Noninvasive Technologies for the Diagnosis of Coronary Artery Disease in Women
Noninvasive Technologies for the Diagnosis of Coronary Artery Disease in Women

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Prepared by:
Duke Evidence-based Practice Center
Durham, NC

Investigators:
Rowena J. Dolor, M.D., M.H.S., Principal Investigator
Manesh R. Patel, M.D., Principal Investigator
Chiara Melloni, M.D., Clinical Investigator
Ranee Chatterjee, M.D., M.P.H., Clinical Investigator
Amanda J. McBroom, Ph.D., EPC Project Manager
Michael D. Musty, EPC Project Coordinator
Liz Wing, M.A., EPC Editor
Remy R. Coeytaux, M.D., Ph.D., EPC Investigator
Adia K. Ross, M.D., M.H.A., Clinical Investigator
Lori A. Bastian, M.D., M.P.H., Clinical Investigator
Monique Anderson, M.D., Clinical Investigator
Andrzej S. Kosinski, Ph.D., Statistical Investigator
Gillian D. Sanders, Ph.D., EPC Director

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None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children’s Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family’s health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (http://www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

Carolyn M. Clancy, M.D.
Director, Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence Agency for Healthcare Research and Quality

Stephanie Chang M.D., M.P.H.
Director, EPC Program
Center for Outcomes and Evidence Agency for Healthcare Research and Quality

Elisabeth U. Kato, M.D., M.R.P.
Task Order Officer
Center for Outcomes and Evidence Agency for Healthcare Research and Quality
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The authors thank Megan von Isenburg, M.L.S., for help with the literature search and retrieval.

Key Informants
Bonnie Arkus, R.N.
Executive Director
Women’s Heart Foundation
West Trenton, NJ

Javed Butler, M.D., M.P.H.
Associate Professor of Medicine
Emory University
Atlanta, GA

Brenda J. Clark
Go Red for Women
American Heart Association

Stacie Daugherty, M.D., M.S.P.H.
Assistant Professor of Cardiology
University of Colorado
Aurora, CO

John F. Heitner, M.D.
Director of Noninvasive Imaging
New York Methodist Hospital
Brooklyn, NY

Neil Jensen, M.B.A., M.H.A.
Director, Cardiology Networks
United HealthCare
Edina, MN

Mark Hlatky, M.D.
Director, Stanford-Kaiser Cardiovascular Outcomes Research Center
Stanford University
Stanford, CA

Neil Jensen, M.B.A., M.H.A.
Director, Cardiology Networks
United HealthCare
Edina, MN

Marcel Salive, M.D., M.P.H.
Director, Division of Medical and Surgical Services
Centers for Medicare and Medicaid
Bethesda, MD

Technical Expert Panel
Matthew J. Budoff, M.D.
Professor of Medicine
University of California, Los Angeles
Los Angeles, CA

Javed Butler, M.D., M.P.H.
Associate Professor of Medicine
Emory University
Atlanta, GA

Stacie Daugherty, M.D., M.S.P.H.
Assistant Professor of Cardiology
University of Colorado
Aurora, CO

John F. Heitner, M.D.
Director of Noninvasive Imaging
New York Methodist Hospital
Brooklyn, NY

Mark Hlatky, M.D.
Director, Stanford-Kaiser Cardiovascular Outcomes Research Center
Stanford University
Stanford, CA

Neil Jensen, M.B.A., M.H.A.
Director, Cardiology Networks
United HealthCare
Edina, MN
Marcel Salive, M.D., M.P.H.
Director, Division of Medical and Surgical Services
Centers for Medicare and Medicaid
Bethesda, MD

Subha V. Raman, M.D., M.S.
Cardiovascular Imaging Research Center
Ohio State University Medical Center
Columbus, OH

Peer Reviewers
Elizabeth Barrett-Connor, M.D.
Professor and Division Chief of Epidemiology
University of California, San Diego
San Diego, CA

Kavitha M. Chinnaiyan, M.D.
Medical Director of Noninvasive Cardiology Education
Beaumont Heart Center
Royal Oak, MI

Nakela L. Cook, M.D., M.P.H.
Division of Cardiology
Washington Hospital Center
Washington, DC

Malissa J. Wood, M.D.
Assistant Professor Medicine
Harvard Medical School
Boston, MA

Jean McSweeney, Ph.D., R.N.
Associate Dean for Research
University of Arkansas for Medical Sciences
Little Rock, AR

Lori Mosca, M.D., Ph.D., M.P.H.
Professor of Medicine
Director of Preventive Cardiology
Columbia University Medical Center
New York, NY

Frank John Rybicki III, M.D., Ph.D.
Associate Professor of Radiology
Brigham and Women’s Hospital
Boston, MA
Noninvasive Technologies for the Diagnosis of Coronary Artery Disease in Women

Structured Abstract

Objectives: To conduct a systematic review of the medical literature assessing (1) accuracy of noninvasive technologies (NITs) for diagnosing coronary artery disease (CAD) in women with symptoms suspicious for CAD, (2) predictors affecting test accuracy, (3) ability of NITs to provide risk stratification, prognostic information, inform decisionmaking about treatment options, and affect clinical outcomes, and (4) risks to women undergoing these tests.

Data Sources: MEDLINE®, PubMed®, Embase®, and Cochrane Database of Systematic Reviews.

Review Methods: Studies published in English through September 2011 with sex-specific outcomes comparing exercise/stress electrocardiography (ECG), echocardiography (ECHO), single proton emission computed tomography (SPECT), cardiac magnetic resonance (CMR), or coronary computed tomography angiography (coronary CTA) with another NIT, or with coronary angiography. We ran separate meta-analyses of the accuracy of each NIT modality compared with coronary angiography on the no known and mixed CAD populations in women and in men.

Results: A total of 104 comparative studies (110 articles) were included. For women with no known CAD, the summary of accuracy for each NIT modality compared with coronary angiography was ECG (29 studies), sensitivity 62 percent, specificity 68 percent; ECHO (14 studies), sensitivity 79 percent, specificity 83 percent; SPECT (14 studies), sensitivity 81 percent, specificity 78 percent; CMR (5 studies), sensitivity 72 percent, specificity 84 percent; and CTA (5 studies), sensitivity 94 percent, specificity 87 percent. Compared with men, in women ECG and coronary CTA modalities were both less sensitive and less specific. The ECHO and SPECT modalities, although less sensitive, appeared to be more specific in women. The lower specificity of the ECG modality in women was the only statistically significant difference. Strength of evidence was high for ECG, ECHO, and SPECT and low for CMR and coronary CTA compared with coronary angiography in women. Eleven comparative studies examined predictors of diagnostic accuracy in women such as postmenopausal status, race/ethnicity, heart size, beta blocker use, and pretest probability; insufficient evidence was available to draw conclusions about predictors that affect accuracy. Eight studies assessed risk stratification and prognostic factors, two studies assessed treatment decisionmaking, and four studies provided comparative clinical outcomes. There is insufficient evidence on the comparative effectiveness of NITs to provide risk stratification, prognostic information, treatment decisionmaking, or impact clinical outcomes in women. Thirteen comparative studies reported risks. Of these, four studies of coronary CTA showed a higher mean effective radiation dose and attributable risk of cancer incidence in women compared with men; however, radiation safety issues were not discussed in other NIT modalities with radiation exposure. Thus, there was insufficient evidence regarding the comparative risks of various NIT modalities in women.
Conclusions: This systematic review provides evidence for the summary sensitivities and specificities of exercise/stress ECG, ECHO, SPECT, CMR, and coronary CTA compared with coronary angiography used for diagnosing CAD in women. There was limited or insufficient evidence from comparative studies to define the influence of clinical and demographic factors on NIT diagnostic accuracy, risk stratification, prognostic information, treatment decisions, clinical outcomes, and harms in women.
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Executive Summary

Background

Cardiovascular disease is the leading cause of mortality for women in the United States. Coronary heart disease—which includes coronary artery (or atherosclerotic) disease (CAD), myocardial infarction (MI), acute coronary syndromes, and angina—is the largest subset of this mortality. According to the American Heart Association (AHA), approximately one in three female adults has some form of cardiovascular disease. Since 1984, the number of deaths attributed to cardiovascular disease in women has exceeded that in men, reaching 454,613 in 2005—more than deaths from all forms of cancer combined. It is estimated that 8.1 million women alive today have a history of heart attack, angina pectoris (chest pain or discomfort caused by reduced blood supply to the heart muscle), or both, and experts predict that in 2010 alone an estimated 370,000 women will have a new or recurrent MI. Overall, women who have had an acute MI—particularly those older than 55 years of age—have a worse prognosis than men, with a greater recurrence of MI and higher mortality. More women (5.5 million) than men (4.3 million) have angina in total numbers. However, the prevalence of CAD in women with chest pain is about 50 percent, compared with 80 percent in men, which complicates diagnosis in women.

The AHA suggests there is evidence showing that women at risk for CAD are less often referred for the appropriate diagnostic test than are men. Coronary anatomy and pathology have traditionally been defined and identified by invasive, catheter-based x-ray angiography, also referred to as coronary angiography. In this invasive procedure, a catheter is inserted into the femoral, brachial, or radial artery and passed up through the aorta to directly engage the right and left coronary arteries; an iodinated contrast agent is then injected into each artery while digital x-ray images are recorded. The major benefits of invasive coronary angiography over noninvasive techniques are that the use of a catheter makes it possible to see the coronary arteries with greater anatomic precision and resolution and to combine diagnosis and treatment in a single procedure. The limitations of the procedure include the invasive nature of the test and the limited data on the functional impact of a luminal obstruction. These limitations are generally considered to be minor when compared with the benefits of the procedure, and coronary angiography is now the reference (gold) standard for clinical care of patients who have chest pain suggestive of CAD.

Coronary angiography, however, is not risk-free. Arterial bleeding can occur at the access site, and manipulation of the catheter within the aorta and coronary arteries may cause an atherosclerotic embolus that, in turn, could result in stroke or heart attack. Separation of material from the inner lining of the artery may also cause a blockage downstream of the catheter tip. The contrast agent used during the procedure to visualize the coronary arteries may cause anaphylaxis, renal impairment, or injury, and there is radiation exposure during the digital x-ray imaging. Although it is a rare occurrence, the catheter can puncture an artery and cause internal bleeding.
Coronary angiography is generally indicated in patients who have chest pain and are at high risk for CAD. For intermediate-risk patients, clinicians have a wide range of noninvasive diagnostic modalities to choose from, with wide variability in reported sensitivities and specificities. Noninvasive technologies (NITs) are especially important options for patients who have contraindications to invasive catheterization, or for those who would be put at higher risk for complications with invasive screening.

**Types of Noninvasive Technologies**

NITs can assess functional status (i.e., ischemia or no ischemia) or visualize anatomic abnormalities (i.e., no CAD, nonobstructive CAD, or obstructive CAD). Types of NITs include the following:

- **Functional modalities:**
  - Exercise/stress electrocardiography (ECG) exercise/stress or resting
  - Exercise/stress echocardiography (ECHO) with or without a contrast agent
  - Exercise/stress radionuclide myocardial perfusion imaging, including single proton emission computed tomography (SPECT) and positron emission tomography (PET)

- **Anatomic modalities:**
  - Stress myocardial perfusion and wall motion magnetic resonance imaging (CMR)
  - Coronary computed tomography angiography (coronary CTA)

The AHA and the American College of Cardiology (ACC) recommend that women with suspected CAD should be classified as either symptomatic or asymptomatic and further classified as being at low, intermediate, or high risk for the disease to guide the decision about which diagnostic test to use first. In 2005, the AHA developed a consensus statement on the role of noninvasive testing in the clinical evaluation of women with suspected CAD. In this statement, the AHA recommended that women who are symptomatic and at intermediate to high risk of having CAD should undergo noninvasive diagnostic studies (i.e., exercise electrocardiography and cardiac imaging studies) and that those who are asymptomatic and at low risk of CAD should not undergo cardiac imaging studies. The AHA consensus statement was a thorough synopsis of the extant literature regarding the diagnosis of CAD in women with expert-guided recommendations for the workup of symptomatic women but did not include a comparative effectiveness review of the accuracy of the various NIT modalities in women.

**Objectives**

The goal of this comparative effectiveness report was to conduct a systematic review of the peer-reviewed medical literature assessing (1) the accuracy of different NITs for diagnosing CAD in women with symptoms suspicious of CAD, (2) the predictors affecting test accuracy, (3) the ability to provide risk stratification and prognostic information, inform decisionmaking about treatment options, and affect clinical outcomes, and (4) the safety concerns and risks to women undergoing these tests. The following Key Questions (KQs) were considered in this comparative effectiveness review:

- **KQ 1.** What is the accuracy of one NIT in diagnosing obstructive and nonobstructive CAD when compared with another NIT or with coronary angiography in women with symptoms suspicious for CAD?
  - Exercise ECG stress test, including resting ECG technology (e.g., multifunctional cardiogram)
• Exercise/stress ECHO with or without a contrast agent
• Exercise/stress radionuclide myocardial perfusion imaging, including SPECT and PET
• CMR imaging
• Coronary CTA

• KQ 2. What are the predictors of diagnostic accuracy (e.g., age, race/ethnicity, body size, heart size, menopausal status, functional status, stress modality) of different NITs in women?

• KQ 3. Is there evidence that the use of NITs (when compared with other NITs or with coronary angiography) in women improves:
  o KQ 3a. Risk stratification/prognostic information?
  o KQ 3b. Decisionmaking regarding treatment options (e.g., revascularization, optimal medical therapy)?
  o KQ 3c. Clinical outcomes (e.g., death, myocardial infarction, unstable angina, hospitalization, revascularization, angina relief, quality of life)?

• KQ 4. Are there significant safety concerns/risks (i.e., radiation exposure, access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, anaphylaxis, arrhythmias) associated with the use of different NITs to diagnose CAD in women with symptoms suspicious for CAD?
Analytic Framework

Figure A shows the analytic framework for the systematic review of NITs for the diagnosis of CAD in women.

Figure A. Analytic framework

Abbreviations: CAD = coronary artery disease; KQ = Key Question; NSF = nephrogenic systemic fibrosis

Methods

Input From Stakeholders

The Evidence-based Practice Center (EPC) followed AHRQ’s recommended methodology, described in Methods Guide for Effectiveness and Comparative Effectiveness Reviews, for literature search strategies, inclusion/exclusion of studies, abstract screening, data abstraction and management, assessment of methodological quality of individual studies, data synthesis, and grading of evidence for each KQ.

During the topic refinement stage, we solicited input from Key Informants, representing clinicians (cardiology, primary care, cardiac imaging), patients, scientific experts, and Federal agencies to help define the KQs. The KQs were then posted for public comment for 30 days, and the comments received were considered in the development of the research protocol. We next convened a Technical Expert Panel (TEP), comprising clinical, content, and methodological experts, to provide input in defining populations, interventions, comparisons, or outcomes as well as identifying particular studies or databases to search. The Key Informants and members of
the TEP were required to disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Any potential conflicts of interest were balanced or mitigated. Neither Key Informants nor members of the TEP did analysis of any kind and did not contribute to the writing of the report.

**Data Sources and Selection**

We included studies published in English from January 1, 2000, through September 12, 2011. Search strategies were specific to each database in order to retrieve the articles most relevant to the KQs. Our search strategy used the National Library of Medicine’s medical subject headings (MeSH) keyword nomenclature developed for MEDLINE® and adapted for use in other databases. We used PubMed®, Embase®, the Cochrane Database of Systematic Reviews, and the Cochrane Central Registry of Controlled Trials for our literature search. We also searched the grey literature of study registries and conference abstracts for relevant articles from completed trials, including Clinicaltrials.gov; metaRegister of Controlled Trials; ClinicalStudyResults.org; WHO: International Clinical Trials Registry Platform Search Portal; CSA Conference Papers Index; and Scopus. The exact search strings used in our strategy are given in Appendix A of the full report. Reference lists of articles applicable to the relevant KQs of previous AHRQ reports on this topic6,7 and from identified systematic reviews and meta-analyses were manually hand-searched and cross-referenced against our library, and additional manuscripts were retrieved. All citations were imported into an electronic bibliographic database (EndNote® Version X4; Thomson Reuters, Philadelphia, PA).

We developed a list of article inclusion and exclusion criteria for the KQs (Table A). Using the prespecified inclusion and exclusion criteria, titles and abstracts were examined independently by two reviewers for potential relevance to the KQs. Articles included by any reviewer underwent full-text screening. At the full-text screening stage, two independent reviewers read each article to determine if it met eligibility criteria. At the full-text review stage, paired researchers independently reviewed the articles and indicated a decision to “include” or “exclude” the article for data abstraction. When the paired reviewers arrived at different decisions about whether to include or exclude an article, we reconciled the difference through a third-party arbitrator. Articles meeting our eligibility criteria were included for data abstraction. Relevant systematic review articles, meta-analyses, and methods articles were flagged for hand-searching and cross-referencing against the library of citations identified through electronic database searching.
<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>Study design</td>
<td>An article was included if the following two criteria were met:</td>
<td>Editorial</td>
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<td></td>
<td>Original data or related methodology paper of an included article</td>
<td>Not a systematic review</td>
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<td>Randomized controlled trial, prospective or retrospective observational study, or registry</td>
<td>Letter to editor</td>
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<td>Case series</td>
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<td>Review article, meta-analysis, or methods paper of an excluded article</td>
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<td>Not peer reviewed</td>
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<td>Population</td>
<td>Study included adult women (age ≥ 18 years of age) who present symptoms of symptoms suspicious for CAD (e.g., exertional dyspnea, shortness of breath, and/or angina) with or without a known diagnosis of CAD; data for women must be presented separately from data for men</td>
<td>All subjects were &lt; 18 years of age, or some subjects were under &lt; 18 but results were not broken down by age</td>
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<td>No patients had symptomatic chest pain (i.e., an asymptomatic population), or some of the patients had symptomatic chest pain but results were not reported separately for this subgroup</td>
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<td>All patients were known to have CAD and were not being tested for chest pain symptoms (e.g., postrevascularization testing to assess for persistent ischemia)</td>
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<td>Interventions</td>
<td>NITs for the diagnosis of obstructive and nonobstructive CAD included:</td>
<td>Coronary artery calcium scoring by electron beam computed tomography since this modality is often used to screen asymptomatic patients for CAD</td>
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<td>Exercise electrocardiogram stress test</td>
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<td>Resting electrocardiogram technology</td>
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<td>Exercise/stress echocardiography with or without a contrast agent</td>
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<td>Exercise/stress radionuclide myocardial perfusion imaging, including single proton emission computed tomography and positron emission tomography</td>
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<td>Stress myocardial perfusion and wall motion magnetic resonance imaging</td>
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<td>Coronary computed tomography angiography</td>
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<tr>
<td>Comparators</td>
<td>Another NIT or coronary angiography</td>
<td>Study did not compare one NIT with another, or with coronary angiography</td>
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<td>Outcomes</td>
<td>Primary outcome—accurate diagnosis of obstructive and nonobstructive CAD</td>
<td>Outcomes not related to diagnostic accuracy for detecting CAD</td>
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<td>KQ 1 patient-level outcomes:</td>
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<td></td>
<td>Sensitivity</td>
<td>Vessel-based outcomes</td>
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<td>Specificity</td>
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<td>True positive, false negative, true negative, false positive</td>
<td>Outcomes of women not reported separately from total population</td>
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<td>Indeterminate or technically inadequate results</td>
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<td></td>
<td>Prevalence</td>
<td></td>
</tr>
<tr>
<td></td>
<td>KQ 2 outcomes: Predictors of diagnostic accuracy—age, race/ethnicity, body size, heart size, menopausal status, functional status, stress modality</td>
<td>Outcomes of women not reported separately from total population</td>
</tr>
<tr>
<td></td>
<td>KQ 3 outcomes:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Risk stratification/prognostic information</td>
<td>Outcomes of women not reported separately from total population</td>
</tr>
<tr>
<td></td>
<td>Treatment —none, medical therapy, percutaneous coronary intervention, or coronary artery bypass surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clinical outcomes—death, myocardial infarction, unstable angina, hospitalization, revascularization, angina relief, quality of life</td>
<td></td>
</tr>
<tr>
<td></td>
<td>KQ 4 outcomes: Safety and adverse events—radiation exposure, access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, anaphylaxis, arrhythmias—and how these events varied by demographic factors</td>
<td>Outcomes of women not reported separately from total population</td>
</tr>
<tr>
<td>Setting</td>
<td>Inpatient or outpatient settings, primarily primary care and cardiology clinics</td>
<td>None</td>
</tr>
<tr>
<td>Publication languages</td>
<td>English only</td>
<td>Given the high volume of English-language publications (including the majority of known important studies), non-English articles were excluded</td>
</tr>
</tbody>
</table>
Data Extraction and Quality Assessment

The investigative team created forms for abstracting the data elements for the KQs. Based on their clinical and methodological expertise, two researchers were assigned to abstract data from the eligible articles pertaining to the research questions. One researcher abstracted the data, and the second overread the article and the accompanying abstraction form to check for accuracy and completeness. Disagreements were resolved by consensus or by obtaining a third reviewer’s opinion if consensus was not reached by the first two researchers. To aid in both reproducibility and standardization of data collection, researchers received data abstraction instructions directly on each form created specifically for this project with the DistillerSR data synthesis software program (Evidence Partners Inc., Manotick, ON, Canada). We designed these forms to collect the data required to evaluate the specified eligibility criteria for inclusion in this review as well as to collect demographics and data needed to determine outcomes (intermediate outcomes, health outcomes, and safety outcomes). Appendix B of the full report lists the elements used in the data abstraction forms.

Appendix C of the full report contains a bibliography of all studies included in this review, organized alphabetically by author. When appropriate, methods articles providing additional detail were considered when abstracting data for an included study.

The studies included in this comparative effectiveness review were assessed on the basis of the quality of their reporting of relevant data. We evaluated the quality of individual studies using the approach described in AHRQ’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews (hereafter referred to as the Methods Guide). To assess study quality, we (1) classified the study design, (2) applied predefined criteria for quality and critical appraisal, and (3) made a summary judgment of the study’s quality. To evaluate methodological quality, we applied criteria for each study type that were derived from the core elements described in the Methods Guide5 and from QUADAS,8 a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. To indicate the summary judgment of the quality of the individual studies, we used the summary ratings of Good, Fair, and Poor based on the study’s adherence to well-accepted standard methodologies (such as QUADAS) and adequate reporting standards.

We used data abstracted on the population studied, the intervention and comparator, the outcomes measured, settings, and timing of assessments to identify specific issues that may have limited the applicability of individual studies or a body of evidence as recommended in the Methods Guide.5,9 We used these data to evaluate the applicability to clinical practice, paying special attention to study eligibility criteria, demographic features of the enrolled population in comparison with the target population, the intervention used in comparison with technologies currently in use, and clinical relevance and timing of the outcome measures. We summarized issues of applicability qualitatively. Appendix D of the full report summarizes our assessment of the quality and applicability for each included study as well as the assessed QUADAS quality scores for diagnostic accuracy.

Data Synthesis and Analysis

We summarized the primary literature by abstracting relevant continuous data (e.g., age, sensitivity, specificity, event rates) and categorical data (e.g., race/ethnicity, presence of CAD). Data for patients with no known diagnosis of CAD were collected and analyzed separately from data for mixed CAD populations that included patients with and without known CAD. We then
determined the feasibility of completing a quantitative synthesis (i.e., summary receiver
operating characteristic [SROC] curves for diagnostic accuracy or meta-analysis for other
outcomes). The feasibility of a meta-analysis or SROC curve depended on the volume of
relevant literature, the homogeneity of the studies in terms of the populations studied, the
interventions included or the outcomes assessed, and the completeness of the results reporting.
For each SROC calculation, we ran separate analyses of the accuracy of each NIT modality
compared with coronary angiography on the no-known CAD and mixed CAD populations using
random-effects models to quantitatively synthesize the available evidence. In our primary
analyses, we evaluated these performance characteristics in the population of women who had no
previously known CAD. In secondary analyses, we explored a broader patient population by
including those studies that had women from mixed populations of known and no known CAD.
We also assessed the impact on our findings if, in each population, we restricted our analyses to
those studies that were assessed to be good quality. We then compared the performance
characteristics of the NIT modalities with each other in a generalized linear mixed model. In a
final exploratory analysis, we evaluated the test performance of the modalities in women
compared with men in a similar generalized linear model with sex as a covariate. We presented
summary estimates and confidence intervals (CIs).

For synthesizing the accuracy data for studies included in our assessment of KQ 1, we used
the following approach as advocated by Leeflang,, et al.10 This approach allows the paired nature
of sensitivity and specificity and randomness between studies to be taken into account. The
analyses are based on true positive (TP), false negative (FN), false positive (FP), and true
negative (TN) frequencies abstracted from relevant publications. Estimated study specific
sensitivity (TP/[TP+FN]) and specificity (TN/[TN+FP]) values are displayed in paired forest
plots together with exact 95% CIs.11 The fixed-effects estimates and their variance–covariance
matrix provided (after reverse logit transformation) summary sensitivity and specificity values
and a joint confidence region (dotted oval shape on figures) as well as separate CIs for summary
sensitivity and specificity as presented on figures and forest plots in the report. We used the
Rutter and Gatsonis12 SROC curve as described by Arends,, et al.,13 and it is presented in figures
as a solid line over the range of the available data.

Grading the Body of Evidence

The strength of evidence for each Key Question was assessed using the approach described
in AHRQ’s Methods Guide on Medical Test Reviews for grading the evidence related to the
diagnostic accuracy of the NITs (KQ 1),14 and the Methods Guide for Effectiveness and
Comparative Effectiveness Reviews for grading the evidence related to the other Key Questions
(KQs 2–4).5,15 The evidence was evaluated using the four required domains: risk of bias (low,
medium, or high), consistency (consistent, inconsistent, or unknown/not applicable), directness
(direct or indirect), and precision (precise or imprecise). Additionally, when appropriate, the
studies were evaluated for the presence of confounders that would diminish an observed effect,
the strength of association (magnitude of effect), and publication bias. The strength of evidence
was assigned an overall grade of High, Moderate, Low, or Insufficient according to the following
four-level scale:

- High—High confidence that the evidence reflects the true effect. Further research is very
  unlikely to change our confidence in the estimate of effect.
• Moderate—Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
• Low—Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
• Insufficient—Evidence either is unavailable or does not permit estimation of effect.

Results
The flow of articles through the literature search and screening process is depicted in Figure B. Of the 8,231 citations identified by our searches, 634 were duplicates. A manual search identified an additional 445 citations for a total of 8,042 citations. After applying inclusion/exclusion criteria at the title-and-abstract level, 1,772 full-text articles were retrieved and screened. Of these, 1,662 articles were excluded at the full-text screening stage. Of these, we excluded 1,376 (83 percent) for not reporting data on women and 615 (37 percent) for looking only at a population with known CAD. (Note that an article may have been excluded for more than one reason.) The final set comprised 110 articles representing 104 studies.

Of the 104 studies, 1 was an RCT, 79 were prospective observational, and 24 were retrospective observational with study cohorts comprising individuals who presented for NIT testing and received diagnostic coronary angiography (100 studies) or another NIT modality only (4 studies). The four studies without coronary angiography compared ECHO with ECG\textsuperscript{16,17} or ECG with SPECT.\textsuperscript{18,19} Three of these studies were applicable to KQ 3,\textsuperscript{16-18} and one was applicable to KQ 2.\textsuperscript{19} Of the 94 studies included in the KQ 1 results, 5 reported NIT versus NIT comparisons in addition to coronary angiography.\textsuperscript{20-24}
Abbreviations: CAD = coronary artery disease; KQ = Key Question; NIT = noninvasive technology; SR = systematic review
Summary of Key Findings

We analyzed the results by study population (no known CAD and mixed CAD populations) and by study quality (good quality rating). Table B and Figure C show the summary sensitivities and specificities for each NIT modality. Table C summarizes our key findings.

Table B. Summary of accuracy of NITs compared with coronary angiography for diagnosing CAD in women

<table>
<thead>
<tr>
<th>Modality</th>
<th>Population</th>
<th>Quality of Included Studies</th>
<th>Number of Studies</th>
<th>Number of Women</th>
<th>Summary Sensitivity (95% CI)</th>
<th>Summary Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>No known CAD</td>
<td>All Good</td>
<td>29</td>
<td>3,392</td>
<td>62% (55%–68%)</td>
<td>70% (58%–73%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All Good</td>
<td>41</td>
<td>4,879</td>
<td>61% (54%–67%)</td>
<td>65% (52%–76%)</td>
</tr>
<tr>
<td>ECHO</td>
<td>No known CAD</td>
<td>All Good</td>
<td>14</td>
<td>1,286</td>
<td>79% (74%–83%)</td>
<td>83% (74%–94%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All Good</td>
<td>22</td>
<td>1,873</td>
<td>78% (73%–83%)</td>
<td>86% (79%–91%)</td>
</tr>
<tr>
<td>SPECT</td>
<td>No known CAD</td>
<td>All Good</td>
<td>14</td>
<td>1,000</td>
<td>81% (76%–86%)</td>
<td>78% (69%–84%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All Good</td>
<td>30</td>
<td>2,146</td>
<td>82% (77%–87%)</td>
<td>81% (74%–86%)</td>
</tr>
<tr>
<td>CMR</td>
<td>No known CAD</td>
<td>All Good</td>
<td>5</td>
<td>501</td>
<td>72% (55%–85%)</td>
<td>84% (69%–93%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All Good</td>
<td>6</td>
<td>778</td>
<td>78% (61%–89%)</td>
<td>84% (74%–90%)</td>
</tr>
<tr>
<td>Coronary CTA</td>
<td>No known CAD</td>
<td>All Good</td>
<td>5</td>
<td>474</td>
<td>93% (69%–99%)</td>
<td>77% (54%–91%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All Good</td>
<td>8</td>
<td>690</td>
<td>94% (81%–98%)</td>
<td>87% (68%–96%)</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; CI = confidence interval; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; SPECT = single proton emission computed tomography
Figure C. Summary of accuracy of NITs compared with coronary angiography for diagnosing CAD in women with no known CAD (all studies)

<table>
<thead>
<tr>
<th>Test</th>
<th>Number of Studies</th>
<th>Number of Patients</th>
<th>Summary Sensitivity (95% CI)</th>
<th>Summary Sensitivity (95% CI)</th>
<th>Summary Specificity (95% CI)</th>
<th>Summary Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR</td>
<td>5</td>
<td>501</td>
<td>0.72 (0.55-0.85)</td>
<td>0.72 (0.55-0.85)</td>
<td>0.84 (0.69-0.93)</td>
<td>0.84 (0.69-0.93)</td>
</tr>
<tr>
<td>CTA</td>
<td>5</td>
<td>474</td>
<td>0.93 (0.69-0.99)</td>
<td>0.93 (0.69-0.99)</td>
<td>0.77 (0.54-0.91)</td>
<td>0.77 (0.54-0.91)</td>
</tr>
<tr>
<td>ECHO</td>
<td>14</td>
<td>1286</td>
<td>0.79 (0.74-0.83)</td>
<td>0.79 (0.74-0.83)</td>
<td>0.83 (0.74-0.89)</td>
<td>0.83 (0.74-0.89)</td>
</tr>
<tr>
<td>SPECT</td>
<td>14</td>
<td>1000</td>
<td>0.81 (0.76-0.86)</td>
<td>0.81 (0.76-0.86)</td>
<td>0.78 (0.69-0.84)</td>
<td>0.78 (0.69-0.84)</td>
</tr>
<tr>
<td>ECG</td>
<td>29</td>
<td>3392</td>
<td>0.62 (0.55-0.68)</td>
<td>0.62 (0.55-0.68)</td>
<td>0.68 (0.63-0.73)</td>
<td>0.68 (0.63-0.73)</td>
</tr>
</tbody>
</table>
Table C. Summary of key findings

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ 1: Diagnostic accuracy of NITs in women</td>
<td>ECG: High, ECHO: High, SPECT: High, CMR: Low, Coronary CTA: Low</td>
<td>94 studies described the diagnostic accuracy of NITs in comparison to another NIT or coronary angiography in women. Of these 94 studies, 78 studies included sufficient data to estimate the sensitivity and specificity of the NIT compared with coronary angiography. Summary from all studies with no known CAD: 41 studies (13 good quality, 22 fair, 6 poor) of exercise ECG showed a summary sensitivity of 62% and specificity of 68%. 22 studies (8 good quality, 13 fair, 1 poor) of exercise/stress ECHO showed a summary sensitivity of 79% and specificity of 83%. 30 studies (10 good quality, 15 fair, 5 poor) of exercise/stress radionuclide perfusion imaging (SPECT, PET) showed a summary sensitivity of 81% and specificity of 78%. 6 studies (5 good quality, 1 fair) of CMR imaging showed a summary sensitivity of 72% and specificity of 84%. 8 studies (4 good quality, 4 fair) of coronary CTA showed a summary sensitivity of 93% and specificity 77%. Overall, within a given modality, the summary sensitivities and specificities were similar for both types of populations (unknown CAD and mixed known and no known CAD) and for all studies when compared with good-quality studies. For the newer technologies (i.e., coronary CTA and CMR), more studies in women would be needed to support these findings since the 95% CIs were quite wide. In testing for a statistically significant difference between the diagnostic accuracy of testing modalities in women, our analyses determined that for women with no previously known CAD, there were differences between the performance of the available modalities (p &lt; 0.001). The sensitivity of ECHO and SPECT was significantly higher than that of ECG. Specificity of ECG was less than that of CMR (borderline) and of ECHO. In the subset of studies that were good-quality and where there was no known CAD in the included population, our analyses again demonstrated differences between performance of tests (p = 0.006) with the specificity of ECG being less than that of CMR and ECHO.</td>
</tr>
</tbody>
</table>
Table C. Summary of key findings (continued)

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KQ 1 (continued)</strong></td>
<td></td>
<td>Sensitivity analyses exploring mixed populations of women with known and no known CAD showed no statistically significant difference in the sensitivities and specificities from our primary analysis. An analysis exploring the prevalence of CAD across the different NIT modality studies also showed no statistically significant difference. In addition, there were very few studies (1 SPECT, 1 ECHO, and 3 ECG) that did not complete a coronary angiography in all patients who underwent the NIT; therefore the results are minimized for verification bias. Finally we found no evidence of publication bias across the different modalities in our 4 populations of interest (studies of women with no known CAD, good quality studies of women with no known CAD, studies of women from mixed populations, and good quality studies of women from mixed populations).</td>
</tr>
</tbody>
</table>
| **KQ 2: Predictors of diagnostic accuracy in women** | Insufficient         | 11 studies (4 good quality, 5 fair, 2 poor) described diagnostic accuracy, and 9 of these examined predictors of diagnostic accuracy of different NITs in women.  
Summary:  
The predictors assessed included (1) postmenopausal women ages 55 to 64 (1 study), (2) race/ethnicity (2 studies), (3) heart size (4 studies), (4) pretest probability (3 studies), and (5) use of beta blocker medications (1 study).  
We identified no studies examining the influence of age alone, functional status, or body size on diagnostic accuracy in women.  
In terms of the NIT modality, we found four studies of stress ECHO, six studies of stress ECG, two studies of CMR, and four studies of SPECT that reported these predictors.  
Insufficient evidence was available to draw definitive conclusions about predictors given the small number of studies for each predictor and for each modality, as well as the combination of predictor by modality. |
| **KQ 3: Improving risk stratification, decisionmaking, and outcomes in women** | Insufficient         | 13 studies (3 good quality, 9 fair, 1 poor) reported prognostic, outcome, or decisionmaking data comparing one NIT with another NIT or with coronary angiography in women with symptoms suspicious for CAD.  
Summary:  
We found 8 studies assessing risk stratification and prognostic information, 2 studies assessing decisionmaking for treatment options, and 4 studies that provided comparative clinical outcomes.  
There were insufficient data to demonstrate that the use of specific NITs (compared with coronary angiography) routinely provided incremental risk stratification, prognostic information, or other meaningful information to improve decisionmaking and improve patient outcomes.  
Most findings reported in the literature would require significant confirmation and replication in larger studies with women. |
### Table C. Summary of key findings (continued)

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
</tr>
</thead>
</table>
| KQ 4: Safety concerns| Insufficient        | 13 studies (9 good quality, 4 fair) reported data pertinent to safety concerns or risks associated with the use of NITs to diagnose CAD in women with symptoms suspicious for CAD.  
Summary:  
Safety data were reported on the following modalities: (1) stress ECG (4 studies), (2) ECHO (6 studies), (3) SPECT (3 studies), (4) CMR (2 studies), and (5) coronary CTA (4 studies).  
Data specific to women on access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, or anaphylaxis associated with NITs were not reported in any of the studies included in this report.  
Other than higher mean effective radiation doses for coronary CTA studies for women compared with men (from 3 out of 4 studies reporting radiation exposure levels), the extant literature does not provide sufficient evidence to conclude whether safety concerns, risks, or radiation exposure associated with different NITs to diagnose CAD in patients with suspected CAD differ significantly between women and men. |
Discussion

In summary, the findings of this comparative effectiveness review provide evidence for the accuracy of exercise/stress ECG, ECHO, SPECT, CMR, and coronary CTA compared with coronary angiography used for diagnosing CAD in women. The diagnostic accuracy appears to be consistent over time except for the sensitivity of CMR, which appears to be increasing over time (although the large confidence intervals reflect the underlying uncertainty in this measure). We are confident that the summary statistics for ECG, ECHO, and SPECT are robust and unlikely to change with the addition of new studies based on both the number of good-quality trials comparing these modalities with coronary angiography and the tight confidence intervals. More good-quality studies comparing CMR or coronary CTA with coronary angiography in the no-known CAD population and reporting sex-based results are needed to strengthen the summary statistics for those modalities.

Decisions around performing tests (either noninvasive or invasive) in patients with symptoms suspicious for CAD revolve around first understanding the pretest probability and testing/action thresholds for patients from the AHA/ACC stable angina guidelines and appropriate use criteria for the various NIT modalities. Specifically, clinicians faced with patients who have a guideline-defined low-to-intermediate pretest probability of CAD may decide to obtain a noninvasive test, ideally with a high negative predictive value in this population and low risk of adverse events, in order to “rule out” disease. These may be patients with atypical chest pain (e.g., reflux or musculoskeletal disease) who are concerned about a heart problem and who require reassurance that their symptoms are not cardiac in origin. In contrast, in patients with high pretest probability of CAD (greater than 90 percent chance), a test with very high positive predictive value in this population and potentially more risk may be chosen since the disease of interest is thought to be present; in these cases, invasive angiography—the gold standard—is recommended by the current clinical practice guidelines. Finally, it is the spectrum of intermediate probability between 10 and 90 percent for which the clinicians must choose noninvasive tests that provide the right balance of sensitivity, specificity, and clinical risk to warrant testing. The choice of NIT may differ by clinician preference, availability, or setting (outpatient vs. chest pain unit of an emergency department).

It is in this context that the findings of this report on the effectiveness of NITs in women must be considered. First, women are thought to be at lower pretest probability of CAD when evaluated in comparison with men of the same age. When comorbidities or risk factors are taken into account, the pretest likelihood increases with a higher number of comorbidities. Second, women susceptible to some of the adverse effects of testing may have poor test performance or have higher rates of complication from invasive arterial access. Third, because of body shape and limited functional capacity, women may not obtain the same test performance that men do from noninvasive testing. Finally, because of the lack of full representation of women across the spectrum of disease, the available literature may not provide data on performance at the ends of the probability spectrum. Spectrum bias may be present since the studies we evaluated had potentially varied populations and varied disease definitions.

While readers may assume that requiring coronary angiography as the comparator would bias this report toward a higher risk CAD population, we found that the mean CAD prevalence ranged from 0.26 to 0.44; thus there was a broad spectrum of CAD prevalence in these studies. In fact, the range of CAD prevalence in this review is similar to a recent analysis of a large administrative database of patients referred for coronary angiography in which the prevalence of
significant obstructive disease was 38 to 40 percent.\textsuperscript{29} The patient population that does not require coronary angiography can be characterized as having symptoms with low suspicion for CAD or pretest probability of less than 10 percent (note that all included studies enrolled patients with “suspected CAD”). Thus, results from this review would not apply to patients with low pretest probability of disease (e.g., gastroesophageal reflux, musculoskeletal pain, or panic attacks) where an NIT may be performed for clinical reassurance that their symptoms are noncardiac in origin.

In general, because there are few patients with high pretest probability, most clinicians would prefer to have patients undergo one NIT prior to determining a treatment choice or referral to coronary angiography. More than one NIT test is often required when the initial test results are equivocal. Our review did not identify studies that discussed the order in which different NITs were used for evaluating CAD. In fact, multiple testing or layered-testing strategies are areas where significant research is needed.

The current data suggest that NITs with higher sensitivity include coronary CTA and SPECT, and stress ECHO may represent an NIT with higher specificity. Stress CMR shows emerging data that may be in the upper range for both sensitivity and specificity. Additionally, the findings also demonstrate that NIT performance in women is not as good as in men, likely due to the reasons addressed above. The accuracy may also be location or operator dependent, and thus the results of published studies conducted at highly specialized centers may not uniformly apply to those seen in routine practice. Choice of NIT—and whether to use exercise or pharmacological stress imaging—may be influenced by functional capacity, which tends to be lower in women compared with men. Of note, the accuracy data for NIT modalities in men appeared a little higher than expected given previous meta-analyses of diagnostic accuracy data in the total population, which is likely because the published literature combined the accuracy data for men and women. Taken in context, these findings give support to the current ACC/AHA recommendations and studies on noninvasive testing in women.

Women are more likely than men to have false-positive stress tests; i.e., abnormal stress imaging with nonobstructive CAD on coronary angiography. In fact, up to 9 percent of women presenting with acute coronary syndrome will not have obstructive CAD when they undergo coronary angiography for potential PCI.\textsuperscript{30} Some experts suggest that these phenomena are due to the presence of microvascular obstruction, the incidence of which is hard to determine since there is no clear diagnostic test used to establish the diagnosis.

Currently, there is debate on whether NITs that measure heart function abnormalities (ECG abnormalities, wall motion abnormality, ischemia), including exercise ECG, stress ECHO, and cardiac nuclear imaging, are equivalent or inferior to NITs that measure anatomic abnormalities (detection of CAD) by CMR or coronary CTA. Will knowing the coronary anatomy (nonobstructive or obstructive) in symptomatic patients lead to better implementation of secondary measures—control of blood pressure, diabetes, and hyperlipidemia—to reduce future cardiac events? Or is it more important to intervene with medications and/or revascularization when ischemia is present? Though this review does not answer these important questions, we describe this evidence gap in the Future Research section.

**Limitations of This Review**

Despite identifying 104 studies (110 articles) that met the inclusion criteria, this systematic review has several limitations. First, our search focused on comparator studies of the various NITs with a gold standard of coronary angiography for establishing the diagnosis of CAD in
symptomatic patients. While this focus was adequate for identifying studies to assess the diagnostic accuracy of the NIT modalities in women, we found very few comparative studies that reported the influence of clinical characteristics or patient demographics on diagnostic accuracy. Few comparative studies (NIT vs. coronary angiography, or NIT vs. NIT) provided information on incremental risk stratification, prognostic information, or meaningful information regarding decisionmaking, and few reported the significant risks in women. Study results on these issues were reported for the total patient population and did not separate the effects by sex. Many of the included studies were single-sex (women) studies and limited our ability to fully evaluate sex differences. Also, by focusing on symptomatic patients, this report did not review the use of coronary artery calcium scoring for asymptomatic, high-risk populations.

We are aware that there are several noncomparator studies of each of the NIT modalities that address these issues in women since routine clinical care does not require two NIT modalities or an NIT modality plus coronary angiography for the diagnostic workup of suspected CAD. Given the focus on comparative effectiveness, we did not include these noncomparator studies in our review. By focusing the review on comparative studies, however, we are reducing the bias that is inherent in noncomparative studies. Noncomparative studies have selection, spectrum, and intervention biases for the following reasons: The choice of NIT is determined by the treating provider; only a subset of patients with indeterminate or positive results are referred for further NIT testing or coronary angiography; and the clinical outcomes may be influenced by the medical treatments or revascularization options that are offered. Second, the sample size and low representation of women in most of the comparator studies may affect the authors’ ability to analyze the results by sex, therefore reducing the number of studies reporting these findings separately. Third, most studies lacked long-term followup of the patient population, which affected our ability to find studies that reported prognostic information on how the different NITs influenced clinical outcomes. Finally, our summary of the harms and risks of NITs is limited by the lack of disclosure of periprocedural and postprocedural complications in most of the studies.

Conclusions

This systematic review has provided evidence for the summary sensitivities and specificities of exercise/stress ECG, ECHO, SPECT, CMR, and coronary CTA compared with coronary angiography in women. There was limited or insufficient evidence on the influence of clinical and demographic factors on comparative diagnostic accuracy, risk stratification, prognostic information, treatment decisions, clinical outcomes, and harms from different NITs specifically in women. Modifying the search criteria to include noncomparator studies of NIT modalities may increase the number of studies that address this limitation.

Future Research

This comprehensive review of the comparative effectiveness of NIT modalities for diagnosing women with suspected CAD identified numerous gaps in evidence that would be suitable for future research and for improving the reporting of findings of NIT studies in the published literature.

Randomized trials comparing functional versus anatomic modalities. Almost all the studies reviewed were prospective observational studies where patients already scheduled for coronary angiography also underwent one or two NIT modalities to assess the diagnostic accuracy of the NITs. In routine clinical practice, clinicians order one type of NIT modality based on a patient’s ability to exercise, test availability, and clinician preference. Exercise ECG,
stress ECHO, and nuclear imaging all measure functional parameters to assess for ischemia and obstructive CAD. Newer technologies such as coronary CTA and CMR offer clinicians the ability to evaluate anatomic parameters to assess both nonobstructive and obstructive CAD. A comparison of a functional testing strategy to an anatomic testing strategy for patients with symptomatic chest pain is currently being done in two large clinical trials (PROMISE [NCT001174550] and RESCUE [NCT01262625]). The information from these clinical trials could inform how the choice of an NIT modality affects prognosis, treatment decisions, and clinical outcomes.

**Studies assessing outcomes beyond diagnostic accuracy.** Our review found very few comparative NIT studies that looked at risk stratification, prognostic information, treatment decisions, and clinical outcomes. Future studies, whether observational or controlled clinical trials, should have long-term followup of patient cohorts to assess these factors. This is important because a positive NIT result could lead to further testing to establish the diagnosis of CAD as well as lead to more attention to secondary prevention for CAD. As stated previously, multiple testing or layered-testing strategies, plus the influence on risk-factor modification (e.g., medication prescriptions and adherence), are areas where significant research is needed.

**Studies of sufficient sample size and representation of women.** Many studies assessing the comparative diagnostic accuracy of an NIT modality with another NIT modality or with coronary angiography did not present a sample size calculation for the numbers needed per group. In addition, after excluding the women-only studies, the studies with both sexes had low representation of women. In order to assess sex differences in NIT diagnostic accuracy or the impact on clinical outcomes, a sufficient sample size is required to have adequate statistical power for subgroup analyses.

**Reporting sex and CAD population subgroups separately.** From 1,662 citations, we excluded 1,376 (83 percent) for not reporting data on women and 615 (37 percent) for looking only at a population with known CAD. Since publication of the AHRQ report on the use of NITs in women,6,7 there has been an increase in the number of studies reporting sex-based differences. We encourage more reporting of women’s results as well as separating the results from no known CAD and known CAD populations. One challenge we encountered in this review was that the primary data representing the numbers of TP, TN, FP, and FN were not presented in most studies and often needed to be back-calculated based on reported sensitivities and specificities and underlying disease prevalence for our quantitative synthesis. It would aid future comparisons of modalities if study authors were to report the primary data for women and men separately either within the article itself or within an online supplementary appendix.

**Assessing clinical and demographic factors that influence diagnostic accuracy.** Clinicians are taught that clinical factors such as weight, heart size, functional status, race/ethnicity, sex, age, and menopausal status can influence the diagnostic accuracy of various NIT modalities. However, we found very few comparative studies that looked at the impact of these clinical and demographic factors on the sensitivity and specificity of NIT results. More evidence about predictors affecting diagnostic cardiac testing is needed to support or dispel these long-held notions. Additional studies of the NIT modalities to assess differing symptomatology and timing at presentation, racial differences, various risk profiles, and different settings (outpatient, inpatient, emergency room) would be help to build the evidence base needed for clinical decisionmaking.

**Reporting of risk, harms, and/or safety outcomes.** Diagnostic procedures to screen for heart disease can result in harmful clinical events (nephropathy, radiation exposure, access site
complications). Systematic reporting of adverse events in publications—in total and by sex—should continue to clarify which NIT modalities are safe after they are approved for use in clinical practice.

Glossary

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Term</th>
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<tbody>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
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<tr>
<td>ACC</td>
<td>American College of Cardiology</td>
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<tr>
<td>CAD</td>
<td>coronary artery disease</td>
</tr>
<tr>
<td>CMR</td>
<td>cardiac magnetic resonance imaging</td>
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<tr>
<td>CTA</td>
<td>coronary computed tomography angiography</td>
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<tr>
<td>ECG</td>
<td>electrocardiogram, electrocardiography</td>
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<tr>
<td>ECHO</td>
<td>echocardiogram, echocardiography</td>
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<tr>
<td>KQ</td>
<td>Key Question</td>
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<tr>
<td>MeSH</td>
<td>Medical Subject Heading</td>
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<tr>
<td>NIT</td>
<td>noninvasive technology</td>
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<td>NSF</td>
<td>nephrogenic systemic fibrosis</td>
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<td>PET</td>
<td>positron emission tomography</td>
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<td>MI</td>
<td>myocardial infarction</td>
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<tr>
<td>SPECT</td>
<td>single photon emission computed tomography</td>
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<td>TEP</td>
<td>Technical Expert Panel</td>
</tr>
</tbody>
</table>

References


Introduction

Background

Cardiovascular disease is the leading cause of mortality for women in the United States. Coronary heart disease—which includes coronary artery (or atherosclerotic) disease (CAD), myocardial infarction (MI), acute coronary syndromes, and angina—is the largest subset of this mortality. According to the American Heart Association (AHA), approximately one in three female adults has some form of cardiovascular disease. Since 1984, the number of deaths attributed to cardiovascular disease in women has exceeded that in men, reaching 454,613 in 2005—more than deaths from all forms of cancer combined. It is estimated that 8.1 million women alive today have a history of heart attack, angina pectoris (chest pain or discomfort caused by reduced blood supply to the heart muscle), or both, and experts predict that in 2010 alone an estimated 370,000 women will have a new or recurrent MI. Overall, women who have had an acute MI—particularly those older than 55 years of age—have a worse prognosis than men, with a greater recurrence of MI and higher mortality. More women (5.5 million) than men (4.3 million) have angina in total numbers. Among women older than 20 years of age, non-Hispanic black women have the highest incidence of angina (6.7 percent) when compared with non-Hispanic whites (4.3 percent) and Mexican Americans (4.5 percent). However, the prevalence of CAD in women with chest pain is about 50 percent, as compared with 80 percent in men, which complicates diagnosis in women.

The AHA suggests there is evidence showing that women at risk for CAD are less often referred for the appropriate diagnostic test than are men. Coronary anatomy and pathology have traditionally been defined and identified by invasive, catheter-based x-ray angiography, also referred to as coronary angiography. In this invasive procedure, a catheter is inserted into the femoral, brachial, or radial artery and passed up through the aorta to directly engage the right and left coronary arteries; an iodinated contrast agent is then injected into each artery while digital x-ray images are recorded. The major benefits of invasive coronary angiography over noninvasive techniques are that the use of a catheter makes it possible to see the coronary arteries with greater anatomic precision and resolution and to combine diagnosis and treatment in a single procedure. The limitations of the procedure include the invasive nature of the test and the limited data on the functional impact of a luminal obstruction. These limitations are generally considered to be minor when compared with the benefits of the procedure, and coronary angiography is now the reference (gold) standard for clinical care of patients who have chest pain suggestive of CAD.

Coronary angiography, however, is not risk-free. Arterial bleeding can occur at the access site, and manipulation of the catheter within the aorta and coronary arteries may cause an atherosclerotic embolus that, in turn, could result in stroke or heart attack. Separation of material from the inner lining of the artery may also cause a blockage downstream of the catheter tip. The contrast agent used during the procedure to visualize the coronary arteries may cause anaphylaxis or renal impairment or injury, and there is radiation exposure during the digital x-ray imaging. Although it is a rare occurrence, the catheter can puncture an artery and cause internal bleeding.

Coronary angiography is generally indicated in patients who have chest pain and are at high risk for CAD. For intermediate-risk patients, clinicians have a wide range of noninvasive diagnostic modalities to choose from, with wide variability in reported sensitivities and specificities. Noninvasive technologies (NITs) are especially important options for patients who...
have contraindications to invasive catheterization, or for those who would be put at higher risk for complications with invasive screening. Included in this group would be patients who have a higher risk of an embolic stroke because of extensive vascular disease in the aorta; those with endocarditis involving the aortic valve; and those who are at high risk for developing a pseudoaneurysm at the site of catheter insertion because of underlying vascular disease.4

**Types of Noninvasive Technologies**

NITs can assess functional status (i.e., ischemia or no ischemia) or visualize anatomic abnormalities (i.e., no CAD, nonobstructive CAD, or obstructive CAD). Types of NITs include:

- **Functional modalities:**
  - Exercise/stress electrocardiography (ECG) exercise/stress or resting
  - Exercise/stress echocardiography (ECHO) with or without a contrast agent
  - Exercise/stress radionuclide myocardial perfusion imaging, including single proton emission computed tomography (SPECT) and positron emission tomography (PET)

- **Anatomic modalities:**
  - Stress myocardial perfusion and wall motion magnetic resonance imaging (CMR)
  - Coronary computed tomography angiography (coronary CTA)

The AHA and the American College of Cardiology (ACC) recommend that women with suspected CAD should be classified as either symptomatic or asymptomatic and further classified as being at low, intermediate, or high risk for the disease to guide the decision about which diagnostic test to use first.1 In 2005, the AHA developed a consensus statement on the role of noninvasive testing in the clinical evaluation of women with suspected CAD. In this statement, the AHA recommended that women who are symptomatic and at intermediate to high risk of having CAD should undergo noninvasive diagnostic studies (i.e., exercise electrocardiography and cardiac imaging studies) and that those who are asymptomatic and at low risk of CAD should not undergo cardiac imaging studies.1 The AHA consensus statement was a thorough synopsis of the extant literature regarding the diagnosis of CAD in women with expert-guided recommendations for the workup of symptomatic women but did not include a comparative effectiveness review of the accuracy of the various NIT modalities in women.

**Functional Modalities**

**Electrocardiographic Modalities**

Treadmill testing with exercise ECG is the oldest and most commonly used form of stress testing. It is widely available and has low initial costs. According to the joint AHA/ACC guidelines, women should undergo exercise testing if they have an intermediate risk of CAD on the basis of symptoms and risk factors.5 Factors that are unique to women (such as hormonal factors) have been reported to induce ECG changes during exercise that diminish the accuracy of the test. For exercise ECG, a positive test is defined, at peak exercise, by a significant ST segment horizontal or downsloping depression (significant level may vary by study as ≥1 mm, 1-2 mm, or ≥2 mm ST). ECG changes alone may not provide adequate prognostication. Exercise ECG has been recognized in the literature as being less sensitive and specific for diagnosing obstructive CAD in women than in men. Additional factors may improve the accuracy of the exercise test, such as chronotropic and hemodynamic responses to exercise. Despite sex-specific limitations, existing ACC/AHA guidelines propose that evidence of sex-specific limitations is
insufficient to remove the stress exercise ECG test as the initial test for symptomatic women at intermediate risk for CAD who have normal resting ECG results and are capable of exercise.\(^1,5\)

The AHA asserts that integrating other parameters into exercise scores (e.g., the Duke Treadmill Score, the ST/heart rate index) may improve the predictive value in women and that a positive ECG result in women indicates more diagnostic tests are necessary.\(^1\)

Another ECG-based test is the newly developed Multifunction Cardiogram\(^\text{®}\) (Cardiac Analytics, Powell, OH). With this resting ECG technology, patients are tested while lying in a supine position. From the multifunction cardiogram machine, five ECG wires with electrodes are attached to the patient at the four standard limb-lead and precordial-lead V5 positions. An automatic simultaneous 2-lead (leads V5 and II) ECG sampling is recorded for 82 seconds with amplification and digitization, and the ECG data are then transmitted to a data center via an encrypted Internet connection. Results are then compiled into a report that can be reviewed on the multifunction cardiogram unit itself or on any computer that has a Web browser. At present, this device is not widely available.\(^6\)

**Echocardiographic Modalities**

Exercise/stress ECHO is another noninvasive method for diagnosing CAD that provides information on the presence of left ventricular systolic or diastolic dysfunction, valvular heart disease, and the extent of infarction and stress-induced ischemia (defined as new or worsening wall motion abnormalities). Exercise ECHO can be performed using a treadmill or upright bicycle. In patients who cannot exercise, dobutamine is the most commonly used pharmacological stress agent. Vasodilator stress ECHO uses dipyridamole or adenosine. Contrast agents available for stress ECHO include SonoVue\(^\text{®}\), Optison\(^\text{TM}\), and Luminity\(^\text{TM}\). For stress ECHO, a positive test is defined by the evidence of new wall motion abnormalities in a different segment of the heart that can occur at stress only or at rest and stress. The AHA asserts that exercise/stress ECHO provides significantly higher specificity and accuracy for diagnosing obstructive CAD in women than standard exercise ECG testing does. Exercise/stress ECHO is recommended for women who are symptomatic and are at intermediate to high risk of CAD (women with suspected CAD must also have abnormal results from resting ECG), and dobutamine stress ECHO is recommended for women with normal or abnormal ECG results who are incapable of exercise.\(^1\) The significant advantages of stress ECHO over ECG are superior diagnostic performance, ability to localize areas of ischemia, and the option of performing stress testing on patients who are unable to exercise.\(^3\) According to a recent review, the overall sensitivities for exercise/stress ECHO are reported to be slightly lower in women than in men, although the specificities appear to be comparable for both.\(^3\)

**Myocardial Perfusion Imaging Modalities**

Exercise/stress myocardial perfusion imaging, which includes SPECT, PET, and scintigraphy, is a nuclear-based technique that uses a combination of test elements to diagnose CAD. Of the imaging modalities, exercise SPECT, PET, and scintigraphy can be performed by using a treadmill or an upright bicycle. In patients who cannot exercise, the pharmacologic stress agents are dobutamine, adenosine, and dipyridamole. The radionuclides commonly used are technetium Tc 99m sestamibi (MIBI), thallous chloride TL-201 (thallium) and fluorodeoxyglucose.
SPECT is the most commonly performed stress imaging test in the United States, especially for men and women who are unable to exercise. Recently, the use of stress PET has increased. Parameters included in this modality are perfusion defects, global and regional left ventricular function, and left ventricular volumes. For myocardial perfusion imaging studies, a positive test is one that demonstrates reversible ischemia, and different scores can be used. The most frequently used is the summed stress score, which is a semiquantitative index obtained by adding the individual score derived from the 17 or 20 segments analyzed and scored during the stress study. Each segment is scored on a 5-point scale (0 = normal, 1 = slight reduction of tracer uptake, 2 = moderate reduction of tracer uptake, 3 = severe reduction of uptake, 4 = absence of uptake). A summed stress score <4 is considered normal; 4 to 8, mildly abnormal; 9 to 13, moderately abnormal; and >13, severely abnormal. Another score is based on the analysis of extent and severity of stress perfusion defect in the different segments of the left ventricle. This modality has been found to have technical limitations in women, including false-positive results, because of breast attenuation and a small left ventricular chamber size; however, recent advances in nuclear imaging have improved its accuracy (i.e., reduced the breast artifact).1

SPECT imaging is recommended for symptomatic women with an intermediate to high risk of CAD in the AHA 2005 consensus statement for the role of NIT in women.1 A higher prevalence of single-vessel CAD among women adversely affects the diagnostic accuracy of this modality (as well as the ECHO modality).3

Anatomic Modalities

ECG, ECHO, and myocardial perfusion imaging techniques do not provide direct visualization of coronary artery anatomy. They evaluate cardiac electrical activity, wall motion, or perfusion at rest and under stress, and any abnormal findings are used to make inferences about the presence and severity of obstructive CAD and the need for invasive coronary artery imaging. Other anatomic modalities provide direct visualization of coronary anatomy similar to that of coronary angiography but without invasive catheterization. These include cardiac magnetic resonance imaging (CMR) and coronary computed tomography angiography (coronary CTA). For CMR, a positive test is defined by the evidence of perfusion defects (extent and severity) and of wall motion abnormalities (at rest and/or at stress) in different left ventricular segments. For coronary CTA, a significant stenosis is defined quantitatively as at least a 50-percent narrowing (stenosis) of the coronary artery lumen.

Recently, the AHA published a scientific statement on CMR and coronary CTA in which recommendations were made for the general population and were not specific to women.7 The AHA states that both tests are suboptimal for patients with atrial fibrillation and other arrhythmias, and image quality may be further reduced by a high body mass index. Overall, the AHA concludes that the potential benefit of noninvasive coronary angiography is likely to be greatest for symptomatic patients who are at intermediate risk for CAD after initial risk stratification, including patients with equivocal stress test results. The AHA does not recommend that CMR or coronary CTA be used to screen for CAD in patients without symptoms; in particular, concerns about the radiation dose limit the use of coronary CTA in patients who have a very low pretest likelihood of coronary stenoses. At the same time, patients with a high pretest likelihood of coronary stenoses are likely to require intervention and invasive catheter angiography for definitive evaluation. The AHA asserts that the main advantages of coronary CTA, compared with CMR, are wider availability, higher spatial resolution, and more consistent, shorter examinations with better patient adherence. Advantages associated with CMR include the
lack of need for ionizing radiation and an iodinated contrast agent. However, it is not clear whether the diagnostic accuracy or the relative balance of benefits and harms associated with either of these techniques differs between men and women.\textsuperscript{3,8}

**Uncertainties Surrounding Noninvasive Diagnosis of CAD in Women**

Noninvasive diagnosis of CAD in women is particularly challenging for many reasons. Women with chest pain demonstrate a lower prevalence of CAD, and their symptoms are less predictive and more often atypical when compared with those of men. Additionally, women are often older at the time of initial diagnosis; therefore, age-related comorbidities limit their tolerance for exercise testing.\textsuperscript{3} Thus, many factors affect the accuracy of diagnostic testing for CAD in women, including:

- Lower prevalence of CAD
- Higher prevalence of nonobstructive CAD (microvascular abnormalities, mitral valve prolapse)
- Less predictive symptomatology
- Limited exercise tolerance because of older age, obesity, and diabetes at initial diagnosis
- Different response to exercise than men
- Lower peak exercise values
- Lesser increase in the left ventricular ejection fraction
- Increase in cardiac output by enhancing end-diastolic volume
- Inappropriate catecholamine release
- Hormonal influences of estrogens mimicking a digitalis-like false-positive ECG response
- Anatomic differences affecting stress test results
- Female breast attenuation artifacts
- Smaller coronary artery size
- Smaller left ventricular chamber size
- Higher prevalence of single-vessel disease
- Poor left ventricular opacification on echocardiography

In addition to all the factors that may affect the accuracy of noninvasive testing in women, there is currently considerable variation in which tests are used and in which order. In the acute-care setting, patients are often referred for early invasive coronary angiography as the initial risk stratification test although lower risk patients may be evaluated first with noninvasive testing.\textsuperscript{4} After undergoing coronary angiography, some patients may be referred for noninvasive stress testing to define the functional significance of a coronary stenosis (constriction or narrowing) that is borderline in severity or is located such that the risk of treatment is increased.\textsuperscript{4} Some cardiovascular experts advocate for a diagnostic strategy that includes both anatomic information (from direct coronary imaging, traditionally performed by using catheter angiography) and functional information collected during exercise or pharmacological stress testing.\textsuperscript{4} Currently, there is no NIT modality that achieves both of these objectives.\textsuperscript{4}
Relevance

The goals of the diagnostic workup for women who have symptoms suspicious for CAD are to identify CAD with optimal accuracy and establish the basis for instituting preventive and therapeutic interventions. More effective diagnostic strategies are critical for women at risk of CAD because up to 40 percent of initial cardiac events are fatal. The literature suggests that, when compared with men, women are initially diagnosed with more advanced CAD because of the lack of early recognition and management. Therefore, a better understanding of how the accuracy of the many different noninvasive tests for CAD varies by sex could dramatically improve outcomes for many women.

Noninvasive testing of women for CAD also raises uncertainty for decisionmakers because invasive coronary angiography has non-negligible patient risk. In addition, it is costly, requiring expensive equipment and the time and skill of highly trained physicians and support staff. Although the use of noninvasive modalities to minimize the need for invasive procedures offers the possibility of better patient outcomes at lower cost, the wide range of diagnostic modalities—each with advantages and disadvantages for their use—makes it difficult for clinicians, patients, and payers to determine which test is best or should be used or covered in a given clinical situation.

Scope and Key Questions

The following Key Questions (KQs) were considered in this comparative effectiveness review:

- **KQ 1.** What is the accuracy of one NIT in diagnosing obstructive and nonobstructive CAD when compared with another NIT or with coronary angiography in women with symptoms suspicious for CAD?
  - Exercise ECG stress test, including resting ECG technology (e.g., multifunctional cardiogram)
  - Exercise/stress ECHO with or without a contrast agent
  - Exercise/stress radionuclide myocardial perfusion imaging, including SPECT and PET
  - CMR imaging
  - Coronary CTA

- **KQ 2.** What are the predictors of diagnostic accuracy (e.g., age, race/ethnicity, body size, heart size, menopausal status, functional status, stress modality) of different NITs in women?

- **KQ 3.** Is there evidence that the use of NITs (when compared with other NITs or with coronary angiography) in women improves:
  - **KQ 3a.** Risk stratification/prognostic information?
  - **KQ 3b.** Decisionmaking regarding treatment options (e.g., revascularization, optimal medical therapy)?
  - **KQ 3c.** Clinical outcomes (e.g., death, myocardial infarction, unstable angina, hospitalization, revascularization, angina relief, quality of life)?
• **KQ 4.** Are there significant safety concerns/risks (i.e., radiation exposure, access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, anaphylaxis, arrhythmias) associated with the use of different NITs to diagnose CAD in women with symptoms suspicious for CAD?
Methods

Topic Development and Refinement

The Evidence-based Practice Center (EPC) followed AHRQ’s recommended methodology, described in Methods Guide for Effectiveness and Comparative Effectiveness Reviews, for literature search strategies, inclusion/exclusion of studies, abstract screening, data abstraction and management, assessment of methodological quality of individual studies, data synthesis, and grading of evidence for each Key Question (KQ).

During the topic refinement stage, we solicited input from Key Informants representing clinicians (cardiology, primary care, cardiac imaging), patients, scientific experts, and Federal agencies, to help define the KQs. The KQs were then posted for public comment for 30 days, and the comments received were considered in the development of the research protocol. We next convened a Technical Expert Panel (TEP), comprising clinical, content, and methodological experts, to provide input in defining populations, interventions, comparisons, or outcomes as well as identifying particular studies or databases to search. The Key Informants and members of the TEP were required to disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Any potential conflicts of interest were balanced or mitigated. Neither Key Informants nor members of the TEP did analysis of any kind and did not contribute to the writing of the report.

Analytic Framework

Figure 1 shows the analytic framework for the systematic review of NITs for the diagnosis of CAD in women.
Literature Search Strategy

Sources Searched

We included studies published in English from January 1, 2000, through September 12, 2011. Search strategies were specific to each database in order to retrieve the articles most relevant to the KQs. Our search strategy used the National Library of Medicine’s medical subject headings (MeSH) keyword nomenclature developed for MEDLINE® and adapted for use in other databases. In consultation with our research librarians, we used PubMed®, Embase®, the Cochrane Database of Systematic Reviews, and the Cochrane Central Registry of Controlled Trials for our literature search. We also searched the grey literature of study registries and conference abstracts for relevant articles from completed trials. Grey literature databases included Clinicaltrials.gov; metaRegister of Controlled Trials; ClinicalStudyResults.org; WHO: International Clinical Trials Registry Platform Search Portal; CSA Conference Papers Index; and Scopus. The exact search strings used in our strategy are given in Appendix A. Reference lists of articles applicable to the relevant KQs of previous AHRQ reports on this topic and from identified systematic reviews and meta-analyses were manually hand-searched and cross-referenced against our library, and additional manuscripts were retrieved. All citations were
imported into an electronic bibliographic database (EndNote® Version X4; Thomson Reuters, Philadelphia, PA).

**Process for Study Selection**

**Screening for Inclusion and Exclusion**

We developed a list of article inclusion and exclusion criteria for the KQs (Table 1). Using the prespecified inclusion and exclusion criteria, titles and abstracts were examined independently by two reviewers for potential relevance to the KQs. Articles included by any reviewer underwent full-text screening. At the full-text screening stage, two independent reviewers read each article to determine if it met eligibility criteria. At the full-text review stage, paired researchers independently reviewed the articles and indicated a decision to “include” or “exclude” the article for data abstraction. When the paired reviewers arrived at different decisions about whether to include or exclude an article, we reconciled the difference through a third-party arbitrator. Articles meeting our eligibility criteria were included for data abstraction. Relevant systematic review articles, meta-analyses, and methods articles were flagged for hand-searching and cross-referencing against the library of citations identified through electronic database searching.
Table 1. Summary of inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>Study design</td>
<td>An article was included if the following two criteria were met:</td>
<td>• Editorial</td>
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<td></td>
<td>• Original data or related methodology paper of an included article</td>
<td>• Letter to editor</td>
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<tr>
<td></td>
<td>• Randomized controlled trial, prospective or retrospective observational study, or registry</td>
<td>• Case series</td>
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<td></td>
<td>Study included adult women (age ≥ 18 years of age) who present symptoms suspicious for CAD (e.g., exertional dyspnea, shortness of breath, and/or angina) with or without a known diagnosis of CAD; data for women must be presented separately from data for men</td>
<td>• Review article, meta-analysis, or methods paper of an excluded article</td>
</tr>
<tr>
<td></td>
<td>• All subjects were &lt; 18 years of age, or some subjects were under &lt; 18 but results were not broken down by age</td>
<td>• Not peer reviewed</td>
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<td></td>
<td>• No patients had symptomatic chest pain (i.e., an asymptomatic population), or some of the patients had symptomatic chest pain but results were not reported separately for this subgroup</td>
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<td></td>
<td>• All patients were known to have CAD and were not being tested for chest pain symptoms (e.g., postrevascularization testing to assess for persistent ischemia)</td>
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<tr>
<td>Interventions</td>
<td>NITs for the diagnosis of obstructive and nonobstructive CAD included:</td>
<td>Coronary artery calcium scoring by electron beam computed tomography since this modality is often used to screen asymptomatic patients for CAD</td>
</tr>
<tr>
<td></td>
<td>• Exercise electrocardiogram stress test</td>
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<td></td>
<td>• Resting electrocardiogram technology</td>
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<td></td>
<td>• Exercise/stress echocardiography with or without a contrast agent</td>
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<td></td>
<td>• Exercise/stress radionuclide myocardial perfusion imaging, including single proton emission computed tomography and positron emission tomography</td>
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<td></td>
<td>• Stress myocardial perfusion and wall motion magnetic resonance imaging</td>
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<td></td>
<td>• Coronary computed tomography angiography</td>
<td></td>
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<tr>
<td>Comparators</td>
<td>Another NIT or coronary angiography</td>
<td>Study did not compare one NIT with another, or with coronary angiography</td>
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Table 1. Summary of inclusion and exclusion criteria (continued)

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Inclusion Criteria</th>
<th>ExclusionCriteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>Primary outcome—accurate diagnosis of obstructive and nonobstructive CAD</td>
<td>Outcomes not related to diagnostic accuracy for detecting CAD</td>
</tr>
<tr>
<td>KQ 1 patient-level outcomes:</td>
<td>• Sensitivity • Specificity • True positive, false negative, true negative, false positive • Indeterminate or technically inadequate results • Prevalence</td>
<td>• Vessel-based outcomes • Outcomes of women not reported separately from total population</td>
</tr>
<tr>
<td>KQ 2 outcomes: Predictors of diagnostic accuracy—age, race/ethnicity, body size, heart size, menopausal status, functional status, stress modality</td>
<td></td>
<td>Outcomes of women not reported separately from total population</td>
</tr>
<tr>
<td>KQ 3 outcomes:</td>
<td>• Risk stratification/prognostic information • Treatment—none, medical therapy, percutaneous coronary intervention, or coronary artery bypass surgery • Clinical outcomes—death, myocardial infarction, unstable angina, hospitalization, revascularization, angina relief, quality of life</td>
<td>Outcomes of women not reported separately from total population</td>
</tr>
<tr>
<td>KQ 4 outcomes: Safety and adverse events—radiation exposure, access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, anaphylaxis, arrhythmias—and how these events varied by demographic factors</td>
<td></td>
<td>Outcomes of women not reported separately from total population</td>
</tr>
<tr>
<td>Setting</td>
<td>Inpatient or outpatient settings, primarily primary care and cardiology clinics</td>
<td>None</td>
</tr>
<tr>
<td>Publication languages</td>
<td>English only</td>
<td>Given the high volume of English-language publications (including the majority of known important studies), non-English articles were excluded</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; KQ = Key Question; NIT = noninvasive technology

Data Extraction and Data Management

The investigative team created forms for abstracting the data elements for the KQs. The data abstraction forms were piloted by two members of the study team, and refinements to clarify the questions and collection of data were added after the first week of data abstraction. The investigators who piloted the forms were also the main data abstractors. Based on their clinical and methodological expertise, two researchers were assigned to abstract data from the eligible articles pertaining to the research questions. One researcher abstracted the data, and the second overread the article and the accompanying abstraction form to check for accuracy and completeness. Disagreements were resolved by consensus or by obtaining a third reviewer’s opinion if consensus was not reached by the first two researchers. Any data changes during overreading were noted in a comment field. The overall interrater reliability was 0.76.
To aid in both reproducibility and standardization of data collection, researchers received data abstraction instructions directly on each form created specifically for this project with the DistillerSR data synthesis software program (Evidence Partners Inc., Manotick, ON, Canada). We designed these forms to collect the data required to evaluate the specified eligibility criteria for inclusion in this review as well as to collect demographics and data needed to determine outcomes (intermediate outcomes, health outcomes, and safety outcomes). The safety outcomes were framed to help identify radiation exposure, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, anaphylaxis, and arrhythmias, which are the more common adverse events resulting from use of the different NITs. The abstraction form templates were pilot tested with a sample of included articles to ensure that all relevant data elements were captured and that there was consistency and reproducibility between abstractors. Appendix B lists the elements used in the data abstraction forms.

Appendix C contains a bibliography of all studies included in this review, organized alphabetically by author. When appropriate, methods articles providing additional detail were considered when abstracting data for an included study. If a methods article was used as a source for information in the abstraction of a study, it was included in the review and is listed in the bibliography in Appendix C.

**Individual Study Quality Assessment**

The studies included in this comparative effectiveness review were assessed on the basis of the quality of their reporting of relevant data. We evaluated the quality of individual studies using the approach described in AHRQ’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews (hereafter referred to as the Methods Guide).\(^9\) To assess study quality, we (1) classified the study design, (2) applied predefined criteria for quality and critical appraisal, and (3) made a summary judgment of the study’s quality. To evaluate methodological quality, we applied criteria for each study type that were derived from the core elements described in the Methods Guide\(^9\) and from QUADAS,\(^12\) a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. To indicate the summary judgment of the quality of the individual studies, we used the summary ratings of Good, Fair, and Poor based on the study’s adherence to well-accepted standard methodologies (such as QUADAS) and adequate reporting standards.

Grading was outcome specific; thus, a given study may have been graded of different quality for two individual outcomes reported within that study. Study design was considered when grading quality. Randomized controlled trials were graded as Good, Fair, or Poor. Observational studies were graded separately also as Good, Fair, or Poor.

We used data abstracted on the population studied, the intervention and comparator, the outcomes measured, settings, and timing of assessments to identify specific issues that may have limited the applicability of individual studies or a body of evidence as recommended in the Methods Guide.\(^9,13\) We used these data to evaluate the applicability to clinical practice, paying special attention to study eligibility criteria, demographic features of the enrolled population in comparison with the target population, the intervention used in comparison with technologies currently in use, and clinical relevance and timing of the outcome measures. We summarized issues of applicability qualitatively. The quality grading and applicability were conducted in similar fashion to the rest of the data abstraction phase, with one investigator entering ratings, a second investigator overreading the entries, and disagreements resolved through consensus or a
third party. Appendix D summarizes our assessment of the quality and applicability for each included study as well as the assessed QUADAS quality scores for diagnostic accuracy.

Data Synthesis

We summarized the primary literature by abstracting relevant continuous data (e.g., age, sensitivity, specificity, event rates) and categorical data (e.g., race/ethnicity, presence of CAD). Data for patients with no known diagnosis of CAD were collected and analyzed separately from data for mixed CAD populations that included patients with and without known CAD. We then determined the feasibility of completing a quantitative synthesis (i.e., summary receiver operating characteristic [SROC] curves for diagnostic accuracy or meta-analysis for other outcomes). The feasibility of a meta-analysis or SROC curve depended on the volume of relevant literature, the homogeneity of the studies in terms of the populations studied, the interventions included, or the outcomes assessed, and the completeness of the results reporting. For each SROC calculation, we ran separate analyses of the accuracy of each NIT modality compared with coronary angiography on the no-known CAD and mixed CAD populations using random-effects models to quantitatively synthesize the available evidence. In our primary analyses, we evaluated these performance characteristics in the population of women who had no previously known CAD. In secondary analyses, we explored a broader patient population by including those studies that had women from a mixed population of known and no known CAD. We also assessed the impact on our findings if, in each population, we restricted our analyses to those studies that were assessed to be good quality. We then compared the performance characteristics of the NIT modalities with each other using a generalized linear mixed model to assess for differences in summary sensitivity and specificity between the NIT modalities (ECG, ECHO, SPECT, CTA, CMR), as well as differences in disease state (no known and mixed CAD). In a final exploratory analysis, we evaluated the test performance of the modalities in women compared with men in a separate generalized linear mixed model with sex (women, men) as a covariate. We presented summary estimates and confidence intervals (CIs).

For synthesizing the accuracy data for studies included in our assessment of KQ 1, we used the following approach as advocated by Leeflang., et al.\cite{14} This approach allows the paired nature of sensitivity and specificity and randomness between studies to be taken into account. The analyses are based on true positive (TP), false negative (FN), false positive (FP), and true negative (TN) frequencies abstracted from relevant publications. Estimated study specific sensitivity (TP/[TP+FN]) and specificity (TN/[TN+FP]) values are displayed in paired forest plots together with exact 95 % CIs.\cite{15} The summary estimates of sensitivity and specificity resulted from random-effects modeling with two random effects, with each study being considered a random realization of the underlying true distribution. In the absence of covariates, both the bivariate random-effects model and the hierarchical model with random effects are mathematically equivalent.\cite{16} We used the GLIMMIX procedure in the SAS statistical package (SAS Institute; Cary, NC) with maximum likelihood estimation. A binomial error model was used with the logit link. The unstructured covariance matrix of the two random effects was considered during the fitting process, and its Cholesky parameterization was used.

The fixed-effects estimates and their variance–covariance matrix provided (after reverse logit transformation) summary sensitivity and specificity values and a joint confidence region (dotted oval shape on figures) as well as separate CIs for summary sensitivity and specificity as presented on figures and forest plots in the report. There were several possible choices for the SROC curve resulting from the random-effects modeling.\cite{17} We used the Rutter and Gatsonis\cite{18}
SROC curve as described by Arends., et al.,\textsuperscript{17} and it is presented in figures as a solid line over the range of the available data.

In addition to our SROC curve estimation, we evaluated other available outcomes. Most outcomes that we analyzed in this comparative effectiveness report were binary or categorical, and so we summarized these outcomes by proportions. We summarized inherently continuous variables, such as age, by mean, median, and standard deviation.

We also evaluated the potential of verification bias and other limitations of our synthesized analyses based on the underlying clinical domain and diagnostic testing practices. For example, angiography is often administered only to a subset of patients who are undergoing diagnostic tests within a studied population. This subset of patients is not a completely random sample because angiography-based verification of disease is often driven by previous test results and/or other considerations. We explored the potential for publication bias across the different modalities in our four populations of interest (studies of women with no known CAD, good-quality studies of women with no known CAD, studies of women from mixed populations, and good-quality studies of women from mixed populations). Using methods advocated by Deeks., et al.,\textsuperscript{19} we computed for each study the diagnostic odds ratio (DOR) and the effective sample size (ESS). Subsequently we performed regression of natural logarithm of DOR against $1/\text{ESS}^{1/2}$ weighing by ESS, and reported the p value for testing whether slope is equal to zero. A nonsignificant p value indicated no evidence for publication bias.

To explore additional sources of potential bias, we also recorded whether the diagnostic tests were interpreted in a blinded fashion; that is, without knowledge of results of other diagnostic tests or clinical history and risk factors, if such information was available in the reviewed studies.
Grading the Body of Evidence

The strength of evidence for each KQ was assessed using the approach described in AHRQ’s Methods Guide on Medical Test Reviews for grading the evidence related to the diagnostic accuracy of the NITs (KQ 1), and the Methods Guide for grading the evidence related to the other KQs (KQs 2–4). The outcomes used for grading the body of evidence for each KQ are outlined in Table 1. The evidence was evaluated using the four required domains: risk of bias (low, medium, or high), consistency (consistent, inconsistent, or unknown/not applicable), directness (direct or indirect), and precision (precise or imprecise). Additionally, when appropriate, the studies were evaluated for the presence of confounders that would diminish an observed effect, the strength of association (magnitude of effect), and publication bias. The strength of evidence was assigned an overall grade of High, Moderate, Low, or Insufficient according to the following four-level scale:

- **High**—High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
- **Moderate**—Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- **Low**—Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
- **Insufficient**—Evidence either is unavailable or does not permit estimation of effect.

Peer Review and Public Commentary

The peer review process was our principal external quality-monitoring device. Nominations for peer reviewers were solicited from several sources, including the TEP and interested Federal agencies. The list of nominees was forwarded to AHRQ for vetting and approval. A list of reviewers submitting comments on this draft is included in the Preface of this report.
Results

The flow of articles through the literature search and screening process is depicted in Figure 2. Of the 8,231 citations identified by our searches, 634 were duplicates. A manual search identified an additional 445 citations for a total of 8,042 citations. After applying inclusion/exclusion criteria at the title-and-abstract level, 1,772 full-text articles were retrieved and screened. Of these, 1,662 articles were excluded at the full-text screening stage. We excluded 1376 (83 percent) for not reporting data on women and 615 (37 percent) for looking only at a population with known CAD. (Note that an article may have been excluded for more than one reason.) The final set comprised 110 articles representing 104 studies.

Of the 104 studies, 1 was an RCT, 79 were prospective observational, and 24 were retrospective observational with study cohorts comprising individuals who presented for NIT testing and received diagnostic coronary angiography (100 studies) or another NIT modality only (4 studies). The four studies without coronary angiography compared ECHO with ECG\textsuperscript{22,23} or ECG with SPECT\textsuperscript{24,25}. Three of these studies were applicable to Key Question (KQ) 3\textsuperscript{22-24} and one was applicable to KQ 2\textsuperscript{25}. Of the 94 studies included in the KQ 1 results, 5 reported NIT versus NIT comparisons in addition to coronary angiography\textsuperscript{26-30}.

Appendix E provides a complete list of articles excluded at the full-text screening stage, with reasons for exclusion.
Figure 2. Literature flow diagram

8231 citations identified by search of electronic databases:
MEDLINE: 6377
EMBASE: 1233
Cochrane: 621

634 duplicates

445 citations identified through manual searching

8042 citations identified

6270 abstracts excluded

1772 passed abstract screening

6270 abstracts excluded

1662 articles excluded

Reasons for exclusion*
Unable to locate full-text: 6

Section 1 exclusion:
Not English-language: 20
Conference abstract or trial registry posting: 14
Not a clinical study report: 34
Not original peer-reviewed data or a secondary analysis or registry: 84
No data for NITs of interest: 43
Population did not include women ≥ age 18: 7

Section 2 exclusion:
No chest pain symptoms: 397
Known CAD: 615
No NIT or catheterization comparator: 273
No data for women: 1376
No outcomes of interest: 167

110 articles** representing 104 studies abstracted into database and included in review:
KQ 1: 94
KQ 2: 11
KQ 3: 13
KQ 4: 13

* The total may exceed the number in the corresponding box because articles could be excluded for more than one reason at this level

** A given article could be used to address more than one KQ

Abbreviations: CAD = coronary artery disease; KQ = Key Question; NIT = noninvasive technology; SR = systematic review
A summary graph of the QUADAS ratings for all 104 studies is shown in Figure 3. (Refer to Table D-2 in Appendix D for a summary table of the QUADAS quality scores for diagnostic accuracy of the 104 studies included in this review.) A majority of studies uniformly applied a reference test (i.e., coronary angiography) that was independently performed, used blinded interpretation of the reference and index test, and had sufficient detail about the index test to allow for replicability. Many studies had a high risk of spectrum bias (i.e., patient representation of those who would receive the test in practice), a poor description of study withdrawals, unclear descriptions of clinical data available during test interpretation, and lacked descriptions of uninterpretable or intermediate test results. There is a possibility that sensitivity and specificity values may be biased because of subjects included in the studies that did not represent the spectrum of the population of interest; we explored the impact of the underlying prevalence of CAD in the population on our findings.

Figure 3. QUADAS elements used to rate diagnostic accuracy
Key Question 1: Diagnostic Accuracy of NITs

KQ 1. What is the accuracy of one NIT in diagnosing obstructive and nonobstructive CAD when compared with another NIT or with coronary angiography in women with symptoms suspicious for CAD?

- Exercise ECG stress test, including resting ECG technology (e.g., multifunctional cardiogram)
- Exercise/stress ECHO with or without a contrast agent
- Exercise/stress radionuclide myocardial perfusion imaging, including SPECT and PET
- CMR imaging
- Coronary CTA

Key Points

Individual study performance characteristics were evaluated for each testing modality, and summary receiver operating characteristic (SROC) curves were calculated. These analyses demonstrated:

- Overall, within a given testing modality, the summary sensitivities and specificities were similar for both types of populations (known and no known CAD) and for all studies when compared with good-quality studies.
- When accounting for only the good-quality studies, it appeared that the diagnostic accuracy of detecting CAD in women was better (in descending order) for coronary CTA, SPECT, ECHO, CMR, and ECG, although the strength of evidence varied markedly for different modalities.
- For the newer technologies (i.e., CMR and coronary CTA), more studies in women would be needed to support the point estimates given the wide confidence intervals (CIs) on the test performance.
- For women without previously known CAD, there were statistically significant differences between the performance of the available modalities (p < 0.001). The sensitivity of ECHO and SPECT was significantly greater than that of ECG. Specificity of ECG was less than that of CMR (borderline) and of ECHO.
- In the subset of studies that were good-quality and where there was no known CAD in the included population, there were statistically significant differences between performance of tests (p = 0.006), with the specificity of ECG being less than that of CMR and ECHO. Our ability to quantify the difference between test performance of the modalities between men and women was inhibited by the limited number of studies that reported both sexes separately in their analysis.
In exploratory analysis of the difference between test performance in men and women, the ECG and coronary CTA modalities were both less sensitive and less specific in women than in men. The ECHO and SPECT modalities, although less sensitive, appeared to be more specific in women. The lower specificity of the ECG modality in women, however, is the only estimate that was determined to be a statistically significant difference.

**Detailed Synthesis**

In KQ 1 we sought to determine the accuracy of each NIT modality in diagnosing obstructive and nonobstructive CAD when compared with coronary angiography in women with symptoms suspicious for CAD. For this analysis, we included 94 studies describing comparative diagnostic accuracy of NITs. Of these 94 studies, 78 studies included sufficient data to estimate the sensitivity and specificity of the NIT compared with coronary angiography. This included 41 studies examining exercise/stress ECG (13 good quality, 22 fair, 6 poor); 22 examining exercise/stress ECHO (8 good quality, 13 fair, 1 poor); 30 examining exercise/stress radionuclide myocardial perfusion imaging (e.g., SPECT or PET) (10 good quality, 15 fair, 5 poor); 6 examining CMR (5 good, 1 fair); and 8 examining coronary CTA (4 good quality, 4 fair).

For each testing modality, we used the individual performance characteristics to calculate an SROC curve and to estimate the summary sensitivity and specificity and CIs of the modality compared with coronary angiography. We present forest plots of the individual study estimates of sensitivity and specificity of each NIT for diagnosing CAD in women. Error bars in these plots represent 95% CIs; the dashed vertical line represents the summary sensitivity and specificity for the included studies. The ROC curve illustrates the tradeoff between sensitivity and specificity since the threshold that defines a positive test result varies from the most stringent to the least stringent. Open circles represent individual study estimates of sensitivity and specificity. The black circle indicates the average sensitivity and specificity estimate of the study results, and the dashed circle represents the 95-percent confidence region around it. In our primary analyses, we evaluated these performance characteristics in the population of women who had no previously known CAD. In secondary analyses we explored a broader patient population including those studies that had women from a mixed population of known and no known CAD. We also assessed the impact on our findings if, in each population, we restricted our analyses to those studies that were assessed to be good quality. We then compared the performance characteristics of the NIT modalities with each other. In a final exploratory analysis, we evaluated the test performance of the modalities in women compared with men. All secondary analyses involved the use of separate generalized linear mixed models with covariates for disease state (no known versus mixed), NIT modality (ECG, ECHO, SPECT, CMR, CTA), or sex (women versus men).
ECG

We identified 41 studies evaluating the accuracy of exercise/stress ECG compared with coronary angiography (Table 2).27-29,31-68 This table lists those studies that focused purely on women with no known CAD and then follows with the additional studies that included a mixed population of known and no known CAD. Within these populations, good-quality studies are listed first, followed by those of fair and poor quality. Twenty-nine of the ECG studies reported accuracy data in women with no known CAD, and these are the studies used in our primary analysis.

In our secondary analysis, we evaluated the accuracy of exercise/stress ECG in diagnosing CAD in mixed populations of known and no known CAD. This analysis included 1 study that reported additional data for a mixed population61 and an additional 12 studies that reported findings with mixed populations of known and no known CAD. Two of these studies evaluated the use of resting ECG,33,49 and two studies35,50 evaluated pharmacological stressed ECG. All other studies evaluated exercise/stress ECG.

Primary Analysis: Population of Women With No Known CAD

The 29 studies represent findings on ECG use in 3,391 women (sample size ranging from 10 to 580 women). Of these studies, 10 were good quality, 15 were fair quality, and 4 were poor quality. Sensitivity varied from 32 to 91 percent, and specificity varied from 40 to 100 percent; the median sensitivity was 61 percent, and the median specificity was 68 percent. Figure 4 presents forest plots of the individual study estimates of sensitivity and specificity of ECG for diagnosing CAD in women with no known CAD. Error bars represent 95 percent CIs; the dashed vertical line represents the summary sensitivity and specificity for the included studies.
Figure 4. Accuracy of ECG in women with no known CAD

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sketch, 1975</td>
<td>5</td>
<td>6</td>
<td>10</td>
<td>35</td>
<td>0.45 (0.17-0.77)</td>
<td>0.78 (0.63-0.89)</td>
</tr>
<tr>
<td>Barolsky, 1979</td>
<td>18</td>
<td>12</td>
<td>20</td>
<td>42</td>
<td>0.60 (0.41-0.77)</td>
<td>0.68 (0.55-0.79)</td>
</tr>
<tr>
<td>Weiner, 1979</td>
<td>128</td>
<td>40</td>
<td>148</td>
<td>264</td>
<td>0.76 (0.69-0.82)</td>
<td>0.64 (0.59-0.69)</td>
</tr>
<tr>
<td>Guteras, 1982</td>
<td>33</td>
<td>9</td>
<td>24</td>
<td>46</td>
<td>0.79 (0.63-0.90)</td>
<td>0.66 (0.53-0.77)</td>
</tr>
<tr>
<td>Masini, 1988</td>
<td>18</td>
<td>8</td>
<td>20</td>
<td>22</td>
<td>0.69 (0.48-0.86)</td>
<td>0.52 (0.36-0.68)</td>
</tr>
<tr>
<td>Robert, 1991</td>
<td>32</td>
<td>22</td>
<td>17</td>
<td>44</td>
<td>0.59 (0.45-0.72)</td>
<td>0.72 (0.59-0.83)</td>
</tr>
<tr>
<td>Agati, 1992</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>6</td>
<td>0.50 (0.07-0.93)</td>
<td>1.00 (0.61-1.00)</td>
</tr>
<tr>
<td>Severi, 1994</td>
<td>29</td>
<td>12</td>
<td>44</td>
<td>37</td>
<td>0.71 (0.54-0.84)</td>
<td>0.46 (0.35-0.57)</td>
</tr>
<tr>
<td>Marwick, 1995</td>
<td>37</td>
<td>11</td>
<td>31</td>
<td>39</td>
<td>0.77 (0.63-0.88)</td>
<td>0.56 (0.43-0.68)</td>
</tr>
<tr>
<td>Morise, 1995</td>
<td>63</td>
<td>52</td>
<td>38</td>
<td>135</td>
<td>0.55 (0.45-0.64)</td>
<td>0.78 (0.71-0.84)</td>
</tr>
<tr>
<td>Morise, 1995</td>
<td>39</td>
<td>80</td>
<td>18</td>
<td>147</td>
<td>0.33 (0.24-0.42)</td>
<td>0.89 (0.83-0.93)</td>
</tr>
<tr>
<td>Richardson, 1995</td>
<td>10</td>
<td>1</td>
<td>25</td>
<td>26</td>
<td>0.91 (0.59-1.00)</td>
<td>0.51 (0.37-0.65)</td>
</tr>
<tr>
<td>Santana-Baodo, 1998</td>
<td>12</td>
<td>8</td>
<td>14</td>
<td>29</td>
<td>0.60 (0.36-0.81)</td>
<td>0.67 (0.51-0.81)</td>
</tr>
<tr>
<td>Morise, 2000</td>
<td>11</td>
<td>5</td>
<td>8</td>
<td>18</td>
<td>0.69 (0.41-0.89)</td>
<td>0.69 (0.48-0.86)</td>
</tr>
<tr>
<td>Gentile, 2001</td>
<td>20</td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>0.71 (0.51-0.87)</td>
<td>0.57 (0.29-0.82)</td>
</tr>
<tr>
<td>Koide, 2001</td>
<td>21</td>
<td>5</td>
<td>17</td>
<td>40</td>
<td>0.81 (0.61-0.93)</td>
<td>0.70 (0.57-0.82)</td>
</tr>
<tr>
<td>Miler, 2001</td>
<td>65</td>
<td>57</td>
<td>26</td>
<td>57</td>
<td>0.53 (0.44-0.62)</td>
<td>0.69 (0.58-0.78)</td>
</tr>
<tr>
<td>Ozdemir, 2002</td>
<td>30</td>
<td>19</td>
<td>20</td>
<td>28</td>
<td>0.61 (0.46-0.75)</td>
<td>0.58 (0.43-0.72)</td>
</tr>
<tr>
<td>Rollan, 2002</td>
<td>22</td>
<td>7</td>
<td>9</td>
<td>10</td>
<td>0.76 (0.56-0.90)</td>
<td>0.53 (0.29-0.76)</td>
</tr>
<tr>
<td>Hollund-Carlsen, 2005</td>
<td>10</td>
<td>9</td>
<td>56</td>
<td>56</td>
<td>0.38 (0.15-0.65)</td>
<td>0.86 (0.75-0.93)</td>
</tr>
<tr>
<td>Lehmkuhl, 2007</td>
<td>29</td>
<td>16</td>
<td>31</td>
<td>38</td>
<td>0.64 (0.49-0.78)</td>
<td>0.55 (0.43-0.67)</td>
</tr>
<tr>
<td>Lew andowski, 2007</td>
<td>22</td>
<td>46</td>
<td>24</td>
<td>100</td>
<td>0.32 (0.22-0.45)</td>
<td>0.61 (0.73-0.87)</td>
</tr>
<tr>
<td>Michaelides, 2007</td>
<td>36</td>
<td>25</td>
<td>32</td>
<td>21</td>
<td>0.59 (0.46-0.71)</td>
<td>0.40 (0.26-0.54)</td>
</tr>
<tr>
<td>Meres, 2007</td>
<td>18</td>
<td>9</td>
<td>5</td>
<td>11</td>
<td>0.67 (0.46-0.83)</td>
<td>0.69 (0.41-0.89)</td>
</tr>
<tr>
<td>Yeih, 2007</td>
<td>12</td>
<td>16</td>
<td>4</td>
<td>19</td>
<td>0.43 (0.24-0.63)</td>
<td>0.83 (0.61-0.95)</td>
</tr>
<tr>
<td>Bokhari, 2008</td>
<td>15</td>
<td>30</td>
<td>6</td>
<td>17</td>
<td>0.33 (0.20-0.49)</td>
<td>0.74 (0.52-0.90)</td>
</tr>
<tr>
<td>Schupbach, 2008</td>
<td>30</td>
<td>19</td>
<td>14</td>
<td>53</td>
<td>0.61 (0.46-0.75)</td>
<td>0.79 (0.67-0.88)</td>
</tr>
<tr>
<td>Sinha, 2008</td>
<td>10</td>
<td>4</td>
<td>12</td>
<td>24</td>
<td>0.71 (0.42-0.92)</td>
<td>0.67 (0.49-0.81)</td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>25</td>
<td>6</td>
<td>20</td>
<td>25</td>
<td>0.81 (0.63-0.93)</td>
<td>0.56 (0.40-0.70)</td>
</tr>
<tr>
<td><strong>Summary values</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>0.62 (0.55-0.68)</strong></td>
<td><strong>0.68 (0.63-0.73)</strong></td>
</tr>
</tbody>
</table>
Figure 5 presents a summary receiver operating characteristic (SROC) curve with an average sensitivity of 62 percent (95% CI, 55 to 68 percent) and specificity of 68 percent (95% CI, 63 to 73 percent). The ROC curve illustrates the tradeoff between sensitivity and specificity since the threshold that defines a positive test result varies from the most stringent to the least stringent. Open circles represent individual study estimates of sensitivity and specificity. The black circle indicates the average sensitivity and specificity estimate of the study results, and the dashed circle represents the 95-percent confidence region around it.

The prevalence of CAD on coronary angiogram in these 29 studies ranged from 18 to 67 percent with a mean prevalence of 41 percent. In the individual studies, the positive predictive value (PPV) ranged from 29 to 100 percent, and the negative predictive value (NPV) ranged from 40 to 100 percent. The positive likelihood ratio (LR+) ranged from 0.98 to 3.00, and the negative likelihood ratio (LR-) ranged from 0.18 to 1.03. Using the summary sensitivity and specificity of 62 and 68 percent, respectively, we calculated an overall PPV of 57 percent and NPV of 72 percent. Similarly, we calculated summary LR+ of 1.94 and LR- of 0.56.
Accuracy of ECG in 10 Good-Quality Studies

Next, we evaluated the accuracy of ECG compared with coronary angiography in the 10 good-quality studies. In these studies, sensitivity varied from 32 to 91 percent, and specificity varied from 46 to 81 percent; the median sensitivity was 71 percent, and the median specificity was 58 percent. Figure 6 presents forest plots of the individual study estimates of sensitivity and specificity of ECG in 10 good-quality studies for diagnosing CAD in women with no known CAD.

Figure 6. Accuracy of ECG in 10 good-quality studies in women with no known CAD

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Weiner, 1979</td>
<td>128</td>
<td>40</td>
<td>148</td>
<td>264</td>
<td>0.76 (0.69-0.82)</td>
<td>0.64 (0.59-0.69)</td>
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<tr>
<td>Severi, 1994</td>
<td>29</td>
<td>12</td>
<td>44</td>
<td>37</td>
<td>0.71 (0.54-0.84)</td>
<td>0.46 (0.35-0.57)</td>
</tr>
<tr>
<td>Richardson, 1995</td>
<td>10</td>
<td>1</td>
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<td>26</td>
<td>0.91 (0.59-1.00)</td>
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<td>Morise, 2000</td>
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<td>18</td>
<td>0.69 (0.41-0.89)</td>
<td>0.69 (0.48-0.86)</td>
</tr>
<tr>
<td>Gentile, 2001</td>
<td>20</td>
<td>8</td>
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<td>8</td>
<td>0.71 (0.51-0.87)</td>
<td>0.57 (0.29-0.82)</td>
</tr>
<tr>
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<td>40</td>
<td>0.81 (0.61-0.93)</td>
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</tr>
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<td>30</td>
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<td>0.61 (0.46-0.75)</td>
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<td>0.64 (0.49-0.78)</td>
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<td>Lewandowski, 2007</td>
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<td>46</td>
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<td>100</td>
<td>0.32 (0.22-0.45)</td>
<td>0.81 (0.73-0.87)</td>
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<td>Lu, 2010</td>
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<td>0.70 (0.58-0.79)</td>
<td>0.62 (0.53-0.69)</td>
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</table>

Figure 7 presents an SROC curve with an average sensitivity of 70 percent (95% CI, 58 to 79 percent) and specificity of 62 percent (95% CI, 53 to 69 percent).
The prevalence of CAD in these 10 good-quality studies ranged from 18 to 67 percent with a mean prevalence of 38 percent. In the individual studies, PPV ranged from 29 to 77 percent, and NPV ranged from 50 to 96 percent. LR+ ranged from 1.30 to 2.71 and LR- from 0.18 to 0.84. Using the summary sensitivity and specificity of 70 and 62 percent, respectively, we calculated an overall PPV of 53 percent and NPV of 77 percent. Similarly, we calculated summary LR+ of 1.84 and LR- of 0.48.

Secondary Analysis: Mixed Population of Women With Known and No Known CAD

We performed a secondary analysis where we expanded our inclusion criteria to include studies whose patient population included a mix of women with known CAD and women with no known CAD. This expanded inclusion criteria allowed an additional 12 studies to be included in the analysis and an additional 83 patients from one study (totaling 41 studies). The 41 studies represent findings on ECG use in 4946 women (sample size ranging from 10 to 613 women). Of these 41 studies, 13 were good quality, 22 were fair quality, and 6 were poor quality (Table 2).

In these 41 studies, sensitivity varied from 26 to 96 percent, and specificity varied from 1 to 100 percent; the median sensitivity was 61 percent, and the median specificity was 65 percent. Figure 8 presents forest plots of the individual study estimates of sensitivity and specificity of ECG for diagnosing CAD in women from mixed populations.
### Figure 8. Accuracy of ECG in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
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<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
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<td>Lu, 2010</td>
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<td>Svart, 2010</td>
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<td>23</td>
<td>42</td>
<td>23</td>
<td>0.52 (0.37-0.67)</td>
<td>0.35 (0.24-0.48)</td>
</tr>
</tbody>
</table>

**Summary values**

- **Sensitivity (95% CI):** 0.61 (0.54-0.67)
- **Specificity (95% CI):** 0.65 (0.58-0.72)
Figure 9 presents an SROC curve demonstrating an average sensitivity of 61 percent (95% CI, 54 to 67 percent) and specificity of 65 percent (95% CI, 58 to 72 percent).

Figure 9. SROC curve for ECG in women from mixed populations

The prevalence of CAD in these 41 studies ranged from 11 to 67 percent with a mean prevalence of 42 percent. In the individual studies, PPV ranged from 4 to 100 percent, and NPV ranged from 1 to 100 percent. LR+ ranged from 0.30 to 5.42 and LR- from 0.05 to 55.3. Using the summary sensitivity and specificity of 61 and 65 percent, respectively, we calculated an overall PPV of 56 percent and NPV of 70 percent. Similarly, we calculated summary LR+ of 1.74 and LR- of 0.60.

Accuracy of ECG in 13 Good-Quality Studies

Next, we evaluated the accuracy of ECG compared with coronary angiography in the 13 good-quality studies. In these studies, sensitivity varied from 26 to 91 percent, and specificity varied from 33 to 81 percent; the median sensitivity was 71 percent, and the median specificity was 58 percent. Figure 10 presents forest plots of the individual study estimates of sensitivity and specificity of ECG in 13 good-quality studies for diagnosing CAD in women from mixed populations.
Figure 10. Accuracy of ECG in 13 good-quality studies in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity 95% CI</th>
<th>Specificity 95% CI</th>
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<td>0.81 (0.63-0.93)</td>
<td>0.56 (0.40-0.70)</td>
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</table>

Summary values

Sensitivity 95% CI: 0.65 (0.52-0.76)
Specificity 95% CI: 0.60 (0.52-0.68)
Figure 11 presents an SROC curve demonstrating an average sensitivity of 65 percent (95% CI, 52 to 76 percent) and specificity of 60 percent (95% CI, 52 to 68 percent).

The prevalence of CAD in these 13 good-quality studies ranged from 18 to 67 percent with a mean prevalence of 37 percent. In the individual studies, PPV ranged from 28 to 77 percent, and NPV ranged from 31 to 96 percent. LR+ ranged from 0.39 to 2.71 and LR- from 0.18 to 2.21. Using the summary sensitivity and specificity of 65 and 60 percent, respectively, we calculated an overall PPV of 49 percent and NPV of 75 percent. Similarly, we calculated summary LR+ of 1.62 and LR- of 0.58.
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<th>LR+ (95% CI)</th>
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<td>Good</td>
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Table 2. Summary of accuracy data evaluating ECG for diagnosing CAD (continued)

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<th>Cath %</th>
<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
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Table 2. Summary of accuracy data evaluating ECG for diagnosing CAD (continued)

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<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
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<th>LR- (95% CI)</th>
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Table 2. Summary of accuracy data evaluating ECG for diagnosing CAD (continued)

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<td>97 (90-100) 96 (91-100)</td>
<td>5.42 (2.61-11.26) 8.19 (4.41-15.18)</td>
<td>0.053 (0.01-036) 0.06 (0.02-0.19)</td>
<td></td>
</tr>
<tr>
<td>Svart, et al., 201034</td>
<td>Mixed</td>
<td>Fair</td>
<td>113 (women) 113 (men)</td>
<td>≥ 50 42</td>
<td>52 (37-67) 35 (24-48)</td>
<td>37 (26-49) 35 (24-48)</td>
<td>50 (36-64) 50 (36-64)</td>
<td>0.81 (0.58-1.12) 1.35 (0.87-2.11)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Elhendy, et al., 199735</td>
<td>Mixed</td>
<td>Fair</td>
<td>88 (women) 177 (men)</td>
<td>≥ 50 65</td>
<td>28 (17-42) 40 (32-49)</td>
<td>81 (63-93) 85 (68-95)</td>
<td>73 (54-91) 92 (85-99)</td>
<td>38 (26-50) 25 (17-32)</td>
<td>1.45 (0.63-3.33) 2.66 (1.16-6.11)</td>
<td>0.89 (0.70-1.13) 0.70 (0.58-0.86)</td>
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</tr>
<tr>
<td>Yamauchi, et al., 198536</td>
<td>Mixed</td>
<td>Fair</td>
<td>43 (women) 90 (men)</td>
<td>≥ 75 47</td>
<td>70 (46-88) 71 (58-81)</td>
<td>87 (66-97) 92 (75-99)</td>
<td>82 (64-100) 96 (90-100)</td>
<td>77 (61-93) 56 (41-71)</td>
<td>5.37 (1.80-16.02) 9.14 (2.39-34.94)</td>
<td>0.35 (0.17-0.69) 0.32 (0.22-0.48)</td>
<td></td>
</tr>
<tr>
<td>Masini, et al., 198831</td>
<td>Mixed</td>
<td>Fair</td>
<td>83 (women) 83 (men)</td>
<td>≥ 70 47</td>
<td>72 (55-85) 71 (58-81)</td>
<td>52 (37-68) 57 (43-71)</td>
<td>68 (52-83) 68 (52-83)</td>
<td>1.50 (1.04-2.17) 1.50 (1.04-2.17)</td>
<td>0.54 (0.29-1.00) 1.67 (1.02-2.73)</td>
<td>0.35 (0.17-0.69) 0.32 (0.22-0.48)</td>
<td></td>
</tr>
<tr>
<td>Friedman, et al., 198237</td>
<td>Mixed</td>
<td>Fair</td>
<td>60 (women) 60 (men)</td>
<td>≥ 70 47</td>
<td>32 (16-52) 41 (24-59)</td>
<td>41 (24-58) 41 (24-58)</td>
<td>0.54 (0.29-1.00) 1.67 (1.02-2.73)</td>
<td>0.35 (0.17-0.69) 0.32 (0.22-0.48)</td>
<td>0.54 (0.30-0.96) 0.35 (0.17-0.69) 0.32 (0.22-0.48)</td>
<td>0.54 (0.30-0.96) 0.35 (0.17-0.69) 0.32 (0.22-0.48)</td>
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Table 2. Summary of accuracy data evaluating ECG for diagnosing CAD (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Mix</th>
<th>Quality</th>
<th>Patients (N)</th>
<th>Cath %</th>
<th>≥ 50</th>
<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maffei, et al., 2010</td>
<td>Mixed</td>
<td>Fair</td>
<td>89 (women)</td>
<td>11</td>
<td>30</td>
<td>30 (7-65)</td>
<td>1 (0-7)</td>
<td>4 (0-8)</td>
<td>13 (0-35)</td>
<td>0.30</td>
<td>(0.12-0.78)</td>
<td>55.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>88 (men)</td>
<td></td>
<td></td>
<td>50 (25-75)</td>
<td>35 (24-47)</td>
<td>15 (5-24)</td>
<td>76 (61-90)</td>
<td>0.76</td>
<td>(0.46-1.28)</td>
<td>1.44</td>
</tr>
<tr>
<td>Ho, et al., 1998</td>
<td>Mixed</td>
<td>Fair</td>
<td>30 (women)</td>
<td>47</td>
<td>71</td>
<td>71 (42-92)</td>
<td>44 (20-70)</td>
<td>53 (30-75)</td>
<td>64 (35-92)</td>
<td>1.27</td>
<td>(0.74-2.19)</td>
<td>0.65</td>
</tr>
<tr>
<td>Cin, et al., 2000</td>
<td>Mixed</td>
<td>Poor</td>
<td>110 (women)</td>
<td>65</td>
<td>86</td>
<td>86 (76-93)</td>
<td>61 (43-76)</td>
<td>81 (72-89)</td>
<td>70 (54-85)</td>
<td>2.18</td>
<td>(1.46-3.27)</td>
<td>0.23</td>
</tr>
<tr>
<td>Hlatky, et al., 1984</td>
<td>Mixed</td>
<td>Poor</td>
<td>613 (women)</td>
<td>41</td>
<td>57</td>
<td>57 (51-63)</td>
<td>86 (82-89)</td>
<td>74 (68-80)</td>
<td>74 (70-79)</td>
<td>4.07</td>
<td>(3.09-5.37)</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1656 (men)</td>
<td>0</td>
<td>72</td>
<td>72 (70-75)</td>
<td>83 (79-86)</td>
<td>92 (90-94)</td>
<td>53 (49-57)</td>
<td>4.28</td>
<td>(3.47-5.27)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

*Resting ECG

Abbreviations: CAD = coronary artery disease; Cath % = % stenosis defined to be positive for CAD on diagnostic cardiac catheterization (coronary angiography); CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NPV = negative predictive value; NR = not reported; PPV = positive predictive value
ECHO

We identified 22 studies evaluating the accuracy of exercise/stress ECHO compared with coronary angiography (Table 3). Twenty-seven of these studies reported accuracy data in women with no known CAD, and these are the studies used in our primary analyses. In our secondary analyses, we evaluated the accuracy of the ECHO in diagnosing CAD including an additional 8 studies that reported findings with mixed populations of known and no known CAD as well as additional patients from one study that had data for those with no known CAD. None of the identified ECHO studies used contrast.

Primary Analysis: Population of Women With No Known CAD

The 14 studies represent findings on ECHO use in 1289 women (sample size ranging from 14 to 192 women). Of these studies, five were good-quality, eight were fair-quality, and one was poor-quality. Sensitivity varied from 57 to 90 percent, specificity varied from 37 to 96 percent; the median sensitivity was 79 percent, and the median specificity was 82 percent. Figure 12 presents forest plots of the individual study estimates of sensitivity and specificity of ECHO for diagnosing CAD in women with no known CAD.

Figure 12. Accuracy of ECHO in women with no known CAD

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masini, 1988</td>
<td>20</td>
<td>6</td>
<td>3</td>
<td>39</td>
<td>0.77 (0.56-0.91)</td>
<td>0.93 (0.81-0.99)</td>
</tr>
<tr>
<td>Sawada, 1989</td>
<td>24</td>
<td>4</td>
<td>4</td>
<td>25</td>
<td>0.86 (0.67-0.96)</td>
<td>0.86 (0.68-0.96)</td>
</tr>
<tr>
<td>Mazeika, 1992</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>0.57 (0.18-0.90)</td>
<td>0.71 (0.29-0.96)</td>
</tr>
<tr>
<td>Severi, 1994</td>
<td>28</td>
<td>13</td>
<td>3</td>
<td>78</td>
<td>0.68 (0.52-0.82)</td>
<td>0.96 (0.90-0.99)</td>
</tr>
<tr>
<td>Williams, 1994</td>
<td>29</td>
<td>4</td>
<td>6</td>
<td>31</td>
<td>0.88 (0.72-0.97)</td>
<td>0.84 (0.68-0.94)</td>
</tr>
<tr>
<td>Marwick, 1995</td>
<td>47</td>
<td>12</td>
<td>19</td>
<td>83</td>
<td>0.80 (0.67-0.89)</td>
<td>0.81 (0.72-0.88)</td>
</tr>
<tr>
<td>Slavich, 1996</td>
<td>13</td>
<td>9</td>
<td>6</td>
<td>18</td>
<td>0.59 (0.36-0.79)</td>
<td>0.75 (0.53-0.90)</td>
</tr>
<tr>
<td>Takeuchi, 1996</td>
<td>15</td>
<td>5</td>
<td>4</td>
<td>46</td>
<td>0.75 (0.51-0.91)</td>
<td>0.92 (0.81-0.98)</td>
</tr>
<tr>
<td>Dionisopoulos, 1997</td>
<td>60</td>
<td>7</td>
<td>7</td>
<td>27</td>
<td>0.90 (0.80-0.96)</td>
<td>0.79 (0.62-0.91)</td>
</tr>
<tr>
<td>Roger, 1997</td>
<td>46</td>
<td>12</td>
<td>24</td>
<td>14</td>
<td>0.79 (0.67-0.89)</td>
<td>0.37 (0.22-0.54)</td>
</tr>
<tr>
<td>Rollan, 2002</td>
<td>29</td>
<td>13</td>
<td>6</td>
<td>51</td>
<td>0.69 (0.53-0.82)</td>
<td>0.89 (0.78-0.96)</td>
</tr>
<tr>
<td>Lehmkuhl, 2007</td>
<td>36</td>
<td>9</td>
<td>13</td>
<td>56</td>
<td>0.80 (0.65-0.90)</td>
<td>0.81 (0.70-0.90)</td>
</tr>
<tr>
<td>Lewandowski, 2007</td>
<td>54</td>
<td>14</td>
<td>36</td>
<td>88</td>
<td>0.79 (0.68-0.88)</td>
<td>0.71 (0.62-0.79)</td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>27</td>
<td>4</td>
<td>8</td>
<td>37</td>
<td>0.87 (0.70-0.96)</td>
<td>0.82 (0.68-0.92)</td>
</tr>
</tbody>
</table>

Summary values

<table>
<thead>
<tr>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.79 (0.74-0.83)</td>
<td>0.83 (0.74-0.89)</td>
</tr>
</tbody>
</table>
Figure 13 presents an SROC curve with an average sensitivity of 79 percent (95% CI, 74 to 83 percent) and specificity of 83 (95% CI, 74 to 89 percent).

The prevalence of CAD in these 14 studies ranged from 29 to 66 percent with a mean prevalence of 44 percent. In the individual studies, PPV ranged from 60 to 90 percent, and NPV ranged from 37 to 96 percent. LR+ ranged from 1.25 to 18.44 and LR- from 0.13 to 0.60. Using the summary sensitivity and specificity of 79 and 83 percent, respectively, we calculated an overall PPV of 78 percent and NPV of 83 percent. Similarly, we calculated summary LR+ of 4.65 and LR- of 0.25.

**Accuracy of ECHO in Five Good-Quality Studies**

Next, we evaluated the accuracy of ECHO compared with coronary angiography in the five good-quality studies. In these studies, sensitivity varied from 68 to 87 percent, specificity varied from 71 to 96 percent; the median sensitivity was 80 percent, and the median specificity was 82 percent. Figure 14 presents forest plots of the individual study estimates of sensitivity and specificity of ECHO for diagnosing CAD in women with no known CAD.
Figure 14. Accuracy of ECHO in five good-quality studies in women with no known CAD

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sawada, 1989</td>
<td>24</td>
<td>4</td>
<td>4</td>
<td>25</td>
<td>0.86 (0.67-0.96)</td>
<td>0.86 (0.68-0.96)</td>
</tr>
<tr>
<td>Severi, 1994</td>
<td>28</td>
<td>13</td>
<td>3</td>
<td>78</td>
<td>0.68 (0.52-0.82)</td>
<td>0.96 (0.90-0.99)</td>
</tr>
<tr>
<td>Lehmkuhl, 2007</td>
<td>36</td>
<td>9</td>
<td>13</td>
<td>56</td>
<td>0.80 (0.65-0.90)</td>
<td>0.81 (0.70-0.90)</td>
</tr>
<tr>
<td>Lewandowski, 2007</td>
<td>54</td>
<td>14</td>
<td>36</td>
<td>88</td>
<td>0.79 (0.68-0.88)</td>
<td>0.71 (0.62-0.79)</td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>27</td>
<td>4</td>
<td>8</td>
<td>37</td>
<td>0.87 (0.70-0.96)</td>
<td>0.82 (0.68-0.92)</td>
</tr>
<tr>
<td>Summary values</td>
<td>9</td>
<td>2</td>
<td>18</td>
<td>78</td>
<td>0.79 (0.69-0.87)</td>
<td>0.85 (0.68-0.94)</td>
</tr>
</tbody>
</table>

Figure 15 presents an SROC curve with an average sensitivity of 79 percent (95% CI, 69 to 87 percent) and specificity of 85 percent (95% CI, 68 to 94 percent).

The prevalence of CAD in these five good-quality studies ranged from 34 to 49 percent with a mean prevalence of 40 percent. In the individual studies, PPV ranged from 60 to 90 percent, and NPV ranged from 86 to 90 percent. LR+ ranged from 2.73 to 18.44 and LR- from 0.16 to 0.33. Using the summary sensitivity and specificity of 79 and 85 percent, respectively, we calculated an overall PPV of 78 percent and NPV of 86 percent. Similarly, we calculated summary LR+ of 5.27 and LR- of 0.25.
Secondary Analysis: Mixed Population of Women With Known and No Known CAD

We performed a secondary analysis where we expanded our inclusion criteria to include studies whose patient population included a mix of women with known CAD and women with no known CAD. This expanded inclusion criteria allowed an additional eight studies to be included in the analysis and an additional group of patients from one study (totaling 22 studies). The 22 studies represent findings on ECHO use in 1944 women (sample size ranging from 7 to 192 women). Of these 22 studies, 8 were good quality, 13 were fair quality, and 1 was poor quality (Table 3).

In these 22 studies, sensitivity varied from 40 to 93 percent, and specificity varied from 37 to 100 percent; the median sensitivity was 79 percent, and the median specificity was 84 percent. Figure 16 presents forest plots of the individual study estimates of sensitivity and specificity of ECHO for diagnosing CAD in women from mixed populations.

Figure 16. Accuracy of ECHO in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masini, 1988</td>
<td>31</td>
<td>8</td>
<td>3</td>
<td>41</td>
<td>0.79 (0.64-0.91)</td>
<td>0.93 (0.81-0.99)</td>
<td></td>
</tr>
<tr>
<td>Sawada, 1989</td>
<td>24</td>
<td>4</td>
<td>4</td>
<td>25</td>
<td>0.86 (0.67-0.96)</td>
<td>0.86 (0.68-0.96)</td>
<td></td>
</tr>
<tr>
<td>Agati, 1992</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>0.80 (0.28-0.99)</td>
<td>1.00 (0.55-1.00)</td>
<td></td>
</tr>
<tr>
<td>Mazeika, 1992</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>0.57 (0.18-0.90)</td>
<td>0.71 (0.29-0.96)</td>
<td></td>
</tr>
<tr>
<td>Severi, 1994</td>
<td>28</td>
<td>13</td>
<td>3</td>
<td>78</td>
<td>0.68 (0.52-0.82)</td>
<td>0.96 (0.90-0.99)</td>
<td></td>
</tr>
<tr>
<td>Williams, 1994</td>
<td>29</td>
<td>4</td>
<td>6</td>
<td>31</td>
<td>0.88 (0.72-0.97)</td>
<td>0.84 (0.68-0.94)</td>
<td></td>
</tr>
<tr>
<td>Bjornstad, 1995</td>
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<td>1</td>
<td>0</td>
<td>1</td>
<td>0.83 (0.36-1.00)</td>
<td>1.00 (0.05-1.00)</td>
<td></td>
</tr>
<tr>
<td>Marwick, 1995</td>
<td>47</td>
<td>12</td>
<td>19</td>
<td>83</td>
<td>0.80 (0.67-0.89)</td>
<td>0.81 (0.72-0.88)</td>
<td></td>
</tr>
<tr>
<td>Slavich, 1996</td>
<td>13</td>
<td>9</td>
<td>6</td>
<td>18</td>
<td>0.59 (0.36-0.79)</td>
<td>0.75 (0.53-0.90)</td>
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</tr>
<tr>
<td>Takeuchi, 1996</td>
<td>15</td>
<td>5</td>
<td>4</td>
<td>46</td>
<td>0.75 (0.51-0.91)</td>
<td>0.92 (0.81-0.98)</td>
<td></td>
</tr>
<tr>
<td>Donisopoulos, 1997</td>
<td>60</td>
<td>7</td>
<td>7</td>
<td>27</td>
<td>0.90 (0.80-0.96)</td>
<td>0.79 (0.62-0.91)</td>
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<tr>
<td>Elhendy, 1997</td>
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<td>15</td>
<td>2</td>
<td>32</td>
<td>0.76 (0.63-0.88)</td>
<td>0.94 (0.80-0.99)</td>
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<td>Laurienzo, 1997</td>
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<td>4</td>
<td>0</td>
<td>62</td>
<td>0.82 (0.60-0.95)</td>
<td>1.00 (0.95-1.00)</td>
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</tr>
<tr>
<td>Roger, 1997</td>
<td>46</td>
<td>12</td>
<td>24</td>
<td>14</td>
<td>0.79 (0.67-0.89)</td>
<td>0.37 (0.22-0.54)</td>
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<tr>
<td>Elhendy, 1998</td>
<td>35</td>
<td>10</td>
<td>2</td>
<td>23</td>
<td>0.78 (0.63-0.89)</td>
<td>0.92 (0.74-0.99)</td>
<td></td>
</tr>
<tr>
<td>Ho, 1998</td>
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<td>2</td>
<td>4</td>
<td>18</td>
<td>0.93 (0.77-0.99)</td>
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<td></td>
</tr>
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<td>Lewis, 1999</td>
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<td>54</td>
<td>0.40 (0.21-0.61)</td>
<td>0.81 (0.69-0.89)</td>
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<tr>
<td>Rollan, 2002</td>
<td>29</td>
<td>13</td>
<td>6</td>
<td>51</td>
<td>0.69 (0.53-0.82)</td>
<td>0.89 (0.78-0.96)</td>
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</tr>
<tr>
<td>Shin, 2003</td>
<td>45</td>
<td>10</td>
<td>31</td>
<td>76</td>
<td>0.82 (0.69-0.91)</td>
<td>0.71 (0.61-0.79)</td>
<td></td>
</tr>
<tr>
<td>Lehmkuhl, 2007</td>
<td>36</td>
<td>9</td>
<td>13</td>
<td>56</td>
<td>0.80 (0.65-0.90)</td>
<td>0.81 (0.70-0.90)</td>
<td></td>
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<tr>
<td>Lewandowski, 2007</td>
<td>54</td>
<td>14</td>
<td>36</td>
<td>88</td>
<td>0.79 (0.68-0.88)</td>
<td>0.71 (0.62-0.79)</td>
<td></td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>27</td>
<td>4</td>
<td>8</td>
<td>37</td>
<td>0.87 (0.70-0.96)</td>
<td>0.82 (0.68-0.92)</td>
<td></td>
</tr>
<tr>
<td>Summary values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.78 (0.73-0.83)</td>
<td>0.86 (0.79-0.91)</td>
<td></td>
</tr>
</tbody>
</table>
Figure 17 presents an SROC curve demonstrating an average sensitivity of 78 percent (95% CI, 73 to 83 percent) and specificity of 86 percent (95% CI, 79 to 91 percent).

The prevalence of CAD in these 22 studies ranged from 26 to 86 percent with a mean prevalence of 46 percent. In the individual studies, PPV ranged from 43 to 100 percent, and NPV ranged from 37 to 100 percent. LR+ ranged from 1.25 to 18.44 and LR- from 0.08 to 0.74. Using the summary sensitivity and specificity of 78 and 86 percent, respectively, we calculated an overall PPV of 82 percent and NPV of 82 percent. Similarly, we calculated summary LR+ of 5.57 and LR- of 0.26.

**Accuracy of ECHO in Eight Good-Quality Studies**

Next, we evaluated the accuracy of ECHO compared with coronary angiography in the eight good-quality studies. In these studies, sensitivity varied from 40 to 87 percent, and specificity varied from 71 to 100 percent; the median sensitivity was 80 percent, and the median specificity was 84 percent. Figure 18 presents forest plots of the individual study estimates of sensitivity and specificity of ECHO for diagnosing CAD in women from mixed populations.
Figure 18. Accuracy of ECHO in eight good-quality studies in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sawada, 1989</td>
<td>24</td>
<td>4</td>
<td>4</td>
<td>25</td>
<td>0.86 (0.67-0.96)</td>
<td></td>
<td>0.86 (0.68-0.96)</td>
<td></td>
</tr>
<tr>
<td>Severi, 1994</td>
<td>28</td>
<td>13</td>
<td>3</td>
<td>78</td>
<td>0.68 (0.52-0.82)</td>
<td></td>
<td>0.80 (0.69-0.99)</td>
<td></td>
</tr>
<tr>
<td>Laurienzo, 1997</td>
<td>18</td>
<td>4</td>
<td>0</td>
<td>62</td>
<td>0.82 (0.60-0.95)</td>
<td></td>
<td>1.00 (0.95-1.00)</td>
<td></td>
</tr>
<tr>
<td>Elhendy, 1998</td>
<td>35</td>
<td>10</td>
<td>2</td>
<td>23</td>
<td>0.78 (0.63-0.89)</td>
<td></td>
<td>0.92 (0.74-0.99)</td>
<td></td>
</tr>
<tr>
<td>Lewis, 1999</td>
<td>10</td>
<td>15</td>
<td>13</td>
<td>54</td>
<td>0.40 (0.21-0.61)</td>
<td></td>
<td>0.81 (0.69-0.89)</td>
<td></td>
</tr>
<tr>
<td>Lehmkuhl, 2007</td>
<td>36</td>
<td>9</td>
<td>13</td>
<td>56</td>
<td>0.80 (0.65-0.90)</td>
<td></td>
<td>0.81 (0.70-0.90)</td>
<td></td>
</tr>
<tr>
<td>Lewandowski, 2007</td>
<td>54</td>
<td>14</td>
<td>36</td>
<td>88</td>
<td>0.79 (0.68-0.88)</td>
<td></td>
<td>0.71 (0.62-0.79)</td>
<td></td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>27</td>
<td>4</td>
<td>8</td>
<td>37</td>
<td>0.87 (0.70-0.96)</td>
<td></td>
<td>0.82 (0.68-0.92)</td>
<td></td>
</tr>
<tr>
<td>Summary values</td>
<td>27</td>
<td>4</td>
<td>8</td>
<td>37</td>
<td>0.77 (0.65-0.85)</td>
<td></td>
<td>0.89 (0.76-0.95)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 19 presents an SROC curve demonstrating an average sensitivity of 77 percent (95% CI, 65 to 85 percent) and specificity of 89 percent (95% CI, 76 to 95 percent).
The prevalence of CAD in these 8 good-quality studies ranged from 26 to 64 percent with a mean prevalence of 40 percent. In the individual studies, PPV ranged from 43 to 100 percent, and NPV ranged from 70 to 94 percent. LR+ ranged from 2.06 to 18.44 and LR- from 0.16 to 0.74. Using the summary sensitivity and specificity of 77 and 89 percent, respectively, we calculated an overall PPV of 82 percent and NPV of 85 percent. Similarly, we calculated summary LR+ of 7.0 and LR- of 0.26.
Table 3. Summary of accuracy data evaluating ECHO for diagnosing CAD

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Mix</th>
<th>Quality</th>
<th>Patients (N)</th>
<th>Cath %</th>
<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lu, et al., 2010</td>
<td>No known CAD</td>
<td>Good</td>
<td>76 (women)</td>
<td>≥ 50</td>
<td>41</td>
<td>87 (75-99)</td>
<td>82 (71-93)</td>
<td>77 (63-91)</td>
<td>90 (81-99)</td>
<td>4.90 (2.58-9.32)</td>
<td>0.16 (0.06-0.40)</td>
</tr>
<tr>
<td>Lewandowski, et al., 2007</td>
<td>No known CAD</td>
<td>Good</td>
<td>192 (women)</td>
<td>≥ 50</td>
<td>35</td>
<td>79 (70-89)</td>
<td>71 (63-79)</td>
<td>60 (50-70)</td>
<td>86 (80-93)</td>
<td>2.74 (2.03-3.70)</td>
<td>0.29 (0.18-0.47)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>359 (men)</td>
<td></td>
<td>75</td>
<td>87 (82-91)</td>
<td>66 (55-76)</td>
<td>88 (84-92)</td>
<td>63 (53-73)</td>
<td>2.55 (1.91-3.41)</td>
<td>0.20 (0.14-0.28)</td>
</tr>
<tr>
<td>Lehmkuhl, et al., 2007</td>
<td>No known CAD</td>
<td>Good</td>
<td>114 (women)</td>
<td>≥ 50</td>
<td>39</td>
<td>80 (68-92)</td>
<td>81 (72-90)</td>
<td>73 (61-86)</td>
<td>86 (78-95)</td>
<td>4.25 (2.55-7.08)</td>
<td>0.26 (0.14-0.45)</td>
</tr>
<tr>
<td>Severi, et al., 1994</td>
<td>No known CAD</td>
<td>Good</td>
<td>122 (women)</td>
<td>≥ 75</td>
<td>34</td>
<td>68 (54-83)</td>
<td>96 (92-100)</td>
<td>90 (80-100)</td>
<td>86 (79-93)</td>
<td>18.44 (5.96-57.07)</td>
<td>0.33 (0.21-0.52)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>307 (men)</td>
<td></td>
<td>67</td>
<td>76 (70-82)</td>
<td>84 (76-91)</td>
<td>91 (86-95)</td>
<td>64 (56-72)</td>
<td>4.85 (3.07-7.66)</td>
<td>0.28 (0.22-0.37)</td>
</tr>
<tr>
<td>Sawada, et al., 1989</td>
<td>No known CAD</td>
<td>Good</td>
<td>57 (women)</td>
<td>≥ 50</td>
<td>49</td>
<td>86 (73-99)</td>
<td>86 (74-99)</td>
<td>86 (73-99)</td>
<td>86 (74-99)</td>
<td>6.21 (2.47-15.63)</td>
<td>0.17 (0.07-0.42)</td>
</tr>
<tr>
<td>Rollan, et al., 2002</td>
<td>No known CAD</td>
<td>Fair</td>
<td>99 (women)</td>
<td>≥ 50</td>
<td>42</td>
<td>69 (55-83)</td>
<td>89 (82-97)</td>
<td>83 (70-95)</td>
<td>80 (70-90)</td>
<td>6.56 (3.00-14.36)</td>
<td>0.35 (0.22-0.55)</td>
</tr>
<tr>
<td>Williams, et al., 1994</td>
<td>No known CAD</td>
<td>Fair</td>
<td>70 (women)</td>
<td>≥ 50</td>
<td>47</td>
<td>88 (77-99)</td>
<td>84 (72-96)</td>
<td>83 (70-95)</td>
<td>89 (78-99)</td>
<td>5.42 (2.58-11.40)</td>
<td>0.14 (0.06-0.37)</td>
</tr>
<tr>
<td>Marwick, et al., 1995</td>
<td>No known CAD</td>
<td>Fair</td>
<td>161 (women)</td>
<td>≥ 50</td>
<td>37</td>
<td>80 (69-90)</td>
<td>81 (74-89)</td>
<td>71 (60-82)</td>
<td>87 (81-94)</td>
<td>4.28 (2.79-6.55)</td>
<td>0.25 (0.15-0.42)</td>
</tr>
<tr>
<td>Dionisopoulos, et al., 1997</td>
<td>No known CAD</td>
<td>Fair</td>
<td>101 (women)</td>
<td>≥ 50</td>
<td>66</td>
<td>90 (82-97)</td>
<td>79 (66-93)</td>
<td>90 (82-97)</td>
<td>79 (86-93)</td>
<td>4.35 (2.24-8.46)</td>
<td>0.13 (0.06-0.27)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>137 (men)</td>
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<td>76</td>
<td>85 (78-91)</td>
<td>96 (85-99)</td>
<td>98 (96-100)</td>
<td>67 (56-79)</td>
<td>19.2 (4.94-74.44)</td>
<td>0.15 (0.10-0.23)</td>
</tr>
<tr>
<td>Mazeika, et al., 1992</td>
<td>No known CAD</td>
<td>Fair</td>
<td>14 (women)</td>
<td>≥ 70</td>
<td>50</td>
<td>57 (20-94)</td>
<td>71 (38-100)</td>
<td>67 (29-100)</td>
<td>63 (29-96)</td>
<td>2.00 (0.53-7.60)</td>
<td>0.6 (0.23-1.60)</td>
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<tr>
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<td></td>
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<td>41 (men)</td>
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<td>80</td>
<td>88 (47-1.00)</td>
<td>92 (76-100)</td>
<td>24 (9-40)</td>
<td>2.67 (0.40-17.76)</td>
<td>0.76 (0.53-1.09)</td>
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<tr>
<td>Slavich, et al., 1996</td>
<td>No known CAD</td>
<td>Fair</td>
<td>49 (women)</td>
<td>≥ 50</td>
<td>45</td>
<td>59 (39-80)</td>
<td>75 (58-92)</td>
<td>68 (48-89)</td>
<td>67 (49-84)</td>
<td>2.36 (1.09-5.13)</td>
<td>0.55 (0.31-0.95)</td>
</tr>
<tr>
<td>Takeuchi, et al., 1996</td>
<td>No known CAD</td>
<td>Fair</td>
<td>70 (women)</td>
<td>≥ 50</td>
<td>29</td>
<td>75 (56-94)</td>
<td>92 (84-100)</td>
<td>79 (61-97)</td>
<td>90 (82-98)</td>
<td>9.38 (3.54-24.82)</td>
<td>0.27 (0.13-0.58)</td>
</tr>
<tr>
<td>Study</td>
<td>Patient Mix</td>
<td>Quality</td>
<td>Patients (N)</td>
<td>Cath %</td>
<td>Prevalence %</td>
<td>Sensitivity % (95% CI)</td>
<td>Specificity % (95% CI)</td>
<td>PPV % (95% CI)</td>
<td>NPV % (95% CI)</td>
<td>LR+ (95% CI)</td>
<td>LR- (95% CI)</td>
</tr>
<tr>
<td>------------------------</td>
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<td>--------------</td>
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<td>------------------------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Masini, et al., 1988</td>
<td>No known CAD</td>
<td>Fair</td>
<td>68 (women)</td>
<td>≥ 70</td>
<td>38</td>
<td>77 (61-93)</td>
<td>93 (85-100)</td>
<td>87 (73-100)</td>
<td>87 (77-97)</td>
<td>10.77 (3.55-32.70)</td>
<td>0.25 (0.12-0.50)</td>
</tr>
<tr>
<td>Roger, et al., 1997</td>
<td>No known CAD</td>
<td>Poor</td>
<td>96 (women)</td>
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<td>60</td>
<td>79 (69-90)</td>
<td>37 (22-52)</td>
<td>66 (55-77)</td>
<td>54 (35-73)</td>
<td>1.26 (0.95-1.66)</td>
<td>0.56 (0.29-1.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>244 (men)</td>
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<td>80</td>
<td>78 (71-83)</td>
<td>44 (30-59)</td>
<td>84 (79-90)</td>
<td>34 (22-45)</td>
<td>1.39 (1.08-1.80)</td>
<td>0.50 (0.33-0.76)</td>
</tr>
<tr>
<td>Laurienzo, et al., 1997</td>
<td>Mixed</td>
<td>Good</td>
<td>84 (women)</td>
<td>≥ 70</td>
<td>26</td>
<td>82 (66-98)</td>
<td>100 (95-100)</td>
<td>100 (83-100)</td>
<td>94 (88-100)</td>
<td>NA</td>
<td>0.18 (0.07-0.44)</td>
</tr>
<tr>
<td>Elhendy, et al., 1997</td>
<td>Mixed</td>
<td>Good</td>
<td>70 (women)</td>
<td>≥ 50</td>
<td>64</td>
<td>78 (66-90)</td>
<td>92 (81-100)</td>
<td>95 (87-100)</td>
<td>70 (54-85)</td>
<td>9.72 (2.55-37.07)</td>
<td>0.24 (0.14-0.42)</td>
</tr>
<tr>
<td>Lewis, et al., 1999</td>
<td>Mixed</td>
<td>Good</td>
<td>92 (women)</td>
<td>≥ 50</td>
<td>27</td>
<td>40 (21-59)</td>
<td>81 (71-90)</td>
<td>43 (23-64)</td>
<td>78 (69-88)</td>
<td>2.06 (1.04-4.09)</td>
<td>0.74 (0.53-1.05)</td>
</tr>
<tr>
<td>Shin, et al., 2003</td>
<td>Mixed</td>
<td>Fair</td>
<td>162 (women)</td>
<td>≥ 50</td>
<td>34</td>
<td>82 (72-92)</td>
<td>71 (62-80)</td>
<td>59 (48-70)</td>
<td>88 (82-95)</td>
<td>2.82 (2.05-3.90)</td>
<td>0.26 (0.14-0.45)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>302 (men)</td>
<td></td>
<td>55</td>
<td>79 (72-85)</td>
<td>80 (72-86)</td>
<td>83 (77-89)</td>
<td>76 (68-83)</td>
<td>3.95 (2.80-5.59)</td>
<td>0.26 (0.19-0.36)</td>
</tr>
<tr>
<td>Elhendy, et al., 1997</td>
<td>Mixed</td>
<td>Fair</td>
<td>96 (women)</td>
<td>≥ 50</td>
<td>65</td>
<td>76 (65-86)</td>
<td>94 (66-100)</td>
<td>96 (90-100)</td>
<td>68 (55-81)</td>
<td>12.89 (3.33-49.80)</td>
<td>0.26 (0.16-0.40)</td>
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<tr>
<td></td>
<td></td>
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<td>210 (men)</td>
<td></td>
<td>81</td>
<td>73 (66-80)</td>
<td>77 (61-89)</td>
<td>93 (89-98)</td>
<td>39 (28-50)</td>
<td>3.17 (1.77-5.66)</td>
<td>0.35 (0.26-0.47)</td>
</tr>
<tr>
<td>Bjornstad, et al., 1995</td>
<td>Mixed</td>
<td>Fair</td>
<td>7 (women)</td>
<td>≥ 50</td>
<td>86</td>
<td>83 (54-100)</td>
<td>100 (NA-100)</td>
<td>100 (40-100)</td>
<td>50 (NA-100)</td>
<td>NA</td>
<td>0.17 (0.03-1.00)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30 (men)</td>
<td></td>
<td>93</td>
<td>68 (48-84)</td>
<td>100 (55-1.00)</td>
<td>100 (84-100)</td>
<td>36 (11-61)</td>
<td>NA</td>
<td>0.32 (0.19-0.55)</td>
</tr>
<tr>
<td>Agati, et al., 1992</td>
<td>Mixed</td>
<td>Fair</td>
<td>10 (women)</td>
<td>≥ 70</td>
<td>50</td>
<td>80 (45-100)</td>
<td>100 (NA-100)</td>
<td>100 (40-100)</td>
<td>100 (NA-100)</td>
<td>NA</td>
<td>0.20 (0.03-1.15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>22 (men)</td>
<td></td>
<td>86</td>
<td>95 (74-1.00)</td>
<td>100 (37-1.00)</td>
<td>100 (83-100)</td>
<td>75 (33-100)</td>
<td>NA</td>
<td>0.05 (0.01-0.35)</td>
</tr>
<tr>
<td>Masini, et al., 1988</td>
<td>Mixed</td>
<td>Fair</td>
<td>83 (women)</td>
<td>≥ 70</td>
<td>47</td>
<td>79 (67-92)</td>
<td>93 (86-100)</td>
<td>91 (82-100)</td>
<td>84 (73-94)</td>
<td>11.66 (3.87-35.16)</td>
<td>0.22 (0.12-0.41)</td>
</tr>
<tr>
<td>Ho, et al., 1998</td>
<td>Mixed</td>
<td>Fair</td>
<td>51 (women)</td>
<td>≥ 50</td>
<td>57</td>
<td>93 (77-99)</td>
<td>82 (60-95)</td>
<td>87 (75-99)</td>
<td>90 (77-100)</td>
<td>5.12 (2.10-12.49)</td>
<td>0.08 (0.02-0.32)</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; Cath % = % stenosis defined to be positive for CAD on diagnostic cardiac catheterization (coronary angiography); CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NPV = negative predictive value; NR = not reported; PPV = positive predictive value
SPECT

We identified 30 studies evaluating the accuracy of SPECT compared with coronary angiography (Table 4). Fourteen of these studies were conducted exclusively in women with no known CAD, and these are the studies used in our primary analysis. In our secondary analysis, we evaluated the accuracy of SPECT in diagnosing CAD in mixed populations of known and no known CAD, including 16 additional studies.

Primary Analysis: Population of Women With No Known CAD

The 14 studies represent findings on SPECT use in 1000 women (sample size ranging from 19 to 184 women). Of these studies, four were good quality, nine were fair quality, and 1 was poor quality. Sensitivity varied from 62 to 93 percent, and specificity varied from 50 to 91 percent; the median sensitivity was 82 percent, and the median specificity was 81 percent. Figure 20 presents forest plots of the individual study estimates of sensitivity and specificity of SPECT for diagnosing CAD in women with no known CAD.

Figure 20. Accuracy of SPECT in women with no known CAD

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hung, 1984</td>
<td>21</td>
<td>7</td>
<td>6</td>
<td>58</td>
<td>0.75 (0.55-0.89)</td>
<td>0.91 (0.81-0.96)</td>
</tr>
<tr>
<td>Slavich, 1996</td>
<td>18</td>
<td>4</td>
<td>4</td>
<td>20</td>
<td>0.82 (0.60-0.95)</td>
<td>0.83 (0.63-0.95)</td>
</tr>
<tr>
<td>Takeuchi, 1996</td>
<td>14</td>
<td>4</td>
<td>13</td>
<td>30</td>
<td>0.78 (0.52-0.94)</td>
<td>0.70 (0.54-0.83)</td>
</tr>
<tr>
<td>Santana-Baodo, 1998</td>
<td>17</td>
<td>3</td>
<td>4</td>
<td>39</td>
<td>0.85 (0.62-0.97)</td>
<td>0.91 (0.78-0.97)</td>
</tr>
<tr>
<td>Abramson, 2000</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>0.89 (0.52-1.00)</td>
<td>0.90 (0.55-1.00)</td>
</tr>
<tr>
<td>Gentile, 2001</td>
<td>26</td>
<td>2</td>
<td>7</td>
<td>7</td>
<td>0.93 (0.76-0.99)</td>
<td>0.50 (0.23-0.77)</td>
</tr>
<tr>
<td>Rollan, 2002</td>
<td>23</td>
<td>3</td>
<td>12</td>
<td>16</td>
<td>0.88 (0.70-0.98)</td>
<td>0.57 (0.37-0.76)</td>
</tr>
<tr>
<td>Doyle, 2003</td>
<td>16</td>
<td>10</td>
<td>28</td>
<td>130</td>
<td>0.62 (0.41-0.80)</td>
<td>0.82 (0.75-0.88)</td>
</tr>
<tr>
<td>Elhendy, 2006</td>
<td>44</td>
<td>9</td>
<td>7</td>
<td>28</td>
<td>0.83 (0.70-0.92)</td>
<td>0.80 (0.63-0.92)</td>
</tr>
<tr>
<td>Mieres, 2007</td>
<td>12</td>
<td>2</td>
<td>4</td>
<td>24</td>
<td>0.86 (0.57-0.98)</td>
<td>0.86 (0.67-0.96)</td>
</tr>
<tr>
<td>Yeih, 2007</td>
<td>20</td>
<td>8</td>
<td>3</td>
<td>20</td>
<td>0.71 (0.51-0.87)</td>
<td>0.87 (0.66-0.97)</td>
</tr>
<tr>
<td>Bokhari, 2008</td>
<td>36</td>
<td>9</td>
<td>5</td>
<td>18</td>
<td>0.80 (0.65-0.90)</td>
<td>0.78 (0.56-0.93)</td>
</tr>
<tr>
<td>Wolak, 2008</td>
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<td>13</td>
<td>12</td>
<td>33</td>
<td>0.81 (0.70-0.90)</td>
<td>0.73 (0.58-0.85)</td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>28</td>
<td>3</td>
<td>21</td>
<td>24</td>
<td>0.90 (0.74-0.98)</td>
<td>0.53 (0.38-0.68)</td>
</tr>
</tbody>
</table>
| **Summary values** &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &nbsp; &n
Figure 21 presents an SROC curve with an average sensitivity of 81 percent (95% CI, 76 to 86 percent) and specificity of 78 percent (95% CI, 69 to 84 percent).

The prevalence of CAD in these 14 studies ranged from 14 to 67 percent with a mean prevalence of 45 percent. In the individual studies, PPV ranged from 36 to 89 percent, and NPV ranged from 50 to 91 percent. LR+ ranged from 1.86 to 9.14 and LR- from 0.12 to 0.47 respectively. Using the summary sensitivity and specificity of 81 and 78 percent, respectively, we calculated an overall PPV of 75 percent and a negative predictive value of 83 percent. Similarly, we calculated summary LR+ of 3.68 and LR- of 0.24.

**Accuracy of SPECT in Four Good-Quality Studies**

Next, we evaluated the accuracy of SPECT compared with coronary angiography in the four good-quality studies. In these studies, sensitivity varied from 62 to 93 percent, and specificity varied from 50 to 91 percent; the median sensitivity was 83 percent, and the median specificity was 68 percent. Figure 22 presents forest plots of the individual study estimates of sensitivity and specificity of SPECT for diagnosing CAD in women with no known CAD.
Figure 22. Accuracy of SPECT in four good-quality studies in women with no known CAD

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hung, 1984</td>
<td>21</td>
<td>7</td>
<td>6</td>
<td>58</td>
<td>0.75 (0.55-0.89)</td>
<td>0.91 (0.81-0.96)</td>
</tr>
<tr>
<td>Gentile, 2001</td>
<td>26</td>
<td>2</td>
<td>7</td>
<td>7</td>
<td>0.93 (0.76-0.99)</td>
<td>0.50 (0.23-0.77)</td>
</tr>
<tr>
<td>Doyle, 2003</td>
<td>16</td>
<td>10</td>
<td>28</td>
<td>130</td>
<td>0.62 (0.41-0.80)</td>
<td>0.82 (0.75-0.88)</td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>28</td>
<td>3</td>
<td>21</td>
<td>24</td>
<td>0.90 (0.74-0.98)</td>
<td>0.53 (0.38-0.68)</td>
</tr>
<tr>
<td>Summary values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.83 (0.52-0.95)</td>
<td>0.72 (0.37-0.92)</td>
</tr>
</tbody>
</table>

Figure 23 presents an SROC curve with an average sensitivity of 83 percent (95% CI, 52 to 95 percent) and specificity of 72 percent (95% CI, 37 to 92 percent). It is important to note that given the small number of studies and wide confidence intervals that these summary statistics should be interpreted with caution.
The prevalence of CAD in these 4 good-quality studies ranged from 14 to 67 percent with a mean prevalence of 38 percent. In the individual studies, PPV ranged from 36 to 79 percent, and NPV ranged from 78 to 93 percent. LR+ ranged from 1.86 to 8.0 and LR- from 0.14 to 0.47. Using the summary sensitivity and specificity of 83 and 72 percent, respectively, we calculated an overall PPV of 65 percent and NPV of 88 percent. Similarly, we calculated summary LR+ of 2.96 and LR- ratio of 0.24.

Secondary Analysis: Mixed Population of Women With Known and No Known CAD

We performed a secondary analysis where we expanded our inclusion criteria to include studies whose patient population included a mix of women with known CAD and women with no known CAD. This expanded inclusion criteria allowed an additional 16 studies to be included in our analysis (totaling 30 studies). The 30 studies represent findings on SPECT use in 2157 women (sample size ranging from 14 to 243 women). Of these 30 studies, 10 were good quality, 15 were fair quality, and 5 were poor quality (Table 4).

In these 30 studies, sensitivity varied from 15 to 100 percent, and specificity varied from 27 to 100 percent; the median sensitivity was 83 percent, and the median specificity was 81 percent. Figure 24 presents forest plots of the individual study estimates of sensitivity and specificity of SPECT for diagnosing CAD in women from mixed populations.
Figure 24. Accuracy of SPECT in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedman, 1982</td>
<td>21</td>
<td>7</td>
<td>1</td>
<td>31</td>
<td>0.75 (0.55-0.89)</td>
<td>0.97 (0.84-1.00)</td>
</tr>
<tr>
<td>Hung, 1984</td>
<td>21</td>
<td>7</td>
<td>6</td>
<td>58</td>
<td>0.75 (0.55-0.89)</td>
<td>0.91 (0.81-0.96)</td>
</tr>
<tr>
<td>DePasquale, 1988</td>
<td>22</td>
<td>3</td>
<td>4</td>
<td>11</td>
<td>0.88 (0.69-0.97)</td>
<td>0.73 (0.45-0.92)</td>
</tr>
<tr>
<td>Kiat, 1990</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>1.00 (0.76-1.00)</td>
<td>0.67 (0.09-0.99)</td>
</tr>
<tr>
<td>Chae, 1993</td>
<td>116</td>
<td>47</td>
<td>28</td>
<td>52</td>
<td>0.71 (0.64-0.78)</td>
<td>0.65 (0.54-0.75)</td>
</tr>
<tr>
<td>Van Train, 1994</td>
<td>16</td>
<td>1</td>
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<td>9</td>
<td>0.94 (0.71-1.00)</td>
<td>0.69 (0.39-0.91)</td>
</tr>
<tr>
<td>Mak, 1995</td>
<td>20</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>0.83 (0.63-0.95)</td>
<td>1.00 (0.05-1.00)</td>
</tr>
<tr>
<td>Mohiuddin, 1996</td>
<td>61</td>
<td>4</td>
<td>2</td>
<td>16</td>
<td>0.94 (0.85-0.98)</td>
<td>0.89 (0.65-0.99)</td>
</tr>
<tr>
<td>Slavich, 1996</td>
<td>18</td>
<td>4</td>
<td>4</td>
<td>20</td>
<td>0.82 (0.60-0.95)</td>
<td>0.83 (0.63-0.95)</td>
</tr>
<tr>
<td>Takeuchi, 1996</td>
<td>14</td>
<td>4</td>
<td>13</td>
<td>30</td>
<td>0.78 (0.52-0.94)</td>
<td>0.70 (0.54-0.83)</td>
</tr>
<tr>
<td>Laurienzo, 1997</td>
<td>19</td>
<td>3</td>
<td>12</td>
<td>48</td>
<td>0.86 (0.65-0.97)</td>
<td>0.80 (0.68-0.89)</td>
</tr>
<tr>
<td>Taillefer, 1997</td>
<td>46</td>
<td>18</td>
<td>3</td>
<td>18</td>
<td>0.72 (0.59-0.82)</td>
<td>0.86 (0.64-0.97)</td>
</tr>
<tr>
<td>Elhendy, 1998</td>
<td>35</td>
<td>10</td>
<td>2</td>
<td>23</td>
<td>0.78 (0.63-0.89)</td>
<td>0.92 (0.74-0.99)</td>
</tr>
<tr>
<td>Ho, 1998</td>
<td>19</td>
<td>5</td>
<td>5</td>
<td>15</td>
<td>0.79 (0.58-0.93)</td>
<td>0.75 (0.51-0.91)</td>
</tr>
<tr>
<td>Santana-Baodo, 1998</td>
<td>17</td>
<td>3</td>
<td>4</td>
<td>39</td>
<td>0.85 (0.62-0.97)</td>
<td>0.91 (0.78-0.97)</td>
</tr>
<tr>
<td>Abramson, 2000</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>9</td>
<td>0.89 (0.52-1.00)</td>
<td>0.90 (0.55-1.00)</td>
</tr>
<tr>
<td>Gentile, 2001</td>
<td>26</td>
<td>2</td>
<td>7</td>
<td>7</td>
<td>0.93 (0.76-0.99)</td>
<td>0.50 (0.23-0.77)</td>
</tr>
<tr>
<td>Kaminek, 2001</td>
<td>60</td>
<td>6</td>
<td>5</td>
<td>62</td>
<td>0.91 (0.81-0.97)</td>
<td>0.93 (0.83-0.98)</td>
</tr>
<tr>
<td>Emmett, 2002</td>
<td>9</td>
<td>1</td>
<td>3</td>
<td>10</td>
<td>0.90 (0.55-1.00)</td>
<td>0.77 (0.46-0.95)</td>
</tr>
<tr>
<td>Rollan, 2002</td>
<td>23</td>
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<td>12</td>
<td>16</td>
<td>0.88 (0.70-0.98)</td>
<td>0.57 (0.37-0.76)</td>
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<tr>
<td>Doyle, 2003</td>
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<td>10</td>
<td>28</td>
<td>130</td>
<td>0.62 (0.41-0.80)</td>
<td>0.82 (0.75-0.88)</td>
</tr>
<tr>
<td>Gulati, 2004</td>
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<td>7</td>
<td>0.15 (0.06-0.30)</td>
<td>1.00 (0.65-1.00)</td>
</tr>
<tr>
<td>Elhendy, 2006</td>
<td>44</td>
<td>9</td>
<td>7</td>
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<td>24</td>
<td>0.86 (0.57-0.98)</td>
<td>0.86 (0.67-0.96)</td>
</tr>
<tr>
<td>Slomka, 2007</td>
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<td>3</td>
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<td>0.83 (0.71-0.91)</td>
<td>0.94 (0.83-0.99)</td>
</tr>
<tr>
<td>Vashist, 2007</td>
<td>34</td>
<td>5</td>
<td>11</td>
<td>4</td>
<td>0.87 (0.73-0.96)</td>
<td>0.27 (0.08-0.55)</td>
</tr>
<tr>
<td>Yeih, 2007</td>
<td>20</td>
<td>8</td>
<td>3</td>
<td>20</td>
<td>0.71 (0.51-0.87)</td>
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</tr>
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<td>Bokhari, 2008</td>
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<td>33</td>
<td>0.81 (0.70-0.90)</td>
<td>0.73 (0.58-0.85)</td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>28</td>
<td>3</td>
<td>21</td>
<td>24</td>
<td>0.90 (0.74-0.98)</td>
<td>0.53 (0.38-0.68)</td>
</tr>
</tbody>
</table>

Summary values

Sensitivity (95% CI): 0.82 (0.77-0.87)
Specificity (95% CI): 0.81 (0.74-0.86)
Figure 25 presents an SROC curve demonstrating an average sensitivity of 82 percent (95% CI, 77 to 87 percent) and specificity of 81 percent (95% CI, 74 to 86 percent).

The prevalence of CAD in the 30 studies ranged from 14 to 96 percent with a mean prevalence of 54 percent. In the individual studies, PPV ranged from 36 to 100 percent, and NPV ranged from 27 to 100 percent. LR+ ranged from 1.89 to 24 and LR- from 0 to 0.89. Using the summary sensitivity and specificity of 82 and 81 percent, respectively, we calculated an overall PPV of 84 percent and NPV of 79 percent. Similarly, we calculated summary LR+ of 4.32 and LR- of 0.22.

**Accuracy of SPECT in 10 Good-Quality Studies**

Next, we evaluated the accuracy of SPECT compared with coronary angiography in the 10 good-quality studies. In these studies, sensitivity varied from 62 to 94 percent, and specificity varied from 50 to 100 percent; the median sensitivity was 81 percent, and the median specificity was 84 percent. Figure 26 presents forest plots of the individual study estimates of sensitivity and specificity of SPECT for diagnosing CAD in women with from mixed populations.
Figure 26. Accuracy of SPECT in 10 good-quality studies in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hung, 1984</td>
<td>21</td>
<td>7</td>
<td>6</td>
<td>58</td>
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<td>47</td>
<td>28</td>
<td>52</td>
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<td>0.65 (0.54-0.75)</td>
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<td>Mak, 1995</td>
<td>20</td>
<td>4</td>
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<td>Elhendy, 1998</td>
<td>35</td>
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<td>2</td>
<td>23</td>
<td>0.78 (0.63-0.89)</td>
<td>0.92 (0.74-0.99)</td>
</tr>
<tr>
<td>Gentile, 2001</td>
<td>26</td>
<td>2</td>
<td>7</td>
<td>7</td>
<td>0.93 (0.76-0.99)</td>
<td>0.50 (0.23-0.77)</td>
</tr>
<tr>
<td>Doyle, 2003</td>
<td>16</td>
<td>10</td>
<td>28</td>
<td>130</td>
<td>0.62 (0.41-0.80)</td>
<td>0.82 (0.75-0.88)</td>
</tr>
<tr>
<td>Lu, 2010</td>
<td>28</td>
<td>3</td>
<td>21</td>
<td>24</td>
<td>0.90 (0.74-0.98)</td>
<td>0.53 (0.38-0.68)</td>
</tr>
<tr>
<td><strong>Summary values</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>0.82 (0.72-0.88)</strong></td>
<td><strong>0.79 (0.66-0.87)</strong></td>
</tr>
</tbody>
</table>

Figure 27 presents an SROC curve demonstrating an average sensitivity of 82 percent (95% CI, 72 to 88 percent) and specificity of 79 percent (95% CI, 66 to 87 percent).

The prevalence of CAD in these 10 good-quality studies ranged from 14 to 96 percent with a mean prevalence of 56 percent. In the individual studies, PPV ranged from 36 to 100 percent, and NPV ranged from 20 to 94 percent. LR+ ranged from 1.86 to 9.72 and LR- from 0.07 to 0.47. Using the summary sensitivity and specificity of 82 and 79 percent, respectively, we calculated an overall PPV of 84 percent and NPV of 78 percent. Similarly, we calculated summary LR+ of 3.90 and LR- of 0.23.
Table 4. Summary of accuracy data evaluating SPECT for diagnosing CAD

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Mix</th>
<th>Quality</th>
<th>Patients (N)</th>
<th>Cath %</th>
<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lu, et al., 2010</td>
<td>No known CAD</td>
<td>Good</td>
<td>76 (women)</td>
<td>≥ 50</td>
<td>41</td>
<td>90 (74-98)</td>
<td>53 (38-68)</td>
<td>57 (43-71)</td>
<td>89 (77-100)</td>
<td>1.94 (1.39-2.70)</td>
<td>0.18 (0.06-0.55)</td>
</tr>
<tr>
<td>Doyle, et al., 2003</td>
<td>No known CAD</td>
<td>Good</td>
<td>184 (women)</td>
<td>≥ 70</td>
<td>14</td>
<td>62 (41-80)</td>
<td>82 (75-88)</td>
<td>36 (22-51)</td>
<td>93 (89-97)</td>
<td>3.47 (2.21-5.46)</td>
<td>0.47 (0.29-0.76)</td>
</tr>
<tr>
<td>Gentile, et al., 2001</td>
<td>No known CAD</td>
<td>Good</td>
<td>42 (women)</td>
<td>≥ 60</td>
<td>67</td>
<td>93 (76-99)</td>
<td>50 (23-77)</td>
<td>79 (65-93)</td>
<td>78 (51-100)</td>
<td>1.86 (1.09-3.17)</td>
<td>0.14 (0.03-0.60)</td>
</tr>
<tr>
<td>Hung, et al., 1984</td>
<td>No known CAD</td>
<td>Good</td>
<td>92 (women)</td>
<td>≥ 70</td>
<td>30</td>
<td>75 (55-89)</td>
<td>91 (81-96)</td>
<td>78 (62-93)</td>
<td>89 (82-97)</td>
<td>8 (3.63-17.6)</td>
<td>0.28 (0.14-0.53)</td>
</tr>
<tr>
<td>Wolak, et al., 2008</td>
<td>No known CAD</td>
<td>Fair</td>
<td>114 (women)</td>
<td>≥ 70</td>
<td>61</td>
<td>81 (70-90)</td>
<td>73 (58-85)</td>
<td>82 (73-91)</td>
<td>72 (59-85)</td>
<td>3.04 (1.85-6.01)</td>
<td>0.26 (0.15-0.43)</td>
</tr>
<tr>
<td>Yeih, et al., 2007</td>
<td>No known CAD</td>
<td>Good</td>
<td>51 (women)</td>
<td>≥ 50</td>
<td>55</td>
<td>71 (51-87)</td>
<td>87 (66-97)</td>
<td>87 (73-100)</td>
<td>71 (55-88)</td>
<td>5.48 (1.86-16.14)</td>
<td>0.33 (0.18-0.60)</td>
</tr>
<tr>
<td>Mieres, et al., 2007</td>
<td>No known CAD</td>
<td>Fair</td>
<td>42 (women)</td>
<td>≥ 50</td>
<td>33</td>
<td>86 (57-98)</td>
<td>86 (67-96)</td>
<td>75 (54-96)</td>
<td>92 (82-100)</td>
<td>6 (2.36-15.24)</td>
<td>0.17 (0.05-0.61)</td>
</tr>
<tr>
<td>Elhendy, et al., 2006</td>
<td>No known CAD</td>
<td>Fair</td>
<td>88 (women)</td>
<td>≥ 50</td>
<td>60</td>
<td>83 (70-92)</td>
<td>80 (63-92)</td>
<td>86 (77-96)</td>
<td>76 (62-90)</td>
<td>4.15 (2.12-8.14)</td>
<td>0.21 (0.11-0.39)</td>
</tr>
<tr>
<td>Rollan, et al., 2002</td>
<td>No known CAD</td>
<td>Fair</td>
<td>54 (women)</td>
<td>≥ 50</td>
<td>48</td>
<td>88 (70-98)</td>
<td>57 (37-76)</td>
<td>66 (50-81)</td>
<td>84 (68-100)</td>
<td>2.06 (1.32-3.24)</td>
<td>0.20 (0.07-0.61)</td>
</tr>
<tr>
<td>Abramson, et al., 2000</td>
<td>No known CAD</td>
<td>Fair</td>
<td>19 (women)</td>
<td>≥ 50</td>
<td>47</td>
<td>89 (52-100)</td>
<td>90 (55-100)</td>
<td>89 (68-100)</td>
<td>90 (71-100)</td>
<td>8.89 (1.36-57.89)</td>
<td>0.12 (0.02-0.8)</td>
</tr>
<tr>
<td>Slavich, et al., 1996</td>
<td>No known CAD</td>
<td>Fair</td>
<td>46 (women)</td>
<td>≥ 50</td>
<td>48</td>
<td>82 (60-95)</td>
<td>83 (63-95)</td>
<td>82 (66-98)</td>
<td>83 (68-98)</td>
<td>4.91 (1.96-12.27)</td>
<td>0.22 (0.09-0.54)</td>
</tr>
<tr>
<td>Takeuchi, et al., 1996</td>
<td>No known CAD</td>
<td>Fair</td>
<td>61 (women)</td>
<td>≥ 50</td>
<td>30</td>
<td>78 (52-94)</td>
<td>70 (54-83)</td>
<td>52 (33-71)</td>
<td>88 (77-99)</td>
<td>2.57 (1.53-4.31)</td>
<td>0.32 (0.13-0.77)</td>
</tr>
<tr>
<td>Santana-Baudo, et al., 1998</td>
<td>No known CAD</td>
<td>Fair</td>
<td>63 (women)</td>
<td>≥ 50</td>
<td>32</td>
<td>85 (62-97)</td>
<td>91 (78-97)</td>
<td>81 (64-98)</td>
<td>93 (85-100)</td>
<td>9.13 (3.53-23.65)</td>
<td>0.16 (0.06-0.47)</td>
</tr>
<tr>
<td>Rollan, et al., 2002</td>
<td>No known CAD</td>
<td>Fair</td>
<td>100 (men)</td>
<td>≥ 50</td>
<td>80</td>
<td>92 (84-97)</td>
<td>90 (68-99)</td>
<td>97 (94-100)</td>
<td>75 (58-92)</td>
<td>9.25 (2.48-34.5)</td>
<td>0.08 (0.04-0.18)</td>
</tr>
<tr>
<td>Study</td>
<td>Patient Mix</td>
<td>Qualit y</td>
<td>Patients (N)</td>
<td>Cath %</td>
<td>Prevalence %</td>
<td>Sensitivity (95% CI)</td>
<td>Specificity (95% CI)</td>
<td>PPV % (95% CI)</td>
<td>NPV % (95% CI)</td>
<td>LR+ (95% CI)</td>
<td>LR- (95% CI)</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------</td>
<td>---------</td>
<td>---------------</td>
<td>-------</td>
<td>--------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>-------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Bokhari, et al., 2008 \cite{52}</td>
<td>No known CAD</td>
<td>Poor</td>
<td>68 (women)</td>
<td>≥ 50</td>
<td>66</td>
<td>80 (65-90)</td>
<td>78 (56-93)</td>
<td>88 (78-98)</td>
<td>67 (49-84)</td>
<td>3.68 (1.67-8.10)</td>
<td>0.26 (0.14-0.48)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>150 (men)</td>
<td></td>
<td>65</td>
<td>82 (73-89)</td>
<td>79 (65-89)</td>
<td>88 (81-95)</td>
<td>69 (58-81)</td>
<td>3.86 (2.26-6.58)</td>
<td>0.23 (0.15-0.36)</td>
</tr>
<tr>
<td>Laurienzo, et al., 1997 \cite{39}</td>
<td>Mixed</td>
<td>Good</td>
<td>84 (women)</td>
<td>&gt; 70</td>
<td>26</td>
<td>86 (65-97)</td>
<td>80 (68-89)</td>
<td>61 (44-78)</td>
<td>94 (88-100)</td>
<td>4.32 (2.54-7.36)</td>
<td>0.17 (0.06-0.49)</td>
</tr>
<tr>
<td>Taillefer, et al., 1997 \cite{57}</td>
<td>Mixed</td>
<td>Good</td>
<td>85 (women)</td>
<td>≥ 50</td>
<td>75</td>
<td>72 (59-82)</td>
<td>86 (64-97)</td>
<td>94 (87-100)</td>
<td>50 (34-66)</td>
<td>5.03 (1.75-14.50)</td>
<td>0.33 (0.21-0.50)</td>
</tr>
<tr>
<td>Mak, et al., 1995 \cite{68}</td>
<td>Mixed</td>
<td>Good</td>
<td>25 (women)</td>
<td>≥ 50</td>
<td>96</td>
<td>83 (63-95)</td>
<td>100 (5-100)</td>
<td>100 (85-100)</td>
<td>20 (15-55)</td>
<td>2.48 (1.31-4.67)</td>
<td>0.11 (0.05-0.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>114 (men)</td>
<td></td>
<td>86</td>
<td>93 (86-97)</td>
<td>63 (35-85)</td>
<td>94 (89-99)</td>
<td>59 (35-82)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Chae, et al., 1993 \cite{60}</td>
<td>Mixed</td>
<td>Good</td>
<td>243 (women)</td>
<td>≥ 50</td>
<td>67</td>
<td>71 (64-78)</td>
<td>65 (54-75)</td>
<td>81 (74-87)</td>
<td>53 (43-62)</td>
<td>2.03 (1.49-2.78)</td>
<td>0.44 (0.33-0.59)</td>
</tr>
<tr>
<td>Elhendy, et al., 1998 \cite{51}</td>
<td>Mixed</td>
<td>Good</td>
<td>70 (women)</td>
<td>≥ 50</td>
<td>64</td>
<td>78 (63-89)</td>
<td>92 (74-99)</td>
<td>95 (87-100)</td>
<td>70 (54-85)</td>
<td>9.72 (2.55-37.07)</td>
<td>0.24 (0.14-0.42)</td>
</tr>
<tr>
<td>Mohiuddin, et al, 1996 \cite{59}</td>
<td>Mixed</td>
<td>Good</td>
<td>83 (women)</td>
<td>≥ 50</td>
<td>78</td>
<td>94 (85-98)</td>
<td>89 (65-99)</td>
<td>97 (92-100)</td>
<td>80 (62-98)</td>
<td>8.45 (2.28-31.25)</td>
<td>0.07 (0.03-0.18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>119 (men)</td>
<td></td>
<td>80</td>
<td>87 (79-93)</td>
<td>83 (63-95)</td>
<td>95 (91-100)</td>
<td>63 (46-79)</td>
<td>5.24 (2.14-12.87)</td>
<td>0.15 (0.09-0.26)</td>
</tr>
<tr>
<td>Vashist, et al., 2007 \cite{53}</td>
<td>Mixed</td>
<td>Fair</td>
<td>54 (women)</td>
<td>≥ 50</td>
<td>72</td>
<td>87 (73-96)</td>
<td>27 (8-55)</td>
<td>76 (63-88)</td>
<td>44 (12-77)</td>
<td>1.19 (0.86-1.65)</td>
<td>0.48 (0.15-1.55)</td>
</tr>
<tr>
<td>Gulati, et al., 2004 \cite{64}</td>
<td>Mixed</td>
<td>Fair</td>
<td>47 (women)</td>
<td>≥ 50</td>
<td>85</td>
<td>15 (6-30)</td>
<td>95 (65-100)</td>
<td>95 (78-100)</td>
<td>16 (5-28)</td>
<td>3.28 (1.10-103.69)</td>
<td>0.89 (0.72-1.10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25 (men)</td>
<td></td>
<td>85</td>
<td>4 (0-21)</td>
<td>100 (5-100)</td>
<td>99 (87-100)</td>
<td>4 (4-12)</td>
<td>7.39 (NA)</td>
<td></td>
</tr>
<tr>
<td>Emmett, et al., 2002 \cite{65}</td>
<td>Mixed</td>
<td>Fair</td>
<td>23 (women)</td>
<td>&gt; 70</td>
<td>43</td>
<td>90 (55-100)</td>
<td>77 (46-95)</td>
<td>75 (51-100)</td>
<td>91 (74-100)</td>
<td>3.90 (1.42-10.75)</td>
<td>0.13 (0.02-0.85)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>77 (men)</td>
<td></td>
<td>78</td>
<td>88 (77-95)</td>
<td>53 (28-77)</td>
<td>87 (78-95)</td>
<td>56 (32-81)</td>
<td>1.88 (1.12-3.13)</td>
<td>0.22 (0.10-0.50)</td>
</tr>
</tbody>
</table>
Table 4. Summary of accuracy data evaluating SPECT for diagnosing CAD (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Mix</th>
<th>Quality</th>
<th>Patients (N)</th>
<th>Cath %</th>
<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiat, et al., 1990&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Fair</td>
<td>14 (women)</td>
<td>≥ 50</td>
<td>79</td>
<td>100 (76-100)</td>
<td>67 (9-99)</td>
<td>92 (76-100)</td>
<td>100 (50-100)</td>
<td>3 (0.61-14.86)</td>
<td>0 (NA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>39 (men)</td>
<td></td>
<td></td>
<td>95</td>
<td>92 (78-98)</td>
<td>50 (1-99)</td>
<td>25 (17-67)</td>
<td>1.84 (0.46-7.37)</td>
<td>0.16 (0.03-0.94)</td>
</tr>
<tr>
<td>Friedman, et al., 1982&lt;sup&gt;37&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Fair</td>
<td>60 (women)</td>
<td>≥ 70</td>
<td>47</td>
<td>75 (55-89)</td>
<td>97 (84-100)</td>
<td>95 (87-100)</td>
<td>82 (69-94)</td>
<td>24 (3.45-167.17)</td>
<td>0.26 (0.14-0.49)</td>
</tr>
<tr>
<td>Ho, et al., 1998&lt;sup&gt;62&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Fair</td>
<td>44 (women)</td>
<td>≥ 50</td>
<td>55</td>
<td>79 (58-93)</td>
<td>75 (51-91)</td>
<td>79 (63-95)</td>
<td>75 (56-94)</td>
<td>3.17 (1.44-6.95)</td>
<td>0.28 (0.12-0.63)</td>
</tr>
<tr>
<td>Slomka, et al., 2007&lt;sup&gt;60&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Poor</td>
<td>113 (women)</td>
<td>≥ 70</td>
<td>57</td>
<td>83 (71-91)</td>
<td>94 (83-99)</td>
<td>95 (89-100)</td>
<td>81 (70-91)</td>
<td>13.53 (4.49-40.71)</td>
<td>0.18 (0.11-0.31)</td>
</tr>
<tr>
<td>Kaminek, et al., 2001&lt;sup&gt;81&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Poor</td>
<td>133 (women)</td>
<td>≥ 50</td>
<td>50</td>
<td>91 (81-97)</td>
<td>93 (83-98)</td>
<td>92 (86-99)</td>
<td>91 (84-98)</td>
<td>12.18 (5.22-28.41)</td>
<td>0.10 (0.046-0.21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>455 (men)</td>
<td></td>
<td></td>
<td>83 (91-96)</td>
<td>82 (71-90)</td>
<td>96 (94-98)</td>
<td>72 (63-82)</td>
<td>5.15 (3.20-8.28)</td>
<td>0.08 (0.05-0.12)</td>
</tr>
<tr>
<td>DePasquale, et al., 1988&lt;sup&gt;64&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Poor</td>
<td>40 (women)</td>
<td>≥ 70</td>
<td>63</td>
<td>88 (69-97)</td>
<td>73 (45-92)</td>
<td>85 (71-98)</td>
<td>79 (57-100)</td>
<td>3.30 (1.41-7.73)</td>
<td>0.16 (0.05-0.49)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>170 (men)</td>
<td></td>
<td></td>
<td>96 (92-99)</td>
<td>25 (7-52)</td>
<td>93 (88-97)</td>
<td>40 (10-70)</td>
<td>1.28 (0.96-1.70)</td>
<td>0.16 (0.05-0.49)</td>
</tr>
<tr>
<td>Van Train, et al., 1994&lt;sup&gt;94&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Poor</td>
<td>39 (women)</td>
<td>≥ 50</td>
<td>44</td>
<td>94 (71-100)</td>
<td>69 (39-91)</td>
<td>80 (62-98)</td>
<td>90 (71-100)</td>
<td>3.06 (1.34-6.97)</td>
<td>0.08 (0.01-0.59)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>94 (men)</td>
<td></td>
<td></td>
<td>90 (81-95)</td>
<td>94 (89-99)</td>
<td>31 (6-56)</td>
<td>1.61 (0.89-2.90)</td>
<td>0.24 (0.09-0.62)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; Cath % = % stenosis defined to be positive for CAD on diagnostic cardiac catheterization (coronary angiography); CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NPV = negative predictive value; NR = not reported; PPV = positive predictive value
CMR

We identified six studies evaluating the accuracy of CMR compared with coronary angiography (Table 5). Five of these studies reported accuracy data in women with no known CAD, and these are the studies used in our primary analysis. In our secondary analysis, we evaluated the accuracy of CMR in diagnosing CAD in mixed populations of known and no known CAD, including additional data from two studies and data from one additional study.

Primary Analysis: Population of Women With No Known CAD

The five studies represent findings on CMR use in 501 women (sample size ranging from 30 to 184 women). All five of these studies were rated good quality. In these studies, sensitivity varied from 58 to 83 percent, and specificity varied from 59 to 96 percent; the median sensitivity was 75 percent, and the median specificity was 88 percent. Figure 28 presents forest plots of the individual study estimates of sensitivity and specificity of CMR for diagnosing CAD in women with no known CAD.

Figure 28. Accuracy of CMR in women with no known CAD

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doyle, 2003</td>
<td>15</td>
<td>11</td>
<td>35</td>
<td>123</td>
<td>0.58 (0.37-0.77)</td>
<td>0.78 (0.71-0.84)</td>
</tr>
<tr>
<td>Klem, 2008</td>
<td>32</td>
<td>14</td>
<td>11</td>
<td>79</td>
<td>0.70 (0.54-0.82)</td>
<td>0.88 (0.79-0.94)</td>
</tr>
<tr>
<td>Langer, 2009</td>
<td>6</td>
<td>2</td>
<td>9</td>
<td>13</td>
<td>0.75 (0.35-0.97)</td>
<td>0.59 (0.36-0.79)</td>
</tr>
<tr>
<td>Gebker, 2010</td>
<td>42</td>
<td>9</td>
<td>8</td>
<td>60</td>
<td>0.82 (0.69-0.92)</td>
<td>0.88 (0.78-0.95)</td>
</tr>
<tr>
<td>Merkle, 2010</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>25</td>
<td>0.83 (0.36-1.00)</td>
<td>0.96 (0.80-1.00)</td>
</tr>
</tbody>
</table>

Summary values: Sensitivity = 0.72 (0.55-0.85); Specificity = 0.84 (0.69-0.93)

Figure 29 presents an SROC curve with an average sensitivity of 72 percent (95% CI, 55 to 85 percent) and specificity of 84 percent (95% CI, 69 to 93 percent).
The prevalence of CAD in these 5 studies ranged from 14 to 43 percent with a mean prevalence of 27 percent. In the individual studies, PPV ranged from 30 to 84 percent, and NPV ranged from 59 to 96 percent. LR+ ranged from 1.83 to 21.67 and LR- from 0.17 to 0.54. Using the summary sensitivity and specificity of 72 and 84 percent, respectively, we calculated an overall PPV of 62 percent and NPV of 89 percent. Similarly, we calculated summary LR+ of 4.5 and LR- of 0.33.

**Secondary Analysis: Mixed Population of Women With Known and No Known CAD**

We performed a secondary analysis where we expanded our inclusion criteria to include studies whose patient population included a mix of women with known CAD and women with no known CAD. This expanded inclusion criteria allowed an additional 64 patients from one study and an additional 45 patients from another study to be included in our analysis—as well as 168 patients from a third study that was not included in our primary analysis (totaling 6 studies). The 6 studies represent findings on CMR use in 778 women (sample size ranging from 30 to 184 women). Five of these studies were good-quality, and one was fair quality (Table 5).

In these 6 studies, sensitivity varied from 58 to 92 percent, and specificity varied from 59 to 91 percent; the median sensitivity was 80 percent, and the median specificity was 83 percent. Figure 30 presents forest plots of the individual study estimates of sensitivity and specificity of CMR for diagnosing CAD in women from mixed populations.
Figure 30. Accuracy of CMR in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doyle, 2003</td>
<td>15</td>
<td>11</td>
<td>35</td>
<td>123</td>
<td>0.58 (0.37-0.77)</td>
<td>0.78 (0.71-0.84)</td>
</tr>
<tr>
<td>Klem, 2008</td>
<td>32</td>
<td>14</td>
<td>11</td>
<td>79</td>
<td>0.70 (0.54-0.82)</td>
<td>0.88 (0.79-0.94)</td>
</tr>
<tr>
<td>Langer, 2009</td>
<td>6</td>
<td>2</td>
<td>9</td>
<td>13</td>
<td>0.75 (0.35-0.97)</td>
<td>0.59 (0.36-0.79)</td>
</tr>
<tr>
<td>Gebker, 2010</td>
<td>84</td>
<td>15</td>
<td>12</td>
<td>72</td>
<td>0.85 (0.76-0.91)</td>
<td>0.86 (0.76-0.92)</td>
</tr>
<tr>
<td>Merkle, 2010</td>
<td>39</td>
<td>4</td>
<td>3</td>
<td>31</td>
<td>0.91 (0.78-0.97)</td>
<td>0.91 (0.76-0.98)</td>
</tr>
<tr>
<td>Coehlo-Filho, 2011</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>0.92 (0.62-1.00)</td>
<td>0.80 (0.44-0.97)</td>
</tr>
<tr>
<td>Summary values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.78 (0.61-0.89)</td>
<td>0.84 (0.74-0.90)</td>
</tr>
</tbody>
</table>

Figure 31 presents an SROC curve demonstrating an average sensitivity of 78 percent (95% CI, 61 to 89 percent) and specificity of 84 percent (95% CI, 74 to 90 percent).

The prevalence of CAD in the 6 studies ranged from 7 to 56 percent with a mean prevalence of 32 percent. In the individual studies, PPV ranged from 30 to 93 percent, and NPV ranged from 59 to 91 percent. LR+ ranged from 1.83 to 10.28 and LR- from 0.102 to 0.54. Using the summary sensitivity and specificity of 78 and 84 percent, respectively, we calculated an overall PPV of 69 percent and NPV of 89 percent. Similarly, we calculated summary LR+ of 4.88 and LR- of 0.26.
Accuracy of CMR in Five Good-quality Studies

Next, we evaluated the accuracy of CMR compared with coronary angiography in the five good-quality studies. In these studies, sensitivity varied from 58 to 91 percent, and specificity varied from 59 to 91 percent; the median sensitivity was 75 percent, and the median specificity was 86 percent. Figure 32 presents forest plots of the individual study estimates of sensitivity and specificity of CMR for diagnosing CAD in women from mixed populations.

Figure 32. Accuracy of CMR in five good-quality studies in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doyle, 2003</td>
<td>15</td>
<td>11</td>
<td>35</td>
<td>123</td>
<td>0.58 (0.37-0.77)</td>
<td>0.78 (0.71-0.84)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Klem, 2008</td>
<td>32</td>
<td>14</td>
<td>11</td>
<td>79</td>
<td>0.70 (0.54-0.82)</td>
<td>0.88 (0.79-0.94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Langer, 2009</td>
<td>6</td>
<td>2</td>
<td>9</td>
<td>13</td>
<td>0.75 (0.35-0.97)</td>
<td>0.59 (0.36-0.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gebker, 2010</td>
<td>42</td>
<td>9</td>
<td>8</td>
<td>60</td>
<td>0.82 (0.69-0.92)</td>
<td>0.88 (0.78-0.95)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merkle, 2010</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>25</td>
<td>0.83 (0.36-1.00)</td>
<td>0.96 (0.80-1.00)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary values</td>
<td>123</td>
<td>54</td>
<td>48</td>
<td>300</td>
<td>0.72 (0.55-0.85)</td>
<td>0.84 (0.69-0.93)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 33 presents an SROC curve demonstrating an average sensitivity of 72 percent (95% CI, 55 to 85 percent) and specificity of 84 percent (95% CI, 69 to 93 percent).

Figure 33. SROC curve for CMR in five good-quality studies in women from mixed populations

Sensitivity (95% CI) = 0.72 (0.55-0.85)
Specificity (95% CI) = 0.84 (0.69-0.93)
The prevalence of CAD in these five good-quality studies ranged from 14 to 56 percent with a mean prevalence of 37 percent. In the individual studies, PPV ranged from 30 to 93 percent, and NPV ranged from 59 to 91 percent. LR+ ranged from 1.83 to 10.28 and LR- from 0.102 to 0.54. Using the summary sensitivity and specificity of 72 and 84 percent, respectively, we calculated an overall PPV of 72 percent and NPV of 84 percent. Similarly, we calculated summary LR+ of 4.5 and LR- of 0.33.
Table 5. Summary of accuracy data evaluating CMR for diagnosing CAD

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Mix</th>
<th>Quality</th>
<th>Patients (N)</th>
<th>Cath %</th>
<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merkle, et al., 2010</td>
<td>No known CAD</td>
<td>Good</td>
<td>32 (women)</td>
<td>≥ 50</td>
<td>19</td>
<td>83 (36-100)</td>
<td>96 (80-100)</td>
<td>83 (54-100)</td>
<td>96 (89-100)</td>
<td>21.67 (3.07-153.05)</td>
<td>0.17 (0.03-1.04)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>41 (men)</td>
<td></td>
<td>34</td>
<td>79 (57-100)</td>
<td>74 (58-91)</td>
<td>61 (39-84)</td>
<td>87 (73-100)</td>
<td>3.03 (1.51-6.07)</td>
<td>0.29 (0.10-0.81)</td>
</tr>
<tr>
<td>Klem, et al., 2008</td>
<td>No known CAD</td>
<td>Good</td>
<td>136 (women)</td>
<td>≥ 50</td>
<td>34</td>
<td>70 (54-82)</td>
<td>88 (79-94)</td>
<td>74 (61-87)</td>
<td>85 (78-92)</td>
<td>5.69 (3.17-10.22)</td>
<td>0.35 (0.22-0.54)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70</td>
<td>70 (50-90)</td>
<td>70 (50-90)</td>
<td>70 (50-90)</td>
<td>70 (50-90)</td>
<td>2.22 (1.06-4.68)</td>
<td>0.48 (0.23-0.97)</td>
</tr>
<tr>
<td>Doyle, et al., 2003</td>
<td>No known CAD</td>
<td>Good</td>
<td>184 (women)</td>
<td>≥ 70</td>
<td>14</td>
<td>58 (37-77)</td>
<td>78 (71-84)</td>
<td>30 (17-43)</td>
<td>92 (87-96)</td>
<td>2.60 (1.68-4.04)</td>
<td>0.54 (0.34-0.86)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70</td>
<td>70 (50-90)</td>
<td>70 (50-90)</td>
<td>70 (50-90)</td>
<td>70 (50-90)</td>
<td>2.22 (1.06-4.68)</td>
<td>0.48 (0.23-0.97)</td>
</tr>
<tr>
<td>Gebker, et al., 2010</td>
<td>No known CAD</td>
<td>Good</td>
<td>119 (women)</td>
<td>≥ 70</td>
<td>43</td>
<td>82 (69-92)</td>
<td>88 (78-95)</td>
<td>84 (74-94)</td>
<td>87 (79-95)</td>
<td>7.00 (3.61-13.59)</td>
<td>0.20 (0.11-0.36)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>70</td>
<td>85 (76-91)</td>
<td>86 (76-92)</td>
<td>88 (81-94)</td>
<td>83 (75-91)</td>
<td>5.94 (3.49-10.09)</td>
<td>0.18 (0.11-0.28)</td>
</tr>
<tr>
<td>Gebker, et al., 2010</td>
<td>Mixed</td>
<td>Good</td>
<td>183 (women)</td>
<td>≥ 70</td>
<td>54</td>
<td>85 (76-91)</td>
<td>86 (76-92)</td>
<td>88 (81-94)</td>
<td>83 (75-91)</td>
<td>5.94 (3.49-10.09)</td>
<td>0.18 (0.11-0.28)</td>
</tr>
<tr>
<td>Merkle, et al., 2010</td>
<td>Mixed</td>
<td>Good</td>
<td>77 (women)</td>
<td>≥ 50</td>
<td>56</td>
<td>91 (78-97)</td>
<td>91 (76-98)</td>
<td>93 (85-100)</td>
<td>89 (78-99)</td>
<td>10.28 (3.47-30.4)</td>
<td>0.10 (0.04-0.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>179 (men)</td>
<td></td>
<td>79</td>
<td>91 (86-96)</td>
<td>91 (76-98)</td>
<td>93 (89-97)</td>
<td>70 (56-84)</td>
<td>3.48 (2.04-5.93)</td>
<td>0.12 (0.06-0.20)</td>
</tr>
<tr>
<td>Coelho-Filho, et al., 2011</td>
<td>Mixed</td>
<td>Fair</td>
<td>168 (women)</td>
<td>≥ 70</td>
<td>7</td>
<td>92 (62-100)</td>
<td>80 (44-97)</td>
<td>85 (65-100)</td>
<td>89 (68-100)</td>
<td>4.58 (1.31-16.02)</td>
<td>0.10 (0.01-0.70)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>237 (men)</td>
<td></td>
<td>15</td>
<td>86 (71-95)</td>
<td>74 (49-91)</td>
<td>86 (75-97)</td>
<td>74 (54-93)</td>
<td>3.27 (1.52-7.02)</td>
<td>0.19 (0.08-0.44)</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; Cath % = % stenosis defined to be positive for CAD on diagnostic cardiac catheterization (coronary angiography); CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NPV = negative predictive value; NR = not reported; PPV = positive predictive value
Coronary CTA

We identified eight studies evaluating the accuracy of coronary CTA compared with coronary angiography (Table 6). Five of these studies were exclusively in women with no known CAD, and these are the studies used in our primary analysis. In our secondary analysis, we evaluated the accuracy of coronary CTA in diagnosing CAD in mixed populations of known and no known CAD, including the three additional studies.

Primary Analysis: Population of Women With No Known CAD

The five studies represent findings on coronary CTA use in 474 women (sample size ranging from 30 to 280 women). Of these studies, three were good quality, two were fair quality, and none were poor quality. Sensitivity varied from 70 to 100 percent, and specificity varied from 46 to 91 percent; the median sensitivity was 89 percent, and the median specificity was 78 percent. Figure 34 presents forest plots of the individual study estimates of sensitivity and specificity of coronary CTA for diagnosing CAD in women with no known CAD.

Figure 34. Accuracy of coronary CTA in women with no known CAD
Figure 35 presents an SROC curve with an average sensitivity of 93 percent (95% CI, 69 to 99 percent) and specificity of 77 percent (95% CI, 54 to 91 percent).

The prevalence of CAD in the 5 studies ranged from 16 to 60 percent with a mean prevalence of 30 percent. In the individual studies, PPV ranged from 23 to 87 percent, and NPV ranged from 46 to 91 percent. LR+ ranged from 1.58 to 11 and LR- from 0 to 0.41. Using the summary sensitivity and specificity of 93 and 77 percent, respectively, we calculated an overall PPV of 63 percent and NPV of 96 percent. Similarly, we calculated summary LR+ of 4.04 and LR- of 0.09.

**Accuracy of Coronary CTA in Three Good-Quality Studies**

Next, we evaluated the accuracy of coronary CTA compared with coronary angiography in the three good-quality studies. In these studies, sensitivity varied from 70 to 100 percent, and specificity varied from 46 to 91 percent; the median sensitivity was 86 percent, and the median specificity was 73 percent. Given the small number of studies and the specific point estimate and CIs of these studies, our meta-analytic modeling was not able to reach convergence and provide a summary sensitivity and specificity for this set of studies.

The prevalence of CAD in these 3 good-quality studies ranged from 16 to 27 percent with a mean prevalence of 21 percent. In the individual studies, PPV ranged from 23 to 80 percent, and NPV ranged from 91 to 100 percent. LR+ ranged from 1.58 to 11 and LR- from 0 to 0.41.
Secondary Analysis: Mixed Population of Women With Known and No Known CAD

We performed a secondary analysis where we expanded our inclusion criteria to include studies whose patient population included a mix of women with known CAD and women with no known CAD. This expanded inclusion criteria allowed three additional studies to be included in our analysis (totaling eight studies). The 8 studies represent findings on coronary CTA use in 690 women (sample size ranging from 30 to 280 women). Of these eight studies, four were good quality, four were fair quality, and none were poor quality (Table 6).

In these 8 studies, sensitivity varied from 70 to 100 percent, and specificity varied from 46 to 100 percent; the median sensitivity was 92 percent, and the median specificity was 88 percent. Figure 36 presents forest plots of the individual study estimates of sensitivity and specificity of coronary CTA for diagnosing CAD in women from mixed populations.

Figure 36. Accuracy of coronary CTA in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shivalkar, 2007</td>
<td>17</td>
<td>2</td>
<td>6</td>
<td>45</td>
<td>0.89 (0.67-0.99)</td>
<td>0.88 (0.76-0.96)</td>
</tr>
<tr>
<td>Dewey, 2008</td>
<td>7</td>
<td>3</td>
<td>11</td>
<td>25</td>
<td>0.70 (0.35-0.93)</td>
<td>0.72 (0.56-0.85)</td>
</tr>
<tr>
<td>Pundziute, 2008</td>
<td>21</td>
<td>1</td>
<td>2</td>
<td>26</td>
<td>0.95 (0.77-1.00)</td>
<td>0.93 (0.76-0.99)</td>
</tr>
<tr>
<td>Langer, 2009</td>
<td>8</td>
<td>0</td>
<td>2</td>
<td>20</td>
<td>1.00 (0.69-1.00)</td>
<td>0.91 (0.71-0.99)</td>
</tr>
<tr>
<td>Dewey, 2010</td>
<td>25</td>
<td>5</td>
<td>6</td>
<td>41</td>
<td>0.83 (0.65-0.94)</td>
<td>0.87 (0.74-0.95)</td>
</tr>
<tr>
<td>Jenkins, 2010</td>
<td>6</td>
<td>1</td>
<td>20</td>
<td>17</td>
<td>0.86 (0.42-1.00)</td>
<td>0.46 (0.29-0.63)</td>
</tr>
<tr>
<td>Maffei, 2010</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>79</td>
<td>1.00 (0.74-1.00)</td>
<td>1.00 (0.96-1.00)</td>
</tr>
<tr>
<td>Dharampal, 2011</td>
<td>166</td>
<td>3</td>
<td>24</td>
<td>87</td>
<td>0.98 (0.95-1.00)</td>
<td>0.78 (0.70-0.86)</td>
</tr>
<tr>
<td><strong>Summary values</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>0.94 (0.81-0.98)</strong></td>
<td><strong>0.87 (0.68-0.96)</strong></td>
</tr>
</tbody>
</table>

Figure 37 presents an SROC curve demonstrating an average sensitivity of 94 percent (95% CI, 81 to 98 percent) and specificity of 87 percent (95% CI, 68 to 96 percent).
The prevalence of CAD in these 8 studies ranged from 11 to 60 percent with a mean prevalence of 31 percent. In the individual studies, PPV ranged from 23 to 100 percent, and NPV ranged from 46 to 100 percent. LR+ ranged from 2.54 to 13.36 and LR- 0 to 0.41. Using the summary sensitivity and specificity of 94 and 87 percent, respectively, we calculated an overall PPV of 76 percent and NPV of 97 percent. Similarly, we calculated summary LR+ of 7.23 and LR- of 0.069.

**Accuracy of Coronary CTA in Four Good-Quality Studies**

Next, we evaluated the accuracy of coronary CTA compared with coronary angiography in the four good-quality studies. In these studies, sensitivity varied from 70 to 100 percent, and specificity varied from 46 to 91 percent; the median sensitivity was 85 percent, and the median specificity was 80 percent. Figure 38 presents forest plots of the individual study estimates of sensitivity and specificity of coronary CTA for diagnosing CAD in women with from mixed populations.
Figure 38. Accuracy of coronary CTA in four good-quality studies in women from mixed populations

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>TP</th>
<th>FN</th>
<th>FP</th>
<th>TN</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dewey, 2008</td>
<td>7</td>
<td>3</td>
<td>11</td>
<td>29</td>
<td>0.70 (0.35-0.93)</td>
<td>0.72 (0.56-0.85)</td>
</tr>
<tr>
<td>Langer, 2009</td>
<td>8</td>
<td>0</td>
<td>2</td>
<td>20</td>
<td>1.00 (0.69-1.00)</td>
<td>0.91 (0.71-0.99)</td>
</tr>
<tr>
<td>Dewey, 2010</td>
<td>25</td>
<td>5</td>
<td>6</td>
<td>41</td>
<td>0.83 (0.65-0.94)</td>
<td>0.87 (0.74-0.95)</td>
</tr>
<tr>
<td>Jenkins, 2010</td>
<td>6</td>
<td>1</td>
<td>20</td>
<td>17</td>
<td>0.86 (0.42-1.00)</td>
<td>0.46 (0.29-0.63)</td>
</tr>
<tr>
<td>Summary values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.83 (0.58-0.94)</td>
<td>0.77 (0.40-0.94)</td>
</tr>
</tbody>
</table>

Figure 39 presents an SROC curve demonstrating an average sensitivity of 83 percent (95% CI, 58 to 94 percent) and specificity of 77 percent (95% CI, 40 to 94 percent). It is important to note that given the small number of studies and wide confidence intervals that these summary statistics should be interpreted with caution.

Figure 39. SROC curve for coronary CTA in four good-quality studies in women from mixed populations

Summary values
Sensitivity (95% CI) = 0.83 (0.58-0.94)
Specificity (95% CI) = 0.77 (0.40-0.94)
The prevalence of CAD in these 4 good-quality studies ranged from 16 to 39 percent with a mean prevalence of 25 percent. In the individual studies, PPV ranged from 23 to 81 percent, and NPV ranged from 89 to 100 percent. LR+ ranged from 1.58 to 11 and LR- from 0 to 0.41. Using the summary sensitivity and specificity of 83 and 77 percent, respectively, we calculated an overall PPV of 55 percent and NPV of 93 percent. Similarly, we calculated summary LR+ of 3.61 and LR- of 0.22.
### Table 6. Summary of accuracy data evaluating coronary CTA for diagnosing CAD

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Mix</th>
<th>Quality</th>
<th>Patients (N)</th>
<th>Cath %</th>
<th>Prevalence %</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>LR+ (95% CI)</th>
<th>LR- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jenkins, et al., 2010$^{102}$</td>
<td>No known CAD</td>
<td>Good</td>
<td>44 (women)</td>
<td>≥ 50</td>
<td>16</td>
<td>86 (42-100)</td>
<td>46 (29-63)</td>
<td>23 (7-39)</td>
<td>94 (84-100)</td>
<td>94 (84-100)</td>
<td>1.59 (1.04-2.42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>55 (men)</td>
<td></td>
<td>56</td>
<td>94 (79-99)</td>
<td>50 (29-71)</td>
<td>71 (57-85)</td>
<td>86 (67-100)</td>
<td>1.87 (1.24-2.82)</td>
<td>0.31 (0.05-1.97)</td>
</tr>
<tr>
<td>Langer, et al., 2009$^{98}$</td>
<td>No known CAD</td>
<td>Good</td>
<td>30 (women)</td>
<td>≥ 50</td>
<td>27</td>
<td>100 (69-100)</td>
<td>91 (71-99)</td>
<td>80 (55-100)</td>
<td>100 (85-100)</td>
<td>11 (2.93-41.24)</td>
<td>0 (NA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>38 (men)</td>
<td></td>
<td>47</td>
<td>94 (73-100)</td>
<td>100 (86-100)</td>
<td>95 (86-100)</td>
<td>NA</td>
<td>0.06 (0.01-0.37)</td>
<td>0.007 (0.002-0.02)</td>
</tr>
<tr>
<td>Dewey, et al., 2008$^{103}$</td>
<td>No known CAD</td>
<td>Good</td>
<td>50 (women)</td>
<td>≥ 50</td>
<td>20</td>
<td>70 (35-93)</td>
<td>73 (56-85)</td>
<td>39 (16-61)</td>
<td>91 (81-100)</td>
<td>2.55 (1.33-4.86)</td>
<td>0.41 (0.16-1.09)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95 (men)</td>
<td></td>
<td>62</td>
<td>95 (86-99)</td>
<td>81 (64-92)</td>
<td>89 (81-97)</td>
<td>91 (81-100)</td>
<td>4.88 (2.50-9.52)</td>
<td>0.06 (0.02-0.19)</td>
</tr>
<tr>
<td>Shivalkar, et al., 2007$^{104}$</td>
<td>No known CAD</td>
<td>Fair</td>
<td>70 (women)</td>
<td>≥ 70</td>
<td>27</td>
<td>89 (67-99)</td>
<td>88 (76-96)</td>
<td>74 (56-92)</td>
<td>96 (90-100)</td>
<td>7.61 (3.53-16.38)</td>
<td>0.12 (0.03-0.44)</td>
</tr>
<tr>
<td>Dharampal, et al., 2011$^{105}$</td>
<td>No known CAD</td>
<td>Fair</td>
<td>280 (women)</td>
<td>≥ 50</td>
<td>60</td>
<td>98 (95-100)</td>
<td>78 (70-86)</td>
<td>87 (83-92)</td>
<td>97 (93-100)</td>
<td>4.54 (3.19-6.48)</td>
<td>0.02 (0.01-0.07)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>636 (men)</td>
<td></td>
<td>76</td>
<td>99 (98-100)</td>
<td>82 (75-88)</td>
<td>95 (93-97)</td>
<td>98 (95-100)</td>
<td>5.56 (3.95-7.82)</td>
<td>0.007 (0.002-0.02)</td>
</tr>
<tr>
<td>Dewey, et al., 2010$^{100}$</td>
<td>Mixed</td>
<td>Good</td>
<td>77 (women)</td>
<td>≥ 50</td>
<td>39</td>
<td>83 (65-94)</td>
<td>87 (74-95)</td>
<td>81 (67-95)</td>
<td>89 (80-98)</td>
<td>6.53 (3.04-14.02)</td>
<td>0.19 (0.09-0.43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>214 (men)</td>
<td></td>
<td>62</td>
<td>86 (79-91)</td>
<td>91 (83-96)</td>
<td>94 (90-98)</td>
<td>80 (71-88)</td>
<td>9.92 (4.87-20.20)</td>
<td>0.16 (0.10-0.24)</td>
</tr>
<tr>
<td>Study</td>
<td>Patient Mix</td>
<td>Quality</td>
<td>Patients (N)</td>
<td>Cath %</td>
<td>Prevalence %</td>
<td>Sensitivity % (95% CI)</td>
<td>Specificity % (95% CI)</td>
<td>PPV % (95% CI)</td>
<td>NPV % (95% CI)</td>
<td>LR+ (95% CI)</td>
<td>LR- (95% CI)</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------</td>
<td>---------</td>
<td>--------------</td>
<td>--------</td>
<td>--------------</td>
<td>-------------------------</td>
<td>-------------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Dewey, et al., 2010&lt;sup&gt;100&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Good</td>
<td>77 (women)</td>
<td>≥50</td>
<td>39</td>
<td>83 (65-94)</td>
<td>87 (74-95)</td>
<td>81 (67-95)</td>
<td>86 (79-91)</td>
<td>89 (80-98)</td>
<td>0.19 (0.09-0.43)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>214 (men)</td>
<td></td>
<td>62</td>
<td>86 (79-91)</td>
<td>91 (83-96)</td>
<td>94 (90-98)</td>
<td></td>
<td>80 (71-88)</td>
<td>9.92 (4.87-20.20)</td>
</tr>
<tr>
<td>Pundziute, et al., 2008&lt;sup&gt;101&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Fair</td>
<td>50 (women)</td>
<td>≥50</td>
<td>44</td>
<td>95 (77-100)</td>
<td>93 (76-99)</td>
<td>91 (80-100)</td>
<td>100 (91-100)</td>
<td>96 (89-100)</td>
<td>13.36 (3.50-50.97)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50 (men)</td>
<td></td>
<td>64</td>
<td>100 (91-100)</td>
<td>89 (65-99)</td>
<td>94 (86-100)</td>
<td></td>
<td>100 (81-100)</td>
<td>0.05 (0.01-0.33)</td>
</tr>
<tr>
<td>Maffei, et al., 2010&lt;sup&gt;106&lt;/sup&gt;</td>
<td>Mixed</td>
<td>Fair</td>
<td>89 (women)</td>
<td>≥50</td>
<td>11</td>
<td>100 (74-100)</td>
<td>100 (96-100)</td>
<td>100 (70-100)</td>
<td>100 (83-100)</td>
<td>100 (96-100)</td>
<td>NA (NA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>88 (men)</td>
<td></td>
<td>18</td>
<td>100 (74-100)</td>
<td>97 (90-100)</td>
<td>89 (74-100)</td>
<td></td>
<td>100 (96-100)</td>
<td>36 (9.18-141)</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; Cath % = % stenosis defined to be positive for CAD on diagnostic cardiac catheterization (coronary angiography); CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NPV = negative predictive value; NR = not reported; PPV = positive predictive value.
KQ 1 Summary

Table 7 and Figure 40 show the summary of the diagnostic accuracy of ECG, ECHO, SPECT, CMR, and coronary CTA modalities in women presented in Figures 4–39. The information is presented separately for no known CAD and mixed CAD populations, as well as for all studies separately from the good-quality studies. Overall, within a given modality, the summary sensitivities and specificities were similar for both types of populations (known and no known CAD) and for all studies when compared with good-quality studies. When accounting for only the good-quality studies, it appeared that the diagnostic accuracy of detecting CAD in women with unknown CAD was better (in descending order) for coronary CTA, SPECT, ECHO, CMR, and ECG. For the newer technologies (i.e., coronary CTA and CMR), more studies in women would be needed to support these findings since the 95% CIs were quite wide.

To minimize the risk of spectrum bias, our primary analysis focused on women with no known CAD. We also explored mixed populations of women with known and no known CAD in sensitivity analyses. These analyses did not demonstrate a significant difference in terms of the sensitivities and specificities from our primary analysis. We also explored whether the accuracy of the modalities were correlated with the underlying prevalence of disease in the population of interest. The mean prevalences and 95% CIs for ECG, SPECT, ECHO, CMR, and coronary CTA with the population of women with no previously known CAD were 0.41 (0.36 to 0.46), 0.44 (0.34 to 0.55), 0.43 (0.37 to 0.50), 0.26 (0.14 to 0.44), and 0.29 (0.13 to 0.54), respectively. We evaluated whether these prevalences were different across modalities using a random-effects model and did not find a statistically significant difference (p = 0.17). Thus, these analyses did not indicate any specific trend or relationship between prevalence and the NIT’s sensitivity or specificity. There did appear to be an increase in the sensitivity of CMR over time, although the wide confidence intervals for this characteristic highlight the uncertainty in this trend.

We assessed the risk of verification bias by exploring the studies in our analysis that did not complete a coronary catheterization in all of the patients who underwent the NIT. In the population of women with no previously known CAD, this represented one study of SPECT, \textsuperscript{52} one study of ECHO, \textsuperscript{79} three studies of ECG, \textsuperscript{29,52,58} and no studies of CMR or coronary CTA. Given the small number of total studies with this potential bias, we felt confident that our primary results were minimized for verification bias.

We explored the potential for publication bias across the different modalities in our four populations of interest (studies of women with no known CAD, good-quality studies of women with no known CAD, studies of women from mixed populations, and good-quality studies of women from mixed populations). Our analyses did not provide evidence for publication bias, with our p values ranging from 0.093 to 0.95.

In a final analysis, we explored whether there was a statistically significant difference between the diagnostic accuracy of testing modalities in women using a generalized linear mixed model, with NIT modality and disease state (no known and mixed CAD) as covariates in the model. Our analyses determined that for women with no previously known CAD, there were differences between the performance of the available modalities (p < 0.001). The sensitivity of ECHO and SPECT was significantly higher than that of ECG. Specificity of ECG was less than that of CMR (borderline) and of ECHO. We similarly explored the differences among the modalities in the subset of studies that were good-quality and also where there was no known CAD in the included population. These analyses again demonstrated differences between
performance of tests ($p = 0.008$) with the specificity of ECG being less than that of CMR and ECHO.

Table 7. Summary of accuracy of NITs compared with coronary angiography for diagnosing CAD in women

<table>
<thead>
<tr>
<th>Modality</th>
<th>Population</th>
<th>Quality of Included Studies</th>
<th>Number of Studies</th>
<th>Number of Women</th>
<th>Summary Sensitivity (95% CI)</th>
<th>Summary Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>No known CAD</td>
<td>All</td>
<td>29</td>
<td>3392</td>
<td>62% (55%-68%)</td>
<td>68% (63%-73%)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td></td>
<td>10</td>
<td>1410</td>
<td>70% (58%-79%)</td>
<td>62% (53%-69%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>41</td>
<td>4879</td>
<td>61% (54%-67%)</td>
<td>65% (58%-72%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>13</td>
<td>1679</td>
<td>65% (52%-76%)</td>
<td>60% (52%-68%)</td>
</tr>
<tr>
<td>ECHO</td>
<td>No known CAD</td>
<td>All</td>
<td>14</td>
<td>1286</td>
<td>79% (74%-83%)</td>
<td>83% (74%-89%)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td></td>
<td>5</td>
<td>561</td>
<td>79% (69%-87%)</td>
<td>85% (68%-94%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>22</td>
<td>1873</td>
<td>78% (73%-83%)</td>
<td>86% (79%-91%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>8</td>
<td>807</td>
<td>77% (65%-85%)</td>
<td>89% (76%-95%)</td>
</tr>
<tr>
<td>SPECT</td>
<td>No known CAD</td>
<td>All</td>
<td>14</td>
<td>1000</td>
<td>81% (76%-86%)</td>
<td>78% (69%-84%)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td></td>
<td>4</td>
<td>394</td>
<td>83% (52%-95%)</td>
<td>72% (37%-92%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>30</td>
<td>2146</td>
<td>82% (77%-87%)</td>
<td>81% (74%-86%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>10</td>
<td>982</td>
<td>82% (72%-88%)</td>
<td>79% (66%-87%)</td>
</tr>
<tr>
<td>CMR</td>
<td>No known CAD</td>
<td>All</td>
<td>5</td>
<td>501</td>
<td>72% (55%-85%)</td>
<td>84% (69%-93%)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td></td>
<td>5</td>
<td>501</td>
<td>72% (55%-85%)</td>
<td>84% (69%-93%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>6</td>
<td>778</td>
<td>78% (61%-89%)</td>
<td>84% (74%-90%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>5</td>
<td>610</td>
<td>76% (55%-89%)</td>
<td>84% (72%-91%)</td>
</tr>
<tr>
<td>Coronary CTA</td>
<td>No known CAD</td>
<td>All</td>
<td>5</td>
<td>474</td>
<td>93% (69%-99%)</td>
<td>77% (54%-91%)</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td></td>
<td>3</td>
<td>124</td>
<td>85% (26%-99%)</td>
<td>73% (17%-97%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>8</td>
<td>690</td>
<td>94% (81%-98%)</td>
<td>87% (68%-96%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>4</td>
<td>201</td>
<td>83% (58%-94%)</td>
<td>77% (40%-94%)</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; CI = confidence interval; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; SPECT = single proton emission computed tomography
Figure 40. Summary of accuracy of NITs compared with coronary angiography for diagnosing CAD in women with no known CAD (all studies)

<table>
<thead>
<tr>
<th>Test</th>
<th>Number of Studies</th>
<th>Number of Patients</th>
<th>Summary Sensitivity (95% CI)</th>
<th>Summary Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR</td>
<td>5</td>
<td>501</td>
<td>0.72 (0.55-0.85)</td>
<td>0.84 (0.69-0.93)</td>
</tr>
<tr>
<td>CTA</td>
<td>5</td>
<td>474</td>
<td>0.93 (0.69-0.99)</td>
<td>0.77 (0.54-0.91)</td>
</tr>
<tr>
<td>ECHO</td>
<td>14</td>
<td>1286</td>
<td>0.79 (0.74-0.83)</td>
<td>0.83 (0.74-0.89)</td>
</tr>
<tr>
<td>SPECT</td>
<td>14</td>
<td>1000</td>
<td>0.81 (0.76-0.86)</td>
<td>0.78 (0.69-0.84)</td>
</tr>
<tr>
<td>ECG</td>
<td>29</td>
<td>3392</td>
<td>0.62 (0.55-0.68)</td>
<td>0.68 (0.63-0.73)</td>
</tr>
</tbody>
</table>

Comparative Accuracy of NIT Modalities in Men

Although it was not the primary goal of this systematic review, we also evaluated, when possible, the accuracy of the five NIT modalities in male patients and specifically how the accuracy of these modalities differed between men and women. Most of the studies included in our analysis, however, did not include data on both sexes. Specifically, of the 41 included studies evaluating ECG in a mixed population, only 20 included data on men as well as women. Similarly for the 22 ECHO, 30 SPECT, 6 CMR, and 8 CTA included studies, only 9, 11, 3, and 7 respectively included data on men.

Although limited, the available studies provided enough data for men to determine summary sensitivity and specificity estimates and to evaluate whether the accuracy of these modalities differed between men and women (Table 8). In Tables 2–6, we provide the accuracy data for the individual studies included in our analysis that had male representation. In Table 7 we list the summary sensitivities and specificities calculated with an SROC curve as described in our primary women analyses. Given the reduced number of available studies, we focused on studies with populations of either no known CAD or a mix of known and no known CAD. When comparing the accuracy of the modalities between men and women enrolled in the same studies, the ECG and coronary CTA modalities were both less sensitive and less specific in women. The ECHO, CMR, and SPECT modalities, although less sensitive, appeared to be more specific in women. The lower specificity of the ECG modality in women, however, is the only estimate that was determined to be a statistically significant difference.
Table 8. Summary of accuracy of NITs for diagnosing CAD in men compared with women from mixed populations

<table>
<thead>
<tr>
<th>Modality</th>
<th>Quality of Include d Studies</th>
<th>Number of Studies</th>
<th>Number of Men</th>
<th>Summary Sensitivity in Men (95% CI)</th>
<th>Summary Sensitivity in Women (95% CI)</th>
<th>p Value (Women vs. Men)</th>
<th>Summary Specificity in Men (95% CI)</th>
<th>Summary Specificity in Women (95% CI)</th>
<th>p Value (Women vs. Men)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>All Good</td>
<td>20</td>
<td>7345</td>
<td>64% (54%-73%)</td>
<td>61% (54%-67%)</td>
<td>0.57</td>
<td>81% (72%-87%)</td>
<td>65% (58%-72%)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>2410</td>
<td>68% (32%-90%)</td>
<td>65% (52%-76%)</td>
<td></td>
<td>74% (49%-90%)</td>
<td>65% (58%-72%)</td>
<td></td>
</tr>
<tr>
<td>ECHO</td>
<td>All Good</td>
<td>9</td>
<td>1705</td>
<td>77% (65%-86%)</td>
<td>78% (73%-83%)</td>
<td>0.80</td>
<td>81% (65%-91%)</td>
<td>86% (79%-91%)</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>666</td>
<td>Insufficient data</td>
<td>77% (65%-85%)</td>
<td></td>
<td>Insufficient data</td>
<td>89% (76%-95%)</td>
<td></td>
</tr>
<tr>
<td>SPECT</td>
<td>All Good</td>
<td>11</td>
<td>1433</td>
<td>88% (73%-95%)</td>
<td>82% (77%-87%)</td>
<td>0.36</td>
<td>74% (50%-89%)</td>
<td>81% (74%-86%)</td>
<td>0.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>323</td>
<td>91% (78%-97%)</td>
<td>82% (72%-88%)</td>
<td></td>
<td>71% (32%-93%)</td>
<td>79% (66%-87%)</td>
<td></td>
</tr>
<tr>
<td>CMR</td>
<td>All Good</td>
<td>3</td>
<td>272</td>
<td>86% (50%-97%)</td>
<td>78% (61%-89%)</td>
<td>0.53</td>
<td>72% (46%-89%)</td>
<td>84% (74%-90%)</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>217</td>
<td>Insufficient data</td>
<td>76% (55%-89%)</td>
<td></td>
<td>Insufficient data</td>
<td>84% (72%-91%)</td>
<td></td>
</tr>
<tr>
<td>Coronary CTA</td>
<td>All Good</td>
<td>7</td>
<td>1176</td>
<td>97% (89%-99%)</td>
<td>94% (81%-98%)</td>
<td>0.36</td>
<td>89% (71%-96%)</td>
<td>87% (68%-96%)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4</td>
<td>402</td>
<td>91% (77%-97%)</td>
<td>83% (58%-94%)</td>
<td></td>
<td>85% (43%-98%)</td>
<td>77% (40%-94%)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; CI = confidence interval; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; SPECT = single proton emission computed tomography
Key Question 2: Predictors of Diagnostic Accuracy

KQ 2. What are the predictors of diagnostic accuracy (e.g., age, race/ethnicity, body size, heart size, menopausal status, functional status, stress modality) of different NITs in women?

Key Points

- Significant variability existed around diagnostic accuracy among studies examining each NIT modality.
- Only one study compared diagnostic accuracy for women with diagnostic accuracy for men.
- The studies reviewed did not examine functional status, age, or body size—the main predictors examined included heart size, pretest probability of CAD, race/ethnicity, postmenopausal status, and beta blocker use.
- There was heterogeneity in the types of predictors reported.
- Studies that examined heart size varied on the effect on diagnostic accuracy by stress modality. These studies suggest that increased heart size reduces the specificity of stress ECG, ECHO, and SPECT.
- One fair-quality study of 51 women reported that beta blocker use reduces the specificity of stress ECG and the sensitivity and specificity of SPECT. Withholding beta blockers prior to exercise stress testing is common to allow patients to achieve a target (or higher) heart rate in assessing for ischemia. One study showed that the PPV increases as the pretest probability of CAD increases for stress ECG and ECHO.
- Insufficient evidence was available to draw definitive conclusions about predictors given the small number of studies for each predictor and for each modality, as well as the combination of predictor by modality.

Detailed Synthesis

Many factors are reported in the literature that affect the diagnostic accuracy of noninvasive testing in women, including (1) higher prevalence in women of nonobstructive CAD (microvascular abnormalities, mitral valve prolapse), (2) less predictive symptomatology, (3) limited exercise tolerance because of older age, obesity, and diabetes at initial diagnosis, (4) different response to exercise than men, (5) lower peak exercise values, (6) lower increase in the left ventricular ejection fraction, (7) an increase in cardiac output by enhancing end-diastolic volume, (8) inappropriate catecholamine release, (9) hormonal influences of estrogens mimicking a digitalis-like false-positive ECG response, (10) anatomic differences affecting stress test results, (11) breast attenuation artifacts, (12) smaller coronary artery size, (13) smaller left ventricular chamber size, (14) higher prevalence of single-vessel disease, and (15) poor left ventricular opacification on echocardiography.
For KQ 2, we examined studies for the following nine predictors of diagnostic accuracy of different NITs in women: age, race/ethnicity, body size, heart size, menopausal status, functional status, stress modality, cardiac risk factors, and pretest probability of CAD. We identified 11 studies\textsuperscript{25,28,31,38,50,55,67,69,83,95,97} that described diagnostic accuracy, but only 9 of these studies examined predictors of diagnostic accuracy. Four of the 11 studies were considered good quality, 5 were fair quality, and 2 were poor quality.

Findings of Diagnostic Accuracy by Predictor

Findings of diagnostic accuracy by predictor in the studies we reviewed are summarized in Tables 9–12. Of the nine predictors we originally searched for, we found studies that addressed four of the predictors: (1) age combined with (2) menopausal status, (3) race/ethnicity, and (4) heart size. We also found two other types of predictors reported in women: (5) pretest probability based on cardiac risk factors and (6) use of beta blockers:

- The study by Cin., et al.\textsuperscript{31} examined the diagnostic accuracy of stress ECG in postmenopausal women ages 55 to 64.
- Two studies examined race/ethnicity: One study by Vashist,, et al.\textsuperscript{83} compared the diagnostic accuracy of SPECT across three race/ethnic categories—African American, Hispanic, and Asian—and another study by Yeih., et al.\textsuperscript{50} examined the diagnostic accuracy of ECG testing and SPECT in Asian women in Taiwan.
- Four studies examined heart size as a predictor of diagnostic accuracy: Lu., et al.\textsuperscript{28} and Gebker,, et al.\textsuperscript{95} compared left ventricular hypertrophy (LVH) with no LVH for ECG, ECHO, SPECT, and CMR. The study by Klem., et al.\textsuperscript{97} examined heart size in grams for CMR testing, and Siegler,, et al.\textsuperscript{25} examined heart size for ECG alone.
- Three studies, Yeih., et al.,\textsuperscript{50} Marwick,, et al.,\textsuperscript{55} and Ho., et al.,\textsuperscript{67} examined pretest probability as a predictor of accuracy for ECG, dobutamine ECHO, and CMR.
- The study by Yeih., et al.,\textsuperscript{50} examined the use of beta blockers on diagnostic accuracy in ECG and SPECT.
- We identified no studies that examined age alone, functional status, or body size as predictors of diagnostic accuracy in women.
Table 9. Age and menopausal status as a predictor

<table>
<thead>
<tr>
<th>Study (predictor)</th>
<th>N Women</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Modality</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cin, et al., 2000&lt;sup&gt;a&lt;/sup&gt; (Postmenopausal, ages 55 to 64)</td>
<td>110</td>
<td>Prospective</td>
<td>Poor</td>
<td>ECG</td>
<td>86</td>
<td>61</td>
<td>81</td>
<td>70</td>
<td>2.18</td>
<td>0.23</td>
</tr>
</tbody>
</table>

<sup>a</sup>This study did not have a premenopausal reference group.

Abbreviations: ECG = exercise/stress electrocardiogram; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; N = number; NPV = negative predictive value; PPV = positive predictive value

Table 10. Race/ethnicity as a predictor

<table>
<thead>
<tr>
<th>Study (predictor)</th>
<th>N Women</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Modality</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vashist, et al., 2007&lt;sup&gt;a&lt;/sup&gt; (Hispanic)</td>
<td>16</td>
<td>Retrospective</td>
<td>Fair</td>
<td>SPECT</td>
<td>71.4</td>
<td>33.3</td>
<td>45.5</td>
<td>60</td>
<td>1.07</td>
<td>0.86</td>
</tr>
<tr>
<td>Vashist, et al., 2007&lt;sup&gt;a&lt;/sup&gt; (African American)</td>
<td>34</td>
<td>Retrospective</td>
<td>Fair</td>
<td>SPECT</td>
<td>90</td>
<td>20</td>
<td>86.7</td>
<td>25</td>
<td>1.12</td>
<td>0.52</td>
</tr>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;a&lt;/sup&gt; (Asian)</td>
<td>51</td>
<td>Prospective</td>
<td>Fair</td>
<td>SPECT</td>
<td>71</td>
<td>87</td>
<td>87</td>
<td>71</td>
<td>5.48</td>
<td>0.33</td>
</tr>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;a&lt;/sup&gt; (Asian)</td>
<td>51</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>43</td>
<td>83</td>
<td>75</td>
<td>54</td>
<td>2.46</td>
<td>0.69</td>
</tr>
</tbody>
</table>

<sup>a</sup>None of these studies reported results for Caucasian women.

Abbreviations: ECG = exercise/stress electrocardiogram; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; N = number; NPV = negative predictive value; PPV = positive predictive value; SPECT = single photon emission computed tomography
<table>
<thead>
<tr>
<th>Study (predictor)</th>
<th>N Women</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Modality</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lu, et al., 2010* (With LVH)</td>
<td>36</td>
<td>Prospective</td>
<td>Good</td>
<td>ECG</td>
<td>NR</td>
<td>31</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Lu, et al., 2010* (Without LVH)</td>
<td>40</td>
<td>Prospective</td>
<td>Good</td>
<td>ECG</td>
<td>NR</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Lu, et al., 2010* (With LVH)</td>
<td>36</td>
<td>Prospective</td>
<td>Good</td>
<td>SPECT</td>
<td>NR</td>
<td>31</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Lu, et al., 2010* (Without LVH)</td>
<td>40</td>
<td>Prospective</td>
<td>Good</td>
<td>SPECT</td>
<td>NR</td>
<td>66</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Lu, et al., 2010* (With LVH)</td>
<td>36</td>
<td>Prospective</td>
<td>Good</td>
<td>ECHO-DOB</td>
<td>NR</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Lu, et al., 2010* (Without LVH)</td>
<td>40</td>
<td>Prospective</td>
<td>Good</td>
<td>ECHO-DOB</td>
<td>NR</td>
<td>89</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Lu, et al., 2010* (With LVH)</td>
<td>36</td>
<td>Prospective</td>
<td>Good</td>
<td>ECHO-DIP</td>
<td>NR</td>
<td>81</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Lu, et al., 2010* (Without LVH)</td>
<td>40</td>
<td>Prospective</td>
<td>Good</td>
<td>ECHO-DIP</td>
<td>NR</td>
<td>96</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gebker, et al., 2010* (With LVH)</td>
<td>56 women 179 men</td>
<td>Prospective</td>
<td>Good</td>
<td>CMR</td>
<td>80 (women) 79 (men)</td>
<td>91 (women) 95 (men)</td>
<td>93 (women) 98 (men)</td>
<td>73 (women) 56 (men)</td>
<td>8.4 (women) 15.46 (men)</td>
<td>0.22 (women) 0.22 (men)</td>
</tr>
<tr>
<td>Gebker, et al., 2010* (Without LVH)</td>
<td>127 women 311 men</td>
<td>Prospective</td>
<td>Good</td>
<td>CMR</td>
<td>87.5 (women) 90 (men)</td>
<td>84 (women) 78 (men)</td>
<td>85 (women) 91 (men)</td>
<td>87 (women) 75 (men)</td>
<td>5.51 (women) 4.08 (men)</td>
<td>0.15 (women) 0.12 (men)</td>
</tr>
<tr>
<td>Study (predictor)</td>
<td>N Women</td>
<td>Study Type</td>
<td>Quality Score</td>
<td>Modality</td>
<td>Sensitivity %</td>
<td>Specificity %</td>
<td>PPV %</td>
<td>NPV %</td>
<td>LR+</td>
<td>LR-</td>
</tr>
<tr>
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<td>---------------</td>
<td>-------</td>
<td>-------</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>Klem, et al., 2008 (≤ 97 g LV mass)</td>
<td>NR</td>
<td>Prospective</td>
<td>Good</td>
<td>CMR</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Klem, et al., 2008 (≥ 97 g LV mass)</td>
<td>NR</td>
<td>Prospective</td>
<td>Good</td>
<td>CMR</td>
<td>95</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Siegler, et al., 2011 (Small heart size)</td>
<td>123</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>57</td>
<td>69</td>
<td>36</td>
<td>85</td>
<td>1.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Siegler, et al., 2011 (Normal heart size)</td>
<td>359</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>61</td>
<td>84</td>
<td>62</td>
<td>83</td>
<td>3.7</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Abbreviations: CMR = cardiac magnetic resonance; ECG = exercise/stress electrocardiogram; ECHO-DOB = echocardiogram with dobutamine; ECHO-DIP = echocardiogram with dipyridamole; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; LVH = left ventricular hypertrophy; N = number; NPV = negative predictive value; NR = not reported; PPV = positive predictive value; SPECT = single proton emission computed tomography
Table 12. Other potential predictors

<table>
<thead>
<tr>
<th>Study (predictor)</th>
<th>N</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Modality</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;ab&lt;/sup&gt; (High pretest probability)</td>
<td>32</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>50</td>
<td>80</td>
<td>85</td>
<td>42</td>
<td>2.5</td>
<td>0.625</td>
</tr>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;ab&lt;/sup&gt; (Low pretest probability)</td>
<td>19</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>33</td>
<td>69</td>
<td>33</td>
<td>69</td>
<td>1.08</td>
<td>0.96</td>
</tr>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;ab&lt;/sup&gt; (With beta blocker)</td>
<td>24</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>53</td>
<td>56</td>
<td>67</td>
<td>42</td>
<td>1.2</td>
<td>0.84</td>
</tr>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;ab&lt;/sup&gt; (Without beta blocker)</td>
<td>27</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>31</td>
<td>86</td>
<td>67</td>
<td>57</td>
<td>2.15</td>
<td>0.81</td>
</tr>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;ab&lt;/sup&gt; (With beta blocker)</td>
<td>24</td>
<td>Prospective</td>
<td>Fair</td>
<td>SPECT</td>
<td>67</td>
<td>78</td>
<td>83</td>
<td>58</td>
<td>3.0</td>
<td>0.43</td>
</tr>
<tr>
<td>Yeih, et al., 2007&lt;sup&gt;ab&lt;/sup&gt; (Without beta blocker)</td>
<td>27</td>
<td>Prospective</td>
<td>Fair</td>
<td>SPECT</td>
<td>77</td>
<td>93</td>
<td>91</td>
<td>81</td>
<td>10.8</td>
<td>0.25</td>
</tr>
<tr>
<td>Marwick, et al., 1995&lt;sup&gt;cd&lt;/sup&gt; (High pretest probability)</td>
<td>25</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>88</td>
<td>44</td>
<td>73</td>
<td>67</td>
<td>1.57</td>
<td>0.28</td>
</tr>
<tr>
<td>Marwick, et al., 1995&lt;sup&gt;cd&lt;/sup&gt; (Intermediate pretest probability)</td>
<td>59</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>68</td>
<td>45</td>
<td>53</td>
<td>61</td>
<td>1.24</td>
<td>0.71</td>
</tr>
<tr>
<td>Marwick, et al., 1995&lt;sup&gt;cd&lt;/sup&gt; (Low pretest probability)</td>
<td>34</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECG</td>
<td>100</td>
<td>70</td>
<td>31</td>
<td>100</td>
<td>3.33</td>
<td>0</td>
</tr>
<tr>
<td>Marwick, et al., 1995&lt;sup&gt;cd&lt;/sup&gt; (High pretest probability)</td>
<td>32</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECHO</td>
<td>82</td>
<td>80</td>
<td>90</td>
<td>67</td>
<td>4.09</td>
<td>0.23</td>
</tr>
<tr>
<td>Marwick, et al., 1995&lt;sup&gt;cd&lt;/sup&gt; (Intermediate pretest probability)</td>
<td>72</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECHO</td>
<td>76</td>
<td>86</td>
<td>78.5</td>
<td>84</td>
<td>5.44</td>
<td>0.28</td>
</tr>
<tr>
<td>Marwick, et al., 1995&lt;sup&gt;cd&lt;/sup&gt; (Low pretest probability)</td>
<td>57</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECHO</td>
<td>88</td>
<td>78</td>
<td>39</td>
<td>97</td>
<td>3.90</td>
<td>0.16</td>
</tr>
<tr>
<td>Ho, et al., 1998&lt;sup&gt;ef&lt;/sup&gt; (≥2 cardiac risk factors)</td>
<td>18</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECHO</td>
<td>92</td>
<td>67</td>
<td>85</td>
<td>80</td>
<td>2.75</td>
<td>0.13</td>
</tr>
<tr>
<td>Ho, et al., 1998&lt;sup&gt;ef&lt;/sup&gt; (≤1 cardiac risk factors)</td>
<td>33</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECHO</td>
<td>94</td>
<td>88</td>
<td>93</td>
<td>89</td>
<td>7.53</td>
<td>0.07</td>
</tr>
<tr>
<td>Ho, et al., 1998&lt;sup&gt;ef&lt;/sup&gt; (&gt;50% pretest probability of CAD)</td>
<td>26</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECHO</td>
<td>94</td>
<td>75</td>
<td>90</td>
<td>86</td>
<td>3.78</td>
<td>0.07</td>
</tr>
<tr>
<td>Ho, et al., 1998&lt;sup&gt;ef&lt;/sup&gt; (&lt;50% pretest probability of CAD)</td>
<td>25</td>
<td>Prospective</td>
<td>Fair</td>
<td>ECHO</td>
<td>91</td>
<td>86</td>
<td>83</td>
<td>92</td>
<td>6.36</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Abbreviations: ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; N = number; NPV = negative predictive value; PPV = positive predictive value; SPECT = single proton emission computed tomography
The following sections focus on differences in predictors, organized by NIT modality. Summaries are in Tables 13–16.

**ECG**

Six studies\(^{25,28,31,38,50,55}\) of stress ECG assessed predictors of diagnostic accuracy in women, including age/menopausal status, disease probability, use of beta blockers, and heart size. There was some variability in diagnostic accuracy using ECG testing (both exercise and with dobutamine) (Table 13).

**Overall accuracy.** For exercise ECG testing, overall sensitivity ranged from 67 to 86 percent, and specificity ranged from 44 to 78 percent. Yeih, et al.,\(^{50}\) examined ECG testing with dobutamine, with a resulting sensitivity of 43 percent and specificity of 83 percent. Ho, et al.,\(^{67}\) examined ECG with exercise treadmill test and found that the sensitivity was 71 percent and specificity was 44 percent.

**Age/menopausal status.** Cin, et al.,\(^{31}\) examined age and menopausal status among women ages 55 to 64 (postmenopausal) and found that ECG testing performed moderately better than in other studies not targeting this age group (sensitivity of 86 percent, specificity of 60 percent). Unfortunately, that study did not have a younger or older age group to compare findings with and was rated poor quality.

**Disease probability.** Marwick, et al.,\(^{55}\) compared ECG testing performance across disease probability categories (low, intermediate, and high as determined by a combination of type of chest pain and age) and found that ECG testing performed better in the low-probability group compared with the intermediate- or high-probability group. The quality of this study was fair.

**Beta blockers.** In the study by Yeih, et al.,\(^{50}\) which compared low and high probability calculated according to age and symptoms, ECG testing performed better in the high-probability group, as expected. This study evaluated only Asian women in Taiwan. Women receiving beta blockers had fewer false positives compared with women not taking beta blockers at the time of the ECG testing.

**Heart size.** In the study by Lewis, et al.,\(^{38}\) ECG testing performed better after excluding nondiagnostic cases (sensitivity 67 percent versus 43 percent, specificity 78 percent versus 66 percent). In the study by Lu, et al.,\(^{28}\) ECG testing performed better in patients without LVH compared with those with LVH (specificity 69 percent versus 31 percent), and this finding may relate to heart size or baseline ECG strain associated with LVH.

Siegler, et al.,\(^{25}\) examined 1011 patients to determine if heart size could lead to higher false-positives rates among patients undergoing stress ECG; 482 women were enrolled in the study. The prevalence of CAD was 28 percent among women enrolled. Overall sensitivity and specificity for women undergoing stress ECG was 60 and 80 percent respectively. There was a significant association between ECG outcome and heart size among women (\(p = 0.03\)), where smaller hearts were associated with a lower specificity compared with normal size hearts.

**ECHO**

Four studies\(^{28,55,67,69}\) examined the predictors of diagnostic accuracy for exercise ECHO in women, specifically disease probability and heart size (Table 14). There was significant variability in the diagnostic accuracy of stress ECHO imaging.

**Overall accuracy.** The overall sensitivity ranged from 61 to 93 percent. The specificity ranged from 71 to 91 percent. Shin, et al.,\(^{69}\) examined 464 patients to determine potential factors that could lead to a higher false-positive rate among patients undergoing exercise ECHO. There
were 162 women enrolled in the study. The prevalence of CAD was 34 percent among the women enrolled. For women undergoing exercise ECHO, the overall sensitivity was 82 percent and specificity was 71 percent, which was less than for men in the study. PPV was 59 percent and NPV was 88 percent; LR+ was 2.82 and LR- was 0.26.

Marwick, et al., 55 found an overall sensitivity of 80 percent (p = 0.050) and specificity of 81 percent (p < 0.004) for exercise ECHO compared with exercise ECG. PPV was 71 percent and NPV was 87 percent. Exercise ECHO was compared with exercise ECG, which had a sensitivity of 77 percent and specificity of 56 percent; LR+ was 4.28 and LR- was 0.25.

Lu, et al., 28 examined the diagnostic accuracy of dipyridamole and dobutamine stress ECHO modalities. The study enrolled 76 Asian women from Taiwan. The prevalence of CAD was 41 percent. For dipyridamole, sensitivity was 61 percent and specificity was 91 percent. PPV was 83 percent and NPV was 77 percent; LR+ was 6.9 and LR- was 0.42. A dobutamine stress ECHO was more sensitive (87 percent) and less specific (82 percent). (Note that the p-value for comparing the sensitivity was 0.02, and for specificity the exact p-value was not reported but was said to be not statistically significant.) PPV was 77 percent and NPV was 90 percent; LR+ was 4.9 and LR- was 0.16.

**Disease probability.** The study by Marwick, et al., 55 also compared the diagnostic accuracy of exercise ECHO in women with different pretest probabilities of CAD (i.e., high probability, intermediate probability, and low probability). The prevalence in each group was 69, 40, and 14 percent respectively. The sensitivity was highest (88 percent) among patients with low probabilities of CAD, second highest (82 percent) among those with high probability of CAD, and lowest (76 percent) among those with an intermediate probability of CAD. However, specificity was highest (86 percent) among patients with intermediate probability of CAD, the next highest (80 percent) was among patients with highest probability of CAD, and the lowest (78 percent) was among those with a low probability of CAD. The quality of this study was fair. In this study, the diagnostic accuracy changed depending on the prevalence of CAD. Ho, et al., 67 examined the diagnostic accuracy of dobutamine stress ECHO. The study enrolled 51 women from Taiwan. The prevalence of CAD was 27 percent. The sensitivity was 93 percent and specificity was 82 percent; PPV was 87 percent and NPV was 90 percent; LR+ was 5.12 and LR- was 0.08. This study also compared the diagnostic accuracy of dobutamine stress ECHO in patients with different coronary risk factors and different pretest probabilities of CAD.

In women with two or more CAD risk factors, Ho, et al., found that the sensitivity was similar to the overall sensitivity (92 percent), but the specificity decreased (67 percent). PPV was 85 percent and NPV was 80 percent; LR+ was 2.75 and LR- was 0.13. For women with zero or one CAD risk factor, sensitivity was 94 percent, specificity was 88 percent; PPV was 93 percent and NPV was 89 percent; LR+ was 7.53 and LR- was 0.07.

In addition, in women with at least a 50-percent pretest probability of CAD, the sensitivity did not change dramatically from the overall sensitivity (94 percent), but the specificity increased (88 percent). PPV was 90 percent and NPV was 86 percent; LR+ was 3.78 and LR- was 0.07. In women with a less than 50 percent pretest probability of CAD, the sensitivity was 91 percent and specificity was 86 percent. PPV was 83 percent and NPV was 92 percent; LR+ was 6.36 and LR- was 0.11. One limitation of this study is that neither beta blockers nor calcium channel blockers were withheld.

**Heart size.** Heart size was also examined in the study by Lu, et al., 28 specifically, the effect that LVH had on diagnostic accuracy. Studies have suggested that LVH is commonly associated with ECG repolarization abnormalities, such as ST elevations in the absence of wall motion.
abnormalities or other evidence of inducible ischemia, leading to a potentially higher false-positive rate. The presence of LVH led to a lower specificity in both dipyridamole and dobutamine (81 percent versus 69 percent) stress test modalities. The sensitivities were not reported. The overall quality of this study was good.

SPECT
Four studies of SPECT assessed predictors of diagnostic accuracy in women, including race/ethnicity, heart size and use of beta blockers. There was considerable variability in diagnostic accuracy using SPECT (Table 15).

Overall accuracy. Overall sensitivity ranged from 71 to 90 percent and specificity ranged from 27 to 88 percent. In the study by Ho, et al., the prevalence of CAD was 27 percent. This study enrolled 51 women, but only 44 of them received SPECT. The overall sensitivity and specificity for SPECT was 79 percent and 75 percent respectively. PPV was 79 percent and NPV was 75 percent; LR+ was 3.17 and LR- was 0.28. It should be noted that, as in the Vashist, et al., study, SPECT was performed by either dipyridamole or dobutamine infusions. Determination of which agent to be used was based on patient preference.

Race/ethnicity. Vashist, et al., examined race/ethnicity differences in performance of SPECT. This retrospective study was noted to have several limitations, including combining exercise SPECT with dipyridamole and dobutamine. This study found a difference in prevalence of CAD but did not find a difference in diagnostic accuracy between Hispanics and African Americans. In the study by Yeih, et al., that focused on Asian women, the sensitivity was similar to other race/ethnic groups, but the specificity was significantly higher than that observed in Vashist, et al., (87 versus 27 percent).

Beta blockers. In the study by Yeih, et al., beta blockers reduced the diagnostic accuracy compared with no beta blockers (sensitivity 67 versus 77 percent, specificity 78 versus 93 percent). This fits with current clinical practice where beta blockers are withheld 48 hours prior to exercise stress to allow patients to achieve a higher (or target) heart rate for the assessment of ischemia.

Heart size. In the study by Lu, et al., SPECT was found to have fewer false positives in the group without LVH versus the group with LVH (specificity 66 versus 31 percent).

CMR
Two studies of CMR examined the influence of heart size on diagnostic accuracy in women (Table 16). The overall sensitivities were similar at 84 percent versus 85 percent, and the specificities ranged from 86 to 88 percent.

Overall accuracy. Klem, et al., studied 136 women at two academic medical centers who presented with chest pain. A multicomponent cardiac MRI (CMR test) that consisted of adenosine stress, rest perfusion, and delayed-enhancement CMR was used. The overall sensitivity and specificity of all three modes were found to be 70 and 81 percent respectively. PPV was 74 percent and NPV was 85 percent. These were reflected in a patient sample where the prevalence of significant CAD was 27 percent. LR+ was 5.96 and LR- was 0.35. Sensitivity and specificity decreased to 78 and 56 percent if perfusion CMR was used alone; LR+ also decreased to 1.77, and LR- increased to 0.39. Also, when coronary angiography results were examined for each patient, the sensitivity for multicomponent CMR was highest when patients with significant CAD had at least two-vessel disease with a sensitivity of 100 percent, as opposed to 71 percent when the patients had only single-vessel disease. The specificity was
unaffected by the extent of CAD and remained 88 percent regardless if the patient had single-vessel or multiple-vessel disease. The overall quality of the study was good.

The study conducted by Gebker, et al.\textsuperscript{95} examined the effectiveness of dobutamine stress CMR in the detection of CAD in women compared with men. The study evaluated 183 women and 541 men for suspected CAD. The prevalence of CAD in women and men was 54 percent (99 women) and 74 percent (365 men). The overall sensitivity and specificity of dobutamine stress CMR was found to be 85 and 86 percent in women and 86 and 83 percent in men. PPV and NPV were 88 and 83 percent in women and 94 and 67 percent in men; LR+ was 5.94 and LR- was 0.18 in women compared with 5.12 and 0.17 in men. The sensitivity of detecting CAD was greater in the presence of multiple-vessel CAD than in single-vessel CAD in both men and women (91 percent compared with 81 percent in women and 91 percent compared with 82 percent in men).

**Heart size.** Klem, et al.,\textsuperscript{97} also analyzed study data to determine if the heart size of patients affected the ability to detect CAD. Investigators divided the patients into two groups—those with LV mass less than 97 grams (defined as “small” hearts) and those with LV mass greater than 97 grams (defined as “large” hearts). The prevalence of significant CAD was found to be similar and was 29 percent in those with small hearts and 26 percent in those with large hearts. The reported sensitivity was 69 percent in those with small hearts and 95 percent in those with large hearts. The authors suggested that this was caused by the limitations in spatial resolution with the 1.5 Tesla MR magnet and by the fact that a smaller heart leads to a smaller number of image pixels that are available to visualize the left ventricular wall.\textsuperscript{97}

Gebker, et al.,\textsuperscript{95} also attempted to understand the relationship between heart size, in particular LVH, and the ability to detect the presence of CAD in women compared with men. Previous studies have shown that the presence of LVH causes a higher rate of false-negative studies.\textsuperscript{107} Women undergoing dobutamine CMR with evidence of LVH had a lower sensitivity but higher specificity than women without LVH (sensitivity 80 percent versus 87.5 percent, specificity 91 percent versus 84 percent). Men undergoing dobutamine CMR with evidence of LVH had a lower sensitivity and a higher specificity than men without LVH (sensitivity 79 percent versus 90 percent, specificity 95 percent versus 78 percent).
### Table 13. Summary table for ECG

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Study</th>
<th>N</th>
<th>Women</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (Dobutamine)</td>
<td>Yeih, et al., 2007</td>
<td>51</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>43</td>
<td>83</td>
<td>75</td>
<td>54</td>
<td>2.46</td>
<td>0.69</td>
</tr>
<tr>
<td>High pretest probability</td>
<td>Yeih, et al., 2007</td>
<td>32</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>50</td>
<td>80</td>
<td>85</td>
<td>42</td>
<td>2.5</td>
<td>0.625</td>
</tr>
<tr>
<td>Low pretest probability</td>
<td>Yeih, et al., 2007</td>
<td>19</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>33</td>
<td>69</td>
<td>33</td>
<td>69</td>
<td>1.08</td>
<td>0.96</td>
</tr>
<tr>
<td>With beta blocker</td>
<td>Yeih, et al., 2007</td>
<td>24</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>53</td>
<td>56</td>
<td>67</td>
<td>42</td>
<td>1.2</td>
<td>0.84</td>
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<tr>
<td>Without beta blocker</td>
<td>Yeih, et al., 2007</td>
<td>27</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>31</td>
<td>86</td>
<td>67</td>
<td>57</td>
<td>2.15</td>
<td>0.81</td>
</tr>
<tr>
<td>Asian</td>
<td>Yeih, et al., 2007</td>
<td>51</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>43</td>
<td>83</td>
<td>75</td>
<td>54</td>
<td>2.46</td>
<td>0.69</td>
</tr>
<tr>
<td>Overall</td>
<td>Ho, et al., 1998</td>
<td>30</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>71</td>
<td>44</td>
<td>0.53</td>
<td>0.64</td>
<td>1.27</td>
<td>0.65</td>
</tr>
<tr>
<td>Overall</td>
<td>Cin, et al., 2000</td>
<td>110</td>
<td></td>
<td>Prospective</td>
<td>Poor</td>
<td>86</td>
<td>61</td>
<td>81</td>
<td>70</td>
<td>2.18</td>
<td>0.23</td>
</tr>
<tr>
<td>Postmenopausal, ages 55 to 64</td>
<td>Cin, et al., 2000</td>
<td>110</td>
<td></td>
<td>Prospective</td>
<td>Poor</td>
<td>86</td>
<td>61</td>
<td>81</td>
<td>70</td>
<td>2.18</td>
<td>0.23</td>
</tr>
<tr>
<td>Overall</td>
<td>Marwick, et al., 1995</td>
<td>118</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>77</td>
<td>56</td>
<td>54</td>
<td>78</td>
<td>1.74</td>
<td>0.41</td>
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<tr>
<td>High pretest probability</td>
<td>Marwick, et al., 1995</td>
<td>25</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>88</td>
<td>44</td>
<td>73</td>
<td>67</td>
<td>1.57</td>
<td>0.28</td>
</tr>
<tr>
<td>Intermediate pretest probability</td>
<td>Marwick, et al., 1995</td>
<td>59</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>68</td>
<td>45</td>
<td>53</td>
<td>61</td>
<td>1.24</td>
<td>0.71</td>
</tr>
<tr>
<td>Low probability</td>
<td>Marwick, et al., 1995</td>
<td>34</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>100</td>
<td>70</td>
<td>31</td>
<td>100</td>
<td>3.33</td>
<td>0</td>
</tr>
<tr>
<td>Overall</td>
<td>Lewis, et al., 2005</td>
<td>96</td>
<td></td>
<td>Prospective</td>
<td>Good</td>
<td>67</td>
<td>78</td>
<td>83</td>
<td>58</td>
<td>3.0</td>
<td>0.43</td>
</tr>
<tr>
<td>Excluding nondiagnostic</td>
<td>Lewis, et al., 2005</td>
<td>74</td>
<td></td>
<td>Prospective</td>
<td>Good</td>
<td>43</td>
<td>66</td>
<td>33</td>
<td>74</td>
<td>1.26</td>
<td>0.86</td>
</tr>
<tr>
<td>Overall</td>
<td>Lu, et al., 2010</td>
<td>76</td>
<td></td>
<td>Prospective</td>
<td>Good</td>
<td>81</td>
<td>56</td>
<td>56</td>
<td>81</td>
<td>1.81</td>
<td>0.35</td>
</tr>
<tr>
<td>With LVH</td>
<td>Lu, et al., 2010</td>
<td>36</td>
<td></td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>31</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Without LVH</td>
<td>Lu, et al., 2010</td>
<td>40</td>
<td></td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Small heart size</td>
<td>Siegler, et al., 2011</td>
<td>123</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>57</td>
<td>69</td>
<td>36</td>
<td>85</td>
<td>1.9</td>
<td>0.6</td>
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<td>Normal heart size</td>
<td>Siegler, et al., 2011</td>
<td>359</td>
<td></td>
<td>Prospective</td>
<td>Fair</td>
<td>61</td>
<td>84</td>
<td>62</td>
<td>83</td>
<td>3.7</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Abbreviations: LR+ = positive likelihood ratio; LR- = negative likelihood ratio; LVH = left ventricular hypertrophy; CMR = cardiac magnetic resonance; N = number; NPV = negative predictive value; NR = not reported; PPV = positive predictive value

Table 14. Summary table for ECHO

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Study</th>
<th>N Women</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Shin, et al., 2003&lt;sup&gt;a&lt;/sup&gt;</td>
<td>162</td>
<td>Prospective</td>
<td>Fair</td>
<td>82</td>
<td>71</td>
<td>59</td>
<td>88</td>
<td>2.82</td>
<td>0.26</td>
</tr>
<tr>
<td>Overall</td>
<td>Marwick, et al., 1995&lt;sup&gt;59&lt;/sup&gt;</td>
<td>161</td>
<td>Prospective</td>
<td>Fair</td>
<td>80</td>
<td>81</td>
<td>71</td>
<td>87</td>
<td>4.28</td>
<td>0.25</td>
</tr>
<tr>
<td>High pretest probability</td>
<td>Marwick, et al., 1995&lt;sup&gt;59&lt;/sup&gt;</td>
<td>32</td>
<td>Prospective</td>
<td>Fair</td>
<td>82</td>
<td>80</td>
<td>90</td>
<td>67</td>
<td>4.09</td>
<td>0.23</td>
</tr>
<tr>
<td>Intermediate pretest probability</td>
<td>Marwick, et al., 1995&lt;sup&gt;59&lt;/sup&gt;</td>
<td>72</td>
<td>Prospective</td>
<td>Fair</td>
<td>76</td>
<td>86</td>
<td>78.5</td>
<td>84</td>
<td>5.44</td>
<td>0.28</td>
</tr>
<tr>
<td>Low pretest probability</td>
<td>Marwick, et al., 1995&lt;sup&gt;59&lt;/sup&gt;</td>
<td>57</td>
<td>Prospective</td>
<td>Fair</td>
<td>88</td>
<td>78</td>
<td>39</td>
<td>97</td>
<td>3.90</td>
<td>0.16</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Lu, et al., 2010&lt;sup&gt;24&lt;/sup&gt;</td>
<td>76</td>
<td>Prospective</td>
<td>Good</td>
<td>61</td>
<td>91</td>
<td>83</td>
<td>77</td>
<td>6.9</td>
<td>0.42</td>
</tr>
<tr>
<td>With LVH</td>
<td>Lu, et al., 2010&lt;sup&gt;24&lt;/sup&gt;</td>
<td>36</td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>81</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Without LVH</td>
<td>Lu, et al., 2010&lt;sup&gt;24&lt;/sup&gt;</td>
<td>40</td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>96</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>Lu, et al., 2010&lt;sup&gt;24&lt;/sup&gt;</td>
<td>76</td>
<td>Prospective</td>
<td>Good</td>
<td>87</td>
<td>82</td>
<td>77</td>
<td>90</td>
<td>4.9</td>
<td>0.16</td>
</tr>
<tr>
<td>With LVH</td>
<td>Lu, et al., 2010&lt;sup&gt;24&lt;/sup&gt;</td>
<td>36</td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Without LVH</td>
<td>Lu, et al., 2010&lt;sup&gt;24&lt;/sup&gt;</td>
<td>40</td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>89</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Overall Dobutamine</td>
<td>Ho, et al., 1998&lt;sup&gt;37&lt;/sup&gt;</td>
<td>51</td>
<td>Prospective</td>
<td>Fair</td>
<td>93</td>
<td>82</td>
<td>87</td>
<td>90</td>
<td>5.12</td>
<td>0.08</td>
</tr>
</tbody>
</table>

<sup>a</sup>Shin, et al. sensitivity/specificity were different in text (88/64)

Abbreviations: LR+ = positive likelihood ratio; LR- = negative likelihood ratio; N = number; NPV = negative predictive value; NR = not reported; PPV = positive predictive value
### Table 15. Summary table for SPECT

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Study</th>
<th>N Women</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
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<tbody>
<tr>
<td>Overall</td>
<td>Ho, et al., 1998&lt;sup&gt;199&lt;/sup&gt;</td>
<td>44</td>
<td>Prospective</td>
<td>Fair</td>
<td>79</td>
<td>75</td>
<td>79</td>
<td>75</td>
<td>3.17</td>
<td>0.28</td>
</tr>
<tr>
<td>Overall</td>
<td>Vashist, et al., 2007&lt;sup&gt;1&lt;/sup&gt;</td>
<td>54</td>
<td>Retrospective</td>
<td>Fair</td>
<td>87</td>
<td>27</td>
<td>75</td>
<td>44</td>
<td>1.19</td>
<td>0.48</td>
</tr>
<tr>
<td>Hispanic</td>
<td>Vashist, et al., 2007&lt;sup&gt;1&lt;/sup&gt;</td>
<td>16</td>
<td>Retrospective</td>
<td>Fair</td>
<td>71.4</td>
<td>33.3</td>
<td>45.5</td>
<td>60</td>
<td>1.07</td>
<td>0.86</td>
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<tr>
<td>African American</td>
<td>Vashist, et al., 2007&lt;sup&gt;1&lt;/sup&gt;</td>
<td>34</td>
<td>Retrospective</td>
<td>Fair</td>
<td>90</td>
<td>20</td>
<td>86.7</td>
<td>25</td>
<td>1.12</td>
<td>0.52</td>
</tr>
<tr>
<td>Overall</td>
<td>Yeih, et al., 2007&lt;sup&gt;1&lt;/sup&gt;</td>
<td>51</td>
<td>Prospective</td>
<td>Fair</td>
<td>71</td>
<td>87</td>
<td>87</td>
<td>71</td>
<td>5.48</td>
<td>0.33</td>
</tr>
<tr>
<td>Hispanic</td>
<td>Yeih, et al., 2007&lt;sup&gt;1&lt;/sup&gt;</td>
<td>51</td>
<td>Prospective</td>
<td>Fair</td>
<td>71</td>
<td>87</td>
<td>87</td>
<td>71</td>
<td>5.48</td>
<td>0.33</td>
</tr>
<tr>
<td>With beta blocker</td>
<td>Yeih, et al., 2007&lt;sup&gt;1&lt;/sup&gt;</td>
<td>24</td>
<td>Prospective</td>
<td>Fair</td>
<td>67</td>
<td>78</td>
<td>83</td>
<td>58</td>
<td>3.0</td>
<td>0.43</td>
</tr>
<tr>
<td>Without beta blocker</td>
<td>Yeih, et al., 2007&lt;sup&gt;1&lt;/sup&gt;</td>
<td>27</td>
<td>Prospective</td>
<td>Fair</td>
<td>77</td>
<td>93</td>
<td>91</td>
<td>81</td>
<td>10.8</td>
<td>0.25</td>
</tr>
<tr>
<td>Overall</td>
<td>Lu, et al., 2010&lt;sup&gt;1&lt;/sup&gt;</td>
<td>76</td>
<td>Prospective</td>
<td>Good</td>
<td>90</td>
<td>53</td>
<td>57</td>
<td>89</td>
<td>1.94</td>
<td>0.18</td>
</tr>
<tr>
<td>With LVH</td>
<td>Lu, et al., 2010&lt;sup&gt;1&lt;/sup&gt;</td>
<td>36</td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>31</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Without LVH</td>
<td>Lu, et al., 2010&lt;sup&gt;1&lt;/sup&gt;</td>
<td>40</td>
<td>Prospective</td>
<td>Good</td>
<td>NR</td>
<td>66</td>
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</table>

Abbreviations: LR+ = positive likelihood ratio; LR- = negative likelihood ratio; LVH = left ventricular hypertrophy; CMR = cardiac magnetic resonance; N = number; NPV = negative predictive value; NR = not reported; PPV = positive predictive value

### Table 16. Summary table for CMR

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Study</th>
<th>N Women</th>
<th>Study Type</th>
<th>Quality Score</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Klem, et al., 2008&lt;sup&gt;1&lt;/sup&gt;</td>
<td>136</td>
<td>Prospective</td>
<td>Good</td>
<td>70</td>
<td>81</td>
<td>74</td>
<td>85</td>
<td>5.96</td>
<td>0.35</td>
</tr>
<tr>
<td>≤ 97 g LV mass</td>
<td>Klem, et al., 2008&lt;sup&gt;1&lt;/sup&gt;</td>
<td>NR</td>
<td>Prospective</td>
<td>Good</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>≥ 97 g LV mass</td>
<td>Klem, et al., 2008&lt;sup&gt;1&lt;/sup&gt;</td>
<td>NR</td>
<td>Prospective</td>
<td>Good</td>
<td>95</td>
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<td>Predictor</td>
<td>Study</td>
<td>N Women</td>
<td>Study Type</td>
<td>Quality Score</td>
<td>Sensitivity %</td>
<td>Specificity %</td>
<td>PPV %</td>
<td>NPV %</td>
<td>LR+</td>
<td>LR-</td>
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<tr>
<td>Dobutamine</td>
<td>Gebker, et al., 2010⁵⁶</td>
<td>183</td>
<td>Prospective</td>
<td>Good</td>
<td>85 (women)</td>
<td>86 (men)</td>
<td>88</td>
<td>83</td>
<td>5.94</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>women</td>
<td></td>
<td></td>
<td>86 (women)</td>
<td>94 (men)</td>
<td></td>
<td></td>
<td>(women)</td>
<td>(men)</td>
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<tr>
<td></td>
<td></td>
<td>490</td>
<td></td>
<td></td>
<td>83 (men)</td>
<td>67 (men)</td>
<td></td>
<td></td>
<td>5.12</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>men</td>
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<td></td>
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</tr>
<tr>
<td>With LVH</td>
<td>Gebker, et al., 2010⁵⁶</td>
<td>56</td>
<td>Prospective</td>
<td>Good</td>
<td>80 (women)</td>
<td>91 (men)</td>
<td>93</td>
<td>73</td>
<td>8.4</td>
<td>0.22</td>
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<tr>
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<td></td>
<td>79 (men)</td>
<td>98 (men)</td>
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<td>56</td>
<td>(women)</td>
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<td>179</td>
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<td>95 (men)</td>
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<td>0.22</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Without LVH</td>
<td>Gebker, et al., 2010⁵⁶</td>
<td>127</td>
<td>Prospective</td>
<td>Good</td>
<td>87.5 (women)</td>
<td>84 (men)</td>
<td>85</td>
<td>87</td>
<td>5.51</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>women</td>
<td></td>
<td></td>
<td>90 (men)</td>
<td>78 (men)</td>
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<td>75</td>
<td>(women)</td>
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<td>4.08</td>
<td>0.12</td>
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<td>men</td>
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Abbreviations: LR+ = positive likelihood ratio; LR- = negative likelihood ratio; LVH = left ventricular hypertrophy; CMR = cardiac magnetic resonance; N = number; NPV = negative predictive value; NR = not reported; PPV = positive predictive value
KQ 2 Summary

To summarize, there was insufficient available evidence to draw definitive conclusions about predictors given the small number of studies for each predictor and for each modality, as well as the combination of predictor by modality. The main predictors examined included heart size, pretest probability of CAD, race/ethnicity, postmenopausal status, and beta blocker use. No studies examined functional status, age alone, or body size. Significant variability around diagnostic accuracy existed among the studies examining each stress modality, and studies that examined heart size varied on the effect on diagnostic accuracy by stress modality.

Key Question 3: Use of NITs To Improve Risk Stratification, Decisionmaking, and Clinical Outcomes

KQ 3. Is there evidence that the use of NITs (when compared with other NITs or with coronary angiography) in women improves:

KQ 3a. Risk stratification/prognostic information?
KQ 3b. Decisionmaking regarding treatment options (e.g., revascularization, optimal medical therapy)?
KQ 3c. Clinical outcomes (e.g., death, myocardial infarction, unstable angina, hospitalization, revascularization, angina relief, quality of life)?

Key Points

- There were insufficient data to demonstrate that the use of specific NITs (compared with coronary angiography) routinely provided incremental risk stratification, prognostic information, or other meaningful information to improve decisionmaking.
- Compared with other NITs, stress ECG testing had higher rates of indeterminate results in women, which limited the ability to compare risk stratification with low-risk and high-risk findings from other stress imaging studies.
- There was insufficient evidence on the comparative effectiveness of different NITs to have an impact on clinical decisionmaking that leads to improved patient outcomes in women.

Detailed Synthesis

For KQ 3, we examined studies that reported prognostic, outcome, or decisionmaking data comparing one NIT with another NIT or with coronary angiography in women with symptoms suspicious for CAD. We identified 13 studies,22-24,30,38,52,83,99,108-112 of which 3 were considered good quality, 9 were fair quality, and 1 was poor quality. The majority of the comparative studies evaluated (n = 7) provided information on risk stratification and prognostic information. Five of these studies evaluated clinical outcomes (two studies with information on both risk stratification and clinical outcomes), and two studies were aimed at clinical decisionmaking.

In order to evaluate the ability of NITs to provide incremental information on risk stratification, prognosis, and decisionmaking, we evaluated studies that reported clinical outcomes for at least two NITs or coronary angiography. Although several studies in women
described observational cohorts of women undergoing an NIT who were followed for findings related to clinical outcomes, these studies were generally excluded since they were limited by the population risk studied, and they did not provide information on evidence for comparative effectiveness. Table 17 summarizes the findings for KQ 3a, 3b, and 3c.

KQ 3a: Risk Stratification and Prognostic Information

Eight studies (two good quality, six fair) provided evidence on risk stratification and prognosis. Of these studies, two from the Women’s Ischemia Study Evaluation (WISE) study evaluated the prognostic significance of CMR for women with suspected myocardial ischemia but without significant obstructive CAD (< 50 percent stenosis) on coronary angiography. In the study by Doyle, et al., two imaging variables—global magnetic resonance-myocardial perfusion imaging ratio of average peak signal-to-normalized uptake slope at stress and ejection fraction—were predictive of events including death, MI, and hospitalization for worsening angina by univariable Cox regression modeling (hazard ratio 0.516; 95% CI, 0.314 to 0.848; p < 0.05 and hazard ratio of 0.949; 95% CI, 0.911 to 0.990; p < 0.05, respectively). Kaplan-Meier survival curves indicated a significant difference in time to adverse events between risk groups (log-rank 15.0, p < 0.0001). Annualized event rates were 12 percent in the high-risk group (2 deaths and 10 hospitalizations for worsening angina) and 4 percent in the not high-risk group (2 MIs and 9 hospitalizations for worsening angina).

Johnson, et al., found that of the 74 women without CAD undergoing CMR, 19 percent had a cardiovascular event (1 heart failure, 12 unstable angina admission, 2 other vascular events). Women without CAD and a negative CMR had an 87-percent cumulative 3-year event-free survival rate. Women with CAD and positive (abnormal) CMR and women in the WISE study (control group, women with angiographically defined CAD) had lower event-free rates (57 percent; p = 0.009, and 52 percent; p < 0.0001 respectively). Among women without CAD, the rate of hospitalization for angina was lower in those with normal CMR compared with abnormal CMR (12 percent versus 36 percent; p < 0.05).

Two other studies described the low event rate and good prognosis in patients with low-risk findings on SPECT with diagnostic validation from coronary angiography. In a retrospective analysis, Vashist, et al., specifically studied the prognostic value of myocardial perfusion imaging in minority women (African American, Hispanic, Asian) and found that low-risk perfusion scanning signified a favorable prognosis for mortality at 2 years. Five of the 54 patients (9.3 percent) had died at 2 years (3 with intermediate-risk scan and 2 with high-risk scan). In the prospective study by Mieres, et al., evaluating the prognostic accuracy of SPECT in symptomatic postmenopausal women (n = 46) with an intermediate pretest likelihood for CAD, the cumulative 3- and 5-year event-free survival was 97 and 94 percent for normal myocardial perfusion scintigraphy (MPS) compared with 60 and 48 percent for those with abnormal MPS findings (p < 0.0001). Using ECG results for risk stratification, a negative exercise ECG was associated with 3- and 5-year event-free survival rates of 89 and 72 percent. When ECG and MPS results were included in a multivariable model, only MPS findings retained statistical significance (p = 0.017).

The prospective analysis by Coelho-Filho, et al., evaluated the prognostic value of stress CMR in a consecutive group of women (n = 177). The myocardial extent of ischemia (ISCH-SCORE) was the strongest predictor of MACE events (cardiac death and acute MI) both with univariate and multivariate analysis: hazard ratio (95% CI) 1.36 (1.23 to 1.5) and 1.49 (1.31 to 1.69) respectively. Women with evidence of ischemia also had a higher annual rate of MACE
and cardiac death compared with women without ischemia (15.1 percent and 8.2 percent versus 0.3 percent and 0 percent respectively).

Finally, three studies\textsuperscript{38,110,111} demonstrated the limitations and prognostic significance of ECG compared with coronary angiography and clinical outcomes. Morise, et al.,\textsuperscript{110} initially developed an exercise ECG score, including clinical and ECG variables to help risk stratify women with suspected CAD into groups of gradually increasing frequency of coronary disease and death. The score was then applied to women enrolled in the WISE study to assess the ability of the pretest and new exercise scores to stratify risk in women with low prevalence of angiographically defined CAD.\textsuperscript{111} Using the pretest score, a Kaplan-Meier curve analysis of the composite endpoint (death, MI, stroke, or late revascularization) revealed a clear separation between the low-risk group and the intermediate- and high-risk groups for as long as 4 years. The intermediate- and high-risk groups were separable for as long as 1.5 years but thereafter became less clearly separable. Using the exercise population, the number of events decreased, and the Kaplan-Meier curve displayed a less clear separation and a nonsignificant difference between the curves (p = 0.11). Using data from the WISE study, Lewis, et al.,\textsuperscript{38} found that the overall sensitivity of ECG was 31 percent for obstructive CAD on coronary angiography and that the inability to perform the ECG, rather than findings on ECG, predicted MI, death, or heart failure. These data emphasize some of the limitations of using ECG in women.

**KQ 3b: Decisionmaking for Treatment Options**

We found two studies\textsuperscript{23,112} with information on clinical decisionmaking that compared different NIT strategies. The prospective analysis by Wong, et al.,\textsuperscript{112} evaluated rates of referral for arteriography and revascularization according to sex. In this study, men were more likely to be referred for percutaneous transluminal coronary angioplasty or coronary artery bypass grafting than were women (59.4 percent versus 32.8 percent; odds ratio 3.0; 95% CI, 2.0 to 4.6). This difference in referral rate seemed to be linked to higher incidence of significant CAD in men (56.2 percent) compared with women (16.4 percent). When accounting for the difference in CAD incidence between men and women, there was no significant difference in revascularization rates, thus no difference in unnecessary referrals.

The study by Sanfilippo, et al.,\textsuperscript{23} was an RCT of three testing strategies in women with chest pain. This fair-quality study included 158 women randomized to ECG, exercise stress ECHO, or dobutamine stress ECHO. All tests resulted in a diagnosis of cardiac chest pain or noncardiac chest pain or were indeterminate. The study found that ECG had a higher likelihood of indeterminate results, and patients with noncardiac chest pain from all modalities had low event rates. Although these two studies were informative, there remains a significant need for studies that evaluate clinical decisionmaking to improve treatment options for patients.

**KQ 3c: Clinical Outcomes**

We found four studies that provided data on the comparative clinical outcomes for different NITs.\textsuperscript{22,24,30,38} As previously stated, the study by Lewis, et al.,\textsuperscript{38} identified limitations in diagnostic accuracy with ECG (overall sensitivity of 31 percent) and associated limitations in prognostic impact. Event-free survival was shorter in women who did not undergo ECG. The proportional hazards model that included ECG, CAD, and age showed estimated hazard ratios (95% CI) of 0.42 (0.18 to 0.97), 3.88 (1.72 to 8.73), and 1.01 (0.98 to 1.05) respectively (p = 0.0003). These results indicate a decreased risk of an event for women who underwent ECG, regardless of outcome, compared with those who did not undergo ECG.
The study by Dodi, et al.,\textsuperscript{22} evaluated 244 women who underwent ECG and exercise ECHO for symptoms suspicious for CAD. This study found that the prognostic information with stress ECHO (odds ratio 40) for death or MI was significantly above the effect of a positive ECG (odds ratio 3.5).

The study by Raman, et al.,\textsuperscript{30} enrolled 23 women who had a positive nuclear scan (SPECT) referred for coronary angiography and who underwent dobutamine stress CMR to assess for ischemia. Followup in this study lasted 20 ± 8 months, and there were no reported MI, hospitalizations, or death in their study sample.

The study by Shaw, et al.,\textsuperscript{24} evaluated women with an intermediate pretest likelihood of CAD. In that study, two diagnostic strategies, exercise ECG and SPECT, had a different effect on the 2-year posttest outcomes for MACE (cardiac death, nonfatal MI) or hospital admission for acute coronary syndrome or heart failure. MACE-free survival was found to be identical (98 percent) for women randomized to the ECG or SPECT arm (p = 0.59), and the observed 2-year MACE rate was 1.7 percent for ECG and 2.3 percent for SPECT (relative hazard, 95\% CI for MACE in SPECT arm versus ECG arm was 1.3; 0.5 to 3.5; p = 0.59). It was noted that the study was underpowered for the MACE outcome (post hoc analysis power of 15 percent at 0.05 significance level).

No articles of coronary CTA reported clinical outcomes data.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>NIT and Reference Test</th>
<th>Outcomes</th>
<th>Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doyle, et al., 2010</td>
<td>Single center Retrospective Consecutive patients Enrollment: Nov 1993–Oct 1998 Followup: 34 ± 16 months</td>
<td>N overall:100 Women: 100 No known CAD</td>
<td>NIT: CMR Reference test: Coronary angiography</td>
<td><strong>Clinical outcomes</strong> Adverse events: Death, MI, hospitalization for worsening angina Imaging variables predictive of events by univariable Cox regression modeling were Global magnetic resonance–myocardial perfusion imaging ratio of average peak signal-to-normalized uptake slope at stress, HR 0.516, 95% CI 0.314 to 0.848 (p &lt;0.05) Ejection fraction, HR 0.949, 95% CI 0.911 to 0.990 (p &lt; 0.05) Event rates High-risk: 2 deaths, 10 hospitalizations for worsening angina; annualized event rate 12% Low-risk: 2 MIs and 9 hospitalizations; annualized event rate 4% Kaplan-Meier survival curve of time to adverse event, log-rank: 15.0, p &lt;0.0001</td>
<td>Fair</td>
</tr>
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</table>
Table 17. Summary of findings for KQ 3 (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>NIT and Reference Test</th>
<th>Outcomes</th>
<th>Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson, et al., 2004</td>
<td>Multicenter</td>
<td>N overall: 74</td>
<td>NIT: CMR</td>
<td>Clinical outcomes</td>
<td>Fair</td>
</tr>
<tr>
<td></td>
<td>Prospective observational</td>
<td>Women: 74</td>
<td>Reference test: Coronary angiography</td>
<td>Death, MI, heart failure, stroke, other vascular events,</td>
<td></td>
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<tr>
<td></td>
<td>Enrollment: NR</td>
<td>Mixed population</td>
<td></td>
<td>hospitalization for unstable angina:</td>
<td></td>
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<tr>
<td></td>
<td>Followup: Median 36.5 months</td>
<td></td>
<td></td>
<td>• In women without CAD (n = 74), 14 (19%) had cardiovascular event (0 death, 0 MI, 1 heart failure, 0 stroke, 12 unstable angina, 2 others)</td>
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<td></td>
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<td></td>
<td>• In women without CAD and normal CMR, 87% 3-year event-free</td>
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<td></td>
<td>• In women without CAD and abnormal CMR, 57% 3-year event-free</td>
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<td>WISE reference women with known CAD (by coronary angiography) had 52% 3-year event-free</td>
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<td><strong>Women without CAD, rate of hospitalization for angina</strong></td>
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<td>Normal CMR: 12%</td>
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<td>Abnormal CMR: 36% (p &lt; 0.05)</td>
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<td><strong>Repeat angiography</strong></td>
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<td>Normal CMR: 3%</td>
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<td></td>
<td>Abnormal CMR: 21% (p &lt; 0.05)</td>
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<tr>
<td>Study</td>
<td>Study Design</td>
<td>Patient Population</td>
<td>NIT and Reference Test</td>
<td>Outcomes</td>
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<td>---------------------------------------------------------------------------</td>
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</tbody>
</table>
| Mieres, et al., 2007<sup>52</sup> | • Single center  
• Prospective observational  
• Consecutive patients  
• Enrollment: NR  
• Followup: 5.0 ± 3 years | N overall: 46  
Women: 46  
No known CAD | NITs:  
• Exercise ECG  
• SPECT  
Reference test:  
Coronary angiography | Clinical outcomes  
Hospitalization for ACS, MI, or new onset or worsening angina  
Normal MPS compared with abnormal MPS  
Cumulative event-free survival at 3 and 5 years was 97% and 94% for normal MPS results compared with 60% and 48% for those with abnormal MPS findings (p < 0.0001)  
Cox models looked at time to cardiovascular event as primary endpoint defined as combination of cardiovascular death, MI, increasing chest pain symptoms with definitive ECG or enzyme marker positive criteria for ACS  
Risk stratification/prognostic outcomes  
A negative exercise ECG was associated with 3- and 5-year event-free survival rates of 89% and 72% respectively  
Occurrence and date of the following cardiac events were noted: death, ACS, and coronary revascularization  
Coronary revascularization procedures were collected for censoring followup in the survival analysis  
Cause of death was defined as cardiovascular when occurring in the setting of a fatal MI, decompensated heart failure, or sudden cardiac death  
ACS was defined after confirmation of pain, ECG, and enzymatic criteria | Fair |
| Vashist, et al., 2007<sup>83</sup> | • Single center  
• Retrospective  
• Consecutive patients  
• Enrollment: NR  
• Followup: 2 years | N overall: 54  
Women: 54  
Minority women  
Mixed population—2% known CAD | NIT: SPECT  
Reference test:  
Coronary angiography | Clinical outcomes  
Death: N = 5 (9.3%)  
• 3 with intermediate-risk perfusion scan  
• 2 with high-risk perfusion scan  
Low-risk perfusion scan with low event rate over 2 years | Fair |
Table 17. Summary of findings for KQ 3 (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>NIT and Reference Test</th>
<th>Outcomes</th>
<th>Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morise, et al., 2002 (^{110})</td>
<td>• Multicenter</td>
<td>N overall: 442</td>
<td>NIT: Exercise ECG</td>
<td>Study developed an exercise ECG score specifically for women.</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td>• Prospective observational</td>
<td>Women: 442</td>
<td>Reference test: Coronary angiography</td>
<td>Factors in score for increase gradations of CAD included age (5), symptoms (2), diabetes (2), smoking (2), and estrogen status (1)</td>
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<tr>
<td></td>
<td>• Enrollment: 1981–1999</td>
<td>No known CAD</td>
<td></td>
<td>Exercise ECG variables selected and their weights included ST depression (2), exercise heart rate (4), and Duke Angina Index (3)</td>
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<tr>
<td></td>
<td>• Followup: 2.6 years</td>
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</tr>
<tr>
<td>Morise, et al., 2004 (^{111})</td>
<td>• Multicenter</td>
<td>N overall: 563</td>
<td>NIT: Exercise ECG</td>
<td>Clinical outcomes</td>
<td>Fair</td>
</tr>
<tr>
<td></td>
<td>• Prospective observational</td>
<td>Women: 563</td>
<td>Reference test: Coronary angiography</td>
<td>Composite death, MI, stroke, late revascularization</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Enrollment: NR</td>
<td>No known CAD</td>
<td></td>
<td>Exercise scores:</td>
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<td></td>
<td>• Followup: mean 3.4 years</td>
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<td>• Low-risk group composite endpoint in 4/83 (4.8%; annualized rate 1.4%)</td>
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<td>• Intermediate-risk group = 13/74 (17.6%; 5.2% annualized rate)</td>
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<td></td>
<td>• High-risk group = 4/32 (12.5%; annualized rate 3.7%, (p = 0.038))</td>
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<tr>
<td>Lewis, et al., 2005 (^{38})</td>
<td>• Single center</td>
<td>N overall: 96</td>
<td>NIT: Exercise ECG</td>
<td>Clinical outcomes</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td>• Prospective observational</td>
<td>Women: 96</td>
<td>Reference test: Coronary angiography</td>
<td>MI: (N = 5)</td>
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<tr>
<td></td>
<td>• Followup: Median 2.82 years</td>
<td>16 known CAD (prior</td>
<td></td>
<td>Death: (N = 12)</td>
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<tr>
<td></td>
<td></td>
<td>revascularization or MI)</td>
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<td></td>
<td>Overall sensitivity of exercise ECG was 31% with CAD on coronary angiography; inability to perform ECG testing, rather than findings on ECG, predicted MI, death, heart failure</td>
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<td>The proportional hazards model that included ECG, CAD, and age revealed estimated hazard ratios (95% CI) of 0.42 (0.18 to 0.97), 3.88 (1.72 to 8.73), and 1.01 (0.98 to 1.05), respectively ((P = 0.0003))</td>
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<td>This indicates a decreased risk of an event for women who underwent ECG, regardless of outcome, compared with those who did not</td>
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</tr>
</tbody>
</table>
### Table 17. Summary of findings for KQ 3 (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>NIT and Reference Test</th>
<th>Outcomes</th>
<th>Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong, et al., 2001&lt;sup&gt;112&lt;/sup&gt;</td>
<td>• Single center&lt;br&gt;• Retrospective observational&lt;br&gt;• Enrollment: Dec 1997–April 2000&lt;br&gt;• Followup: NA</td>
<td>N overall: 1522&lt;br&gt;Women: 601&lt;br&gt;No known CAD</td>
<td>NIT: Exercise ECG&lt;br&gt;N = 423 (137 women 286 men)&lt;br&gt;Reference test: Coronary angiography</td>
<td>Decisionmaking for treatment&lt;br&gt;Men were more likely to be referred for percutaneous transluminal coronary angioplasty or coronary artery bypass grafting than women—59.4% vs. 32.8% (OR 3.0, 95% CI 2.0 to 4.6) but men had a higher incidence of both significant and prognostic CAD (56.2% of women were found to have normal coronary arteries compared with only 16.4% of men). When this was taken into account, there was no significant difference in revascularization rates</td>
<td>Poor</td>
</tr>
<tr>
<td>Sanfilippo, et al., 2005&lt;sup&gt;23&lt;/sup&gt;</td>
<td>• Multicenter&lt;br&gt;• Prospective observational&lt;br&gt;• Enrollment: NR&lt;br&gt;• Followup: 28.1 ± 14.2 months</td>
<td>N overall: 158&lt;br&gt;Women: 158&lt;br&gt;No known CAD</td>
<td>NIT: Exercise ECG&lt;br&gt;Reference test: Stress ECHO</td>
<td>Decisionmaking for treatment&lt;br&gt;Exercise ECG had higher likelihood of indeterminate results, patients with noncardiac chest pain from all modalities had low event rate</td>
<td>Fair</td>
</tr>
<tr>
<td>Dodi, et al., 2001&lt;sup&gt;22&lt;/sup&gt;</td>
<td>• Multicenter&lt;br&gt;• Prospective observational&lt;br&gt;• Enrollment: Nov 1990–Oct 1996&lt;br&gt;• Followup: 36 ± 18 months</td>
<td>N overall: 244&lt;br&gt;Women: 244&lt;br&gt;No known CAD</td>
<td>NIT: Exercise ECG&lt;br&gt;Reference test: Stress ECHO</td>
<td>Clinical outcomes&lt;br&gt;All-cause mortality: N = 2&lt;br&gt;Nonfatal MI: N = 5&lt;br&gt;Unstable angina: N = 7&lt;br&gt;Prognosis for death or MI&lt;br&gt;Positive stress ECHO (OR 40)&lt;br&gt;Positive ECG (OR 3.5)</td>
<td>Good</td>
</tr>
<tr>
<td>Raman, et al., 2008&lt;sup&gt;30&lt;/sup&gt;</td>
<td>• Single center&lt;br&gt;• Prospective observational&lt;br&gt;• Consecutive patients&lt;br&gt;• Enrollment: NR&lt;br&gt;• Followup: 20 ± 8 months</td>
<td>N overall: 23&lt;br&gt;Women: 23&lt;br&gt;No known CAD</td>
<td>NITs: Exercise ECG&lt;br&gt;SPECT&lt;br&gt;CMR&lt;br&gt;Reference test: Coronary angiography</td>
<td>Clinical outcomes&lt;br&gt;MI: N = 0&lt;br&gt;Hospitalization: N = 0&lt;br&gt;Death: N = 0</td>
<td>Fair</td>
</tr>
</tbody>
</table>
Table 17. Summary of findings for KQ 3 (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>NIT and Reference Test</th>
<th>Outcomes</th>
<th>Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coelho-Filho, et al., 2011</td>
<td>• Single center&lt;br&gt;• Prospective observational&lt;br&gt;• Consecutive patients&lt;br&gt;• Enrollment: NR&lt;br&gt;• Followup: median 30 months</td>
<td>N overall: 405&lt;br&gt;Women: 168&lt;br&gt;Mixed population 180 with known CAD (history of MI, PCI, or CABG)</td>
<td>NIT: Stress CMR&lt;br&gt;Reference test: (only in a minority of patients; N = 77)&lt;br&gt;Coronary angiography</td>
<td>MACE (overall)&lt;br&gt;Death: N = 15 (cardiac N = 7, noncardiac N = 8)&lt;br&gt;Mi: N = 7&lt;br&gt;Ischemia (+) N = 36&lt;br&gt;MACE: 15%&lt;br&gt;Cardiac death: 8.2%&lt;br&gt;Ischemia (-) N = 132&lt;br&gt;MACE: 0.3%&lt;br&gt;Cardiac death: 0.02%&lt;br&gt;ISCH-SCORE&lt;br&gt;MACE HR 1.49, 95% CI 1.31 to 1.69; p&lt;0.0001</td>
<td>Fair</td>
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</tbody>
</table>
Table 17. Summary of findings for KQ 3 (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>NIT and Reference Test</th>
<th>Outcomes</th>
<th>Quality Score</th>
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</thead>
<tbody>
<tr>
<td>Shaw, et al., 2011</td>
<td>Multicenter RCT</td>
<td>N overall: 772</td>
<td>NITs: Exercise ECG, SPECT</td>
<td>MACE: Composite of cardiac death, nonfatal MI, or hospital admission for an acute coronary syndrome or heart failure</td>
<td>Fair</td>
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<td></td>
<td>Enrollment: NR</td>
<td>Women: 772</td>
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<td>MACE-free survival was identical (98%) for women randomized to the exercise ECG arm or SPECT arm (p = 0.59)</td>
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<td>Followup: 24 months</td>
<td>No known CAD</td>
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<td>The observed 2-year MACE rate was 1.7% for ECG and 2.3% for SPECT. The relative hazard for MACE was 1.3 (95% CI, 0.5 to 3.5) for the SPECT arm compared with the ECG arm (P = 0.59)</td>
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<td>Note: The study was underpowered for MACE outcome (post hoc analysis power of 15% at 0.05 significance level)</td>
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<td>An additional 6 women died from noncardiac causes (ECG arm, 0.5%; exercise SPECT arm, 1%; P = 0.39)</td>
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<td>By 6 months, 50% of enrolled women were symptom-free. By 2 years, 60% of ECG and 65% of SPECT women were symptomatic (p = 0.25)</td>
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<td>All Seattle Angina Questionnaire (SAQ) subscales were similar by randomized groups during followup. Cumulative incidence of worsening SAQ angina frequency or stability was 5% for both ECG and SPECT arms (p = 0.75)</td>
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Abbreviations: CAD = coronary artery disease; CMR = cardiac magnetic resonance; ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; HR = hazard ratio; MACE = major adverse cardiovascular event; MI = myocardial infarction; NIT = noninvasive technology; NA = not applicable; NR = not reported; SPECT = single proton emission computed tomography
KQ 3 Summary

We identified 13 comparative studies for KQ 3 that evaluated NITs for risk stratification, prognosis, and decisionmaking affecting clinical outcomes. Two studies reported that women with abnormal CMR and normal coronary angiography had lower event-free survival rates. One study found that an abnormal SPECT resulted in a lower event-free survival rate. One study found that a negative stress ECG and diagnosis of noncardiac chest pain translated into lower event rates. Another study found that a positive stress ECHO had higher prognosis of worse cardiovascular events than a positive stress ECG. However, the studies were small and underpowered, and therefore all these findings would require significant confirmation and replication in larger studies with women. Overall, the literature identified was insufficient in demonstrating that the use of a specific NIT provided incremental risk stratification, prognostic information, or other meaningful information to improve decisionmaking and improve patient outcomes. There were specific limitations for the populations studied, including baseline risk, comparative outcomes, and relationship to diagnostic accuracy.

Key Question 4: Safety Concerns and Risks

KQ 4. Are there significant safety concerns/risks (i.e., radiation exposure, access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, anaphylaxis, arrhythmias) associated with the use of different NITs to diagnose CAD in women with symptoms suspicious for CAD?

Key Points

- Data specific to women on access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, or anaphylaxis associated with NITs were not reported in any of the studies included in this report.
- One study showed a significantly lower rate of supraventricular tachycardia (SVT) in women undergoing dobutamine ECHO compared with men.
- A study of adenosine thallium SPECT showed higher rates of ST depression in women compared with men.
- The results of one study suggested that lifetime attributable risk of both cancer incidence and fatal cancer incidence associated with a single coronary CTA examination was approximately twice as high in women compared with men for 50-, 60-, and 70-year old patients. These estimates are derived from projected data rather than from direct observation. The mean effective dose associated with coronary CTA in four studies ranged from 13.7 to 16.0 mSv for women and 11.1 to 16.4 for men. Radiation safety issues were not discussed in the studies that reported on other NITs.
- Other than higher mean effective radiation doses for coronary CTA studies for women compared with men, from three of the four studies reporting radiation exposure levels, there is insufficient evidence to conclude that safety concerns, risks, or radiation exposure associated with different NITs to diagnose CAD in patients with symptoms suspicious for CAD differ significantly between women and men.
Detailed Synthesis

Tests and procedures are associated with varying degrees of risk. In the case of NITs intended to diagnose CAD in women with symptoms suspicious for CAD, physiological stress, contrast agents, and exposure to radiation may cause immediate or long-term harm. Exercise or pharmacological stressors, for example, may cause arrhythmias, acute or worsening ischemia, hypotension, or cardiac arrest. The contrast agents used in conjunction with ECHO, radionuclide myocardial perfusion imaging, CMR, and coronary CTA can cause anaphylaxis, nephrotoxicity, arrhythmias, or thromboembolism. The Food and Drug Administration (FDA) has issued a boxed warning for ECHO contrast agents that contain microscopic gas-filled spheres as well as for gadolinium-based contrast agents because of apparent risk of causing nephrogenic systemic fibrosis. CMR introduces the unique risk from metallic objects in or on the body (e.g., an aneurysm clip) causing bodily harm if moved by the magnetic forces used in CMR. Furthermore, radiation exposure associated with radionuclide myocardial perfusion imaging and coronary CTA may be carcinogenic. These safety concerns and risks may differ for women compared with men, in part because of differences in radiosensitivity between female and male reproductive organs as well as differences between reproductive organs and other organs or tissues. In the next sections, we summarize the evidence pertaining to safety concerns and risks of NITs among women, as reported and discussed in the studies included in this review (Table 18).

For KQ 4, we examined studies that reported data pertinent to safety concerns or risks associated with the use of NITs to diagnose CAD in women. We identified 13 studies, of which 9 were good quality and 5 were fair quality.

ECG

Five studies reported sex-specific safety data among women who underwent exercise or stress ECG and at least one other diagnostic test for CAD. Of these studies, one was a good-quality RCT, two were good-quality prospective cohort studies, and two were fair-quality prospective cohort studies, representing a total of 413 women. Only one study reported side effects specifically for stress ECG. In the study by Lu, et al., that reported adverse events among 76 hypertensive women who underwent dobutamine ECHO, dipyridamole ECHO, and exercise ECG, the rates of adverse events associated with dobutamine ECHO were 4 percent for symptomatic hypotension, 0 percent for dyspnea, 1 percent for nausea or vomiting, severe headache, flushing, left branch bound block (LBBB), and supraventricular tachycardia (SVT). The other four studies reported side effects associated with ECHO but not with exercise/stress ECG.

ECHO

Data pertaining to safety in women who underwent exercise/stress ECHO testing were reported in six studies. Of these, four were good-quality prospective cohort studies, and two were fair-quality prospective cohort studies, representing a total of 513 women. One study compared dobutamine ECHO with dipyridamole ECHO, and five studies used dobutamine as the pharmacological stressor.

In the study by Lu, et al., that reported adverse events among 76 hypertensive women who underwent dobutamine ECHO, dipyridamole ECHO, and exercise ECG, the rates of adverse events associated with dobutamine ECHO were 4 percent for symptomatic hypotension, 0 percent for dyspnea, 1 percent for nausea or vomiting, 3 percent for severe headache, 0 percent for flushing, 16 percent for rhythm disturbances, 13 percent for frequent and severe PVCs, 1
percent for LBBB, and 1 percent for SVT. In contrast, the rates of adverse events associated with
dipyridamole ECHO were 1 percent for symptomatic hypotension, 3 percent for dyspnea, 7
percent for nausea or vomiting, 12 percent for severe headache, 13 percent for flushing, 4 percent
for rhythm disturbances, 4 percent for frequent and severe PVCs, and 0 percent each for LBBB
and SVT.

In the study by Laurienzo, et al.,39 that evaluated transesophageal dobutamine stress ECHO,
2 out of 84 women (2.4 percent) developed supraventricular arrhythmias, and 3 (3.6 percent) had
intolerance to the probe. The study by Elhendy, et al.,71 reported the symptoms and
complications of dobutamine ECHO (with atropine administered as indicated) in 96 women and
210 men. Rates of reported events among the women were 5 percent for nausea, 0 percent for
flushing, 2 percent for dizziness, 1 percent for anxiety, 4 percent for chills, 5 percent for
headache, 1 percent for symptomatic hypotension, 38 percent for typical angina, 2 percent for
SVT, 0 percent for atrial fibrillation, 1 percent for VT < 10 beats, and 0 percent for VT > 10
beats. Women experienced significantly lower rates (at the p < 0.05 level) of SVT and runs of
VT < 10 beats compared with men who experienced these events at rates of 9 percent and 7
percent, respectively. A study by Lewis, et al.,72 that evaluated dobutamine ECHO in 92 women
reported early termination of the stress test in 2 percent of patients because of VT or sustained
SVT. Eight participants (9 percent) experienced dyspnea or extreme anxiety but did not require
the study to be prematurely terminated, while 18 participants (20 percent) experienced mild
symptoms of nausea and 8 participants (9 percent) had lightheadedness. A study of a cohort of
114 women by Lehmkuhl, et al.,27 reported incidence rates of 2.6 percent for arterial
hypotension, 17 percent for PVCs, and 1.7 percent for nonsustained VT with a maximum of 7
beats associated with dobutamine.

Finally, a study by Ho, et al.,67 reported the following complications during dobutamine
infusion for ECHO testing: frequent ventricular premature contractions (24 percent); chest pain
(24 percent); palpitations (20 percent); frequent atrial premature contractions (18 percent); ST-
segment change (16 percent); atrial fibrillation (2 percent); nonsustained ventricular tachycardia
(2 percent); hypotension (2 percent); headache (2 percent); and yawning (2 percent).

**SPECT**

Data pertaining to safety in women who underwent exercise/stress SPECT were reported in
four prospective cohort studies28,39,67,89 representing 294 women. Three studies were good-
quality and one was fair-quality. The study by Lu, et al.,28 evaluated technetium-99 sestamibi
SPECT, the study by Ho, et al.,67 compared dobutamine ECHO with SPECT, coronary
angiography, and exercise ECG, and two studies, by Laurienzo, et al.,39 and Mohiuddin, et al.,89
evaluated thallium-201 myocardial perfusion imaging. Only one of the four studies89 reported
sex-specific safety data associated with SPECT. In this study of adenosine thallium-201
myocardial perfusion imaging, the rates of adverse effects of adenosine were 41 percent for
flushing, 25 percent for neck or jaw pain, 30 percent for dyspnea, 12 percent for lightheadedness,
10 percent for nausea, 8 percent for headache, 4 percent for second-degree atrioventricular (AV)
block, 1 percent for third-degree AV block, 48 percent for hypotension, and 20 percent for
miscellaneous. Compared with men in the same study, women experienced significantly higher
rates of chest pain (21 percent in men) and ST segment depression (8 percent in men) but had no
significant differences in rates of other side effects.
CMR

Two studies reported data pertaining to safety in women undergoing CMR. A study by Gebker, et al.,95 reported safety data in women undergoing dobutamine stress CMR. This good-quality, prospective cohort study included 204 consecutive women and 541 men with suspected and known CAD scheduled for clinically indicated coronary angiography. In general, severe side effects likely attributable to dobutamine occurred uncommonly but tended to occur less often in women than men, with incidences of severe dyspnea of 1 percent versus 0.7 percent; severe increase in blood pressure of 0.5 percent versus 0.6 percent; paroxysmal atrial fibrillation in 1.5 percent versus 2.4 percent; incidence of ventricular tachycardia in 0.5 percent versus 0.6 percent—all in women compared with men. None of these incidences of side effects in women were statistically significantly different. The study by Merkle, et al.,96 was a good-quality prospective cohort study that included 77 women who underwent both CMR and coronary angiography. This study reported no adverse events associated with adenosine infusion. Neither of the two studies reported adverse events potentially associated with CMR itself; the adverse events assessed in these two studies were limited to the pharmacological stress component of the testing procedure.

Coronary CTA

Four studies included sex-specific data on radiation dose associated with coronary CTA.103,105,113,114 All four were prospective cohort studies that compared coronary CTA with conventional coronary angiography. Of these, two were good quality and two were fair quality. Collectively, they included 486 women.

The estimated radiation exposure associated with a single 64-slice, contrast-enhanced coronary CTA was 14.4 mSv for women compared with 11.1 mSv for men in a study by Weustink, et al., (2007)113 evaluating the accuracy of a 32-slice dual-source CT. A study by Dewey, et al.,103 that used a 16-slice multislice CT scanner reported that the effective dose of a 16-slice coronary CTA examination was significantly higher by approximately 17 percent for women compared with men (13.7 ± 1.2 mSv versus 11.7 ± 0.9 mSv, p < 0.001). The largest contributor to dose among women were the lungs (average of 5.2 mSv, 37.8 percent of the effective dose), with breasts contributing 24.5 percent of the effective dose (3.35 mSv, on average). A study by Dharampal, et al.,105 included 280 women and 636 men. Single-source CT was used for the 385 patients enrolled between July 2004 and March 2006, and dual-source CT was used for the 531 patients enrolled between April 2006 and April 2009. Unlike the previous two studies, this study found the mean effective radiation dose for single-source CT to be slightly higher in men compared with women with levels of 16.4 mSv (SD = 1.1) and 16.0 mSv (SD = 1.3) respectively (p = 0.002). The mean effective radiation dose for dual-source CT was lower compared with single-source CT and was not significantly different between the sexes, with levels of 14.4 mSv (SD = 4.6) and 15.2 mSv (SD = 4.8) for women and men, respectively (p = 0.10).

The fourth study, by Weustink, et al.,114 included sex-specific radiation data and involved 436 symptomatic patients (301 men, 135 women; mean age of 61.6 years) who underwent both conventional coronary angiography and coronary CTA. Standard and ECG pulsing were performed in 327 and 109 patients, respectively. The authors of this study applied the Biological Effects of Ionizing Radiation (BEIR) VII approach115 to estimate sex-dependent and age-dependent whole-body lifetime attributable risk of cancer incidence and mortality from a single coronary CTA examination. Risks were estimated for 50-, 60-, and 70- year-old men and women.
for each of three coronary CTA techniques: no ECG pulsing, standard ECG pulsing, and optimal ECG pulsing. The findings of this study suggest that lifetime attributable risk of both cancer incidence and fatal cancer incidence was approximately double in women, compared with men for 50-, 60-, and 70-year old patients. Attributable risk was highest for no ECG pulsing and lowest for optimal ECG pulsing across all three age groups and both sexes. Attributable risk was highest for 50-year old patients and lowest for 70-year patients across all three ECG pulsing approaches and both sexes. Lifetime attributable risk of cancer associated with a single coronary CTA examination with standard ECG pulsing was estimated at approximately 0.15 percent for 60-year-old women and 0.08 percent for 60-year-old men. Lifetime attributable risk of fatal cancer associated with a single coronary CTA examination with standard ECG pulsing was estimated at approximately 0.13 percent for 60-year-old women and 0.07 percent for 60-year-old men. These estimates are derived from projected data rather than from direct observation. Of note, reproductive organs are generally more sensitive to radiation than other tissues or organs; radiation exposure to reproductive organs may therefore result in higher projected cancer risk.
Table 18. Adverse effects of different NITs for screening of CAD in women

<table>
<thead>
<tr>
<th>Study</th>
<th>Stress Test Modality</th>
<th>Comparator</th>
<th>Study Type</th>
<th>N</th>
<th>Adverse Events in Women</th>
<th>Adverse Events in Men</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lu, et al., 2010&lt;sup&gt;28&lt;/sup&gt;</td>
<td>Exercise ECG</td>
<td>Exercise MIBI scanning Dobutamine ECHO Dipyridamole ECHO</td>
<td>Prospective observational cohort</td>
<td>76 (76)</td>
<td><strong>Arrhythmias</strong>: PVCs in 8 (11%); rhythm disturbances noted in 8 (11%). No development of LBBB or SVT</td>
<td>NA (women-only study)</td>
<td>Good</td>
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</tbody>
</table>

Radiation: NR

Clinical events: No hypotension, dyspnea, nausea or vomiting, severe headache, flushing

Other: NR
<table>
<thead>
<tr>
<th>Study</th>
<th>Stress Test  Modality</th>
<th>Comparator</th>
<th>Study Type</th>
<th>N Women (Total)</th>
<th>Adverse Events in Women</th>
<th>Adverse Events in Men</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lu, et al., 2010</td>
<td>Dobutamine ECHO, Dipyridamole ECHO</td>
<td>Exercise ECG, Exercise MIBI scanning</td>
<td>Prospective observational cohort</td>
<td>76 (76)</td>
<td>Dobutamine vs. dipyridamole Arrhythmias: Rhythm disturbances: 12 (16%) vs. 3 (4%) Frequent and severe PVCs: 10 (13%) vs. 3 (4%) LBBB: 1 (1%) vs. 0 SVT: 1 (1%) vs. 0 Contrast issues: NA Radiation: NR Clinical events: Symptomatic hypotension: 3 (4%) vs. 1 (1%) Dyspnea: 0 vs. 2 (3%) Nausea or vomiting: 1 (1%) vs. 5 (7%) Severe headache: 2 (3%) vs. 9 (12%) Flushing: 0 vs. 10 (13%) Other: NR</td>
<td>NA (women-only study)</td>
<td>Good</td>
</tr>
<tr>
<td>Lehmkuhl, et al., 2007</td>
<td>Dobutamine ECHO</td>
<td>Exercise ECG</td>
<td>Prospective observational cohort</td>
<td>114 (114)</td>
<td>Arrhythmias: Frequent premature ventricular beats (17%) Non-sustained ventricular tachycardia of maximal 7 beats (1.7%) Contrast issues: NA Radiation: NA Clinical events: Arterial hypotension (2.6%) Others: NR</td>
<td>NA (women-only study)</td>
<td>Good</td>
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</table>
Table 18. Adverse effects of different NITs for screening of CAD in women (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Stress Test Modality</th>
<th>Comparator</th>
<th>Study Type</th>
<th>N Women (Total)</th>
<th>Adverse Events in Women</th>
<th>Adverse Events in Men</th>
<th>Quality</th>
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<tbody>
<tr>
<td>Laurienzo, et al., 1997&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Transesophageal dobutamine ECHO</td>
<td>Thallium scintigraphy Exercise ECG Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>84 (84)</td>
<td>Arrhythmias: SVT: 2&lt;br&gt;Contrast issues: NR&lt;br&gt;Radiation: NR&lt;br&gt;Clinical events: Severe chest pain: 14&lt;br&gt;Severe hypertension (&gt; 250 mm Hg): 3&lt;br&gt;Dobutamine-induced chest pain: 61&lt;br&gt;Other: Extensive wall motion abnormalities: 5&lt;br&gt;Intolerance to probe: 3</td>
<td>NA (women-only study)</td>
<td>Good</td>
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<tr>
<td>Elhendy, et al., 1997&lt;sup&gt;35&lt;/sup&gt;</td>
<td>Dobutamine ECHO</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>96 (306)</td>
<td>Arrhythmias: SVT: 2 (2)<em>&lt;br&gt;AF: 0&lt;br&gt;VT &lt; 10 beats: 1 (1)</em>&lt;br&gt;VT &gt; 10 beats: 0&lt;br&gt;*Significantly lower rates in women compared with men; others not significantly different&lt;br&gt;Contrast issues: NR&lt;br&gt;Radiation: NR&lt;br&gt;Clinical events: Nausea: 5 (5)&lt;br&gt;Flushing: 0&lt;br&gt;Dizziness: 2 (2)&lt;br&gt;Anxiety: 1 (1)&lt;br&gt;Chills: 4 (4)&lt;br&gt;Headache: 5 (5)&lt;br&gt;Symptomatic hypotension: 1 (1)&lt;br&gt;Typical angina: 36 (38)&lt;br&gt;Other: NR</td>
<td>Arrhythmias: SVT: 18 (9)<em>&lt;br&gt;AF: 1 (0.5)&lt;br&gt;VT &lt; 10 beats: 14 (7)</em>&lt;br&gt;VT &gt; 10 beats: 1 (0.5)&lt;br&gt;*Significantly lower rates in women compared with men; others not significantly different&lt;br&gt;Contrast issues: NR&lt;br&gt;Radiation: NR&lt;br&gt;Clinical events: Nausea: 4 (2)&lt;br&gt;Flushing: 1 (0.5)&lt;br&gt;Dizziness: 2 (1)&lt;br&gt;Anxiety: 1 (0.5)&lt;br&gt;Chills: 11 (5)&lt;br&gt;Headache: 10 (5)&lt;br&gt;Symptomatic hypotension: 1 (0.5)&lt;br&gt;Typical angina: 92 (44)&lt;br&gt;Other: NR</td>
<td>Fair</td>
</tr>
<tr>
<td>Study</td>
<td>Stress Test Modality</td>
<td>Comparator</td>
<td>Study Type</td>
<td>N Women (Total)</td>
<td>Adverse Events in Women</td>
<td>Adverse Events in Men</td>
<td>Quality</td>
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<tr>
<td>Lewis, et al., 1999&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Dobutamine ECHO</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>92 (92)</td>
<td><strong>Arrhythmias:</strong> VT or sustained SVT requiring termination of study: 2 (2)</td>
<td>NA (women-only study)</td>
<td>Good</td>
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<td>Dyspnea or extreme anxiety: 8 (9)</td>
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<td><strong>Contrast issues:</strong> NR</td>
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<td><strong>Radiation:</strong> NR</td>
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<td><strong>Clinical events:</strong></td>
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<td></td>
<td></td>
<td>Nausea: 18 (20)</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Lightheadedness: 8 (9)</td>
<td></td>
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<td></td>
<td></td>
<td>Anginal chest pain: 15 (16)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Hypotension: 3 (3),</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hypertension: 4 (4),</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Atypical chest pain: 43 (47)</td>
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<td></td>
<td></td>
<td></td>
<td><strong>Other:</strong> NR</td>
<td></td>
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</tr>
<tr>
<td>Ho, et al., 1998&lt;sup&gt;31&lt;/sup&gt;</td>
<td>Dobutamine ECHO</td>
<td>Exercise ECG SPECT Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>51 (51)</td>
<td><strong>Arrhythmias:</strong> Frequent PVCs: 24%</td>
<td>NA (women-only study)</td>
<td>Fair</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Atrial fibrillation: 2%</td>
<td></td>
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<td></td>
<td></td>
<td>Nonsustained VT: 2%</td>
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<td></td>
<td></td>
<td></td>
<td>Frequent PACs: 18%</td>
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<td></td>
<td></td>
<td></td>
<td><strong>Contrast issues:</strong> NR</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Radiation:</strong> NR</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Clinical events:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chest pain: 24%</td>
<td></td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Palpitations: 20%</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hypotension: 2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Headache: 2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Stress Test Modality</td>
<td>Comparator</td>
<td>Study Type</td>
<td>N Women (Total)</td>
<td>Adverse Events in Women</td>
<td>Adverse Events in Men</td>
<td>Quality</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>--------------------------</td>
<td>-----------------------</td>
<td>-----------------------------------------------</td>
<td>----------------</td>
<td>----------------------------------------------------------------------------------------</td>
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<td>---------</td>
</tr>
<tr>
<td>Mohiuddin, et al., 1996&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Adenosine thallium 201 SPECT scans</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>83 (202)</td>
<td><strong>Arrhythmias:</strong> Second-degree AV block: 3 (4) Third-degree AV block: 1 (1.2)</td>
<td><strong>Arrhythmias:</strong> Second-degree AV block: 4 (3) Third-degree AV block: 1 (0.8)</td>
<td>Good</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td><strong>Contrast issues:</strong> NR Radiation: NR Clinical events: Flushing: 34 (41)</td>
<td><strong>Radiation:</strong> NR Clinical events: Flushing: 48 (40)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*Significantly higher rates in women compared with men (p &lt; 0.05); others not significantly different</td>
<td>Miscellaneous 28 (24) *Significantly higher rates in women compared with men (p &lt; 0.05); others not significantly different</td>
<td></td>
</tr>
<tr>
<td>Gebker, et al., 2010&lt;sup&gt;30&lt;/sup&gt;</td>
<td>Dobutamine stress CMR</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>204 (745)</td>
<td><strong>Arrhythmias:</strong> Paroxysmal AF: 3 (1.5), Self-limiting VT: 1 (0.5%)</td>
<td><strong>Arrhythmias:</strong> Paroxysmal AF: 13 (2.4) Self-limiting VT: 3 (0.6)</td>
<td>Good</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td><strong>Contrast issues:</strong> NR Radiation: NR Clinical events: Severe chest pain 4 (2)</td>
<td><strong>Contrast issues:</strong> NR Clinical events: Severe chest pain 20 (3.7) Severe dyspnea 4 (0.7)</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Severe dyspnea 2 (1), Severe increase in blood pressure (&gt;240/12) 1 (0.5) Other: NR</td>
<td>Severe increase in blood pressure (&gt;240/120 mm Hg) 3 (0.6) Other: NR</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>*Rates of side effects were not statistically significantly different from men in the study</td>
<td></td>
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</tr>
</tbody>
</table>

**Note:** NR indicates not reported.
## Table 18. Adverse effects of different NITs for screening of CAD in women (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Stress Test Modality</th>
<th>Comparator</th>
<th>Study Type</th>
<th>N Women (Total)</th>
<th>Adverse Events in Women</th>
<th>Adverse Events in Men</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merkle, et al., 2010⁴⁸⁵</td>
<td>Adenosine stress CMR</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>77 (256)</td>
<td>Arrhythmias: NR</td>
<td>Clinical events: No adverse events associated with adenosine infusion</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Contrast issues: NR</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Radiation: NR</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinical events: No adverse events associated with adenosine infusion</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>*Significantly higher in women compared with men (p &lt; 0.001)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Contrast issues: NR</td>
<td>Contrast issues: NR</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Radiation: 13.7 ± 1.2 mSv*</td>
<td>Radiation: 11.7 ± 0.9 mSv*</td>
<td></td>
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<td></td>
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<td></td>
<td>Clinical events: NR</td>
<td>Clinical events: NR</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other: NR</td>
<td>Other: NR</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*Significantly higher in women compared with men (p &lt; 0.001)</td>
<td>*Significantly higher in women compared with men (p &lt; 0.001)</td>
<td></td>
</tr>
<tr>
<td>Weustink, et al., 2007¹¹³</td>
<td>Coronary CTA (32-slice)</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>21 (100)</td>
<td>Arrhythmias: NR</td>
<td>Arrhythmias: NR</td>
<td>Fair</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>Contrast issues: NR</td>
<td>Contrast issues: NR</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Radiation: 14.4 mSv</td>
<td>Radiation: 11.1 mSv</td>
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<td></td>
<td></td>
<td></td>
<td>Clinical events: NR</td>
<td>Clinical events: NR</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other: NR</td>
<td>Other: NR</td>
<td></td>
</tr>
<tr>
<td>Weustink, et al., 2009¹¹⁴</td>
<td>Coronary CTA (64-slice with optimal ECG pulsing)</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>135 (436)</td>
<td>Arrhythmias: NR</td>
<td>Arrhythmias: NR</td>
<td>Good</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>Contrast issues: NR</td>
<td>Contrast issues: NR</td>
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<td></td>
<td></td>
<td></td>
<td>Radiation: NR</td>
<td>Radiation: NR</td>
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<tr>
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<td></td>
<td></td>
<td>Clinical events: Approximately double lifetime attributable risk of both cancer incidence and fatal cancer incidence in women, compared with men, for 50-, 60-, and 70-year old patients</td>
<td>Clinical events: Approximately double lifetime attributable risk of both cancer incidence and fatal cancer incidence in women, compared with men, for 50-, 60-, and 70-year old patients</td>
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<td></td>
<td></td>
<td>Other: NR</td>
<td>Other: NR</td>
<td></td>
</tr>
</tbody>
</table>
### Table 18. Adverse effects of different NITs for screening of CAD in women (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Stress Test Modality</th>
<th>Comparator</th>
<th>Study Type</th>
<th>N Women (Total)</th>
<th>Adverse Events in Women</th>
<th>Adverse Events in Men</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dharampal, et al., 2011</td>
<td>Coronary CTA (single-source CT, dual-source CT)</td>
<td>Coronary angiography</td>
<td>Prospective observational cohort</td>
<td>280 (916)</td>
<td>Arrhythmia: NR</td>
<td>Arrhythmia: NR</td>
<td>Fair</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Contrast issues: NR</td>
<td>Contrast issues: NR</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Radiation: Single-source CT effective radiation dose: 16.0 ± 1.3 mSv* (SD = 1.3)</td>
<td>Radiation: Single-source CT effective radiation dose: 16.4 ± 1.1 mSv*</td>
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<td></td>
<td></td>
<td>Dual-source CT effective radiation dose: 14.4 ± 4.6 mSv</td>
<td>Dual-source CT effective radiation dose: 15.2 ± 4.8 mSv†</td>
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<td></td>
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<td></td>
<td></td>
<td>*Significantly higher in men compared with women (p = 0.002)</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>†No significant difference in men compared with women (p = 0.10)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AF = atrial fibrillation; CTA = computed tomography angiography; CMR = cardiac magnetic resonance imaging; ECG = electrocardiography; ECHO = echocardiography; MIBI = methoxyisobutyl; NR = not reported; NA = not applicable; PAC = premature atrial contraction; PVC = premature ventricular contraction; SVT = supraventricular tachycardia; VT = ventricular tachycardia
KQ 4 Summary

Thirteen studies reported data pertinent to safety concerns or risks associated with the use of NITs to diagnose CAD in women with suspected CAD. Nine of these studies were rated good quality and four fair quality. Data pertinent to safety concerns specifically for women for a given NIT were reported in six studies for ECHO, five for coronary CTA, two for CMR, and one each for exercise/stress ECG and SPECT.

Data specific to women on access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, or anaphylaxis associated with NITs were not reported in any of the studies included in this review. There was insufficient information in the extant literature to draw conclusions about sex-specific concerns about arrhythmias associated with different NITs. Total-body radiation exposure from coronary CTA examinations appeared to be higher in women compared with men; lifetime attributable risk of both cancer incidence and fatal cancer incidence associated with a single coronary CTA examination was estimated in one study to be twice as high in women compared with men. However, recent advancements in technology have reduced the radiation exposure for coronary CTA, suggesting that these estimates may not be applicable to newer testing protocols. Radiation safety issues were not discussed for NITs other than coronary CTA.
Summary and Discussion

For this report, we conducted a systematic review of the peer-reviewed medical literature to evaluate the accuracy of different NIT modalities for diagnosing CAD in women with symptoms suspicious for CAD.

KQ 1: Diagnostic Accuracy of NITs

For diagnostic accuracy, we identified the following number of studies for each NIT modality:

- **ECG**: 41 studies (13 good quality, 22 fair, 6 poor)
- **ECHO**: 22 studies (8 good, 13 fair, 1 poor)
- **SPECT**: 30 studies (10 good, 15 fair, 5 poor)
- **CMR**: 6 studies (5 good quality, 1 fair)
- **Coronary CTA**: 8 studies (4 good, 4 fair)

We analyzed the results by study population (no known CAD and mixed CAD populations) and by study quality (good quality rating). Table 19 and Figure 41 show the summary sensitivities and specificities for each NIT modality.

<table>
<thead>
<tr>
<th>Modality</th>
<th>Population</th>
<th>Quality of Included Studies</th>
<th>Number of Studies</th>
<th>Number of Women</th>
<th>Summary Sensitivity (95% CI)</th>
<th>Summary Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>No known CAD</td>
<td>All</td>
<td>29</td>
<td>3392</td>
<td>62% (55%-68%)</td>
<td>68% (63%-73%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>10</td>
<td>1410</td>
<td>70% (58%-79%)</td>
<td>62% (53%-69%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>41</td>
<td>4879</td>
<td>61% (54%-67%)</td>
<td>65% (58%-72%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>13</td>
<td>1679</td>
<td>65% (52%-76%)</td>
<td>60% (52%-68%)</td>
</tr>
<tr>
<td>ECHO</td>
<td>No known CAD</td>
<td>All</td>
<td>14</td>
<td>1286</td>
<td>79% (74%-83%)</td>
<td>83% (74%-89%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>5</td>
<td>561</td>
<td>79% (69%-87%)</td>
<td>85% (68%-94%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>22</td>
<td>1873</td>
<td>78% (73%-83%)</td>
<td>86% (79%-91%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>8</td>
<td>807</td>
<td>77% (65%-85%)</td>
<td>89% (76%-95%)</td>
</tr>
<tr>
<td>SPECT</td>
<td>No known CAD</td>
<td>All</td>
<td>14</td>
<td>1000</td>
<td>81% (76%-86%)</td>
<td>78% (69%-84%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>4</td>
<td>394</td>
<td>83% (52%-95%)</td>
<td>72% (37%-92%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>30</td>
<td>2146</td>
<td>82% (77%-87%)</td>
<td>81% (74%-86%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>10</td>
<td>982</td>
<td>82% (72%-88%)</td>
<td>79% (66%-87%)</td>
</tr>
<tr>
<td>CMR</td>
<td>No known CAD</td>
<td>All</td>
<td>5</td>
<td>501</td>
<td>72% (55%-85%)</td>
<td>84% (69%-93%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>5</td>
<td>501</td>
<td>72% (55%-85%)</td>
<td>84% (69%-93%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>6</td>
<td>777</td>
<td>78% (61%-89%)</td>
<td>84% (74%-90%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>5</td>
<td>610</td>
<td>76% (55%-89%)</td>
<td>84% (72%-91%)</td>
</tr>
<tr>
<td>Coronary CTA</td>
<td>No known CAD</td>
<td>All</td>
<td>5</td>
<td>474</td>
<td>93% (69%-99%)</td>
<td>77% (54%-91%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>3</td>
<td>124</td>
<td>85% (26%-99%)</td>
<td>73% (17%-97%)</td>
</tr>
<tr>
<td></td>
<td>Mixed population</td>
<td>All</td>
<td>8</td>
<td>690</td>
<td>94% (81%-98%)</td>
<td>87% (68%-96%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
<td>4</td>
<td>201</td>
<td>83% (58%-94%)</td>
<td>77% (40%-94%)</td>
</tr>
</tbody>
</table>
Abbreviations: CAD = coronary artery disease; CI = confidence interval; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; SPECT = single proton emission computed tomography

Figure 41. Summary of accuracy of NITs for diagnosing CAD in women with no known CAD (all studies)

Overall, within a given modality, the summary sensitivities and specificities were similar for both types of populations (known and no known CAD) and for all studies when compared with good-quality studies. When accounting for only the good-quality studies, it appears that the diagnostic accuracy of detecting CAD in women was better (in descending order) for coronary CTA, SPECT, ECHO, CMR, and ECG. For the newer technologies (i.e., coronary CTA and CMR), more studies in women would be needed to support these findings since the 95% CIs were quite wide. In testing for a statistically significant difference between the diagnostic accuracy of testing modalities in women, our analyses determined that for women with no previously known CAD, there were differences between the performance of the available modalities (p < 0.001). The sensitivity of ECHO and SPECT was significantly greater than that of ECG. Specificity of ECG was less than that of CMR (borderline) and of ECHO. In the subset of studies that were good-quality and where there was no known CAD in the included population, our analyses again demonstrated differences between performance of tests (p = 0.006) with the specificity of ECG being less than that of CMR and ECHO.

To minimize the risk of spectrum bias, our primary analysis focused on women with no known CAD. We also explored mixed populations of women with known and no known CAD in sensitivity analyses. These analyses did not demonstrate a significant difference in terms of the sensitivities and specificities from our primary analysis. We also explored the prevalence of CAD across the different NIT modality studies. The mean prevalences and 95% CIs for ECG, SPECT, ECHO, CMR, and coronary CTA with the population of women with no previously known CAD was 0.41 (0.36 to 0.46), 0.44 (0.34 to 0.55), 0.43 (0.37 to 0.50), 0.26 (0.14 to 0.44), and 0.29 (0.13 to 0.54), respectively. We evaluated whether these prevalences were different across modalities using a random-effects model and did not find a statistically significant difference (p = 0.17).

We assessed the risk of verification bias by exploring the studies in our analysis that did not complete a coronary catheterization in all of the patients who underwent the NIT. In the population of women with no previously known CAD, this represented one study of SPECT.
one study of ECHO,\textsuperscript{79} three studies of ECG,\textsuperscript{29,52,58} and no studies of CMR or coronary CTA. Given the small number of total studies with this potential bias, we felt confident that our primary results were minimized for verification bias. We explored the potential for publication bias across the different modalities in our four populations of interest (studies of women with no known CAD, good-quality studies of women with no known CAD, studies of women from mixed populations, and good-quality studies of women from mixed populations). Our analyses did not provide evidence for publication bias, with our p values ranging from 0.093 to 0.95.

Table 20 shows the GRADE for the accuracy of all the NIT modalities in women with no known CAD. The number of observational studies, summary sensitivity/specificity results, and starting grade are listed for each modality. The change in the GRADE score—based on the risk of bias, consistency, directness, precision, and publication bias—is designated as “0” for no change and “-1” for a decrease due to inconsistency or imprecision. The overall strength of evidence was then determined for each modality.
Table 20. GRADE table for accuracy of NIT modalities in women with no known CAD

<table>
<thead>
<tr>
<th>NIT and Outcome</th>
<th>Quantity and Type of Evidence</th>
<th>Finding</th>
<th>Starting Grade</th>
<th>Decrease GRADE</th>
<th>GRADE of Evidence for Outcome</th>
<th>Overall GRADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMR</td>
<td>5</td>
<td>72%</td>
<td>High</td>
<td>-1</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>5</td>
<td>84%</td>
<td>High</td>
<td>-1</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>Specificity</td>
<td>5</td>
<td>93%</td>
<td>High</td>
<td>-1</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>Coronary CTA</td>
<td>5</td>
<td>77%</td>
<td>High</td>
<td>-1</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>ECG</td>
<td>29</td>
<td>62%</td>
<td>High</td>
<td>0</td>
<td>0</td>
<td>High</td>
</tr>
<tr>
<td>Specificity</td>
<td>29</td>
<td>68%</td>
<td>High</td>
<td>0</td>
<td>0</td>
<td>High</td>
</tr>
<tr>
<td>ECHO</td>
<td>14</td>
<td>79%</td>
<td>High</td>
<td>0</td>
<td>0</td>
<td>High</td>
</tr>
<tr>
<td>Specificity</td>
<td>14</td>
<td>83%</td>
<td>High</td>
<td>0</td>
<td>0</td>
<td>High</td>
</tr>
<tr>
<td>SPECT</td>
<td>14</td>
<td>81%</td>
<td>High</td>
<td>0</td>
<td>0</td>
<td>High</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>14</td>
<td>78%</td>
<td>High</td>
<td>0</td>
<td>0</td>
<td>High</td>
</tr>
<tr>
<td>Specificity</td>
<td>14</td>
<td>78%</td>
<td>High</td>
<td>0</td>
<td>0</td>
<td>High</td>
</tr>
</tbody>
</table>

Abbreviations: CAD = coronary artery disease; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; SPECT = single proton emission computed tomography
KQ 2: Predictors of Diagnostic Accuracy

The predictors of diagnostic accuracy of the various NIT modalities in women were seldom reported. From 11 studies (4 good quality, 5 fair, and 2 poor), the predictors assessed included (1) postmenopausal women ages 55 to 64 (1 study), (2) race/ethnicity (2 studies), (3) heart size (4 studies), (4) pretest probability (3 studies), and (5) use of beta blocker medications (1 study). Despite widespread acknowledgment that patient variables can affect the accuracy of NITs, we identified no studies examining the influence of age alone, functional status, or body size on diagnostic accuracy in women. In terms of the NIT modality, we found four studies of stress ECHO, six studies of stress ECG, two studies of CMR, and four studies of SPECT that reported these predictors. There was significant variability in diagnostic accuracy as well as significant heterogeneity in the types of the predictors reported in the NIT literature. From a limited number of studies, it appeared that (1) the presence of LVH reduced the specificity of stress ECG, SPECT, and ECHO, (2) the use of beta blocker agents reduced the specificity of stress ECG and the sensitivity and specificity of SPECT, and (3) the positive predictive value increased as the pretest probability rose for ECG and ECHO.

KQ 3: Improving Risk Stratification, Decisionmaking, and Outcomes

An essential clinical question in the management of women with suspected CAD is whether NITs have the ability to provide risk stratification (low, medium, or high risk) and prognostic information (good, fair, or poor); inform decisionmaking about treatment options (medical therapy or revascularization); and affect clinical outcomes (MI, angina, quality of life, hospitalization, and death). From 13 comparative studies (3 good quality, 9 fair, 1 poor), we found 8 studies assessing risk stratification and prognostic information, 2 studies assessing decisionmaking for treatment options, and 4 studies that provided comparative clinical outcomes. Most of these findings came from subpopulations of the WISE study and assessed the prognosis and outcomes of women with normal coronary arteries on coronary angiography who underwent CMR and exercise/stress ECG. Women with normal coronary arteries by angiography and abnormal CMR or exercise ECG were more likely to have future cardiac events when compared with women with normal CMR or stress ECG findings. Therefore, the study authors speculated that microvascular coronary disease could be the cause of the abnormal NIT findings and an increase in cardiovascular events. One study found that an abnormal SPECT resulted in a lower event-free survival rate. One study found that a negative stress ECG and diagnosis of noncardiac chest pain translated into lower event rates. Another study found that a positive stress ECHO had higher prognosis of worse cardiovascular events than a positive stress ECG. However, all these findings would require significant confirmation and replication in larger studies with women. Overall, the level of evidence was insufficient to make any conclusions about the relative utility of different NITs to provide risk stratification and prognostic information, inform decisionmaking, or impact clinical outcomes.

KQ 4: Safety Concerns

The safety concerns and risks to women undergoing NIT procedures were underreported in the literature. We identified 13 studies (9 good quality, 4 fair) with safety data on the following modalities: (1) stress ECG (4 studies), (2) ECHO (6 studies), (3) SPECT (3 studies), (4) CMR (2 studies), and (5) coronary CTA (5 studies). One study showed a significantly lower rate of SVT in women undergoing dobutamine ECHO. A study of adenosine thallium SPECT showed higher
rates of ST depression in women. Four studies showed higher mean effective radiation dose or higher lifetime attributable risk of cancer incidence in women compared with men. However, recent advancements in technology and revised testing protocols have reduced the radiation exposure for coronary CTA. Radiation safety issues were not discussed in other NIT modalities that employ radiation exposure (i.e., SPECT, PET, MIBI scans). The remaining studies did not show any significant adverse events in women compared with men. However, we did not find data specific to women on access site complications, contrast-agent induced nephropathy, nephrogenic systemic fibrosis, or anaphylaxis.

Discussion

In summary, the findings of this comparative effectiveness review provide evidence for the accuracy of exercise/stress ECG, ECHO, SPECT, CMR, and coronary CTA used for diagnosing CAD in women. The diagnostic accuracy appears to be consistent over time except for the sensitivity of CMR, which appears to be increasing over time (although the large confidence intervals reflect the underlying uncertainty in this measure). We are confident that the summary statistics for ECG, ECHO, and SPECT are robust and unlikely to change with the addition of new studies based on both the number of good-quality studies comparing these modalities with coronary angiography and the tight confidence intervals. More good-quality studies comparing CMR or coronary CTA with coronary angiography in the no-known CAD population and reporting sex-based results are needed to strengthen the summary statistics for those modalities. Of note, this report focused on clinical comparative effectiveness, and so the cost of the various diagnostic strategies was not evaluated.

Decisions around performing tests (either noninvasive or invasive) in patients with symptoms suspicious for CAD revolve around first understanding the pretest probability and testing/action thresholds for patients from the AHA/ACC stable angina guidelines and appropriate use criteria for the various NIT modalities. Pretest probability is classically defined by age, sex, and type of chest pain (e.g., Diamond-Forrester or CASS study), or the Duke database criteria, which adds risk factors/comorbidities. Specifically, clinicians faced with patients who have a guideline-defined low-to-intermediate pretest probability of CAD may decide to obtain a noninvasive test, ideally with a high negative predictive value in this population and low risk of adverse events, in order to “rule out” disease. These may be patients with atypical chest pain (e.g., reflux or musculoskeletal disease) who are concerned about a heart problem and who require reassurance that their symptoms are not cardiac in origin. In contrast, in patients with high pretest probability of CAD (greater than 90 percent chance), a test with very high positive predictive value in this population and potentially more risk may be chosen since the disease of interest is thought to be present; in these cases, invasive angiography—the gold standard—is recommended by the current clinical practice guidelines. Finally, it is the spectrum of intermediate probability between 10 and 90 percent for which the clinicians must choose noninvasive tests that provide the right balance of sensitivity, specificity, and clinical risk to warrant testing. The choice of NIT may differ by clinician preference, availability, or setting (outpatient versus chest pain unit of an emergency department).

It is in this context that the findings of this report on the effectiveness of NITs in women must be considered. First, women are thought to be at lower pretest probability of CAD when evaluated in comparison with men of the same age. When comorbidities or risk factors are taken into account, the pretest likelihood increases with a higher number of comorbidities. Second, women susceptible to some of the adverse effects of testing may have poor test performance or
have higher rates of complication from invasive arterial access. Third, because of body shape and limited functional capacity, women may not obtain the same test performance that men do from noninvasive testing. Finally, because of the lack of full representation of women across the spectrum of disease, the available literature may not provide data on performance at the ends of the probability spectrum. Spectrum bias may be present since the studies we evaluated had potentially varied populations and varied disease definitions. However, this review has made a step forward in reducing the risk of spectrum bias for women by focusing on the no-known CAD subpopulation. By requiring coronary angiography as the gold standard, the pretest probability may be higher in the study population than in a routine clinical population that has a mixture of low-, intermediate-, and high-risk populations.

While readers may assume that requiring coronary angiography as the comparator would bias this report toward a higher risk CAD population, we found that the mean CAD prevalence ranged from 0.26 to 0.44; thus there was a broad spectrum of CAD prevalence in these studies. In fact, the range of CAD prevalence in this review is similar to a recent analysis of a large administrative database of patients referred for coronary angiography in which the prevalence of significant obstructive disease was 38 to 40 percent. The patient population that does not require coronary angiography can be characterized as having symptoms with low suspicion for CAD or pretest probability of less than 10 percent (note that all included studies enrolled patients with “suspected CAD”). Thus, results from this review would not apply to patients with low pretest probability of disease (e.g., gastroesophageal reflux, musculoskeletal pain, or panic attacks) where an NIT may be performed for clinical reassurance that their symptoms are noncardiac in origin.

In general, because there are few patients with high pretest probability, most clinicians would prefer to have patients undergo one NIT prior to determining a treatment choice or referral to coronary angiography. Circumstances where patients may require more than one NIT include the detection of lesions suspicious for obstructive CAD on coronary CTA with a need to assess for ischemia from stress ECHO or SPECT prior to revascularization. Our review did not identify studies that discussed the order in which different NITs were used for evaluating CAD. In fact, multiple testing or layered-testing strategies are areas where significant research is needed.

The current data suggest that NITs with higher sensitivity include coronary CTA and SPECT, and stress ECHO may represent an NIT with higher specificity. Stress CMR shows emerging data that may be in the upper range for both sensitivity and specificity. Additionally, the findings also demonstrate that NIT performance in women is not as good as in men, likely due to the reasons addressed above. The accuracy may also be location or operator dependent, and thus the results of published studies conducted at highly specialized centers may not uniformly apply to those seen in routine practice. Choice of NIT—and whether to use exercise or pharmacological stress imaging—may be influenced by functional capacity, which tends to be lower in women compared with men. Of note, the accuracy data for NIT modalities in men appeared a little higher than expected, which is likely because the published literature combined the accuracy data for men and women. Taken in context, these findings support the current ACC/AHA recommendations and studies on noninvasive testing in women.

Women are more likely than men to have false positive stress tests; i.e., abnormal stress imaging with nonobstructive CAD on coronary angiography. In fact, up to 9 percent of women presenting with acute coronary syndrome will not have obstructive CAD when they undergo coronary angiography for potential PCI. Some experts suggest that these phenomena are due
to the presence of microvascular obstruction, the incidence of which is hard to determine since there is no clear diagnostic test used to establish the diagnosis.

Currently, there is debate on whether NITs that measure heart function abnormalities (ECG abnormalities, wall motion abnormality, ischemia), including exercise ECG, stress ECHO, and cardiac nuclear imaging, are equivalent or inferior to NITs that measure anatomic abnormalities (detection of CAD) by CMR or coronary CTA. Will knowing the coronary anatomy (nonobstructive or obstructive) in symptomatic patients lead to better implementation of secondary measures—control of blood pressure, diabetes, and hyperlipidemia—to reduce future cardiac events? Or is it more important to intervene with medications and/or revascularization when ischemia is present? Though this review does not answer these important questions, we describe this evidence gap in the Future Research section.

**Limitations of This Review**

Despite identifying 104 studies (110 articles) that met the inclusion criteria, this systematic review has several limitations. First, our search focused on comparator studies of the various NITs with a gold standard of coronary angiography for establishing the diagnosis of CAD in symptomatic patients. While this focus was adequate for identifying studies to assess the diagnostic accuracy of the NIT modalities in women, we found very few comparative studies that reported the influence of clinical characteristics or patient demographics on diagnostic accuracy. Few comparative studies (NIT versus coronary angiography, or NIT versus NIT) provided information on incremental risk stratification, prognostic information, or meaningful information regarding decisionmaking, and few reported the significant risks in women. Study results on these issues were reported for the total patient population and did not separate the effects by sex. Many of the included studies were single-sex (women) studies and limited our ability to fully evaluate sex differences. Also, by focusing on symptomatic patients, this report did not review the use of coronary artery calcium scoring for asymptomatic, high-risk populations.

We are aware that there are several noncomparator studies of each of the NIT modalities that address these issues in women since routine clinical care does not require two NIT modalities or an NIT modality plus coronary angiography for the diagnostic workup of suspected CAD. Given the focus on comparative effectiveness, we did not include these noncomparator studies in our review. By focusing the review on comparative studies, however, we are reducing the bias that is inherent in noncomparative studies. Noncomparative studies have selection, spectrum, and intervention biases for the following reasons: the choice of NIT is determined by the treating provider; a subset of patients with indeterminate or positive results are referred for further NIT testing or coronary angiography; and the clinical outcomes may be influenced by the medical treatments or revascularization options that are offered. Second, the sample size and low representation of women in most of the comparator studies may affect the authors’ ability to analyze the results by sex, therefore reducing the number of studies reporting these findings separately. Third, most studies lacked long-term followup of the patient population, which affected our ability to find studies that reported prognostic information on how the different NITs influenced clinical outcomes. Finally, our summary of the harms and risks of NITs is limited by the lack of disclosure of periprocedural and postprocedural complications in most of the studies.
Conclusions

This systematic review has provided evidence for the summary sensitivities and specificities of exercise/stress ECG, ECHO, SPECT, CMR, and coronary CTA compared with coronary angiography in women. There was limited or insufficient evidence on the influence of clinical and demographic factors on comparative diagnostic accuracy, risk stratification, prognostic information, treatment decisions, clinical outcomes, and harms from different NITs specifically in women. Modifying the search criteria to include noncomparator studies of NIT modalities may increase the number of studies that address this limitation. Table 21 summarizes the strength of supporting evidence for each KQ.
Table 21. Summary of key findings

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ 1: Diagnostic accuracy of NITs in women</td>
<td>ECG: High ECHO: High SPECT: High CMR: Low Coronary CTA: Low</td>
<td>94 studies described the diagnostic accuracy of NITs in comparison to another NIT or coronary angiography in women. Of these 94 studies, 78 studies included sufficient data to estimate the sensitivity and specificity of the NIT compared with coronary angiography. Summary from all studies with no known CAD: 41 studies (13 good quality, 22 fair, 6 poor) of exercise ECG showed a summary sensitivity of 62% and specificity of 68%. 22 studies (8 good quality, 13 fair, 1 poor) of exercise/stress ECHO showed a summary sensitivity of 79% and specificity of 83%. 30 studies (10 good quality, 15 fair, 5 poor) of exercise/stress radionuclide perfusion imaging (SPECT, PET) showed a summary sensitivity of 81% and specificity of 78%. 6 studies (5 good quality, 1 fair) of CMR imaging showed a summary sensitivity of 72% and specificity of 84%. 8 studies (4 good quality, 4 fair) of coronary CTA showed a summary sensitivity of 93% and specificity 77%. Overall, within a given modality, the summary sensitivities and specificities were similar for both types of populations (mixed populations of known and unknown CAD and no known CAD) and for all studies when compared with good-quality studies. When accounting for only the good-quality studies, it appeared that the diagnostic accuracy of detecting CAD in women with unknown CAD was better (in descending order) for coronary CTA, SPECT, ECHO, CMR, and ECG. For the newer technologies (i.e., coronary CTA and CMR), more studies in women would be needed to support these findings since the 95% CIs were quite wide. In testing for a statistically significant difference between the diagnostic accuracy of testing modalities in women, our analyses determined that for women with no previously known CAD, there were differences between the performance of the available modalities (p &lt; 0.001). The sensitivity of ECHO and SPECT was significantly higher than that of ECG. Specificity of ECG was less than that of CMR (borderline) and of ECHO. In the subset of studies that were good-quality and where there was no known CAD in the included population, our analyses again demonstrated differences between performance of tests (p = 0.006) with the specificity of ECG being less than that of CMR and ECHO.</td>
</tr>
</tbody>
</table>
Table 21. Summary of key findings (continued)

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>(KQ 1 continued)</td>
<td></td>
<td>Sensitivity analyses exploring mixed populations of women with known and no known CAD showed no statistically significant difference in the sensitivities and specificities from our primary analysis. An analysis exploring the prevalence of CAD across the different NIT modality studies also showed no statistically significant difference. In addition, there were very few studies (1 SPECT, 1 ECHO, and 3 ECG) that did not complete a coronary angiography in all patients who underwent the NIT; therefore the results are minimized for verification bias. Finally we found no evidence of publication bias across the different modalities in our 4 populations of interest (studies of women with no known CAD, good-quality studies of women with no known CAD, studies of women from mixed populations, and good-quality studies of women from mixed populations).</td>
</tr>
<tr>
<td>KQ 2: Predictors of diagnostic accuracy in women</td>
<td>Insufficient</td>
<td>11 studies (4 good quality, 5 fair, 2 poor) described diagnostic accuracy, and 9 of these examined predictors of diagnostic accuracy of different NITs in women. Summary: The predictors assessed included (1) postmenopausal women ages 55 to 64 (1 study), (2) race/ethnicity (2 studies), (3) heart size (4 studies), (4) pretest probability (3 studies), and (5) use of beta blocker medications (1 study). We identified no studies examining the influence of age alone, functional status, or body size on diagnostic accuracy in women. In terms of the NIT modality, we found four studies of stress ECHO, six studies of stress ECG, two studies of CMR, and four studies of SPECT that reported these predictors. Insufficient evidence was available to draw definitive conclusions about predictors given the small number of studies for each predictor and for each modality, as well as the combination of predictor by modality.</td>
</tr>
<tr>
<td>KQ 3: Improving risk stratification, decisionmaking, and outcomes in women</td>
<td>Insufficient</td>
<td>13 studies (3 good quality, 9 fair, 1 poor) reported prognostic, outcome, or decisionmaking data comparing one NIT with another NIT or with coronary angiography in women with symptoms suspicious for CAD. Summary: We found 8 studies assessing risk stratification and prognostic information, 2 studies assessing decisionmaking for treatment options, and 4 studies that provided comparative clinical outcomes. There were insufficient data to demonstrate that the use of specific NITs (compared with coronary angiography) routinely provided incremental risk stratification, prognostic information, or other meaningful information to improve decisionmaking and improve patient outcomes. Most findings reported in the literature would require significant confirmation and replication in larger studies with women.</td>
</tr>
</tbody>
</table>
### Table 21. Summary of key findings (continued)

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Strength of Evidence</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ 4: Safety concerns</td>
<td>Insufficient</td>
<td>13 studies (9 good quality, 4 fair) reported data pertinent to safety concerns or risks associated with the use of NITs to diagnose CAD in women with symptoms suspicious for CAD. Summary: Safety data were reported on the following modalities: (1) stress ECG (4 studies), (2) ECHO (6 studies), (3) SPECT (3 studies), (4) CMR (2 studies), and (5) coronary CTA (4 studies). Data specific to women on access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, or anaphylaxis associated with NITs were not reported in any of the studies included in this report. Other than higher mean effective radiation doses for coronary CTA studies for women compared with men (from 3 out of 4 studies reporting radiation exposure levels), the extant literature does not provide sufficient evidence to conclude whether safety concerns, risks, or radiation exposure associated with different NITs to diagnose CAD in patients with suspected CAD differ significantly between women and men.</td>
</tr>
</tbody>
</table>
Future Research

This comprehensive review of the comparative effectiveness of NIT modalities for diagnosing women with suspected CAD identified numerous gaps in evidence that would be suitable for future research and for improving the reporting of findings of NIT studies in the published literature.

**Randomized trials comparing functional versus anatomic modalities.** Almost all the studies reviewed were prospective observational studies where patients already scheduled for coronary angiography also underwent one or two NIT modalities to assess the diagnostic accuracy of the NITs. In routine clinical practice, clinicians order one type of NIT modality based on a patient’s ability to exercise, test availability, and clinician preference. Exercise ECG, stress ECHO, and nuclear imaging all measure functional parameters to assess for ischemia and obstructive CAD. Newer technologies such as coronary CTA and CMR offer clinicians the ability to evaluate anatomic parameters to assess both nonobstructive and obstructive CAD. A comparison of a functional testing strategy to an anatomic testing strategy for patients with symptomatic chest pain is currently being done in two large clinical trials (PROMISE [NCT001174550] and RESCUE [NCT01262625]). The information from these clinical trials could inform how the choice of an NIT modality affects the prognosis, treatment decisions, and clinical outcomes.

**Studies assessing outcomes beyond diagnostic accuracy.** Our review found very few comparative NIT studies that looked at the risk stratification, prognostic information, treatment decisions, and clinical outcomes. Future studies, whether observational or controlled clinical trials, should have long-term followup of patient cohorts to assess these factors. This is important because a positive NIT result could lead to further testing to establish the diagnosis of CAD as well as lead to more attention to secondary prevention for CAD. As stated previously, multiple testing or layered-testing strategies, plus the influence on risk-factor modification (e.g., medication prescriptions and adherence), are areas where significant research is needed.

**Studies of sufficient sample size and representation of women.** Many studies assessing the comparative diagnostic accuracy of an NIT modality with another NIT modality or with coronary angiography did not present a sample size calculation for the numbers needed per group. In addition, after excluding the women-only studies, the trials with both sexes had low representation of women. In order to assess sex differences in NIT diagnostic accuracy or the impact on clinical outcomes, a sufficient sample size is required to have adequate statistical power for subgroup analyses.

**Reporting sex and CAD population subgroups separately.** From 1662 citations, we excluded 1376 (83 percent) for not reporting data on women and 615 (37 percent) for looking only at a population with known CAD. Since publication of the AHRQ report on the use of NITs in women, there has been an increase in the number of studies reporting sex-based differences. We encourage more reporting of women results as well as separating the results from no known CAD and known CAD populations. One challenge we encountered in this review was that the primary data representing the numbers of TP, TN, FP, and FN were not presented in most studies and often needed to be back-calculated based on reported sensitivities and specificities and underlying disease prevalence for our quantitative synthesis. It would aid future comparisons of modalities if study authors were to report the primary data for women and men separately either within the article itself or within an online supplementary appendix.
Assessing clinical and demographic factors that influence diagnostic accuracy. Clinicians are taught that clinical factors such as weight, heart size, functional status, race/ethnicity, sex, age, and menopausal status can influence the diagnostic accuracy of various NIT modalities. However, we found very few comparative studies that looked at the impact of these clinical and demographic factors on the sensitivity and specificity of NIT results. More evidence about predictors affecting diagnostic cardiac testing is needed to support or dispel these long-held notions. Additional studies of the NIT modalities to assess differing symptomatology and timing at presentation, racial differences, various risk profiles, and different settings (outpatient, inpatient, emergency room) would be help to build the evidence base needed for clinical decisionmaking.

Reporting of risk, harms, and/or safety outcomes. Diagnostic procedures to screen for heart disease can result in harmful clinical events (nephropathy, radiation exposure, access site complications). Systematic reporting of adverse events in publications—in total and by sex—should continue to clarify which NIT modalities are safe after they are approved for use in clinical practice.
References


6. Strobeck JE, Shen JT, Singh B, et al. Comparison of a two-lead, computerized, resting ECG signal analysis device, the MultiFunction-CardioGram or MCG (a.k.a. 3DMP), to quantitative coronary angiography for the detection of relevant coronary artery stenosis (>70%)—a meta-analysis of all published trials performed and analyzed in the US. Int J Med Sci 2009;6(4):143-55. PMID: 19381351


30. Raman SV, Donnally MR, McCarthy B. Dobutamine stress cardiac magnetic resonance imaging to detect myocardial ischemia in women. Prev Cardiol 2008;11(3):135-40. PMID: 18607148


33. Hosokawa J, Shen JT, Imhoff M. Computerized 2-lead resting ECG analysis for the detection of relevant coronary artery stenosis in comparison with angiographic findings. Congest Heart Fail 2008;14(5):251-60. PMID: 18983288


41. Morise AP. Are the American College of Cardiology/American Heart Association guidelines for exercise testing for suspected coronary artery disease correct? Chest 2000;118(2):55-41. PMID: 10936152


<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ACC</td>
<td>American College of Cardiology</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>AV</td>
<td>atrioventricular</td>
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<tr>
<td>CABG</td>
<td>coronary artery bypass grafting</td>
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<tr>
<td>CAD</td>
<td>coronary artery disease</td>
</tr>
<tr>
<td>CMR</td>
<td>cardiac magnetic resonance imaging</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>CTA</td>
<td>coronary computed tomography angiography</td>
</tr>
<tr>
<td>ECHO</td>
<td>echocardiography/echocardiogram</td>
</tr>
<tr>
<td>ECG</td>
<td>electrocardiography/electrocardiogram</td>
</tr>
<tr>
<td>KQ</td>
<td>Key Question</td>
</tr>
<tr>
<td>LBBB</td>
<td>left bundle branch block</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricle</td>
</tr>
<tr>
<td>LVH</td>
<td>left ventricular hypertrophy</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarction</td>
</tr>
<tr>
<td>MIBI</td>
<td>methoxyisobutyl</td>
</tr>
<tr>
<td>MPS</td>
<td>myocardial perfusion scintigraphy</td>
</tr>
<tr>
<td>NA</td>
<td>not applicable</td>
</tr>
<tr>
<td>NIT</td>
<td>noninvasive technology</td>
</tr>
<tr>
<td>NR</td>
<td>not reported</td>
</tr>
<tr>
<td>PET</td>
<td>positron emission tomography</td>
</tr>
<tr>
<td>PVC</td>
<td>premature ventricular contractions</td>
</tr>
<tr>
<td>SPECT</td>
<td>single proton emission computed tomography</td>
</tr>
<tr>
<td>SVT</td>
<td>supraventricular tachycardia</td>
</tr>
<tr>
<td>VT</td>
<td>ventricular tachycardia</td>
</tr>
</tbody>
</table>
Appendix A. Exact Search Strings

PubMed® search strategy (September 12, 2011):

(((/diagnosis OR diagnos* OR predict* OR predictive value of tests OR sensitivity OR specificity) OR (sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR diagnos*[Title/Abstract] OR diagnosis[MeSH:noexp] OR diagnostic *[MeSH:noexp] OR diagnosis, differential[MeSH:noexp] OR diagnosis[Subheading:noexp]]) AND ((women OR woman OR female OR females OR sex factors) AND (((CAD[tiab]) OR (coronary artery disease[mesh] OR "coronary artery disease"[tiab] OR coronary disease[mesh] OR "coronary disease"[tiab] OR "coronary heart disease"[tiab])) OR (Chest pain OR dyspnea OR shortness of breath OR angina)) AND (((echocardiography OR echo OR cardiogram) AND ((electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardiogram OR exercise test OR treadmill) OR (single photon emission computed tomography OR SPECT OR positron emission tomography OR "PET" OR myocardial perfusion imaging OR "nuclear scan" OR radionuclide imaging) OR (((cardio* OR heart OR coronary OR cardiac) AND "Tomography, X-Ray Computed"[Mesh]) OR ("CT angiography" OR CTA OR "Cardiac Computed Tomography" OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR "cardiac CT" OR "Cardiovascular CT")) OR ((cardiac OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) OR (cardiac catheterization OR angiography OR invasive coronary angiography OR heart catheterization OR coronary angiography OR "X-ray angiography" OR "Xray angiography"))) OR ((electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardiogram OR exercise test OR treadmill) AND ((echocardiography OR echo OR cardiogram) OR (single photon emission computed tomography OR SPECT OR positron emission tomography OR "PET" OR myocardial perfusion imaging OR "nuclear scan" OR radionuclide imaging) OR (((cardio* OR heart OR coronary OR cardiac) AND "Tomography, X-Ray Computed"[Mesh]) OR ("CT angiography" OR CTA OR "Cardiac Computed Tomography" OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR "cardiac CT" OR "Cardiovascular CT")) OR ((cardiac OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) OR (cardiac catheterization OR angiography OR invasive coronary angiography OR heart catheterization OR coronary angiography OR "X-ray angiography" OR "Xray angiography"))) OR ((single photon emission computed tomography OR SPECT OR...
positron emission tomography OR "PET" OR myocardial perfusion imaging OR "nuclear scan" OR radionuclide imaging) AND ((echocardiography OR echo OR cardigram) OR (electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardigram OR exercise test OR treadmill) OR (((cardio* OR heart OR coronary OR cardiac) AND "Tomography, X-Ray Computed"[Mesh]) OR ("CT angiography" OR CTA OR "Cardiac Computed Tomography" OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR "cardiac CT" OR "Cardiovascular CT")) OR ((cardiac OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) OR (cardiac catheterization OR angiography OR invasive coronary angiography OR heart catheterization OR coronary angiography OR "X-ray angiography" OR "Xray angiography")) OR (((cardio* OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) AND ((echocardiography OR echo OR cardigram) OR (electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardigram OR exercise test OR treadmill) OR (single photon emission computed tomography OR SPECT OR positron emission tomography OR "PET" OR myocardial perfusion imaging OR "nuclear scan" OR radionuclide imaging) OR ((cardiac OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) OR (cardiac catheterization OR angiography OR invasive coronary angiography OR heart catheterization OR coronary angiography OR "X-ray angiography" OR "Xray angiography")) OR (((cardio* OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) AND ((echocardiography OR echo OR cardigram) OR (electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardigram OR exercise test OR treadmill) OR (single photon emission computed tomography OR SPECT OR positron emission tomography OR "PET" OR myocardial perfusion imaging OR "nuclear scan" OR radionuclide imaging) OR ((cardio* OR heart OR coronary OR cardiac) AND "Tomography, X-Ray Computed"[Mesh]) OR ("CT angiography" OR CTA OR "Cardiac Computed Tomography" OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR "cardiac CT" OR "Cardiovascular CT")) OR ((cardiac OR heart OR coronary OR cardio*) AND (magnetic
resonance imaging OR MRI OR Magnetic resonance angiography OR MRA))))))) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp]) NOT (Animals[Mesh:noexp])

Limits:
Publication Date: 2000 – present
Language: English
Embase® search strategy (September 12, 2011):

'echocardiography'/exp OR echo OR echocardiogram AND ('electrocardiography'/exp OR 'electrocardiogram'/exp OR electrocardiography OR ecg OR ekg OR electrocardio* OR mcg OR 'multifunction cardiogram' OR ('cardiopulmonary exercise test'/exp AND 'exercise test'/exp OR exercise AND test) OR treadmill) OR ('echocardiography'/exp OR echo OR echocardiogram AND ('single photon emission computer tomography'/exp OR 'computer assisted emission tomography'/exp OR 'myocardial perfusion imaging'/exp OR 'single photon emission computed tomography' OR spect OR 'positron emission tomography' OR pet OR 'myocardial perfusion imaging' OR 'nuclear scan' OR 'radionuclide imaging' OR 'heart scintiscanning'/exp)) OR ('echocardiography'/exp OR echo OR echocardiogram AND (cardio* OR heart OR coronary OR cardiac) AND ('computer assisted tomography'/exp OR 'computed tomographic angiography'/exp OR 'multidetector computed tomography'/exp OR 'ct angiography' OR cta OR 'cardiac computed tomography' OR 'msct' OR 'multislice computed tomography' OR 'multi-slice computed tomography' OR m dct OR 'multidetector computed tomography' OR 'multi-detector computed tomography' OR 'cardiac ct' OR 'cardiovascular ct')) OR ('echocardiography'/exp OR echo OR echocardiogram AND (cardio* OR heart OR coronary OR cardiac) AND ('nuclear magnetic resonance imaging'/exp OR 'magnetic resonance angiography'/exp OR 'magnetic resonance imaging' OR mri OR 'magnetic resonance angiography' OR mra) OR ('electrocardiography'/exp OR 'electrocardiogram'/exp OR electrocardiography OR ecg OR ekg OR electrocardio* OR mcg OR 'multifunction cardiogram' OR ('cardiopulmonary exercise test'/exp AND 'exercise test'/exp OR exercise AND test) OR treadmill AND (single photon emission computer tomography'/exp OR 'computer assisted emission tomography'/exp OR 'myocardial perfusion imaging'/exp OR 'single photon emission computed tomography' OR spect OR 'positron emission tomography' OR pet OR 'myocardial perfusion imaging' OR 'nuclear scan' OR 'radionuclide imaging' OR 'heart scintiscanning'/exp)) OR ('electrocardiography'/exp OR echo OR echocardiogram AND (cardio* OR heart OR coronary OR cardiac) AND ('computer assisted tomography'/exp OR 'computed tomographic angiography'/exp OR 'multidetector computed tomography'/exp OR 'ct angiography' OR cta OR 'cardiac computed tomography' OR 'msct' OR 'multislice computed tomography' OR 'multi-slice computed tomography' OR m dct OR 'multidetector computed tomography' OR 'multi-detector computed tomography' OR 'cardiac ct' OR 'cardiovascular ct')) OR ('electrocardiography'/exp OR 'electrocardiogram'/exp OR electrocardiography OR ecg OR ekg OR electrocardio* OR mcg OR 'multifunction cardiogram' OR ('cardiopulmonary exercise test'/exp AND 'exercise test'/exp OR exercise AND test) OR treadmill AND (cardio* OR heart OR coronary OR cardiac) AND ('computer assisted tomography'/exp OR 'computed tomographic angiography'/exp OR 'multidetector computed tomography'/exp OR 'ct angiography' OR cta OR 'cardiac computed tomography' OR 'msct' OR 'multislice computed tomography' OR 'multi-slice computed tomography' OR m dct OR 'multidetector computed tomography' OR 'multi-detector computed tomography' OR 'cardiac ct' OR 'cardiovascular ct')) OR ('electrocardiography'/exp OR 'electrocardiogram'/exp OR electrocardiography OR ecg OR ekg OR electrocardio* OR mcg OR 'multifunction cardiogram' OR ('cardiopulmonary exercise test'/exp AND 'exercise test'/exp OR exercise AND test) OR treadmill AND (cardio* OR heart OR coronary OR cardiac) AND ('nuclear magnetic resonance imaging'/exp OR 'magnetic resonance angiography'/exp OR 'magnetic resonance imaging' OR mri OR 'magnetic resonance angiography' OR mra) OR ('single photon emission computer tomography'/exp OR 'computer assisted emission tomography'/exp OR 'myocardial perfusion imaging' OR 'single photon emission computed tomography' OR spect OR 'positron emission tomography' OR pet OR 'myocardial perfusion imaging' OR 'nuclear scan' OR 'radionuclide imaging' OR 'heart scintiscanning'/exp AND (cardio* OR heart OR coronary OR cardiac) AND ('computer assisted tomography'/exp OR 'computed tomographic angiography'/exp OR 'multidetector computed tomography'/exp OR 'ct angiography' OR cta OR 'cardiac computed
Cochrane search strategy (September 12, 2011):  

[Cochrane Central Registry of Controlled Trials and Cochrane Database of Systematic Reviews]  

Chest pain OR dyspnea OR shortness of breath OR angina OR CAD OR coronary artery disease OR coronary disease OR coronary heart disease  

AND  

((echocardiography OR echo OR cardiogram) AND ((electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardiogram OR exercise test OR treadmill) OR (single photon emission computed tomography OR SPECT OR positron emission tomography OR PET OR myocardial perfusion imaging OR nuclear scan OR radionuclide imaging)) OR (((cardio* OR heart OR coronary OR cardiac) AND X-Ray computed Tomography) OR (CT angiography OR CTA OR Cardiac Computed Tomography OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR cardiac CT OR Cardiovascular CT)) OR ((cardiac OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) OR (cardiac catheterization OR angiography OR invasive coronary angiography OR heart catheterization OR coronary angiography OR X-ray angiography OR X-ray angiography)) OR ((electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardiogram OR exercise test OR treadmill) AND (echocardiography OR echo OR cardiogram) OR (single photon emission computed tomography OR SPECT OR positron emission tomography OR PET OR myocardial perfusion imaging OR nuclear scan OR radionuclide imaging)) OR (((cardio* OR heart OR coronary OR cardiac) AND X-Ray computed Tomography) OR (CT angiography OR CTA OR Cardiac Computed Tomography OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR cardiac CT OR Cardiovascular CT)) OR ((cardiac OR heart OR coronary OR cardio*) AND (magnetic resonance imaging OR MRI OR Magnetic resonance angiography OR MRA)) OR (cardiac catheterization OR angiography OR invasive coronary angiography OR heart catheterization OR coronary angiography OR X-ray angiography OR X-ray angiography)) OR ((single photon emission computed tomography OR SPECT OR positron emission tomography OR PET OR myocardial perfusion imaging OR nuclear scan OR radionuclide imaging) AND ((echocardiography OR echo OR cardiogram) OR (electrocardiography OR ECG OR EKG OR electrocardio* OR MCG OR multifunction cardiogram OR exercise test OR treadmill)) OR (((cardio* OR heart OR coronary OR cardiac) AND X-Ray computed Tomography) OR (CT angiography OR CTA OR Cardiac Computed Tomography OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR cardiac CT OR Cardiovascular CT)) OR ((cardiac OR heart OR coronary OR cardiac) AND X-Ray computed Tomography) OR (CT angiography OR CTA OR Cardiac Computed Tomography OR MSCT OR Multislice computed tomography OR Multi-slice computed tomography OR MDCT OR multidetector computed tomography OR multi-detector computed tomography OR cardiac CT OR Cardiovascular CT))
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AND

women OR woman OR female OR females OR sex factors

AND
diagnosis OR diagnos* OR predict* OR predictive value of tests OR sensitivity OR specificity OR sensitive OR diagnostic OR differential diagnosis
Grey Literature Searches:

ClinicalTrials.gov
searched: 12-6-2010

metaRegister of Controlled Trials (mRCT)
searched: 12-6-2010
(noninvasive OR non-invasive OR "non invasive") AND ("coronary artery disease" OR CAD) [no results]
coronary artery disease [26 results scanned for completed trials related to diagnosis - no results]

ClinicalStudyResults.org
searched: 12-6-2010
CAD OR "coronary artery disease" [no results]

WHO: International Clinical Trials Registry Platform Search Portal
searched: 12-6-2010
(noninvasive OR non-invasive OR "non invasive") in Title
AND
("coronary artery disease" OR CAD) in Indication
scanned for completed trials related to diagnosis

CSA Conference Papers Index
searched: 12-6-2010
Search Query #2 KW=(noninvasive or non-invasive or (non invasive)) and KW=(cad or (coronary artery disease)) and KW=(diagnosis or detection or screening) (Copy Query)
24 Published Works results found in Conference Papers Index
Date Range: Earliest to 2011

Scopus
searched: 12-6-2010
Your query: (TITLE-ABS-KEY(screening OR detection OR diagnosis OR assessment)) AND ((TITLE-ABS-KEY(noninvasive OR "non invasive" OR non-invasive)) AND (TITLE-ABS-KEY("coronary artery disease" OR cad))) AND (LIMIT-TO(DOCTYPE, "cp"))
Appendix B. Data Abstraction Elements

I. Study Characteristics

- Study dates
- Study sites
- Geographic location
- Funding source
- Study design
- If discernable: Is this article known to be a report of data from a population discussed in another article?
  - If Yes, note the primary publication for the study by entering the citation information or study identifier (trial name, acronym, or NCT number). Citation information is preferred.
- Testing setting (select all that apply)
  - Emergency Department/ Chest Pain Unit
  - Outpatient
  - Inpatient
  - Other (specify)
  - Not Reported/Unclear
- Duration of longest follow-up after completion of final test. Enter with units (days, weeks, months). NR if Not Reported. Enter NA if Not Applicable (i.e. if the study did not include a follow-up period).
- Was screening and enrollment consecutive?
- Inclusion criteria: Copy/paste inclusion criteria as reported in the article.
- Exclusion criteria: Copy/paste exclusion criteria as reported in the article.
- Study Enrollment
  - Total population
    - Number of subjects enrolled
    - Number of subjects with known CAD
    - Number of subjects without known CAD
    - If applicable, enter the definition of known CAD
  - Female
    - Number of subjects enrolled
    - Number of subjects with known CAD
    - Number of subjects without known CAD
    - If applicable, enter the definition of known CAD
  - Male
    - Number of subjects enrolled
    - Number of subjects with known CAD
    - Number of subjects without known CAD
    - If applicable, enter the definition of known CAD
- Study Completion
  - Total population
II. Baseline Demographics

- No known CAD reported
  - Age in years (Total, Female, and Male)
    - p value (Female vs. Male data)
    - Mean
    - SD
    - Min age
    - Max age
    - 25% IQR
    - 75% IQR
  - Ethnicity (Total, Female, and Male)
    - Hispanic or Latino
    - Not Hispanic or Latino
  - Race (Total, Female, and Male)
    - American Indian or Alaska Native
    - Asian
    - Black or African American
    - Native Hawaiian or other Pacific Islander
    - White
    - Other
    - Multiracial
    - Not reported
  - Was body size reported?
    - If yes, describe the measurement type and units.
    - If yes, provide the characteristics as reported (e.g. range, mean with standard deviation, etc.)
  - Was heart size reported?
    - If yes, describe the measurement type and units.
    - If yes, provide the characteristics as reported (e.g. range, mean with standard deviation, etc.)
  - Was functional status (exercise capacity) reported?
    - If yes, describe the measurement type and units
    - If yes, provide the characteristics as reported (e.g. range, mean with standard deviation, etc.)

- Mixed known/no known CAD reported
  - Age in years (Total, Female, and Male)
    - p value (Female vs. Male data)
- Mean
- SD
- Min age
- Max age
- 25% IQR
- 75% IQR

○ Ethnicity (Total, Female, and Male)
  - Hispanic or Latino
  - Not Hispanic or Latino

○ Race (Total, Female, and Male)
  - American Indian or Alaska Native
  - Asian
  - Black or African American
  - Native Hawaiian or other Pacific Islander
  - White
  - Other
  - Multiracial
  - Not reported

○ Was body size reported?
  - If yes, describe the measurement type and units.
  - If yes, provide the characteristics as reported (e.g. range, mean with standard deviation, etc.)

○ Was heart size reported?
  - If yes, describe the measurement type and units.
  - If yes, provide the characteristics as reported (e.g. range, mean with standard deviation, etc.)

○ Was functional status (exercise capacity) reported?
  - If yes, describe the measurement type and units
  - If yes, provide the characteristics as reported (e.g. range, mean with standard deviation, etc.)

### III. NIT and Comparator Characteristics

- NITs included in study
  - Electrocardiogram (exercise/stress or resting) = ECG
  - Echocardiography (with or without contrast) = ECHO
  - Exercise/stress radionuclide myocardial perfusion imaging (MPI). Includes:
    - Single proton emission computed tomography = SPECT,
    - Positron emission tomography = PET,
    - Scintigraphy
  - Cardiac perfusion and stress magnetic resonance imaging = CMR
  - Multidetector cardiac computed tomography angiography = CTA

### IV. ECG Module

- Type (multiple selections)
  - Exercise stress
  - Pharmacologic stress
- Multifunction Cardiogram [MCG]
  - If exercise stress, type of exercise performed (multiple selections)
    - Treadmill
    - Bicycle
    - Step
    - Other (specify)
    - Not exercise stress
  - If pharmacologic stress, type of agent used.
    - Dobutamine
    - Adenosine
    - Dipyridamole
    - Other (specify)
    - Not pharmacologic stress
- Definition of a positive result
  - $\geq 1$ mm ST depression
  - 1-2 mm ST depression
  - $\geq 2$ mm ST depression
  - Other (specify)

V. Stress ECHO Module
- Type of stressor (multiple selections)
  - Exercise stress
  - Pharmacologic stress
- If exercise stress, type of exercise performed (multiple selections)
  - Treadmill
  - Bicycle
  - Other (specify)
  - Not exercise stress
- If pharmacologic stress, type of agent used.
  - Dobutamine
  - Adenosine
  - Dipyridamole
  - Other (specify)
  - Not pharmacologic stress
- Was contrast agent used?
- Definition of a positive result
  - Wall Motion Abnormality (WMA) at rest and at stress
  - Wall Motion Abnormality (WMA) at stress, but not at rest
  - Wall Motion Abnormality (WMA) not otherwise specified
- If ECG used, definition of a positive result
  - $\geq 1$ mm ST depression
  - 1-2 mm ST depression
  - $\geq 2$ mm ST depression
  - Other (specify)
VI. Exercise/stress myocardial perfusion imaging Module

- Modality
  - Single selection: SPECT, PET, scintigraphy
- Type of stressor
  - Exercise stress, Pharmacologic stress
  - If exercise stress, type of exercise performed.
    - Treadmill
    - Bicycle
    - Other (specify)
    - Not exercise stress
- If pharmacologic stress, type of agent used.
  - Dobutamine
  - Adenosine
  - Dipyridamole
  - Other (specify)
  - Not pharmacologic stress
- Radionuclide used
  - Technetium Tc 99m sestamibi (MIBI)
  - Thallous chloride TL-201 (thallium)
  - Fluorodeoxyglucose (FDG)
  - Other (specify)
- Definition of a positive result
  - Reported by Sum Stress Score (SSS)?
    - If yes, enter threshold value for positive result
  - Reported by % ischemic LV?
    - If yes, enter threshold value for positive result
  - Reported by evidence of ischemia in any segment?
    - If yes, enter number of segments considered a positive result
  - Reported by Transient Ischemic Dilation (or Total Perfusion Deficit)?
    - If yes, enter threshold value for positive result
- If ECG used, definition of a positive result
  - ≥ 1 mm ST depression
  - 1-2 mm ST depression
  - ≥ 2 mm ST depression
  - Other (specify)

VII. Cardiac perfusion and stress magnetic resonance imaging (CMR) Module

- Type of test (multiple selections):
  - Dobutamine cine CMR
  - Vasodilator stress perfusion
  - Delayed enhanced (DE-CMR)
  - Other (specify)
- Type of stressor (multiple selections):
  - Exercise stress
  - Pharmacologic stress
• If exercise stress, type of exercise performed. If not exercise, select “Not exercise stress.” (multiple selections):
  ▪ Bicycle
  ▪ Other (specify)
  ▪ Not exercise stress
• If pharmacologic stress, type of agent used (multiple selections):
  o Dobutamine
  o Adenosine
  o Dipyridamole
  o Other (specify w/free text field)
  o Not pharmacologic stress
• Was contrast agent used?
  ▪ If yes, specify the contrast agent.
• Definition of positive result
  ▪ Reported by perfusion defect?
    ▪ If yes, enter threshold value for positive result
  ▪ MRA of coronary arteries performed?
    ▪ If yes, enter threshold value for positive result
  ▪ Wall Motion Abnormalities (WMA) assessed?
    ▪ If yes, select definition of positive result
      o Wall Motion Abnormality (WMA) at rest and at stress
      o Wall Motion Abnormality (WMA) at stress, but not at rest
      o Wall Motion Abnormality (WMA) not otherwise specified

VIII. Multidetector cardiac computed tomography angiography (CTA) Module
• Was contrast agent used?
  ▪ If yes, specify the contrast agent and dose (including units).
• Number of slices (multiple selections):
  o 4-slice
  o 16-slice
  o 32-slice
  o Other number less than 64 (specify w/text box)
  o 64-slice or greater
• Was calcium score testing performed?
• Definition of positive result (multiple selections):
  ▪ ≥ 50% stenosis
  ▪ ≥ 70% stenosis
  ▪ ≥ 50% Left Main
  ▪ Other (specify)

IX. Diagnostic catheterization Module
• Angiographic definition of disease (multiple selections):
  o ≥ 50% stenosis
X. Modality comparisons
- Specify modality comparisons [one NIT to another (different) NIT, or a NIT to diagnostic cardiac catheterization].

XI. Applicability to Key Questions
- KQ 1:
  - What is the accuracy of one noninvasive technology (NIT) in diagnosing obstructive and nonobstructive CAD when compared to another NIT or to coronary angiography in women with chest pain syndrome?
    - Exercise electrocardiogram (ECG) stress test (including resting ECG technology, such as a multifunctional cardiogram)
    - Exercise/stress echocardiography (ECHO) with or without a contrast agent
    - Exercise/stress radionuclide myocardial perfusion imaging (including single proton emission computed tomography [SPECT] and positron emission tomography [PET])
    - Cardiac perfusion and stress magnetic resonance imaging (CMR)
    - Multidetector cardiac computed tomography angiography (CTA)

- KQ 2:
  - What are the predictors of diagnostic accuracy (age, race/ethnicity, body size, heart size, menopausal status, functional status, stress modality) of different NITs in women?

- KQ 3:
  - Is there evidence that the use of NITs (when compared to other NITs or to diagnostic cardiac catheterization) in women improves:
    a. Risk stratification/prognostic information?
    b. Decisionmaking regarding treatment options (e.g., revascularization, optimal medical therapy)?
    c. Clinical outcomes (e.g., death, myocardial infarction, unstable angina, hospitalization, revascularization, angina relief, quality of life)?

- KQ 4:
  - Are there significant safety concerns/risks (i.e., radiation exposure, access site complications, contrast agent-induced nephropathy, nephrogenic systemic fibrosis, anaphylaxis, arrhythmias) associated with the use of different NITs to diagnose CAD in women with chest pain syndromes?

XII. KQ 1
- Which modality-level comparison(s) from the “NIT and Comparators” form does this data correspond to? Select all that apply. Space is provided for up to 6 modality-level comparisons.
• Enter total N for each category, NR for not reported, or NA for not applicable (Total population, Female, Male)
• Number of subjects with known CAD
• Number of subjects without known CAD
• If applicable, enter the definition of known CAD
• For the modality-level comparison(s) indicated above, does the article present data separately for both “no known CAD” and “mixed known/ no known CAD” populations?
  o If data is reported for a “no known CAD” population, enter age, ethnicity, race, body size, heart size, and functional status information for the “no known CAD” population in the section below labeled “No known CAD.”
  o If data is reported for a “mixed known/ no known CAD” population, enter age, ethnicity, race, body size, heart size, and functional status information for the mixed population in the section below labeled “Mixed known/ no known CAD.”
• Enter by Total population, Female, Male:
  o SD
  o Min age
  o Max age
  o 25% IQR
  o 75% IQR
  o Ethnicity
    ▪ Hispanic
    ▪ Non-Hispanic or Latino
  o Race
    ▪ American Indian or Alaska Native
    ▪ Asian
    ▪ Black or African American
    ▪ Native Hawaiian or other Pacific Islander
    ▪ White
    ▪ Other
    ▪ Multiracial
    ▪ Not reported
  o Was body size reported?
  o Was heart size reported?
  o Was functional status (exercise capacity) reported?

XIII. KQ 2
• Indicate test modalities compared
• Indicate which predictive factor this data addresses
  o Age
  o Race/ethnicity
  o Body size
  o Heart size
  o Menopausal status
  o Functional status

B-8
- Stress modality
  - Indicate CAD status of the population
    - No known CAD
    - Mixed known/ no known CAD
  - Specify the female subgroups analyzed for this predictor and pair of test modalities. Columns are provided to capture up to 5 subgroup categories. Complete only the number needed to capture the data presented in the study.
  - Define the groups
  - Number of patients who received the index test
  - Number of patients who received diagnostic cardiac cath
  - Number of patients with adequate exercise for index test (if exercise is applicable)
  - Number of patients with positive index test
  - Number of patients with negative index test
  - Disease prevalence (\# of patients)
  - Disease prevalence (\%)
  - True positive (\# of patients)
  - True negative (\# of patients)
  - False positive (\# of patients)
  - False negative (\# of patients)
  - Indeterminate or technically inadequate results (\# of patients)
  - Sensitivity (\%)
  - Sensitivity (Std dev)
  - Sensitivity (Upper confidence interval bound)
  - Sensitivity (Lower confidence interval bound)
  - Specificity (\%)
  - Specificity (Std dev)
  - Specificity (Upper confidence interval bound)
  - Specificity (Lower confidence interval bound)
  - Positive predictive value (\%)
  - Positive predictive value (Std dev)
  - Positive predictive value (Upper confidence interval bound)
  - Positive predictive value (Lower confidence interval bound)
  - Negative predictive value (\%)
  - Negative predictive value (Std dev)
  - Negative predictive value (Upper confidence interval bound)
  - Negative predictive value (Lower confidence interval bound)
  - Negative likelihood ratio
  - Positive likelihood ratio
  - Cath results
    - Number of patients with single-vessel disease
    - Number of patients with 2-vessel disease
    - Number of patients with 3-vessel disease
    - Number of patients with Left Main disease

### XIV. KQ 3
- Indicate test modalities compared
• Indicate CAD status of the population
• Does the study provide data on risk stratification/prognostic information?
• Describe the risk/prognostic findings by gender
• Risk/prognostic information
  o Decisionmaking about treatment (Treatments may include: None, Medical management, Invasive management)
  o Describe any decisionmaking findings not captured by gender
• Clinical outcomes measured by Total population, Female, Male: (multiple selections):
  o MI
  o Unstable angina
  o Hospitalization
  o Mortality
  o Revascularization
  o Angina relief
  o Quality of life
  o Composite (specify)

XV. KQ 4a
• Indicate test modalities compared
• Indicate CAD status of the population
• Data by gender for each category of adverse outcome.
  o Average total body radiation exposure (specify units)
  o Access site complications
  o IV site complications
  o Contrast-agent induced nephropathy
  o Nephrogenic systemic fibrosis
  o Anaphylaxis
  o Arrhythmias
• If access site complications were reported, describe how these complications were defined.
• Does the article report tissue-level radiation data?
• Describe tissue-level radiation findings

XVI. KQ 4b
• Does the article report harms data broken down by any demographic factors other than gender? (Gender data is to be captured in form KQ 4a.)
• Indicate test modalities compared
• Indicate CAD status of the population
• Specify the categories for this subgroup analysis. Columns are provided to capture up to 5 categories. Complete only the number needed to capture the data presented in the study. Define the categories, then complete the tables below with as much information as is provided in the study.
• Harms
  o Average total body radiation exposure (specify units)
  o Access site complications
• IV site complications
• Contrast-agent induced nephropathy
• Nephrogenic systemic fibrosis
• Anaphylaxis
• Arrhythmias

• If access site complications were reported, describe how these complications were defined.
• Does the article report tissue-level radiation data?
• Describe tissue-level radiation findings

XVII. Quality Assessment

• QUADAS Tool for Quality Assessment of Studies of Diagnostic Accuracy
• Answer each of the 14 questions below. A user's guide explaining each question and how to score your responses is available in the 2003 QUADAS article here:  http://www.biomedcentral.com/1471-2288/3/25
  1. Was the spectrum of patients representative of the patients who will receive the test in practice?
  2. Were selection criteria clearly described?
  3. Is the reference standard likely to correctly classify the target condition?
  4. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?
  5. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?
  6. Did patients receive the same reference standard regardless of the index test result?
  7. Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?
  8. Was the execution of the index test described in sufficient detail to permit replication of the test?
  9. Was the execution of the reference standard described in sufficient detail to permit its replication?
 10. Were the index test results interpreted without knowledge of the results of the reference standard?
 11. Were the reference standard results interpreted without knowledge of the results of the index test?
 12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?
 13. Were uninterpretable/intermediate test results reported?
 14. Were withdrawals from the study explained?

• Summary Judgment
  o Good (low risk of bias). No major features that risk biased results. RCTs are considered a high study design type, but studies that include consecutive patients representative of the intended sample for whom diagnostic uncertainty exists may also meet this standard. A “good” study avoids the multiple biases to which
medical test studies are subject (e.g., use of an inadequate reference standard, verification bias), and key study features are clearly described, including the comparison groups, measurement of outcomes, and the characteristics of patients who failed to have actual state (diagnosis or prognosis) verified.

- Fair. Susceptible to some bias, but flaws not sufficient to invalidate the results. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

- Poor (high risk of bias). Significant flaws that imply biases of various types that may invalidate the results. The study has significant biases determined a priori to be major or “fatal” (i.e., likely to make the results either uninterpretable or invalid).

- If the study is rated as “Fair” or “Poor,” provide rationale for decision.

XVIII. Applicability Assessment

- Use the PICOTS format to identify specific issues that may limit the applicability of the study as described in the draft Methods Guide for Medical Test Reviews. Indicate the most important limitations affecting applicability, if any, from the list below.

- Population (P)
  - Source of population not described
  - Study population poorly specified
  - Key characteristics not reported

- Intervention (I)
  - Version/instrumentation not specified
  - Training/quality control not described
  - Screening and diagnostic uses mixed

- Comparator (C)
  - Gold standard not applied
  - Correlational data only

- Outcome of use of the test (O)
  - Failure to test “normals” or subset with gold standard
  - Precision of estimates not provided

- Clinical outcomes from test results (O)
  - Populations and study designs heterogeneous with varied findings
  - Data not stratified or adjusted for key predictors

- Timing (T)
  - Sequence of use of other diagnostics unclear
  - Time from results to treatment not reported
  - Order of testing varies across subjects and was not randomly assigned

- Setting (S)
  - Resources available to providers for diagnosis and treatment of condition vary widely
  - Provider type/specialty varies across settings
  - Comparability of care in international settings unclear
Appendix C. List of Included Studies


Hosokawa J, Shen JT, Imhoff M. Computerized 2-lead resting ECG analysis for the detection of relevant coronary artery stenosis in comparison with angiographic findings. Congest Heart Fail 2008;14(5):251-60. PMID: 18983288


Kiat H, Van Train KF, Maddahi J., et al. Development and prospective application of quantitative 2-day stress-rest Tc-99m methoxy isobutyl isonitrile SPECT for the diagnosis of


Laurienzo JM, Cannon RO, 3rd, Quyyumi AA,, et al. Improved specificity of transesophageal dobutamine stress echocardiography compared to standard tests for evaluation of coronary artery disease in women presenting with chest pain. Am J Cardiol 1997;80(11):1402-7. PMID: 9399711


Morise AP. Are the American College of Cardiology/American Heart Association guidelines for exercise testing for suspected coronary artery disease correct? Chest 2000;118(2):535-41. PMID: 10936152


Raman SV, Donnally MR, McCarthy B. Dobutamine stress cardiac magnetic resonance imaging to detect myocardial ischemia in women. Prev Cardiol 2008;11(3):135-40. PMID: 18607148


Roger VL, Pellikka PA, Bell MR., et al. Sex and test verification bias. Impact on the diagnostic value of
exercise echocardiography. Circulation 1997;95(2):405-10. PMID: 9008457


Tailerre R, DePuey EG, Udelson JE,, et al. Comparative diagnostic accuracy of Tl-201 and Tc-99m sestamibi SPECT imaging (perfusion and ECG-gated SPECT) in detecting coronary artery disease in


## Appendix D. Quality and Applicability of Included Studies

Table D-1. Quality, applicability, and relevant Key Questions (KQs)

<table>
<thead>
<tr>
<th>Study</th>
<th>NIT Modality</th>
<th>KQ 1</th>
<th>KQ 2</th>
<th>KQ 3</th>
<th>KQ 4</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
</table>
| Abramson, et al., 2000 | • SPECT/PET/Scintigraphy | X    |      |      |      | Fair    | • Key characteristics not reported
|                        |                        |      |      |      |      |         | • Failure to test “normals” or subset with gold standard
|                        |                        |      |      |      |      |         | • Data not stratified or adjusted for key predictors                                           |
| Agati, et al., 1992    | • ECG • ECHO          | X    |      |      |      | Fair    | • Source of population not described
|                        |                        |      |      |      |      |         | • Key characteristics not reported
|                        |                        |      |      |      |      |         | • Training/quality control not described                                                     |
|                        |                        |      |      |      |      |         | • Precision of estimates not provided                                                        |
| Barolsky, et al., 1979 | • ECG                 | X    |      |      |      | Fair    | • Key characteristics not reported
|                        |                        |      |      |      |      |         | • Training/quality control not described                                                     |
|                        |                        |      |      |      |      |         | • Precision of estimates not provided                                                        |
|                        |                        |      |      |      |      |         | • Data not stratified or adjusted for key predictors                                           |
| Bjornstad, et al., 1995| • ECHO                | X    |      |      |      | Fair    | • Key characteristics not reported
|                        |                        |      |      |      |      |         | • Training/quality control not described                                                     |
|                        |                        |      |      |      |      |         | • Failure to test “normals” or subset with gold standard                                     |
|                        |                        |      |      |      |      |         | • Precision of estimates not provided                                                        |
| Bokhari, et al., 2008  | • ECG • SPECT/PET/scintigraphy | X    |      |      |      | Poor    | • Training/quality control not described                                                     |
|                        |                        |      |      |      |      |         | • Data not stratified or adjusted for key predictors                                           |
|                        |                        |      |      |      |      |         | • Sequence of use of other diagnostics unclear                                               |
| Burgi Wegmann, et al., 2003 | • ECG        | X    |      |      |      | Fair    | • Source of population not described
<p>|                        |                        |      |      |      |      |         | • Study population poorly specified                                                           |
|                        |                        |      |      |      |      |         | • Version/instrumentation not specified                                                       |
|                        |                        |      |      |      |      |         | • Training/quality control not described                                                     |
|                        |                        |      |      |      |      |         | • Sequence of use of other diagnostics unclear                                               |
|                        |                        |      |      |      |      |         | • Comparability of care in international settings unclear                                     |
| Chae, et al., 1993     | • SPECT/PET/scintigraphy | X    |      |      |      | Good    | • Training/quality control not described                                                     |
|                        |                        |      |      |      |      |         | • Precision of estimates not provided                                                        |
| Cin, et al., 2000      | • ECG                | X    | X    |      |      | Poor    | • Training/quality control not described                                                     |
|                        |                        |      |      |      |      |         | • Precision of estimates not provided                                                        |
|                        |                        |      |      |      |      |         | • Data not stratified or adjusted for key predictors                                           |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>NIT Modality</th>
<th>KQ 1</th>
<th>KQ 2</th>
<th>KQ 3</th>
<th>KQ 4</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coelho-Filho, et al., 2011</td>
<td>CMR, Coronary CTA</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>Fair</td>
<td>• Training/quality control not described</td>
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<tr>
<td>DePasquale, et al., 1988</td>
<td>SPECT/PET/scintigraphy</td>
<td>X</td>
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<td>Poor</td>
<td>• Source of population not described</td>
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<td>• Precision of estimates not provided</td>
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<tr>
<td>Dewey, et al., 2008&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>X</td>
<td></td>
<td>Good</td>
<td>• Precision of estimates not provided</td>
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<td>Dewey, et al., 2010&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Good</td>
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<td>Fair</td>
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<td>• Limitation from use of two types of CTA technology within study</td>
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<td>• Precision of estimates not provided</td>
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<td>Dodi, et al., 2001</td>
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<td>Good</td>
<td>• Precision of estimates not provided</td>
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<td>Doyle, et al., 2010&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>Fair</td>
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<td>• Resources available to providers for diagnosis and treatment of condition varied widely</td>
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<td>Elhendy, et al., 1997</td>
<td>ECH, ECHO</td>
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<td>Fair</td>
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<td></td>
<td>• Comparability of care in international settings unclear</td>
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<td>Study</td>
<td>NIT Modality</td>
<td>KQ 1</td>
<td>KQ 2</td>
<td>KQ 3</td>
<td>Quality</td>
<td>Limitations to Applicability</td>
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</table>
| Elhendy, et al., 2006 | • SPECT/PET/scintigraphy | X    |      |      | Fair    | • Study population poorly specified  
• Key characteristics not reported  
• Training/quality control not described  
• Failure to test “normals” or subset with gold standard  
• Comparability of care in international settings unclear |
| Elhendy, et al., 1998 | • ECHO  
• SPECT/PET/scintigraphy | X    |      |      | Good    | • Training/quality control not described |
| Emmett, et al., 2002  | • SPECT/PET/scintigraphy | X    |      |      | Fair    | • Source of population not described  
• Key characteristics not reported  
• Precision of estimates not provided  
• Comparability of care in international settings unclear |
| Faisal, et al., 2007  | • ECG                | X    |      |      | Poor    | • Source of population not described  
• Study population poorly specified  
• Training/quality control not described  
• Failure to test “normals” or subset with gold standard  
• Precision of estimates not provided  
• Sequence of use of other diagnostics unclear  
• Resources available to providers for diagnosis and treatment of condition varied widely |
| Friedman, et al., 1982| • ECG  
• SPECT/PET/scintigraphy | X    |      |      | Fair    | • Source of population not described  
• Precision of estimates not provided |
| Gebker, et al., 2010  | • CMR                | X    | X    | X    | Good    | • Source of population not described  
• Precision of estimates not provided  
• Training/quality control not described  
• Data not stratified or adjusted for key predictors |
| Gentile, et al., 2001 | • ECG  
• SPECT/PET/scintigraphy | X    |      |      | Good    | • Training/quality control not described  
• Data not stratified or adjusted for key predictors |
| Guiteras, et al., 1982| • ECG                | X    |      |      | Fair    | • Source of population not described  
• Training/quality control not described  
• Precision of estimates not provided  
• Comparability of care in international settings unclear |
| Gulati, et al., 2004  | • SPECT/PET/scintigraphy | X    |      |      | Fair    | • Source of population not described  
• Comparability of care in international settings unclear |
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<th>Study</th>
<th>NIT Modality</th>
<th>KQ 1</th>
<th>KQ 2</th>
<th>KQ 3</th>
<th>KQ 4</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
</table>
| Hlatky, et al., 1984     | ECG                | X    |      |      |      | Poor    | • Source of population not described  
|                          |                    |      |      |      |      | • Key characteristics not reported  
|                          |                    |      |      |      |      | • Version/instrumentation not specified  
|                          |                    |      |      |      |      | • Training/quality control not described  
|                          |                    |      |      |      |      | • Precision of estimates not provided  
|                          |                    |      |      |      |      | • Time from results to treatment not reported  
| Ho, et al., 1998         | ECHO               | X    | X    |      |      | Fair    | • Source of population not described  
|                          | SPECT/PET/scintigraphy |      |      |      |      | • Precision of estimates not provided  
|                          |                    |      |      |      |      | • Comparability of care in international settings unclear  
| Hoolund-Carlsen, et al., | ECG                | X    |      |      |      | Fair    | • Source of population not described  
| 2005                     | SPECT/PET/scintigraphy |      |      |      |      | • Study population poorly specified  
|                          |                    |      |      |      |      | • Version/instrumentation not specified  
|                          |                    |      |      |      |      | • Training/quality control not described  
|                          |                    |      |      |      |      | • Precision of estimates not provided  
|                          |                    |      |      |      |      | • Comparability of care in international settings unclear  
| Hoolund-Carlsen, et al., | SPECT/PET/scintigraphy |      |      |      |      | Good    | • Training/quality control not described  
| 2007                     |                    |      |      |      |      |         |                                                                                                                   |
| Hosokawa, et al., 2008   | ECG                | X    |      |      |      | Fair    | • Source of population not described  
|                          |                    |      |      |      |      | • Study population poorly specified  
|                          |                    |      |      |      |      | • Key characteristics not reported  
|                          |                    |      |      |      |      | • Precision of estimates not provided  
|                          |                    |      |      |      |      | • Time from results to treatment not reported  
|                          |                    |      |      |      |      | • Comparability of care in international settings unclear  
| Hung, et al., 1984       | SPECT/PET/scintigraphy |      |      |      |      | Good    | • Training/quality control not described  
|                          |                    |      |      |      |      | • Precision of estimates not provided  
| Jenkins, et al., 2010    | Coronary CTA       | X    |      |      |      | Good    | • Training/quality control not described  
| Johansen, et al., 2004   | ECG                | X    |      |      |      | Fair    | • Source of population not described  
|                          | SPECT/PET/scintigraphy |      |      |      |      | • Study population poorly specified  
|                          |                    |      |      |      |      | • Version/instrumentation not specified  
|                          |                    |      |      |      |      | • Training/quality control not described  
|                          |                    |      |      |      |      | • Precision of estimates not provided  
|                          |                    |      |      |      |      | • Comparability of care in international settings unclear  
| Johnson, et al., 2004    | CMR                | X    |      |      |      | Fair    | • Populations and study designs heterogeneous with varied findings  
|                          |                    |      |      |      |      | • Comparability of care in international settings unclear  

D-4
<table>
<thead>
<tr>
<th>Study</th>
<th>NIT Modality</th>
<th>KQ 1</th>
<th>KQ 2</th>
<th>KQ 3</th>
<th>KQ 4</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
</table>
| Kaminek, et al., 2001 | SPECT/PET/scintigraphy       | X    |      |      |      | Poor    | • Source of population not described  
• Study population poorly specified  
• Key characteristics not reported  
• Training/quality control not described  
• Precision of estimates not provided  
• Sequence of use of other diagnostics unclear  
• Comparability of care in international settings unclear |
| Kiat, et al., 1990    | SPECT/PET/scintigraphy       | X    |      |      |      | Fair    | • Source of population not described  
• Study population poorly specified  
• Key characteristics not reported  
• Training/quality control not described  
• Precision of estimates not provided  
• Data not stratified or adjusted for key predictors |
| Klem, et al., 2008    | CMR                           | X    | X    |      |      | Good    | • Training/quality control not described  
• Precision of estimates not provided |
| Koide, et al., 2001   | ECG                           | X    |      |      |      | Good    | • Training/quality control not described |
| Langer, et al., 2009  | CMR, Coronary CTA             | X    |      |      |      | Good    | • Precision of estimates not provided |
| Laurienzo, et al., 1997 | ECG, ECHO, SPECT/PET/scintigraphy | X    | X    |      |      | Good    | • Training/quality control not described  
• Precision of estimates not provided  
• Data not stratified or adjusted for key predictors  
• Order of testing varied across subjects and was not randomly assigned |
| Lehmkuhl, et al., 2007 | ECG, ECHO                     | X    | X    |      |      | Good    | • Precision of estimates not provided |
| Lewandowski, et al., 2007 | ECG, ECHO                    | X    |      |      |      | Good    | • Version/instrumentation not specified  
• Training/quality control not described  
• Comparability of care in international settings unclear |
| Lewis, et al., 1999*  | ECHO                          | X    |      | X    |      | Good    | • Precision of estimates not provided |
| Lewis, et al., 2005*  | ECG                           | X    | X    | X    |      | Good    | • Key characteristics not reported  
• Time from results to treatment not reported |
| Lu, et al., 2010      | ECG, ECHO, SPECT/PET/scintigraphy | X    | X    | X    |      | Good    | • Training/quality control not described  
• Precision of estimates not provided |
<table>
<thead>
<tr>
<th>Study</th>
<th>NIT Modality</th>
<th>KQ 1</th>
<th>KQ 2</th>
<th>KQ 3</th>
<th>KQ 4</th>
<th>Quality</th>
<th>Limitations to Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maffei, et al., 2010</td>
<td>• ECG</td>
<td>X</td>
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<td></td>
<td>Fair</td>
<td>• Source of population not described&lt;br&gt;• Precision estimates not provided&lt;br&gt;• Sequence of use of other diagnostics unclear&lt;br&gt;• Comparability of care in international settings unclear</td>
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<tr>
<td>Majstorov, et al., 2005</td>
<td>• SPECT/PET/scintigraphy</td>
<td>X</td>
<td></td>
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• Version/instrumentation not specified  
• Training/quality control not described  
• Precision of estimates not provided  
• Comparability of care in international settings unclear                                                                                                                                 |
| Mieres, et al., 2007   | • ECG, SPECT/PET/scintigraphy |      |      |      |      | Fair    | • Source of population not described  
• Version/instrumentation not specified  
• Training/quality control not described  
• Failure to test “normals” or subset with gold standard  
• Precision of estimates not provided  
• Time from results to treatment not reported  
• Comparability of care in international settings unclear                                                                                                                                 |
| Miller, et al., 2001   | • ECG, SPECT/PET/scintigraphy |      |      |      |      | Fair    | • Training/quality control not described  
• Precision of estimates not provided  
• Data not stratified or adjusted for key predictors                                                                                                                                 |
| Mohiuddin, et al., 1996| • SPECT/PET/scintigraphy      |      |      |      |      | Good    | • Training/quality control not described                                                                                                                                 |
| Morise, et al., 2000   | • ECG                         |      |      |      |      | Good    | • None                                                                                                                                                                    |
| Morise, et al., 1995-A | • ECG                         |      |      |      |      | Fair    | • Training/quality control not described  
• Precision of estimates not provided                                                                                                                                                                                                 |
| Morise, et al., 1995-B | • SPECT/PET/scintigraphy      |      |      |      |      | Poor    | • Study population poorly specified  
• Training/quality control not described  
• Precision of estimates not provided  
• Data not stratified or adjusted for key predictors                                                                                                                                 |
| Morise, et al., 2002   | • ECG                         |      |      |      |      | Good    | • Precision of estimates not provided  
• Comparability of care in international settings unclear                                                                                                                                 |
| Morise, et al., 2004<sup>a</sup> | • ECG                         |      |      |      |      | Fair    | • Source of population not described  
• Study population poorly specified  
• Version/instrumentation not specified  
• Training/quality control not described  
• Precision of estimates not provided  
• Sequence of use of other diagnostics unclear  
• Comparability of care in international settings unclear                                                                                                                                 |
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<th>Quality</th>
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- Data not stratified or adjusted for key predictors  
- Sequence of use of other diagnostics unclear                                                                 |
| Ozdemir, et al., 2002  | ECG                            | X    |      |      |      | Good    | - Training/quality control not described  
- Precision of estimates not provided  
- Data not stratified or adjusted for key predictors                                                                 |
| Pundziute, et al., 2008 | Coronary CTA                    | X    |      |      |      | Fair    | - Source of population not described  
- Sequence of use of other diagnostics unclear  
- Comparability of care in international settings unclear                                                                 |
| Raman, et al., 2008    | ECG, SPECT/PET/scintigraphy, CMR | X    | X    |      |      | Fair    | - Source of population not described  
- Training/quality control not described  
- Comparability of care in international settings unclear                                                                 |
| Richardson, et al., 1995 | ECG                            | X    |      |      |      | Good    | - Training/quality control not described  
- Precision of estimates not provided  
- Data not stratified or adjusted for key predictors                                                                 |
| Robert, et al., 1991   | ECG                            | X    |      |      |      | Fair    | - Source of population not described  
- Key characteristics not reported  
- Training/quality control not described  
- Precision of estimates not provided  
- Comparability of care in international settings unclear                                                                 |
| Roger, et al., 1997    | ECHO                            | X    |      |      |      | Poor    | - Source of population not described  
- Study population poorly specified  
- Training/quality control not described                                                                 |
| Rollan, et al., 2002   | ECG, ECHO, SPECT/PET/scintigraphy | X    |      |      |      | Fair    | - Source of population not described  
- Training/quality control not described  
- Sequence of use of other diagnostics unclear  
- Comparability of care in international settings unclear                                                                 |
| San Roman, et al., 1998 | ECG, ECHO, SPECT/PET/scintigraphy | X    |      |      |      | Good    | - Source of population not described  
- Study population poorly specified  
- Version/instrumentation not specified  
- Precision of estimates not provided  
- Comparability of care in international settings unclear                                                                 |
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• Precision of estimates not provided  
• Data not stratified or adjusted for key predictors  
• Comparability of care in international settings unclear |
| Shin, et al., 2003    | ECHO                 |      |      | X    | X    | Fair    | • Source of population not described  
• Training/quality control not described  
• Precision of estimates not provided  
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| Shivalkar, et al., 2007 | Coronary CTA        | X    |      |      |      | Fair    | • Source of population not described  
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• Comparability of care in international settings unclear |
| Siegler, et al., 2011 | ECG, SPECT/PET/scintigraphy |      |      | X    | X    | Fair    | • Gold standard not applied  
• Precision of estimates not provided |
| Sinha, et al., 2008   | ECG                  | X    |      |      |      | Poor    | • Key characteristics not reported  
• Training/quality control not described  
• Precision of estimates not provided  
• Data not stratified or adjusted for key predictors |
| Sketch, et al., 1975  | ECG                  | X    |      |      |      | Poor    | • Source of population not described  
• Study population poorly specified  
• Precision of estimates not provided  
• Sequence of use of other diagnostics unclear  
• Comparability of care in international settings unclear |
| Slavich, et al., 1996 | ECHO, SPECT/PET/scintigraphy |      |      | X    |      | Fair    | • Source of population not described  
• Study population poorly specified  
• Key characteristics not reported  
• Training/quality control not described  
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|                        |                            |      |      |      |      | • Training/quality control not described  
|                        |                            |      |      |      |      | • Comparability of care in international settings unclear                                  |
| Weiner, et al., 1985   | • ECG                      |      | X    |      |      | Poor    | • Source of population not described  
|                        |                            |      |      |      |      | • Study population poorly specified  
|                        |                            |      |      |      |      | • Key characteristics not reported  
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| Weiner, et al., 1979   | • ECG                      |      | X    |      |      | Good    | • Study population poorly specified  
|                        |                            |      |      |      |      | • Key characteristics not reported  
|                        |                            |      |      |      |      | • Training/quality control not described  
|                        |                            |      |      |      |      | • Precision of estimates not provided  
| Weustink, et al., 2007 | • Coronary CTA             |      |      | X    |      | Fair    | • Source of population not described  
|                        |                            |      |      |      |      | • Precision of estimates not provided  
|                        |                            |      |      |      |      | • Comparability of care in international settings unclear                                  |
| Weustink, et al., 2009 | • Coronary CTA             |      |      | X    |      | Good    | • None                                                                                     |
| Williams, et al., 1994 | • ECHO                     |      | X    |      |      | Fair    | • Key characteristics not reported  
|                        |                            |      |      |      |      | • Training/quality control not described  
|                        |                            |      |      |      |      | • Precision of estimates not provided  
|                        |                            |      |      |      |      | • Data not stratified or adjusted for key predictors                                      |
| Wolak, et al., 2008    | • SPECT/PET/scintigraphy  | X    |      |      |      | Fair    | • Source of population not described  
|                        |                            |      |      |      |      | • Comparability of care in international settings unclear                                  |
| Wong, et al., 2001     | • ECG                      |      |      |      | X    | Poor    | • Source of population not described  
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|                        |                            |      |      |      |      | • Training/quality control not described  
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|                        |                            |      |      |      |      | • Time from results to treatment not reported                                             |
| Yamauchi, et al., 1985 | • ECG                      |      |      |      | X    | Fair    | • Source of population not described  
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|                        |                            |      |      |      |      | • Training/quality control not described  
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|                        |                            |      |      |      |      | • Sequence of use of other diagnostics unclear                                           
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Table D-2. QUADAS tool for quality assessment of diagnostic accuracy

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| Yeih, et al., 2007      | ECG, SPECT/PET/scintigraphy | X    | X    |      |      | Fair                         | • Source of population not described  
• Study population poorly specified  
• Precision of estimates not provided  
• Comparability of care in international settings unclear |

\[a\]Related methods article: Dewey, et al., 2006 (refer to Appendix C for full citation).

\[b\]Related methods article: Miller, et al., 2009 (refer to Appendix C for full citation).

\[c\]Related methods articles: Meijboom, et al., 2007 and Meijboom, et al., 2008 (refer to Appendix C for full citations).

\[d\]Related methods article: Merz, et al., 1999 (refer to Appendix C for full citation).

\[e\]Related methods article: Mieres, et al., 2009 (refer to Appendix C for full citation).

Abbreviations: CAD = coronary artery disease; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = exercise/stress electrocardiogram; ECHO = echocardiogram; KQ = Key Question; PET = positron emission tomography; SPECT = single photon emission computed tomography

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*aRefer to Appendix B in this report for the 14 QUADAS questions. (For full details on QUADAS methodology, see: http://www.biomedcentral.com/1471-2288/3/25.)*

*bRelated methods article: Dewey, et al., 2006 (refer to Appendix C for full citation).*

*cRelated methods article: Miller, et al., 2009 (refer to Appendix C for full citation).*

*dRelated methods articles: Meijboom, et al., 2007 and Meijboom, et al., 2008 (refer to Appendix C for full citations).*

*eRelated methods article: Merz, et al., 1999 (refer to Appendix C for full citation).*

*fRelated methods article: Mieres, et al., 2009 (refer to Appendix C for full citation).*

Abbreviations: N = No; U = Unclear, Y = Yes
Appendix E. List of Excluded Studies

All studies listed below were reviewed in their full-text version and excluded. Following each reference, in italics, is the reason for exclusion. Reasons for exclusion signify only the usefulness of the articles for this study and are not intended as criticisms of the articles.


Abitbol E, Monin JL, Garot J, et al. Relationship between the ischemic threshold at the onset of wall-motion abnormality on semisupine exercise echocardiography and the extent of coronary artery disease. J Am Soc Echocardiogr 2004;17(2):121-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Adams GL, Trimble MA, Brosnan RB, et al. Evaluation of combined cardiac positron emission tomography and coronary computed tomography angiography for the detection of coronary artery disease. Nucl Med Commun 2008;29(7):593-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Adamu U, Knollmann D, Almutairi B, et al. Stress/rest myocardial perfusion scintigraphy in patients without significant coronary artery disease. J Nucl Cardiol 2010;17(1):38-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Aepfelbacher FC, Johnson RB, Schwartz JG, et al. Validation of a model of left ventricular segmentation for interpretation of SPET myocardial perfusion images. Eur J Nucl Med 2001;28(11):1624-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.
Aessopos A, Tsironi M, Vassiliadis I,, et al. Exercise-induced myocardial perfusion abnormalities in sickle beta-thalassemia: Tc-99m tetrofosmin gated SPECT imaging study. Am J Med 2001;111(5):355-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; No outcomes of interest.

Afonso L, Mahajan N. Single-photon emission computed tomography myocardial perfusion imaging in the diagnosis of left main disease. Clin Cardiol 2009;32(12):E11-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD.

Agarwal PP, Patel S, Corbett J,, et al. Left ventricular functional analysis with 16- and 64-row multidetector computed tomography: comparison with gated single-photon emission computed tomography. J Comput Assist Tomogr 2009;33(1):8-14. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Ahlberg AW, Baghdasarian SB, Athar H,, et al. Symptom-limited exercise combined with dipyridamole stress: prognostic value in assessment of known or suspected coronary artery disease by use of gated SPECT imaging. J Nucl Cardiol 2008;15(1):42-56. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; No outcomes of interest.

Ahmadi N, Nabavi V, Hajsadeghi F., et al. Impaired aortic distensibility measured by computed tomography is associated with the severity of coronary artery disease. Int J Cardiovasc Imaging 2010. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; No outcomes of interest.

Ahmadi N, Nabavi V, Hajsadeghi F., et al. Mortality incidence of patients with non-obstructive coronary artery disease diagnosed by computed tomography angiography. Am J Cardiol 2011;107(1):10-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Ahmadi N, Shavelle D, Nabavi V., et al. Coronary distensibility index measured by computed tomography is associated with the severity of coronary artery disease. J Cardiovasc Comput Tomogr 2010;4(2):119-26. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Akram K, Voros S. Absolute coronary artery calcium scores are superior to MESA percentile rank in predicting obstructive coronary artery disease. Int J Cardiovasc Imaging 2008;24(7):743-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Al Moudi M, Sun Z, Lenzo N. Diagnostic value of SPECT, PET and PET/CT in the diagnosis of coronary artery disease: A systematic review. Biomedical Imaging and Intervention Journal 2011;7(2). Full-text exclusion reason(s): Conference abstract or trial registry posting.

Al-Attar AT, Mahussain SA, Sadanandan S. Cardiac tests in asymptomatic type 2 diabetics. Med Princ Pract 2002;11(4):171-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Aldrovandi A, Maffei E, Palumbo A, et al. Prognostic value of computed tomography coronary angiography in patients with suspected coronary artery disease: a 24-month follow-up study. Eur Radiol 2009;19(7):1653-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Al-Khalili F, Janszky I, Andersson A, et al. Physical activity and exercise performance predict long-term prognosis in middle-aged women surviving acute coronary syndrome. J Intern Med 2007;261(2):178-87. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; No outcomes of interest.

Allison JS, Heo J, Iskandrian AE. Artificial neural network modeling of stress single-photon emission computed tomographic imaging for detecting extensive coronary artery disease. Am J Cardiol 2005;95(2):178-81. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Allman KC, Berry J, Sucharski LA, et al. Determination of extent and location of coronary artery disease in patients without prior myocardial infarction by thallium-201 tomography with pharmacologic stress. J Nucl Med 1992;33(12):2067-73. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Al-Mallah M, Alqaisi F, Arafeh A, et al. Long term favorable prognostic value of negative treadmill echocardiogram in the setting of abnormal treadmill electrocardiogram: a 95 month median duration follow-up study. J Am Soc Echocardiogr 2008;21(9):1018-22. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Al-Mallah MH, Hachamovitch R, Dorbala S, et al. Incremental prognostic value of myocardial perfusion imaging in patients referred to stress single-photon emission computed tomography with renal dysfunction. Circ Cardiovasc Imaging 2009;2(6):429-36. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Almeida MC, Markman Filho B. Prognostic value of dipyridamole stress echocardiography in women. Arq Bras Cardiol 2011;96(1):31-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.


Al-Saadi N, Nagel E, Gross M, et al. Noninvasive detection of myocardial ischemia from perfusion reserve based on cardiovascular magnetic resonance. Circulation 2000;101(12):1379-83. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Amanullah AM. Diagnostic and prognostic value of myocardial perfusion imaging in patients with known or suspected stable coronary artery disease. Echocardiography 2000;17(6 Pt 1):587-95. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Amanullah AM, Bevegard S, Lindvall K., et al. Assessment of left ventricular wall motion in angina pectoris by two-dimensional echocardiography and myocardial perfusion by technetium-99m sestamibi tomography during adenosine-induced coronary vasodilation and comparison with coronary angiography. Am J Cardiol 1993;72(14):983-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Amici E, Cortigiani L, Coletta C., et al. Usefulness of pharmacologic stress echocardiography for the long-term prognostic assessment of patients with typical versus atypical chest pain. Am J Cardiol 2003;91(4):440-2. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Anagnostopoulos C, Almonacid A, El Fakhri G., et al. Quantitative relationship between coronary vasodilator reserve assessed by 82Rb PET imaging and coronary artery stenosis severity. Eur J Nucl Med Mol Imaging 2008;35(9):1593-601. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Anand DV, Lim E, Raval U., et al. Prevalence of silent myocardial ischemia in asymptomatic individuals with subclinical atherosclerosis detected by electron beam tomography. J Nucl Cardiol 2004;11(4):450-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Andrade JM, Gowdak LH, Giorgi MC., et al. Cardiac MRI for detection of unrecognized myocardial infarction in patients with end-stage renal disease: comparison with ECG and scintigraphy. AJR Am J Roentgenol 2009;193(1):W25-32. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Andrade MJ, Picano E, Pingitore A., et al. Dipyridamole stress echocardiography in patients with severe left main coronary artery narrowing. Echo Persantine International Cooperative (EPIC) Study Group—Subproject "Left Main Detection". Am J Cardiol 1994;73(7):450-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Andreini D, Pontone G, Ballerini G., et al. Feasibility and diagnostic accuracy of 16-slice multidetector computed tomography coronary angiography in 500 consecutive patients: critical role of heart rate. Int J Cardiovasc Imaging 2007;23(6):789-801. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Anthopoulos LP, Bonou MS, Sioras EP, et al. Echocardiographic detection of the extent of coronary artery disease in the elderly using dobutamine and adenosine infusion. Coron Artery Dis 1997;8(10):633-43. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Arruda AL, Barretto RB, Shub C, et al. Prognostic significance of ST-segment elevation during dobutamine stress echocardiography. Am Heart J 2006;151(3):744 e1-744 e6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Arruda AM, Das MK, Roger VL, et al. Prognostic value of exercise echocardiography in 2,632 patients > or = 65 years of age. J Am Coll Cardiol 2001;37(4):1036-41. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ariff B, Thom SA, Foale RA, et al. Stress echocardiography for the diagnosis of ischaemia in hypertensives. Journal of human hypertension 2000(6):399-401. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Arruda OL, Barretto RB, Shub C, et al. Prognostic significance of ST-segment elevation during dobutamine stress echocardiography. Am Heart J 2006;151(3):744 e1-744 e6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Arruda AM, Das MK, Roger VL, et al. Prognostic value of exercise echocardiography in 2,632 patients > or = 65 years of age. J Am Coll Cardiol 2001;37(4):1036-41. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Arruda-Olson AM, Juracan EM, Mahoney DW, et al. Prognostic value of exercise echocardiography in 5,798 patients: is there a gender difference? J Am Coll Cardiol 2002;39(4):625-31. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.
Ashley EA, Myers J, Froelicher V. Exercise testing in clinical medicine. Lancet 2000;356(9241):1592-1597. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Atar S, Cercek B, Nagai T, et al. Transthoracic stress echocardiography with transesophageal atrial pacing for bedside evaluation of inducible myocardial ischemia in patients with new-onset chest pain. Am J Cardiol 2000;86(1):12-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Atar S, Feldman A, Darawshe A, et al. Utility and diagnostic accuracy of hand-carried ultrasound for emergency room evaluation of chest pain. Am J Cardiol 2004;94(3):408-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Atar S, Nagai T, Cercek B, et al. Pacing stress echocardiography: an alternative to pharmacologic stress testing. J Am Coll Cardiol 2000;36(6):1935-41. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Atchley AE, Iskandrian AE, Bensimhon D, et al. Relationship of technetium-99m tetrofosmin-gated rest single-photon emission computed tomography myocardial perfusion imaging to death and hospitalization in heart failure patients: Results from the nuclear ancillary study of the HF-ACTION trial. Am Heart J 2011;161(6):1038-1045. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Atsma DE, Bavelaar-Croon CD, Germano G, et al. Good correlation between gated single photon emission computed myocardial tomography and contrast ventriculography in the assessment of global and regional left ventricular function. Int J Card Imaging 2000;16(6):447-53. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Attar MN, Wong K, Groves DG, et al. Clinical implications of QRS duration and QT peak prolongation in patients with suspected coronary disease referred for elective cardiac catheterization. Ann Noninvasive Electrocardiol 2008;13(2):106-12. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.
Auseon AJ, Advani SS, Bush CA, et al. Impact of 64-slice multidetector computed tomography on other diagnostic studies for coronary artery disease. Am J Med 2009;122(4):387-91. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Auseon AJ, Tran T, Garcia AM, et al. Aortic pathophysiology by cardiovascular magnetic resonance in patients with clinical suspicion of coronary artery disease. J Cardiovasc Magn Reson 2007;9(1):43-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Bacci S, Villega M, Villeda A, et al. Screening for silent myocardial ischaemia in type 2 diabetic patients with additional atherogenic risk factors: applicability and accuracy of the exercise stress test. Eur J Endocrinol 2002;147(5):649-54. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Bachar GN, Atar E, Fuchs S, et al. Prevalence and clinical predictors of atherosclerotic coronary artery disease in asymptomatic patients undergoing coronary multidetector computed tomography. Coron Artery Dis 2007;18(5):353-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Baghdasarian SB, Heller GV. The role of myocardial perfusion imaging in the diagnosis of patients with coronary artery disease: developments over the past year. Curr Opinion Cardiol 2005;20(5):369-74. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Bamberg F, Truong QA, Blankstein R., et al. Usefulness of age and gender in the early triage of patients with acute chest pain having cardiac computed tomographic angiography. Am J Cardiol 2009;104(9):1165-70. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization.


Banerjee SK, Haque KM, Sharma AK., et al. Role of exercise tolerance test (ETT) and gated single photon emission computed tomography-myocardial perfusion imaging (SPECT-MPI) in predicting severity of ischemia in patients with chest pain. Bangladesh Med Res Counc Bull 2005;31(1):27-35. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Barbirato GB, Azevedo JC, Felix RC., et al. Use of resting myocardial scintigraphy during chest pain to exclude diagnosis of acute myocardial infarction. Arq Bras Cardiol 2009;92(4):269-74. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Bart BA, Cen YY, Hendel RC., et al. Comparison of dobutamine stress echocardiography, dobutamine SPECT, and adenosine SPECT myocardial perfusion imaging in patients with end-stage renal disease. J Nucl Cardiol 2009;16(4):507-15. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Bart BA, Erlien DA, Herzog CA., et al. Marked differences between patients referred for stress echocardiography and myocardial perfusion imaging studies. Am Heart J 2005;149(5):888-93. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Bartel T, Yang Y, Muller S., et al. Noninvasive assessment of microvascular function in arterial hypertension by transthoracic Doppler harmonic echocardiography. J Am Coll Cardiol 2002;39(12):2012-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Basic D, Siu SC, Skyba DM., et al. Prognostic value of myocardial perfusion contrast echocardiography in patients with suggested or known ischemic heart disease. J Am Soc Echocardiogr 2006;19(10):1203-10. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one
NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Bastarrika G, Ramos-Duran L, Rosenblum MA, et al. Adenosine-stress dynamic myocardial CT perfusion imaging: initial clinical experience. Invest Radiol 2010;45(6):306-13. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bateman TM, Heller GV, McGhie AI, et al. Multicenter investigation comparing a highly efficient half-time stress-only attenuation correction approach against standard rest-stress Tc-99m SPECT imaging. J Nucl Cardiol 2009;16(5):726-735. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bateman TM, Heller GV, McGhie AI, et al. Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: comparison with ECG-gated Tc-99m sestamibi SPECT. J Nucl Cardiol 2006;13(1):24-33. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Bauer RW, Thilo C, Chiaramida SA, et al. Noncalcified atherosclerotic plaque burden at coronary CT angiography: a better predictor of ischemia at stress myocardial perfusion imaging than calcium score and stenosis severity. AJR Am J Roentgenol 2009;193(2):410-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Bayrak F, Guneysu T, Gemici G, et al. Diagnostic performance of 64-slice computed tomography coronary angiography to detect significant coronary artery stenosis. Acta Cardiol 2008;63(1):11-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Beanlands RS, Nichol G, Huszti E, et al. F-18-fluorodeoxyglucose positron emission tomography imaging-assisted management of patients with severe left ventricular dysfunction and suspected coronary disease: a randomized, controlled trial (PARR-2). J Am Coll Cardiol 2007;50(20):2002-12. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Beck T, Burgstahler C, Kuettnert A, et al. Clinical use of multislice spiral computed tomography in 210 highly preselected patients: experience with 4 and 16 slice technology. Heart 2005;91(11):1423-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Becker A, Leber A, Becker C, et al. Predictive value of coronary calcifications for future cardiac events in asymptomatic individuals. Am Heart J 2008;155(1):154-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Becker A, Leber AW, Becker C,, et al. Predictive value of coronary calcifications for future cardiac events in asymptomatic patients with diabetes mellitus: a prospective study in 716 patients over 8 years. BMC Cardiovasc Disord 2008;8:27. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Becker CR, Knez A, Leber A,, et al. Detection of coronary artery stenoses with multislice helical CT angiography. J Comput Assist Tomogr 2002;26(5):750-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.


Bedetti G, Pasanisi EM, Pizzi C,, et al. Economic analysis including long-term risks and costs of alternative diagnostic strategies to evaluate patients with chest pain. Cardiovasc Ultrasound 2008;6:21. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry; Data for women not reported as a subgroup; No outcomes of interest.


Beleslin BD, Ostojic M, Stepanovic J,, et al. Stress echocardiography in the detection of myocardial ischemia. Head-to-head comparison of exercise, dobutamine, and dipyridamole tests. Circulation 1994;90(3):1168-76. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Belge B, Coche E, Pasquet A,, et al. Accurate estimation of global and regional cardiac function by retrospectively gated multidetector row computed tomography: comparison with cine magnetic resonance imaging. Eur Radiol 2006;16(7):1424-33. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bell GW, Edwards M, Dunning AM,, et al. Periprocedural safety of 64-detector row coronary computed tomographic angiography: results from the prospective multicenter ACCURACY trial. J Cardiovasc Comput Tomogr 2010;4(6):375-80. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Ben-Gal T, Zafrir N. Utility of stress myocardial perfusion imaging in hospitalized patients with chest pain and normal or nondiagnostic electrocardiograms. Cardiovascular Reviews and Reports 2001;22(10):600-606. Full-text exclusion reason(s): Data for women not reported as a subgroup.

Berger BC, Watson DD, Taylor GJ,, et al. Quantitative thallium-201 exercise scintigraphy for detection of coronary artery disease. J Nucl Med 1981;22(7):585-93. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bergeron S, Ommen SR, Bailey KR,, et al. Exercise echocardiographic findings and outcome of patients referred for evaluation of dyspnea. J Am Coll Cardiol 2004;43(12):2242-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Berman DS, Hachamovitch R, Shaw Ll,, et al. Roles of nuclear cardiology, cardiac computed tomography, and cardiac magnetic resonance: Noninvasive risk stratification and a conceptual framework for the selection of noninvasive imaging tests in patients with known or suspected coronary artery disease. J Nucl Med 2006;47(7):1107-18. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Berman DS, Kang X, Gransar H,, et al. Quantitative assessment of myocardial perfusion abnormality on SPECT myocardial perfusion imaging is more reproducible than expert visual analysis. J Nucl Cardiol 2009;16(1):45-53. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Berman DS, Kang X, Hayes SW,, et al. Adenosine myocardial perfusion single-photon emission computed tomography in women compared with men. Impact of diabetes mellitus on incremental prognostic value and effect on patient management. J Am Coll Cardiol 2003;41(7):1125-33. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Berman DS, Kang X, Schisterman EF,, et al. Serial changes on quantitative myocardial perfusion SPECT in patients undergoing revascularization or conservative therapy. J Nucl Cardiol 2001;8(4):428-37. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Berman DS, Wong ND, Gransar H,, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. J Am Coll Cardiol 2004;44(4):923-30. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bernhardt P, Levenson B, Albrecht A, et al. Detection of cardiac small vessel disease by adenosine-stress magnetic resonance. Int J Cardiol 2007;121(3):261-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Bernheim AM, Kittipovanonth M, Scott CG, et al. Relation of dyspnea in patients unable to perform exercise stress testing to outcome and myocardial ischemia. Am J Cardiol 2009;104(2):265-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Bernheim AM, Kittipovanonth M, Takahashi PY, et al. Does the prognostic value of dobutamine stress echocardiography differ among different age groups? Am Heart J 2011;161(4):740-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Beslic N, Kucukalic-Selimovic E. Comparison of the diagnostic capabilities of noninvasive methods for early detection of coronary artery disease. Med Arh 2011;65(2):96-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Bestetti A, Di Leo C, Alessi A, et al. Post-stress end-systolic left ventricular dilation: a marker of endocardial post-ischemic stunning. Nucl Med Commun 2001;22(6):685-93. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Bhat A, Desai A, Amsterdam EA. Usefulness of high functional capacity in patients with exercise-induced ST-depression to predict a negative result on exercise echocardiography and low prognostic risk. Am J Cardiol 2008;101(11):1541-3. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Bholasingh R, Cornel JH, Kamp O, et al. Prognostic value of predischarge dobutamine stress echocardiography in chest pain patients with a negative cardiac troponin T. J Am Coll Cardiol 2003;41(4):596-602. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Biagini E, Elhendy A, Bax JJ, et al. Seven-year follow-up after dobutamine stress echocardiography: impact of gender on prognosis. J Am Coll Cardiol 2005;45(1):93-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.


Bigi R, Bax JJ, van Domburg RT, et al. Simultaneous echocardiography and myocardial perfusion single photon emission computed tomography associated with dobutamine stress to predict long-term cardiac mortality in normotensive and hypertensive patients. J Hypertens 2005;23(7):1409-15. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Bigi R, Occhi G, Fiorentini C., et al. Dobutamine stress echocardiography for the identification of multivessel coronary artery disease after uncomplicated myocardial infarction: the importance of test end-point. Int J Cardiol 1995;50(1):51-60. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bingham SE, Hachamovitch R. Incremental prognostic significance of combined cardiac magnetic resonance imaging, adenosine stress perfusion, delayed enhancement, and left ventricular function over preimaging information for the prediction of adverse events. Circulation 2011;123(14):1509-18. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bischoff B, Hein F, Meyer T., et al. Comparison of sequential and helical scanning for radiation dose and image quality: results of the Prospective Multicenter Study on Radiation Dose Estimates of Cardiac CT Angiography (PROTECTION) I Study. AJR Am J Roentgenol; 2010:1495-9. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Blankstein R, Shurman LD, Rogers IS., et al. Adenosine-induced stress myocardial perfusion imaging using dual-source cardiac computed tomography. J Am Coll Cardiol 2009;54(12):1072-84. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Blinder G, Benhorin J, Koukoui D., et al. The value of electrocardiography-gated multi-slice computed tomography in the evaluation of patients with chest pain. Isr Med Assoc J 2005;7(4):419-23. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Blumenthal RS, Becker DM, Yanek LR., et al. Detecting occult coronary disease in a high-risk asymptomatic population. Circulation 2003;107(5):702-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Blumenthal RS, Becker DM, Yanek LR., et al. Comparison of coronary calcium and stress myocardial perfusion imaging in apparently healthy siblings of individuals with premature coronary artery disease. Am J Cardiol 2006;97(3):328-33. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Circulation 1979;60(6):1270-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bodi V, Sanchis J, Lopez-Lereu MP, et al. Prognostic value of dipyridamole stress cardiovascular magnetic resonance imaging in patients with known or suspected coronary artery disease. J Am Coll Cardiol 2007;50(12):1174-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Bodi V, Sanchis J, Lopez-Lereu MP, et al. Prognostic and therapeutic implications of dipyridamole stress cardiovascular magnetic resonance on the basis of the ischaemic cascade. Heart 2009;95(1):49-55. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Bogaert J, Kuzo R, Dymarkowski S, et al. Coronary artery imaging with real-time navigator three-dimensional turbo-field-echo MR coronary angiography: initial experience. Radiology 2003;226(3):707-16. Full-text exclusion reason(s): All women in the study are known to have CAD; No outcomes of interest.

Bokhari S, Blood DK, Bergmann SR. Failure of right precordial electrocardiography during stress testing to identify coronary artery disease. J Nucl Cardiol 2001;8(3):325-31. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bonmassari R, Muraglia S, Centonze M, et al. Noninvasive detection of coronary artery stenosis with 16-slice spiral computed tomography in a population at low to moderate risk for coronary artery disease. J Cardiovasc Med (Hagerstown) 2006;7(11):817-25. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Boogers MJ, Schuijf JD, Kitslaar PH, et al. Automated quantification of stenosis severity on 64-slice CT: A comparison with quantitative coronary angiography. JACC: Cardiovascular Imaging 2010;3(7):699-709. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Borges-Neto S, Shaw LK, Tuttle RH, et al. Incremental prognostic power of single-photon emission computed tomographic myocardial perfusion imaging in patients with known or suspected coronary artery disease. Am J Cardiol 2005;95(2):182-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Borges-Neto S, Tuttle RH, Shaw LK, et al. Outcome prediction in patients at high risk for coronary artery disease: comparison between 99mTc tetrofosmin and 99mTc sestamibi. Radiology 2004;232(1):58-65. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Boshchenko AA, Vrublevsky AV, Karpov RS. Transthoracic echocardiography in the detection of chronic total coronary artery occlusion. Eur J Echocardiogr 2009;10(1):62-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Boudik F, Anger Z, Aschermann M, et al. Dipyridamole body surface potential mapping: noninvasive differentiation of syndrome X from coronary artery disease. J Electrocardiol 2002;35(3):181-91. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Bourque JM, Charlton GT, Holland BH, et al. Prognosis in patients achieving >/=10 METS on exercise stress testing: was SPECT imaging useful? J Nucl Cardiol 2011;18(2):230-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bourque JM, Holland BH, Watson DD, et al. Achieving an exercise workload of > or = 10 metabolic equivalents predicts a very low risk of inducible ischemia: does myocardial perfusion imaging have a role? J Am Coll Cardiol 2009;54(6):538-45. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Boussel L, Gamondes D, Staat P, et al. Acute chest pain with normal coronary angiogram: role of contrast-enhanced multidetector computed tomography in the differential diagnosis between myocarditis and myocardial infarction. J Comput Assist Tomogr 2008;32(2):228-32. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Bouvier E, Logeart D, Sablayrolles JL, et al. Diagnosis of aortic valvular stenosis by multislice cardiac computed tomography. Euro Heart J 2006(24):3033-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Bouzas-Mosquera A, Peteiro J, Alvarez-Garcia N, et al. Prediction of mortality and major cardiac events by exercise echocardiography in patients with normal exercise electrocardiographic testing. J Am Coll Cardiol 2009;53(21):1981-90. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Boyne TS, Koplan BA, Parsons WJ, et al. Predicting adverse outcome with exercise SPECT technetium-99m sestamibi imaging in patients with suspected or known coronary artery disease. Am J Cardiol 1997;79(3):270-4. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Brodoefel H, Burgstahler C, Tsiflikas I, et al. Dual-source CT: effect of heart rate, heart rate variability, and calcification on image quality and diagnostic accuracy. Radiology 2008;247(2):346-55. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Brook RD, Bard RL, Patel S, et al. A negative carotid plaque area test is superior to other noninvasive atherosclerosis studies for reducing the likelihood of having underlying significant coronary artery disease. Arterioscler Thromb Vasc Biol 2006;26(3):656-62. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging. A diagnostic tool comes of age. Circulation 1991;83(2):363-81. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Brown TL, Voicu C, Merrill J., et al. Pathophysiologic correlates of 82Rb biodistribution in cardiac PET/CT. Eur J Nucl Med Mol Imaging 2011;38(3):479-84. *Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.*

Bruder O, Schneider S, Nothnagel D., et al. EuroCMR (European Cardiovascular Magnetic Resonance) registry: results of the German pilot phase. J Am Coll Cardiol 2009;54(15):1457-66. *Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.*


Bucerius J, Joe AY, Herder E., et al. Hemodynamic variables during stress testing can predict referral to early catheterization but failed to show a prognostic impact on emerging cardiac events in patients aged 70 years and older undergoing exercise (99m)Tc-sestamibi myocardial perfusion scintigraphy. Int J Cardiovasc Imaging 2009;25(6):569-79. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*

Bucerius J, Joe AY, Herder E., et al. Pathological 99mTc-sestamibi myocardial perfusion scintigraphy is independently associated with emerging cardiac events in elderly patients with known or suspected coronary artery disease. Acta Radiol 2011;52(1):52-8. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.*

Bucerius J, Joe AY, Herder E., et al. Significant association of female gender with lower degree of pathological 99mTc-sestamibi scintigraphy results as well as higher cardiac-related deaths free survival in elderly patients. Med Klin (Munich) 2010;105(12):901-9. *Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.*


Budoff MJ, Gopal A, Gopalakrishnan D. Cardiac computed tomography: Diagnostic utility and integration in clinical practice. Clin Cardiol 2006;29(SUPPL. 1):14-114. *Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.*
Burgstahler C, Reimann A, Drosch T., et al. Cardiac dual-source computed tomography in patients with severe coronary calcifications and a high prevalence of coronary artery disease. J Cardiovasc Comput Tomogr 2007;1(3):143-51. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Bybee KA, Lee J, Markiewicz R., et al. Diagnostic and clinical benefit of combined coronary calcium and perfusion assessment in patients undergoing PET/CT myocardial perfusion stress imaging. J Nucl Cardiol 2010;17(2):188-196. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Cademartiri F, Carli MF. MSCT is better than stress perfusion imaging for detecting CAD. European Journal of Nuclear Medicine and Molecular Imaging 2006;33(3):353-359. Full-text exclusion reason(s): Data for women not reported as a subgroup.


Cademartiri F, Maffei E, Notarangelo F., et al. 64-slice computed tomography coronary angiography: diagnostic accuracy in the real world. Radiol Med 2008;113(2):163-80. Full-text exclusion reason(s): All women in the study are known to have CAD; No outcomes of interest.


Cademartiri F, Romano M, Seitun S., et al. Prevalence and characteristics of coronary artery disease in a population with suspected ischemic heart disease using CT coronary angiography: correlations with cardiovascular risk factors and clinical presentation. Radiol Med 2008;113(3):363-72. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Cademartiri F, Seitun S, Romano M., et al. Prognostic value of 64-slice coronary angiography in diabetes mellitus patients with known or suspected coronary artery disease compared with a nondiabetic population. Radiol Med 2008;113(5):627-43. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Campos AM, da Cunha AB. Dobutamine stress echocardiography as a predictor of coronary lesion severity on coronary angiography. Rev Port Cardiol 2007;26(5):505-18. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Candell-Riera J, Oller-Martinez G, de Leon G., et al. Yield of early rest and stress myocardial perfusion single-photon emission computed tomography and electrocardiographic exercise test in patients with atypical chest pain, nondiagnostic electrocardiogram, and negative biochemical markers in the emergency department. Am J Cardiol 2007;99(12):1662-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Carmo MM, Ferreira T, Quininha J., et al. Non-invasive coronary artery evaluation with multidetector computed tomography. Rev Port Cardiol 2005;24(5):667-79. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Carrascosa P, Capunay C, Deviggiano A., et al. Feasibility of 64-slice gadolinium-enhanced cardiac CT for the evaluation of obstructive coronary artery disease. Heart 2010;96(19):1543-1549. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Carrascosa PM, Capunay CM, Parodi JC., et al. General utilities of multislice tomography in the cardiac field. Herz 2003;28(1):44-51. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Carrinho M, Moraes A, Morcerf F, et al. Myocardial contrast echocardiography in patients with suspected or known coronary artery disease: comparison with myocardial nuclear scintigraphy. Arq Bras Cardiol 2004;83(5):419-23; 414-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Casolo G, Del Meglio J, Rega L, et al. Detection and assessment of coronary artery anomalies by three-dimensional magnetic resonance coronary angiography. Int J Cardiol 2005;103(3):317-22. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Catalan P, Leta R, Hidalgo A, et al. Ruling out coronary artery disease with noninvasive coronary multidetector CT angiography before noncoronary cardiovascular surgery. Radiology 2011;258(2):426-34. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Caussin C, Daoud B, Ghostine S, et al. Comparison of lumens of intermediate coronary stenosis using 16-slice computed tomography versus intravascular ultrasound. Am J Cardiol 2005;96(4):524-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Caussin C, Ohanessian A, Ghostine S, et al. Characterization of vulnerable nonstenotic plaque with 16-slice computed tomography compared with intravascular ultrasound. Am J Cardiol 2004;94(1):99-104. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.


Cerci MSJ, Cerci JJ, Cerci RJ, et al. Myocardial perfusion imaging is a strong predictor of death in women. JACC: Cardiovascular Imaging 2011;4(8):880-888. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization.


with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Chang SA, Choi SI, Choi EK, et al. Usefulness of 64-slice multidetector computed tomography as an initial diagnostic approach in patients with acute chest pain. Am Heart J 2008;156(2):375-83. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Chang SM, Nabi F, Xu J, et al. The coronary artery calcium score and stress myocardial perfusion imaging provide independent and complementary prediction of cardiac risk. J Am Coll Cardiol 2009;54(20):1872-82. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Chao SP, Law WY, Kuo CJ, et al. The diagnostic accuracy of 256-row computed tomographic angiography compared with invasive coronary angiography in patients with suspected coronary artery disease. Euro Heart J 2010;31(15):1916-1923. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Chatziioannou SN, Moore WH, Ford PV, et al. Prognostic value of myocardial perfusion imaging in patients with high exercise tolerance. Circulation 1999;99(7):867-72. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.


Chen LC, Chen JW, Wu MH, et al. Differential coronary artery calcification detected by electron beam computed tomography as an indicator of coronary stenosis among patients with stable angina pectoris. Can J Cardiol 2001;17(6):667-76. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Chen LC, Ding PY, Chen JW, et al. Coronary artery calcium determined by electron beam computed tomography for predicting angiographic coronary artery disease in moderate- to high-risk Chinese patients. Cardiology 2001;95(4):183-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Cheng V, Gutstein A, Wolak A, et al. Moving beyond binary grading of coronary arterial stenoses on coronary computed tomographic angiography: insights for the imager and referring clinician. JACC Cardiovasc Imaging 2008;1(4):460-71. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Cheng W, Zeng M, Arellano C, et al. Detection of myocardial perfusion abnormalities: Standard dual-source coronary computed tomography angiography versus rest/stress technetium-99m single-photo emission CT. Br J Radiol 2010;83(992):652-660. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Chikamori T, Doi YL, Yonezawa Y, et al. Noninvasive identification of significant narrowing of the left main coronary artery by dipyridamole thallium scintigraphy. Am J Cardiol 1991;68(5):472-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Choi EK, Chun EJ, Choi SI., et al. Assessment of subclinical coronary atherosclerosis in asymptomatic patients with type 2 diabetes mellitus with single photon emission computed tomography and coronary computed tomography angiography. Am J Cardiol 2009;104(7):890-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Chotenimitkhun R, Hundley WG. Pharmacological stress cardiovascular magnetic resonance. Postgrad Med 2011;123(3):162-70. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study; or registry.


Chow BJ, Al Shammeri OM, Beanlands RS., et al. Prognostic value of treadmill exercise and dobutamine stress positron emission tomography. Can J Cardiol 2009;25(7):e220-4. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Chow BJ, Ananthasubramaniam K, dekemp RA., et al. Comparison of treadmill exercise versus dipyridamole stress myocardial perfusion imaging using rubidium-82 positron emission tomography. J Am Coll Cardiol 2005;45(8):1227-34. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Choy JB, Leslie WD. Clinical correlates of Tc-99m sestamibi lung uptake. J Nucl Cardiol 2001;8(6):639-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Christian TF, Miller TD, Bailey KR, et al. Noninvasive identification of severe coronary artery disease using exercise tomographic thallium-201 imaging. Am J Cardiol 1992;70(1):14-20. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Christiansen JP, Edwards C, Sinclair T, et al. Detection of myocardial scar by contrast-enhanced cardiac magnetic resonance imaging in patients with troponin-positive chest pain and minimal angiographic coronary artery disease. Am J Cardiol 2006;97(6):768-71. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Chu ZG, Yang ZG, Dong ZH, et al. Characteristics of coronary artery disease in symptomatic type 2 diabetic patients: evaluation with CT angiography. Cardiovasc Diabetol 2010;9:74. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Chung WY, Sir JJ, Cho YS, et al. Additive value of B-type natriuretic peptide on rest 201 Tl-dipyridamole stress 99m Tc-sestamibi gated myocardial SPECT in patients with normal left ventricular systolic function. Cardiol Res Pract 2010;1(1). Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Cilli A, Batmaz F, Demir I, et al. The diagnostic yield of exercise stress testing as a screening tool for subclinical coronary artery disease in patients with moderate to severe obstructive sleep apnea. J Clin Sleep Med 2011;7(1):25-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Clouse ME, Sabir A, Yam CS, et al. Measuring noncalcified coronary atherosclerotic plaque using voxel analysis with MDCT angiography: a pilot clinical study. AJR Am J Roentgenol 2008;190(6):1553-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Coffey JP, Hill JC. Cardiac output and index in obese and non-obese patients using gated single photon emission computed tomography sestamibi pertusion imaging. Journal of the Hong Kong College of Radiologists 2005;8(4):226-232. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Cohen JL, Greene TO, Ottenweller J, et al. Dobutamine digital echocardiography for detecting coronary artery disease. Am J Cardiol 1991;67(16):1311-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.
Cohen JL, Ottenweller JE, George AK, et al. Comparison of dobutamine and exercise echocardiography for detecting coronary artery disease. Am J Cardiol 1993;72(17):1226-31. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Cole JH, Chunm VM, Morrow JA, et al. Cost implications of initial computed tomography angiography as opposed to catheterization in patients with mildly abnormal or equivocal myocardial perfusion scans. J Cardiovasc Comput Tomogr 2007;1(1):21-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.


Coles DR, Wilde P, Oberhoff M, et al. Multislice computed tomography coronary angiography in patients admitted with a suspected acute coronary syndrome. Int J Cardiovasc Imaging 2007;23(5):603-14. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Coma-Canella I, Palazuelos J, Bravo N, et al. Myocardial perfusion imaging with adenosine triphosphate predicts the rate of cardiovascular events. J Nucl Cardiol 2006;13(3):316-323. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Costa MA, Shoemaker S, Futamatsu H, et al. Quantitative magnetic resonance perfusion imaging detects anatomic and physiologic coronary artery disease as measured by coronary angiography and fractional flow reserve. J Am Coll Cardiol 2007;50(6):514-22. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Cosyns B, Lancellotti P, Van Camp G, et al. Head to head comparison of transesophageal and transthoracic contrast-enhanced echocardiography during dobutamine administration for the detection of coronary artery disease. Int J Cardiol 2008;129(1):105-10. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Coyne EP, Belvedere DA, Vande Streek PR, et al. Thallium-201 scintigraphy after intravenous infusion of adenosine compared with exercise thallium testing in the diagnosis of coronary artery disease. J Am Coll Cardiol 1991;17(6):1289-94. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Crouse LJ, Harbrecht JJ, Vacek JL, et al. Exercise echocardiography as a screening test for coronary artery disease and correlation with coronary arteriography. Am J Cardiol 1991;67(15):1213-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Cury RC, Pomerantsev EV, Ferencik M, et al. Comparison of the degree of coronary stenoses by multidetector computed tomography versus by quantitative coronary angiography. Am J Cardiol 2005;96(6):784-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Cwajg J, Xie F, O'Leary E, et al. Detection of angiographically significant coronary artery disease with accelerated intermittent imaging after intravenous administration of ultrasound contrast material. Am Heart J 2000;139(4):675-83. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dagianti A, Penco M, Agati L, et al. Stress echocardiography: comparison of exercise, dipyridamole and dobutamine in detecting and predicting the extent of coronary artery disease. J Am Coll Cardiol 1995;26(1):18-25. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dahan M, Viron BM, Poiseau E, et al. Combined dipyridamole-exercise stress echocardiography for detection of myocardial ischemia in hemodialysis patients: an alternative to stress nuclear imaging. Am J Kidney Dis 2002;40(4):737-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Daimon M, Watanabe H, Yamagishi H,, et al. Physiologic assessment of coronary artery stenosis by coronary flow reserve measurements with transthoracic Doppler echocardiography: comparison with exercise thallium-201 single piston emission computed tomography. J Am Coll Cardiol 2001;37(5):1310-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dal Porto R, Faletra F, Picano E,, et al. Safety, feasibility, and diagnostic accuracy of accelerated high-dose dipyridamole stress echocardiography. Am J Cardiol 2001;87(5):520-4. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dasciu SC, Herrera CJ, Stecy PJ,, et al. Usefulness of multislice computed tomographic coronary angiography to identify patients with abnormal myocardial perfusion stress in whom diagnostic catheterization may be safely avoided. Am J Cardiol 2007;100(11):1605-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Damins PG, Ahlberg AW, Travin MI,, et al. Visual assessment of left ventricular perfusion and function with electrocardiography-gated SPECT has high intraobserver and interobserver reproducibility among experienced nuclear cardiologists and cardiology trainees. J Nucl Cardiol 2002;9(3):263-70. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; No outcomes of interest.

Daoud D, Delahaye N, Vilain D,, et al. Identification of extensive coronary artery disease: incremental value of exercise TI-201 SPECT to clinical and stress test variables. J Nucl Cardiol 2002;9(2):161-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Davin L, Lancellotti P, Bruyere PJ,, et al. Diagnostic accuracy of computed tomography coronary angiography in routine practice. Acta Cardiol 2007;62(4):339-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Dawson D, Kaul S, Peters D,, et al. Prognostic value of dipyridamole stress myocardial contrast echocardiography: comparison with single photon emission computed tomography. J Am Soc Echocardiogr 2009;22(8):954-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for
symptomatic subgroup: All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dawson D, Rinkevich D, Belcik T., et al. Measurement of myocardial blood flow velocity reserve with myocardial contrast echocardiography in patients with suspected coronary artery disease: comparison with quantitative gated Technetium 99m sestamibi single photon emission computed tomography. J Am Soc Echocardiogr 2003;16(11):1171-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

de Albuquerque Fonseca L, Picano E. Comparison of dipyridamole and exercise stress echocardiography for detection of coronary artery disease (a meta-analysis). Am J Cardiol 2001;87(10):1193-6; A4. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

De Almeida MC, Markman Filho B. Prognostic value of dipyridamole stress echocardiography in women. Arq Bras Cardiol 2011;96(1):31-37. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization.


de Graaf FR, Schuijf JD, Scholte AJ., et al. Usefulness of hypertriglyceridemic waist phenotype in type 2 diabetes mellitus to predict the presence of coronary artery disease as assessed by computed tomographic coronary angiography. Am J Cardiol 2010;106(12):1747-53. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

De Graaf FR, Schuijf JD, Van Velzen JE., et al. Diagnostic accuracy of 320-row multidetector computed tomography coronary angiography in the non-invasive evaluation of significant coronary artery disease. Euro Heart J 2010;31(15):1908-1915. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

De Graaf FR, Schuijf JD, Van Velzen JE., et al. Assessment of global left ventricular function and volumes with 320-row multidetector computed tomography: A comparison with 2D-echocardiography. J Nucl Cardiol 2010;17(2):225-231. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

de Leon G, Aguade-Bruix S, Aliaga V., et al. Submaximal exercise testing plus atropine in myocardial perfusion SPECT. Rev Esp Cardiol 2010;63(10):1155-61. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

De Lima JJ, Sabbaga E, Vieira ML., et al. Coronary angiography is the best predictor of events in renal transplant candidates compared with noninvasive testing. Hypertension 2003;42(3):263-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

De Lorenzo A, Hachamovitch R, Kang X., et al. Prognostic value of myocardial perfusion SPECT versus exercise electrocardiography in patients with ST-segment depression on resting electrocardiography. J Nucl Cardiol 2005;12(6):653-61. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


De Vries ST, Kleijn SA, Van THAWJ., et al. Impact of high altitude on echocardiographically determined cardiac morphology and function in patients with coronary artery disease and healthy controls. European Journal of
DeCara JM. Noninvasive cardiac testing in women. J Am Med Womens Assoc 2003;58(4):254-63. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Deetjen A, Mollmann S, Conradi G., et al. Use of automatic exposure control in multislice computed tomography of the coronaries: comparison of 16-slice and 64-slice scanner data with conventional coronary angiography. Heart 2007;93(9):1040-3. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Demir H, Erbay G, Kir KM., et al. Clinical validation of technetium-99m MIBI-gated single photon emission computed tomography (SPECT) for avoiding false positive results in patients with left bundle-branch block: comparison with stress-rest nongated SPECT. Clin Cardiol 2003;26(4):182-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Dendukuri N, Chiu K, Brophy JM. Validity of electron beam computed tomography for coronary artery disease: a systematic review and meta-analysis. BMC Med 2007:5:35. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

DePuey EG, Guertler-Krawczynska E, D’Amato PH. Thallium-201 single photon emission computed tomography with intravenous dipyridamole to diagnose coronary artery disease. Coron Artery Dis 1990;75-82. Full-text exclusion reason(s): Data for women not reported as a subgroup.


Detrano R, Gianrossi R, Froelicher V. The diagnostic accuracy of the exercise electrocardiogram: a meta-analysis of 22 years of research. Prog Cardiovasc Dis 1989;32(3):173-206. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Dewey M, Rutsch W, Schnapauff D., et al. Coronary artery stenosis quantification using multislice computed tomography. Invest Radiol 2007;42(2):78-84. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*

Dewey M, Schnapauff D, Laule M., et al. Multislice CT coronary angiography: evaluation of an automatic vessel detection tool. Rofo 2004;176(4):478-83. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.*

Dewey M, Teige F, Rutsch W., et al. CT coronary angiography: influence of different cardiac reconstruction intervals on image quality and diagnostic accuracy. Eur J Radiol 2008;67(1):92-9. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.*

Dewey M, Zimmermann E, Deissenrieder F., et al. Noninvasive coronary angiography by 320-row computed tomography with lower radiation exposure and maintained diagnostic accuracy: comparison of results with cardiac catheterization in a head-to-head pilot investigation. Circulation 2009;120(10):867-75. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.*


Di Carli MF, Dorbala S. Cardiac PET-CT. J Thorac Imaging 2007;22(1):101-106. *Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.*

Di Carli MF, Dorbala S, Curillova Z., et al. Relationship between CT coronary angiography and stress perfusion imaging in patients with suspected ischemic heart disease assessed by integrated PET-CT imaging. J Nucl Cardiol 2007;14(6):799-809. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.*

Di Cesare E, Battisti S, Riva A., et al. Parallel imaging and dobutamine stress magnetic resonance imaging in patients with atypical chest pain or equivocal ECG not suitable for stress echocardiography. Radiol Med 2009;114(2):216-28. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*


Diederichsen AC, Petersen H, Jensen LO., et al. Diagnostic value of cardiac 64-slice computed tomography: importance of coronary calcium. Scand Cardiovasc J 2009;43(5):337-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Diederichsen ACP, Petersen H, Jensen LO., et al. Diagnostic value of cardiac 64-slice computed tomography: Importance of coronary calcium. Scand Cardiovasc J 2009;43(5):337-344. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dill T, Deetjen A, Ekinci O., et al. Radiation dose exposure in multislice computed tomography of the coronaries in comparison with conventional coronary angiography. Int J Cardiol 2008;124(3):307-11. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dirksen MS, Jukema JW, Bax JJ., et al. Cardiac multidetector-row computed tomography in patients with unstable angina. Am J Cardiol 2005;95(4):457-61. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Dodd JD, Rieber J, Pomerantsev E., et al. Quantification of nonculprit coronary lesions: comparison of cardiac 64-MDCT and invasive coronary angiography. AJR Am J Roentgenol 2008;191(2):432-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dodla S, Xie F, Smith M., et al. Real-time perfusion echocardiography during treadmill exercise and dobutamine stress testing. Heart 2010;96(3):220-5. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Dolan MS, Riad K, El-Shafei A., et al. Effect of intravenous contrast for left ventricular opacification and border definition on sensitivity and specificity of dobutamine stress echocardiography compared with coronary angiography in technically difficult patients. Am Heart J 2001;142(5):908-15. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Donati OF, Scheffel H, Stolzmann P., et al. Combined cardiac CT and MRI for the comprehensive workup of hemodynamically relevant coronary stenoses. AJR Am J Roentgenol 2010;194(4):920-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Dou KF, Yang MF, Yang YJ., et al. Myocardial 18F-FDG uptake after exercise-induced myocardial ischemia in patients with coronary artery disease. J Nucl Med 2008;49(12):1986-91. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. Journal of Epidemiology and Community Health 1998;52(6):377-84. Full-text exclusion reason(s): No data for NITs of interest (ECG, ECHO, SPECT, PET, CMR, CTA).

Dragu R, Kerner A, Gruberg L, et al. Angiographically uncertain left main coronary artery narrowings: correlation with multidetector computed tomography and intravascular ultrasound. Int J Cardiovasc Imaging 2008;24(5):557-63. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Drosch T, Tsiflikas I, Brodoefel H, et al. Semi-automatic assessment of global left ventricular function and left ventricular parameters with dual-source computed tomography: comparison with invasive angiography. Heart Vessels 2010;25(1):57-62. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Duarte R, Bettencourt N, Costa JC, et al. Coronary computed tomography angiography in a single cardiac cycle with a mean radiation dose of approximately 1 mSv: initial experience. Rev Port Cardiol 2010;29(11):1667-76. Full-text exclusion reason(s): Data for women not reported as a subgroup.


Dunn RF, Kelly DT, Bailey IK, et al. Serial exercise thallium myocardial perfusion scanning and exercise electrocardiography in the diagnosis of coronary artery disease. Aust N Z J Med 1979;9(5):547-53. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ebersole DG, Heironimus J, Toney MO, et al. Comparison of exercise and adenosine technetium-99m sestamibi myocardial scintigraphy for diagnosis of coronary artery disease in patients with left bundle branch block. Am J Cardiol 1993;71(5):450-3. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Eek C, Grenne B, Brunvand H, et al. Strain echocardiography predicts acute coronary occlusion in patients with non-ST-segment elevation acute coronary syndrome. European Journal of Echocardiography 2010;11(6):501-508. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ehara M, Surmely JF, Kawai M, et al. Diagnostic accuracy of 64-slice computed tomography for detecting angiographically significant coronary artery stenosis in an unselected consecutive patient population: comparison
with conventional invasive angiography. Circ J 2006;70(5):564-71. *Full-text exclusion reason(s):* No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Eisenberg MJ, Afilalo J, Lawler PR,, et al. Cancer risk related to low-dose ionizing radiation from cardiac imaging in patients after acute myocardial infarction. CMAJ 2011;183(4):430-6. *Full-text exclusion reason(s):* All women in the study are known to have CAD.

Elamin MS, Boyle R, Kardash MM,, et al. Accurate detection of coronary heart disease by new exercise test. Br Heart J 1982;48(4):311-20. *Full-text exclusion reason(s):* All women in the study are known to have CAD; Data for women not reported as a subgroup.

Elhendy A, Bax JJ, van Domburg RT,, et al. Dobutamine stress thallium-201 single-photon emission tomography versus echocardiography for evaluation of the extent and location of coronary artery disease late after myocardial infarction. Eur J Nucl Med 1999;26(5):467-73. *Full-text exclusion reason(s):* All women in the study are known to have CAD; Data for women not reported as a subgroup.

Elhendy A, Geleijnse L, Salustri A,, et al. T wave normalization during dobutamine stress testing in patients with non-Q wave myocardial infarction. A marker of myocardial ischaemia? Eur Heart J 1996;17(4):526-31. *Full-text exclusion reason(s):* All women in the study are known to have CAD.

Elhendy A, Geleijnse ML, Roelandt JR,, et al. Comparison of dobutamine stress echocardiography and 99m-technetium sestamibi SPECT myocardial perfusion scintigraphy for predicting extent of coronary artery disease in patients with healed myocardial infarction. Am J Cardiol 1997;79(1):7-12. *Full-text exclusion reason(s):* All women in the study are known to have CAD; Data for women not reported as a subgroup.

Elhendy A, Geleijnse ML, van Domburg RT,, et al. Comparison of dobutamine stress echocardiography and technetium-99m sestamibi single-photon emission tomography for the diagnosis of coronary artery disease in hypertensive patients with and without left ventricular hypertrophy. Eur J Nucl Med 1998;25(1):69-78. *Full-text exclusion reason(s):* All women in the study are known to have CAD; Data for women not reported as a subgroup.

Elhendy A, O'Leary EL, Xie F,, et al. Comparative accuracy of real-time myocardial contrast perfusion imaging and wall motion analysis during dobutamine stress echocardiography for the diagnosis of coronary artery disease. J Am Coll Cardiol 2004;44(11):2185-91. *Full-text exclusion reason(s):* No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Elhendy A, van Domburg RT, Roelandt JR, et al. Accuracy of dobutamine stress echocardiography for the diagnosis of coronary artery stenosis in patients with myocardial infarction: the impact of extent and severity of left ventricular dysfunction. Heart 1996;76(2):123-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


El-Mahalawy N, Abdel-Salam Z, Samir A, et al. Left ventricular transient ischemic dilation during dobutamine stress echocardiography predicts multi-vessel coronary artery disease. J Cardiol 2009;54(2):255-61. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Emre A, Ersek B, Gursurer M, et al. Angiographic and scintigraphic (perfusion and electrocardiogram-gated SPECT) correlates of clinical presentation in unstable angina. Clin Cardiol 2000;23(7):495-500. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Eren S, Bayram E, Fil F, et al. An investigation of the association between coronary artery dominance and coronary artery variations with coronary artery disease by multidetector computed tomographic coronary angiography. J Comput Assist Tomogr 2008;32(6):929-33. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Erhard I, Rieber J, Jung P, et al. The validation of fractional flow reserve in patients with coronary multivessel disease: a comparison with SPECT and contrast-enhanced dobutamine stress echocardiography. Z Kardiol 2005;94(5):321-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Eriksson SV. Vectorcardiography: A tool for non-invasive detection of reperfusion and reocclusion? Thromb Haemost 1999;82(SUPPL. 1):64-67. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Eskola MJ, Nikus KC, Holmvang L, et al. Value of the 12-lead electrocardiogram to define the level of obstruction in acute anterior wall myocardial infarction: correlation to coronary angiography and clinical outcome in the
DANAMI-2 trial. Int J Cardiol 2009(3):378-83. Full-text exclusion reason(s): No data for NITs of interest (ECG, ECHO, SPECT, PET, CMR, CTA).


Fallahi B, Beiki D, Fard-Esfahani A, et al. The additive value of transient left ventricular dilation using two-day dipyridamole 99mTc-MIBI SPET for screening coronary artery disease in patients with otherwise normal myocardial perfusion: a comparison between diabetic and non-diabetic cases. Hell J Nucl Med 2010;13(3):246-52. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Farzaneh-Far A, Kwong RY. Detecting acute coronary syndromes by magnetic resonance imaging. Heart and Metabolism 2011(50):15-19. Full-text exclusion reason(s): Not a clinical study report; Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry; Data for women not reported as a subgroup.


Feldman C, Vitola D, Schiavo N. Detection of coronary artery disease based on the calcification index obtained by helical computed tomography. Arq Bras Cardiol 2000;75(6):471-80. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Feola M, Biggi A, Ribichini F, et al. The diagnosis of coronary artery disease in hypertensive patients with chest pain and complete left bundle branch block: utility of adenosine Tc-99m tetrofosmin SPECT. Clin Nucl Med 2002;27(7):510-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Feencik M, Nomura CH, Maurovich-Horvat P, et al. Quantitative parameters of image quality in 64-slice computed tomography angiography of the coronary arteries. Eur J Radiol 2006;57(3):373-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Feencik M, Ropers D, Abbara S, et al. Diagnostic accuracy of image postprocessing methods for the detection of coronary artery stenoses by using multidetector CT. Radiology 2007;243(3):696-702. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Fernandes LP, Tardif JC, Arsenault A, et al. Detection of myocardial perfusion abnormalities after a recent acute coronary syndrome by quantitative Levovist myocardial contrast echocardiography: comparison with 99mTc-Myoview SPECT imaging. Can J Cardiol 2003;19(3):251-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Fesmire FM, Hughes AD, Stout PK, et al. Selective dual nuclear scanning in low-risk patients with chest pain to reliably identify and exclude acute coronary syndromes. Ann Emerg Med 2001;38(3):207-15. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Feuchtner G, Postel T, Weidinger F, et al. Is there a relation between non-calcifying coronary plaques and acute coronary syndromes? A retrospective study using multislice computed tomography. Cardiology 2008;110(4):241-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Fine JJ, Hopkins CB, Ruff N, et al. Comparison of accuracy of 64-slice cardiovascular computed tomography with coronary angiography in patients with suspected coronary artery disease. Am J Cardiol 2006;97(2):173-4. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Finkelhor RS, Newhouse KE, Vrobel TR, et al. The ST segment/heart rate slope as a predictor of coronary artery disease: comparison with quantitative thallium imaging and conventional ST segment criteria. Am Heart J 1986;112(2):296-304. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

E-39

Fleischmann S, Koepfli P, Namdar M, et al. Gated (99m)Tc-tetrofosmin SPECT for discriminating infarct from artifact in fixed myocardial perfusion defects. J Nucl Med 2004;45(5):754-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Fleming RM. High-dose dipyridamole and gated sestamibi SPECT imaging provide diagnostic resting and stress ejection fractions useful for predicting extent of coronary artery disease. Angiology 2002;53(4):415-21. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Florh TG, McCollough CH, Bruder H, et al. First performance evaluation of a dual-source CT (DSCT) system. Eur Radiol 2006;16(2):256-68. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Forster S, Rieber J, Ubleis C, et al. Tc-99m sestamibi single photon emission computed tomography for guiding percutaneous coronary intervention in patients with multivessel disease: a comparison with quantitative coronary angiography and fractional flow reserve. Int J Cardiovasc Imaging 2010;26(2):203-13. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Forster T, McNeill AJ, Salustri A, et al. Simultaneous dobutamine stress echocardiography and technetium-99m isonitrile single-photon emission computed tomography in patients with suspected coronary artery disease. J Am Coll Cardiol 1993;21(7):1591-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Fragasso G, Lu C, Dabrowski P, et al. Comparison of stress/rest myocardial perfusion tomography, dipyridamole and dobutamine stress echocardiography for the detection of coronary disease in hypertensive patients with chest pain and positive exercise test. J Am Coll Cardiol 1999;34(2):441-7. Full-text exclusion reason(s): All women in the study are known to have CAD.


Freeman JA, Corbin M, Dunn M, et al. Correlation of single lead telemetric treadmill exercise testing with coronary angiography. J Electrocardiol 1973;6(3):231-4. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.
E-41


Fujitaka K, Nakamura S, Sugiura T., et al. Combined analysis of multislice computed tomography coronary angiography and stress-rest myocardial perfusion imaging in detecting patients with significant proximal coronary artery stenosis. Nucl Med Commun 2009;30(10):789-96. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Gaemperli O, Schepis T, Valenta I., et al. Functionally relevant coronary artery disease: comparison of 64-section CT angiography with myocardial perfusion SPECT. Radiology 2008;248(2):414-23. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Gaibazzi N, Reverberi C, Badano L. Usefulness of contrast stress-echocardiography or exercise-electrocardiography to predict long-term acute coronary syndromes in patients presenting with chest pain without electrocardiographic abnormalities or 12-hour troponin elevation. Am J Cardiol 2011;107(2):161-7. Full-text exclusion reason(s): Data for women not reported as a subgroup.


Gaibazzi N, Rigo F, Squeri A, et al. Incremental value of contrast myocardial perfusion to detect intermediate versus severe coronary artery stenosis during stress-echocardiography. Cardiovasc Ultrasound 2010;8:16. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Data for women not reported as a subgroup.


Galassi AR, Azzarelli S, Lupo L, et al. Accuracy of exercise testing in the assessment of the severity of myocardial ischemia as determined by means of technetium-99m tetrofosmin SPECT scintigraphy. J Nucl Cardiol 2000;7(6):575-83. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. Ann Intern Med 1999;130(9):719-28. **Full-text exclusion reason(s):** Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Garcia MJ, Lessick J, Hoffmann MH. Accuracy of 16-row multidetector computed tomography for the assessment of coronary artery stenosis. JAMA 2006;296(4):403-11. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Data for women not reported as a subgroup.

Gaspar T, Dvir D, Peled N. The role of 16-slice computed tomography angiography in the diagnosis of coronary artery disease: large sample analysis. Isr Med Asso J 2005;7(7):424-7. **Full-text exclusion reason(s):** No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Gebker R, Jahnke C, Manka R, et al. Additional value of myocardial perfusion imaging during dobutamine stress magnetic resonance for the assessment of coronary artery disease. Circ Cardiovasc Imaging 2008;1(2):122-30. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Data for women not reported as a subgroup.

Gebker R, Jahnke C, Paetsch I, et al. Diagnostic performance of myocardial perfusion MR at 3 T in patients with coronary artery disease. Radiology 2008;247(1):57-63. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Data for women not reported as a subgroup.

Geleijnse ML, Elhendy A. Can stress echocardiography compete with perfusion scintigraphy in the detection of coronary artery disease and cardiac risk assessment? Eur J Echocardiogr 2000;1(1):12-21. **Full-text exclusion reason(s):** Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Geleijnse ML, Krenning BJ, Soliman OL, et al. Dobutamine stress echocardiography for the detection of coronary artery disease in women. Am J Cardiol 2007;99(5):714-7. **Full-text exclusion reason(s):** Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry; Data for women not reported as a subgroup.


George RT, Arbab-Zadeh A, Miller JM, et al. Adenosine stress 64- and 256-row detector computed tomography angiography and perfusion imaging: a pilot study evaluating the transmural extent of perfusion abnormalities to predict atherosclerosis causing myocardial ischemia. Circ Cardiovasc Imaging 2009;2(3):174-82. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ghersin E, Litmanovich D, Dragu R, et al. 16-MDCT coronary angiography versus invasive coronary angiography in acute chest pain syndrome: a blinded prospective study. AJR Am J Roentgenol 2006;186(1):177-84. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ghaffari S, Caussin C, Daoud B, et al. Noninvasive Detection of Coronary Artery Disease in Patients with Left Bundle Branch Block Using 64-Slice Computed Tomography. 55th Annual Scientific Session of the American College of Cardiology, Georgia World Congress Center, Atlanta, Georgia (USA), 11-14 Mar 2006 2006. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Gibson PB, Demus D, Noto R, et al. Low event rate for stress-only perfusion imaging in patients evaluated for chest pain. J Am Coll Cardiol 2002;39(6):999-1004. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Gigli G, Cortigiani L, Vallebona A, et al. Vasodilator stress echocardiography for risk stratification of medically stabilized unstable angina. Eur J Echocardiogr 2002;3(1):59-66. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Giorgetti A, Marzullo P, Sambuceti G, et al. Baseline/post-nitrate Tc-99m tetrofosmin mismatch for the assessment of myocardial viability in patients with severe left ventricular dysfunction: comparison with baseline Tc-99m tetrofosmin scintigraphy FDG PET imaging. J Nucl Cardiol 2004;11(2):142-51. Full-text exclusion reason(s): All women in the study are known to have CAD.

Giorgetti A, Rossi M, Stanislao M, et al. Feasibility and diagnostic accuracy of a gated SPECT early-imaging protocol: a multicenter study of the Myoview Imaging Optimization Group. J Nucl Med 2007;48(10):1670-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Girotra S, Keelan M, Weinstein AR, et al. Relation of heart rate response to exercise with prognosis and atherosclerotic progression after coronary artery bypass grafting. Am J Cardiol 2009;103(10):1386-90. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Go RT, Marwick TH, MacIntyre WJ, et al. A prospective comparison of rubidium-82 PET and thallium-201 SPECT myocardial perfusion imaging utilizing a single dipyridamole stress in the diagnosis of coronary artery disease. J Nucl Med 1990;31(12):1899-905. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Goldschlager N, Selzer A, Cohn K. Treadmill stress tests as indicators of presence and severity of coronary artery disease. Ann Intern Med 1976;85(3):277-86. Full-text exclusion reason(s): Population does not include women ≥ age 18; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Gonzalez P, Massardo T, Jofre MJ, et al. (201)T1 myocardial SPECT detects significant coronary artery disease between 50% and 75% angiogram stenosis. Revista Espanola de Medicina Nuclear 2005;24(5):305-311. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Gonzalez P, Massardo T, Jofre MJ, et al. 201T1 myocardial SPECT detects significant coronary artery disease between 50% and 75% angiogram stenosis. Rev Esp Med Nucl 2005;24(5):305-11. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Gould KL. Positron emission tomography and interventional cardiology. Am J Cardiol 1990;66(14):51F-58F. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Gotthardt H, Varenne O, Trinquart L, et al. Coronary artery stenosis in high-risk patients: 64-section CT and coronary angiography—prospective study and analysis of discordance. Radiology 2009;252(2):377-85. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Grover-McKay M, Milne N, Atwood JE, et al. Comparison of thallium-201 single-photon emission computed tomographic scintigraphy with intravenous dipyridamole and arm exercise. Am Heart J 1994;127(6):1516-20. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.
Grover-McKay M, Ratib O, Schwaiger M, et al. Detection of coronary artery disease with positron emission tomography and rubidium 82. Am Heart J 1992;123(3):646-52. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Groves AM, Speechly-Dick ME, Dickson JC, et al. Cardiac 82Rubidium PET/CT: initial European experience. Eur J Nucl Med Mol Imaging 2007;34(12):1965-72. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Gu X, He Y, Li Z, et al. Relation between the incidence, location, and extent of thoracic aortic atherosclerosis detected by transesophageal echocardiography and the extent of coronary artery disease by angiography. Am J Cardiol 2011;107(2):175-8. Full-text exclusion reason(s): All women in the study are known to have CAD.


Gunes Y, Gumrukcuoglu HA, Kaya Y, et al. Incremental diagnostic value of color M-mode propagation velocity of the descending thoracic aorta to exercise electrocardiography. Turk Kardiyoloji Dernek Arsivi 2010;38(8):551-557. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Guo SZ, Shu XH, Pan CZ, et al. Usefulness of dobutamine stress myocardial contrast echocardiography for assessing coronary artery disease. Chin Med J (Engl) 2005;118(21):1766-72. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Gupta NC, Esterbrooks DJ, Hilleman DE, et al. Comparison of adenosine and exercise thallium-201 single-photon emission computed tomography (SPECT) myocardial perfusion imaging. The GE SPECT Multicenter Adenosine Study Group. J Am Coll Cardiol 1992;19(2):248-57. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Hachamovitch R, Johnson JR, Hlatky MA, et al. The study of myocardial perfusion and coronary anatomy imaging roles in CAD (SPARC): design, rationale, and baseline patient characteristics of a prospective, multicenter observational registry comparing PET, SPECT, and CTA for resource utilization and clinical outcomes. J Nucl Cardiol 2009;16(6):935-48. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Hacker M, Jakobs T, Hack N, et al. Combined use of 64-slice computed tomography angiography and gated myocardial perfusion SPECT for the detection of functionally relevant coronary artery stenoses. First results in a clinical setting concerning patients with stable angina. Nuklearmedizin 2007;46(1):29-35. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Hacker M, Jakobs T, Matthiesen F, et al. Comparison of spiral multidetector CT angiography and myocardial perfusion imaging in the noninvasive detection of functionally relevant coronary artery lesions: first clinical experiences. J Nucl Med 2005;46(8):1294-300. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Hajduczki I, Berenyi I, Enghoff E, et al. Qualitative and quantitative evaluation of the exercise electrocardiogram in assessing the degree of coronary heart disease. J Electrocardiol 1985;18(1):55-62. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Hajjiri MM, Leavitt MB, Zheng H, et al. Comparison of positron emission tomography measurement of adenosine-stimulated absolute myocardial blood flow versus relative myocardial tracer content for physiological assessment of coronary artery stenosis severity and location. JACC Cardiovasc Imaging 2009;2(6):751-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Halon DA, Gaspar T, Adawi S, et al. Uses and limitations of 40 slice multi-detector row spiral computed tomography for diagnosing coronary lesions in unselected patients referred for routine invasive coronary angiography. Cardiology 2007;108(3):200-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Halpern EJ, Halpern DJ. Diagnosis of coronary stenosis with CT angiography comparison of automated computer diagnosis with expert readings. Acad Radiol 2011;18(3):324-33. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Halaska B, Case C, Short L, et al. Effect of power Doppler and digital subtraction techniques on the comparison of myocardial contrast echocardiography with SPECT. Heart 2001;85(5):549-55. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Hamdan A, Asbach P, Wellnhofer E., et al. A prospective study for comparison of MR and CT imaging for detection of coronary artery stenosis. JACC Cardiovasc Imaging 2011;4(1):50-61. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Hamirani YS, Isma'eel H, Larijani V., et al. The diagnostic accuracy of 64-detector cardiac computed tomography compared with stress nuclear imaging in patients undergoing invasive cardiac catheterization. J Comput Assist Tomogr 2010;34(5):645-51. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Hamon M, Morello R, Riddell JW. Coronary arteries: diagnostic performance of 16- versus 64-section spiral CT compared with invasive coronary angiography—meta-analysis. Radiology 2007;245(3):720-31. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Han SC, Fang CC, Chen Y., et al. Coronary computed tomography angiography—a promising imaging modality in diagnosing coronary artery disease. J Chin Med Assoc 2008;71(5):241-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Haramati LB, Levsky JM, Jain VR., et al. CT angiography for evaluation of coronary artery disease in inner-city outpatients: an initial prospective comparison with stress myocardial perfusion imaging. Int J Cardiovasc Imaging 2009;25(3):303-13. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Harinstein ME, Flaherty JD, Ansari AH., et al. Predictive value of dobutamine stress echocardiography for coronary artery disease detection in liver transplant candidates. American Journal of Transplantation 2008;8(7):1523-1528. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Hart CY, Miller TD, Hodge DO., et al. Specificity of the stress electrocardiogram during adenosine myocardial perfusion imaging in patients taking digoxin. Am Heart J 2000;140(6):937-40. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Hatanaka K, Doi M, Hirohata S., et al. Safety of and tolerance to adenosine infusion for myocardial perfusion single-photon emission computed tomography in a Japanese population. Circ J 2007;71(6):904-10. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Hausleiter J, Meyer T, Hadamitzky M., et al. Non-invasive coronary computed tomographic angiography for patients with suspected coronary artery disease: the Coronary Angiography by Computed Tomography with the Use of a Submillimeter resolution (CACTUS) trial. Eur Heart J 2007;28(24):3034-41. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Hausleiter J, Meyer T, Hermann F., et al. Estimated radiation dose associated with cardiac CT angiography. JAMA 2009;301(5):500-7. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


He Q, Yao Z, Yu X., et al. Evaluation of (99m)Tc-MIBI myocardial perfusion imaging with intravenous infusion of adenosine triphosphate in diagnosis of coronary artery disease. Chin Med J (Engl) 2002;115(11):1603-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

He ZX, Shi RF, Wu YJ., et al. Direct imaging of exercise-induced myocardial ischemia with fluorine-18-labeled deoxyglucose and Tc-99m-sestamibi in coronary artery disease. Circulation 2003;108(10):1208-13. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Hecht HS, Blumfield DE, Hopkins JM., et al. Single dose exercise and redistribution 201thallium scanning in the diagnosis of myocardial ischemia and coronary artery disease. Comparison with exercise and rest electrocardiography, coronary arteriography and left ventriculography. Chest 1980;77(3):359-68. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Hecht HS, DeBord L, Shaw R., et al. Supine bicycle stress echocardiography versus tomographic thallium-201 exercise imaging for the detection of coronary artery disease. J Am Soc Echocardiogr 1993;6(2):177-85. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Heinicke N, Benesch B, Kaiser T., et al. Mechanisms of regional wall motion abnormalities in contrast-enhanced dobutamine stress echocardiography. Clin Res Cardiol 2006;95(12):650-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Heinle SK, Noblin J, Goree-Best P., et al. Assessment of myocardial perfusion by harmonic power Doppler imaging at rest and during adenosine stress: comparison with (99m)Tc-sestamibi SPECT imaging. Circulation 2000;102(1):55-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not...
Hendel RC, Layden JJ, Leppo JA. Prognostic value of dipyridamole thallium scintigraphy for evaluation of ischemic heart disease. J Am Coll Cardiol 1990;15(1):109-16. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Herzog BA, Husmann L, Burkhard N., et al. Accuracy of low-dose computed tomography coronary angiography using prospective electrocardiogram-triggering: first clinical experience. Eur Heart J 2008;29(24):3037-42. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Herzog BA, Wyss CA, Husmann L., et al. First head-to-head comparison of effective radiation dose from low-dose 64-slice CT with prospective ECG-triggering versus invasive coronary angiography. Heart 2009;95(20):1656-61. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Hida S, Chikamori T, Tanaka H, et al. Sex-specific approach to gated SPECT volumetric analysis after stress and at rest to detect high-risk coronary artery disease. Nucl Med Commun 2010;31(9):800-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Hirano Y, Ozasa Y, Yamamoto T, et al. Diagnosis of vasospastic angina by hyperventilation and cold-pressor stress echocardiography: comparison to I-MIBG myocardial scintigraphy. J Am Soc Echocardiogr 2002;15(6):617-23. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Hlaihel C, Boussel L, Cochet H, et al. Dose and image quality comparison between prospectively gated axial and retrospectively gated helical coronary CT angiography. Br J Radiol 2011;84(997):51-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Ho JS, Barlow CE, Reinhardt DB, et al. Effect of increasing body mass index on image quality and positive predictive value of 100-kV coronary computed tomographic angiography. Am J Cardiol 2010;106(8):1182-1186. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.
Ho KT, Chua KC, Klotz E., et al. Stress and rest dynamic myocardial perfusion imaging by evaluation of complete time-attenuation curves with dual-source CT. JACC: Cardiovascular Imaging 2010;3(8):811-820. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Hoffmann MH, Shi H, Schmitz BL., et al. Noninvasive coronary angiography with multislice computed tomography. JAMA 2005;293(20):2471-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Hoffmann R, Borges AC, Kasprzak JD., et al. Analysis of myocardial perfusion or myocardial function for detection of regional myocardial abnormalities. An echocardiographic multicenter comparison study using myocardial contrast echocardiography and 2D echocardiography. Eur J Echocardiogr 2007;8(6):438-48. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Hoffmann R, Lethen H, Kleinmans E., et al. Comparative evaluation of bicycle and dobutamine stress echocardiography with perfusion scintigraphy and bicycle electrocardiogram for identification of coronary artery disease. Am J Cardiol 1993;72(7):555-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.


Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Hoffmann S, Mogelvang R, Sogaard P., et al. Tissue Doppler echocardiography reveals impaired cardiac function in patients with reversible ischaemia. European Journal of Echocardiography 2011;12(8):628-634. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Hoffmann U, Nagurney JT, Moselewski F., et al. Coronary multidetector computed tomography in the assessment of patients with acute chest pain. Circulation 2006;114(21):2251-60. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Hoppe H, Spagnuolo S, Froehlich JM., et al. Retrospective analysis of patients for development of nephrogenic systemic fibrosis following conventional angiography using gadolinium-based contrast agents. Euro Radiol 2010;20(3):595-603. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Hou Y, Yue Y, Guo W., et al. Prospectively versus retrospectively ECG-gated 256-slice coronary CT angiography: image quality and radiation dose over expanded heart rates. Int J Cardiovasc Imaging 2010. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

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Hozumi T, Yoshida K, Ogata Y., et al. Noninvasive assessment of significant left anterior descending coronary artery stenosis by coronary flow velocity reserve with transthoracic color Doppler echocardiography. Circulation 1998;97(16):1557-62. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Hu SJ, Liu SX, Katus HA., et al. The value of contrast dobutamine stress echocardiography on detecting coronary artery disease in overweight and obese patients. Can J Cardiol 2007;23(11):885-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Huixing D, Aiqun M, Aimin Y., et al. Clinical evaluation of Technetium-99m sestamibi myocardial perfusion SPECT in diabetes with suspected coronary artery diseases. Journal of Medical Colleges of PLA 2010;25(4):220-225. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Hung GU, Lee KW, Chen CP., et al. Relationship of transient ischemic dilation in dipyridamole myocardial perfusion imaging and stress-induced changes of functional parameters evaluated by TI-201 gated SPECT. J Nucl Cardiol 2005;12(3):268-75. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Husmann L, Herzog BA, Burger IA., et al. Usefulness of additional coronary calcium scoring in low-dose CT coronary angiography with prospective ECG-triggering impact on total effective radiation dose and diagnostic accuracy. Acad Radiol 2010;17(2):201-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Husmann L, Scheffel H, Valenta I., et al. Impact of hypertension on the diagnostic accuracy of coronary angiography with computed tomography. Int J Cardiovasc Imaging 2008;24(7):763-70. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Husmann L, Schepis T, Scheffel H., et al. Comparison of diagnostic accuracy of 64-slice computed tomography coronary angiography in patients with low, intermediate, and high cardiovascular risk. Acad Radiol 2008;15(4):452-61. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Husmann L, Valenta I, Gaemperli O., et al. Feasibility of low-dose coronary CT angiography: first experience with prospective ECG-gating. Eur Heart J 2008;29(2):191-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Husmann L, Wiegand M, Valenta I., et al. Diagnostic accuracy of myocardial perfusion imaging with single photon emission computed tomography and positron emission tomography: a comparison with coronary angiography. Int J Cardiovasc Imaging 2008;24(5):511-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Husser O, Bodi V, Sanchis J., et al. Additional diagnostic value of systolic dysfunction induced by dipyridamole stress cardiac magnetic resonance used in detecting coronary artery disease. Rev Esp Cardiol 2009;62(4):383-91. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ikonen AE, Manninen HI, Vainio P., et al. Three-dimensional respiratory-gated coronary MR angiography with reference to X-ray coronary angiography. Acta Radiol 2003;44(6):583-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Imamura Y, Fukuyama T, Nishimura S., et al. Normal myocardial perfusion scan portends a benign prognosis independent from the pretest probability of coronary artery disease. Sub-analysis of the J-ACCESS study. J Cardiol 2009;54(1):93-100. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Iskandrian AS, Hakki AH, Kane-Marsch S. Prognostic implications of exercise thallium-201 scintigraphy in patients with suspected or known coronary artery disease. Am Heart J 1985;110(1 Pt 1):135-43. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Iskandrian AS, Heo J, Decoskey D, et al. Use of exercise thallium-201 imaging for risk stratification of elderly patients with coronary artery disease. Am J Cardiol 1988;61(4):269-72. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Iskandrian AS, Heo J, Kong B, et al. Effect of exercise level on the ability of thallium-201 tomographic imaging in detecting coronary artery disease: analysis of 461 patients. J Am Coll Cardiol 1989;14(6):1477-86. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Isebe S, Sato K, Sugiuara K, et al. Feasibility of intravenous administration of landiolol hydrochloride for multislice computed tomography coronary angiography: initial experience. Circ J 2008;72(11):1814-20. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Iwakoshi K, Matsumoto T, Aono H, et al. Prevalence of subclinical atherosclerosis in asymptomatic patients with low-to-intermediate risk by 64-slice computed tomography. Coron Artery Dis 2011;22(1):18-25. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Jahnke C, Paetsch I, Nehlke K, et al. Rapid and complete coronary arterial tree visualization with magnetic resonance imaging: feasibility and diagnostic performance. Eur Heart J 2005;26(21):2313-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Jahnke C, Paetsch I, Schnackenburg B, et al. Coronary MR angiography with steady-state free precession: individually adapted breath-hold technique versus free-breathing technique. Radiology 2004;232(3):669-76. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Jeetley P, Burden L, Greaves K, et al. Prognostic value of myocardial contrast echocardiography in patients presenting to hospital with acute chest pain and negative troponin. Am J Cardiol 2007;99(10):1369-73. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Jeetley P, Burden L, Senior R. Stress echocardiography is superior to exercise ECG in the risk stratification of patients presenting with acute chest pain with negative Troponin. Eur J Echocardiogr 2006;7(2):155-64. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Jeetley P, Burden L, Stoykova B, et al. Clinical and economic impact of stress echocardiography compared with exercise electrocardiography in patients with suspected acute coronary syndrome but negative troponin: a prospective randomized controlled study. Eur Heart J 2007;28(2):204-11. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Jeetley P, Hickman M, Kamp O, et al. Myocardial contrast echocardiography for the detection of coronary artery stenosis: a prospective multicenter study in comparison with single-photon emission computed tomography. J Am Coll Cardiol 2006;47(1):141-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Jeong DW, Choo KS, Baik SK, et al. Step-and-shoot prospectively ECG-gated versus retrospectively ECG-gated with tube current modulation coronary CT angiography using the 128-slice MDCT: comparison of image quality and radiation dose. Acta Radiol 2011;52(2):155-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Jeong HC, Ahn Y, Ko JS, et al. The role of 64-slice multi-detector computed tomography in the detection of subclinical atherosclerosis of the coronary artery. Int J Cardiovasc Imaging 2010;26(Suppl 2):253-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Jiang B, Gai L, Sun Z, et al. The combination of 64 multislice CT angiography and optical coherence tomography optimally characterizes coronary plaques. Acta Cardiol 2011;66(2):213-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Jinza M, Sato K, Tanami Y, et al. Diagnostic accuracy of angiographic view image for the detection of coronary artery stenoses by 64-detector row CT: a pilot study comparison with conventional post-processing methods and axial images alone. Circ J 2009;73(4):691-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Johansen AH, Poulsen TS, Hoilund-Carlsen PF, et al. Myocardial perfusion imaging and coronary angiography in patients with known or suspected stable angina pectoris. Dan Med Bull 2001;48(2):80-3. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Johnson NP, Schimmel DR, Jr., Dyer SP, et al. Survival by stress modality in patients with a normal myocardial perfusion study. Am J Cardiol 2011;107(7):986-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Johnson TR, Nikolaou K, Busch S, et al. Diagnostic accuracy of dual-source computed tomography in the diagnosis of coronary artery disease. Invest Radiol 2007;42(10):684-91. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Johnson TR, Nikolaou K, Wintersperger BJ, et al. ECG-gated 64-MDCT angiography in the differential diagnosis of acute chest pain. AJR Am J Roentgenol 2007;188(1):76-82. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Jonsbu E, Dammen T, Morken G, et al. Cardiac and psychiatric diagnoses among patients referred for chest pain and palpitations. Scand Cardiovasc J 2009;43(4):256-9. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Kachenoura N, Gaspar T, Lodato JA, et al. Combined assessment of coronary anatomy and myocardial perfusion using multidetector computed tomography for the evaluation of coronary artery disease. Am J Cardiol 2009;103(11):1487-94. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Kamal AM, Fattah AA, Pancholy S., et al. Prognostic value of adenosine single-photon emission computed tomographic thallium imaging in medically treated patients with angiographic evidence of coronary artery disease. J Nucl Cardiol 1994;1(3):254-61. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kaneko K, Ito M, Takanashi T., et al. Computed tomography and scintigraphy vs. cardiac catheterization for coronary disease screening prior to noncardiac surgery. Internal Medicine 2010;49(16):1703-1710. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kanzaki H, Nakatani S, Kandori A., et al. A new screening method to diagnose coronary artery disease using multichannel magnetocardiogram and simple exercise. Basic Res Cardiol 2003;98(2):124-32. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Karabinos IK, Papadopoulos A, Karvouni E., et al. Reliability and safety of dobutamine stress echocardiography for detection of myocardial ischemia-viability: Experience from 802 consecutive studies. Hellenic Journal of Cardiology 2004;45(2):71-83. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Karagiannis SE, Bax JJ, Elhendy A., et al. Enhanced sensitivity of dobutamine stress echocardiography by observing wall motion abnormalities during the recovery phase after acute beta-blocker administration. Am J Cardiol 2006;97(4):462-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

2009;25(3):277-83. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Kasalicky J, Kovac I, Lanska V. Pretest clinical diagnosis of coronary artery disease and stress myocardial perfusion scintigram. Nucl Med Rev Cent East Eur 2001;4(2):89-92. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Katayama T, Ogata N, Tsuruya Y. Diagnostic accuracy of supine and prone thallium-201 stress myocardial perfusion single-photon emission computed tomography to detect coronary artery disease in inferior wall of left ventricle. Ann Nucl Med 2008;22(4):317-21. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kato S, Kitagawa K, Ishida N, et al. Assessment of coronary artery disease using magnetic resonance coronary angiography: A national multicenter trial. J Am Coll Cardiol 2010;56(12):983-991. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kaul S, Boucher CA, Newell JB, et al. Determination of the quantitative thallium imaging variables that optimize detection of coronary artery disease. J Am Coll Cardiol 1986;7(3):527-37. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kawase Y, Nishimoto M, Hato K, et al. Assessment of coronary artery disease with nicorandil stress magnetic resonance imaging. Osaka City Med J 2004;50(2):87-94. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Kefer J, Coche E, Legros G, et al. Head-to-head comparison of three-dimensional navigator-gated magnetic resonance imaging and 16-slice computed tomography to detect coronary artery stenosis in patients. J Am Coll Cardiol 2005;46(1):92-100. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Kelle S, Hamdan A, Schnackenburg B, et al. Dobutamine stress cardiovascular magnetic resonance at 3 Tesla. J Cardiovasc Magn Reson 2008;10:44. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Khan MF, Wesarg S, Gurung J,, et al. Facilitating coronary artery evaluation in MDCT using a 3D automatic vessel segmentation tool. Eur Radiol 2006;16(8):1789-95. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Khorsand A, Graf S, Sochor H,, et al. Automated assessment of myocardial SPECT perfusion scintigraphy: a comparison of different approaches of case-based reasoning. Artif Intell Med 2007;40(2):103-13. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Khorsand A, Haddad M, Graf S,, et al. Automated assessment of dipyridamole 201Tl myocardial SPECT perfusion scintigraphy by case-based reasoning. J Nucl Med 2001;42(2):189-93. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Kiat H, Maddahi J, Roy LT,, et al. Comparison of technetium 99m methoxy isobutyl isonitrile and thallium 201 for evaluation of coronary artery disease by planar and tomographic methods. Am Heart J 1989;117(1):1-11. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Kim J, Lee H, Song S,, et al. Efficacy and safety of the computed tomography coronary angiography based approach for patients with acute chest pain at an emergency department: one month clinical follow-up study. J Korean Med Sci 2010;25(3):466-71. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kim TH, Yu SH, Choi SH,, et al. Pericardial fat amount is an independent risk factor of coronary artery stenosis assessed by multidetector-row computed tomography: The korean atherosclerosis study 2. Obesity 2011;19(5):1028-1034. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Kim WY, Danias PG, Stuber M., et al. Coronary magnetic resonance angiography for the detection of coronary stenoses. N Engl J Med 2001;345(26):1863-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kim YJ, Seo JS, Choi BW,, et al. Feasibility and diagnostic accuracy of whole heart coronary MR angiography using free-breathing 3D balanced turbo-field-echo with SENSE and the half-fourier acquisition technique. Korean J Radiol 2006;7(4):235-42. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kirchin MA, Pirovano G, Venetianer C., et al. Safety assessment of gadobenate dimeglumine (MultiHance): extended clinical experience from phase I studies to post-marketing surveillance. J Magn Reson Imaging 2001;14(3):281-94. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.


Kisacik HL, Ozdemir K, Altinyay E, et al. Comparison of exercise stress testing with simultaneous dobutamine stress echocardiography and technetium-99m isonitrile single-photon emission computerized tomography for diagnosis of coronary artery disease. Eur Heart J 1996;17(1):113-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kitagawa K, Sakuma H, Nagata M, et al. Diagnostic accuracy of stress myocardial perfusion MRI and late gadolinium-enhanced MRI for detecting flow-limiting coronary artery disease: a multicenter study. Eur Radiol 2008;18(12):2808-16. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Klmpp B, Hoevelborn T, Fenchel M, et al. Magnetic resonance myocardial perfusion imaging-First experience at 3.0T. Eur J Radiol 2009;69(1):165-72. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Klmpp BD, Seeger A, Doesch C, et al. High resolution myocardial magnetic resonance stress perfusion imaging at 3 T using a 1 M contrast agent. Eur Radiol 2010;20(3):533-41. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Knez A, Becker CR, Leber A, et al. Usefulness of multislice spiral computed tomography angiography for determination of coronary artery stenoses. Am J Cardiol 2001;88(10):1191-4. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ko SM, Kim NR, Kim DH, et al. Assessment of image quality and radiation dose in prospective ECG-triggered coronary CT angiography compared with retrospective ECG-gated coronary CT angiography. Int J Cardiovasc Imaging 2010;26 Suppl 1:93-101. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Koh AS, Flores JLS, Keng FYJ, et al. Evaluation of the American College of Cardiology Foundation/American Society of Nuclear Cardiology appropriateness criteria for SPECT myocardial perfusion imaging in an Asian tertiary cardiac center. J Nucl Cardiol 2011;18(2):323-330. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Koide Y, Yotsukura M, Yoshino H, et al. Usefulness of QT dispersion immediately after exercise as an indicator of coronary stenosis independent of gender or exercise-induced ST-segment depression. Am J Cardiol 2000;86(12):1312-7. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Kolnes K, Velle OH, Hareide S, et al. Multislice computed tomography coronary angiography at a local hospital: Pitfalls and potential. Acta Radiol 2006;47(7):680-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kontos MC, Dilsizian V, Weiland F, et al. Iodofiltic acid I 123 (BMIPP) fatty acid imaging improves initial diagnosis in emergency department patients with suspected acute coronary syndromes: a multicenter trial. J Am Coll Cardiol 2010;56(4):290-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kontos MC, Hinchman D, Cunningham M, et al. Comparison of contrast echocardiography with single-photon emission computed tomographic myocardial perfusion imaging in the evaluation of patients with possible acute coronary syndromes in the emergency department. Am J Cardiol 2003;91(9):1099-102. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kontos MC, Schmidt KL, McCue M, et al. A comprehensive strategy for the evaluation and triage of the chest pain patient: a cost comparison study. J Nucl Cardiol 2003;10(3):284-90. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Kopp AF, Schroeder S, Kuettner A, et al. Non-invasive coronary angiography with high resolution multidetector-row computed tomography. Results in 102 patients. Eur Heart J 2002;23(21):1714-25. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Korosoglou G, Dubart AE, DaSilva KG, Jr., et al. Real-time myocardial perfusion imaging for pharmacologic stress testing: added value to single photon emission computed tomography. Am Heart J 2006;151(1):131-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Korosoglou G, Elhmiyi Y, Steen H, et al. Prognostic value of high-dose dobutamine stress magnetic resonance imaging in 1,493 consecutive patients: assessment of myocardial wall motion and perfusion. J Am Coll Cardiol 2010;56(15):1225-34. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Korosoglou G, Labadze N, Hansen A, et al. Usefulness of real-time myocardial perfusion imaging in the evaluation of patients with first time chest pain. Am J Cardiol 2004;94(10):1225-31. Full-text exclusion reason(s): All women in the study are known to have CAD.

Kostkiewicz M, Konieczynska M, Szot WM, et al. Comparison between (99m)Tc-MIBI myocardial perfusion SPECT and multi-slice computed tomography for identifying and assessing coronary artery disease. Hellenic Journal of Nuclear Medicine 2004;7(1):48-51. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kowatsch I, Tsutsui JM, Osorio AF, et al. Head-to-head comparison of dobutamine and adenosine stress real-time myocardial perfusion echocardiography for the detection of coronary artery disease. J Am Soc Echocardiogr 2007;20(9):1109-17. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Krishnam MS, Tomasian A, Iv M, et al. Left ventricular ejection fraction using 64-slice CT coronary angiography and new evaluation software: initial experience. Br J Radiol 2008;81(966):450-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Krittayaphong R, Chaithiraphan V, Maneesai A, et al. Prognostic value of combined magnetic resonance myocardial perfusion imaging and late gadolinium enhancement. Int J Cardiovasc Imaging 2011;27(5):705-14. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Kuettnner A, Beck T, Drosch T, et al. Image quality and diagnostic accuracy of non-invasive coronary imaging with 16 detector slice spiral computed tomography with 188 ms temporal resolution. Heart 2005;91(7):938-41. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kumar R, Patel CD, Marwah A., et al. Detection of coronary artery disease by stress thallium scintigraphy in diabetic patients. Nucl Med Commun 2001;22(3):287-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kunimasa T, Sato Y, Matsumoto N., et al. Detection of coronary artery disease by free-breathing, whole heart coronary magnetic resonance angiography: our initial experience. Heart Vessels 2009;24(6):429-33. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Kurita A, Chaitman BR, Bourassa MG. Significance of exercise-induced junctional S-T depression in evaluation of coronary artery disease. Am J Cardiol 1977;40(4):492-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Kurrelmeyer KM. Noninvasive evaluation of women with coronary artery disease. Curr Opin Cardiol 2002;17(5):464-9. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Kurt M, Shaikh KA, Peterson L., et al. Impact of contrast echocardiography on evaluation of ventricular function and clinical management in a large prospective cohort. J Am Coll Cardiol 2009;53(9):802-10. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Kwon SW, Kim YJ, Shim J., et al. Coronary artery calcium scoring does not add prognostic value to standard 64-section CT angiography protocol in low-risk patients suspected of having coronary artery disease. Radiology 2011;259(1):92-9. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Kwong RY, Schussheim AE, Rekhraj S., et al. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. Circulation 2003;107(4):531-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


LaBounty TM, Earls JP, Leipsic J., et al. Effect of a standardized quality-improvement protocol on radiation dose in coronary computed tomographic angiography. Am J Cardiol 2010;106(11):1663-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


LaBounty TM, Leipsic J, Srichai MB., et al. What is the optimal number of readers needed to achieve high diagnostic accuracy in coronary computed tomographic angiography? A comparison of alternate reader

Ladenheim ML, Pollock BH, Rozanski A,, et al. Extent and severity of myocardial hypoperfusion as predictors of prognosis in patients with suspected coronary artery disease. J Am Coll Cardiol 1986;7(3):464-71. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

LaManna MM, Mohama R, Slavich IL, 3rd,, et al. Intravenous adenosine (adenoscan) versus exercise in the noninvasive assessment of coronary artery disease by SPECT. Clin Nucl Med 1990;15(11):804-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lamont DH, Budoff MJ, Shavell DM,, et al. Coronary calcium scanning adds incremental value to patients with positive stress tests. Am Heart J 2002;143(5):861-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Lancellotti P, Benoit T, Rigo P,, et al. Dobutamine stress echocardiography versus quantitative technetium-99m sestamibi SPECT for detecting residual stenosis and multivessel disease after myocardial infarction. Heart 2001;86(5):510-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lancerak SE, Vliegen HW, Jukema JW,, et al. Value of magnetic resonance imaging for the noninvasive detection of stenosis in coronary artery bypass grafts and recipient coronary arteries. Circulation 2003;107(11):1502-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lanza GA, Buffon A, Sestito A,, et al. Relation between stress-induced myocardial perfusion defects on cardiovascular magnetic resonance and coronary microvascular dysfunction in patients with cardiac syndrome X. J Am Coll Cardiol 2008;51(4):466-72. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Laraudogoitia Zaldumbide E, Perez-David E, Larena JA,, et al. The value of cardiac magnetic resonance in patients with acute coronary syndrome and normal coronary arteries. Rev Esp Cardiol 2009;62(9):976-83. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Larsen J, Birkke M, Sandvik L,, et al. Silent coronary atheromatosis in type 1 diabetic patients and its relation to long-term glycemic control. Diabetes 2002;51(8):2637-41. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Laspas F, Tsantioti D, Roussakis A,, et al. Correlation of radiation dose and heart rate in dual-source computed tomography coronary angiography. Acta Radiol 2011;52(3):273-7. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Lavoie KL, Fleet RP, Lesperance F,, et al. Are exercise stress tests appropriate for assessing myocardial ischemia in patients with major depressive disorder? Am Heart J 2004;148(4):621-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Law WY, Yang CC, Chen LK,, et al. Retrospective gating vs. prospective triggering for noninvasive coronary angiography: Assessment of image quality and radiation dose using a 256-slice CT scanner with 270 ms gantry rotation. Acad Radiol 2011;18(1):31-9. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


le Polain de Waroux JB, Pouleur AC, Goffinet C,, et al. Combined coronary and late-enhanced multidetector-computed tomography for delineation of the etiology of left ventricular dysfunction: comparison with coronary angiography and contrast-enhanced cardiac magnetic resonance imaging. Eur Heart J 2008;29(20):2544-51. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Leao Lima Rde S, De Lorenzo A, Issa A. Reduced adverse effects with an accelerated dobutamine stress protocol compared with the conventional protocol: a prospective, randomized myocardial perfusion scintigraphy study. Int J Cardiovasc Imaging 2008;24(1):55-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Leber AW, Becker A, Knez A,, et al. Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: a comparative study using intravascular ultrasound. J Am Coll Cardiol 2006;47(3):672-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Leber AW, Johnson T, Becker A,, et al. Diagnostic accuracy of dual-source multi-slice CT-coronary angiography in patients with an intermediate pretest likelihood for coronary artery disease. Eur Heart J 2007;28(19):2354-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Leber AW, Knez A, Becker C,, et al. Non-invasive intravenous coronary angiography using electron beam tomography and multislice computed tomography. Heart 2003;89(6):633-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Lee DH, Youn HJ, Choi YS., et al. Coronary flow reserve is a comprehensive indicator of cardiovascular risk factors in subjects with chest pain and normal coronary angiogram. Circ J 2010;74(7):1405-14. Full-text exclusion reason(s): Data for women not reported as a subgroup; No outcomes of interest.


Lee DS, Paeng JC, Lee MC. Implication of prognostically significant negative results on prone SPECT. J Nucl Med 2003;44(10):1641-3. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Lee JH, Kim JS, Kim YJ., et al. Diagnostic accuracy of 64-slice multidetector computed tomography for selecting coronary artery bypass graft surgery candidates. J Thorac Cardiovasc Surg 2010. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Lee JH, Crump R, Ellestad MH. Significance of precordial T-wave increase during treadmill stress testing. Am J Cardiol 1995;76(17):1297-9. Full-text exclusion reason(s): Data for women not reported as a subgroup.

Lee KH, Jang HJ, Lee SC., et al. Myocardial thallium defects in apical hypertrophic cardiomyopathy are associated with a benign prognosis. Thallium defects in apical hypertrophy. Int J Cardiovasc Imaging 2003;19(5):381-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Lee TC, O'Malley PG, Feuerstein I., et al. The prevalence and severity of coronary artery calcification on coronary artery computed tomography in black and white subjects. J Am Coll Cardiol 2003;41(1):39-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Legare JF, Haddad H, Barnes D., et al. Myocardial scintigraphy correlates poorly with coronary angiography in the screening of transplant arteriosclerosis. Can J Cardiol 2001;17(8):866-72. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Lehman SJ, Abbara S, Cury RC., et al. Significance of cardiac computed tomography incidental findings in acute chest pain. Am J Med 2009;122(6):543-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Leipsic J, Labounty TM, Heilbron B., et al. Estimated radiation dose reduction using adaptive statistical iterative reconstruction in coronary CT angiography: the ERASIR study. AJR Am J Roentgenol 2010;195(3):655-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.


with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Leite WA, Gil MA, Lima VC, et al. Exercise testing early after myocardial infarction: comparison with echocardiography, electrocardiographic monitoring and coronary arteriography. Arq Bras Cardiol 2008;90(3):176-81. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lele RD, Luthra K, Sawant Y. Assessment of diastolic heart function—experience with 16-gated myocardial perfusion SPECT. J Assoc Physicians India 2008;56:763-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Leschka S, Alkadhi H, Plass A, et al. Accuracy of MSCT coronary angiography with 64-slice technology: first experience. Eur Heart J 2005;26(15):1482-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Leschka S, Scheffel H, Desbiolles L, et al. Combining dual-source computed tomography coronary angiography and calcium scoring: added value for the assessment of coronary artery disease. Heart 2008;94(9):1154-61. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Leschka S, Scheffel H, Husmann L, et al. Effect of decrease in heart rate variability on the diagnostic accuracy of 64-MDCT coronary angiography. AJR Am J Roentgenol 2008;190(6):1583-90. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Lesser JR, Flygenring B, Knickelbine T, et al. Clinical utility of coronary CT angiography: coronary stenosis detection and prognosis in ambulatory patients. Catheter Cardiovasc Interv 2007;69(1):64-72. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Leung DY, Lo ST, Liew CT, et al. Use of functional tests before angiography in patients with normal coronary arteries. Int J Cardiol 2005;104(3):326-31. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Levine MG, McGill CC, Ahlberg AW, et al. Functional assessment with electrocardiographic gated single-photon emission computed tomography improves the ability of technetium-99m sestamibi myocardial perfusion imaging to predict myocardial viability in patients undergoing revascularization. Am J Cardiol 1999;83(1):1-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.
Lewis JF, McGorray SP, Pepine CJ. Assessment of women with suspected myocardial ischemia: review of findings of the Women's Ischemia Syndrome Evaluation (WISE) Study. Curr Womens Health Rep 2002;2(2):110-4. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Lewis WR, Ganim R, Sabapathy R. Utility of stress echocardiography in identifying significant coronary artery disease in patients with left bundle-branch block. Crit Pathw Cardiol 2007;6(3):127-30. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Li J, Li X, Wei M., et al. Diagnostic accuracy of dual-source computed tomography in the detection of coronary chronic total occlusion:Comparison with invasive angiography. African Journal of Biotechnology 2011;10(19):3854-3858. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Liao L, Smith WTt, Tuttle RH., et al. Prediction of death and nonfatal myocardial infarction in high-risk patients: a comparison between the Duke treadmill score, peak exercise radionuclide angiography, and SPECT perfusion imaging. J Nucl Med 2005;46(1):5-11. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lim MC, Wong TW, Yaneza LO., et al. Non-invasive detection of significant coronary artery disease with multi-section computed tomography angiography in patients with suspected coronary artery disease. Clin Radiol 2006;61(2):174-80. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Lin FY, Saba S, Weinsaft JW., et al. Relation of plaque characteristics defined by coronary computed tomographic angiography to ST-segment depression and impaired functional capacity during exercise treadmill testing in patients suspected of having coronary heart disease. Am J Cardiol 2009;103(1):50-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Lin GA, Dudley RA, Lucas FL., et al. Frequency of stress testing to document ischemia prior to elective percutaneous coronary intervention. JAMA 2008;300(15):1765-73. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; No outcomes of interest.

with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Lipiec P, Wejner-Mik P, Krzeminska-Pakula M, et al. Gated 99mTc-MIBI single-photon emission computed tomography for the evaluation of left ventricular ejection fraction: comparison with three-dimensional echocardiography. Ann Nucl Med 2008;22(8):723-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Lipiec P, Wejner-Mik P, Krzeminska-Pakula M, et al. Detection of single-vessel coronary artery disease by dipyridamole stress echocardiography: no longer a problem? Clin Physiol Funct Imaging 2009;29(2):151-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD.

Lipiec P, Wejner-Mik P, Krzeminska-Pakula M, et al. Accelerated stress real-time myocardial contrast echocardiography for the detection of coronary artery disease: comparison with 99mTc single photon emission computed tomography. J Am Soc Echocardiogr 2008;21(8):941-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lipinski M, Do D, Froelicher V, et al. Comparison of exercise test scores and physician estimation in determining disease probability. Arch Intern Med 2001;161(18):2239-44. Full-text exclusion reason(s): Data for women not reported as a subgroup; No outcomes of interest.

Lipton JA, Nelwan SP, van Domburg RT, et al. Abnormal spatial QRS-T angle predicts mortality in patients undergoing dobutamine stress echocardiography for suspected coronary artery disease. Coron Artery Dis 2010;21(1):26-32. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Liu X, Zhao X, Huang J, et al. Comparison of 3D free-breathing coronary MR angiography and 64-MDCT angiography for detection of coronary stenosis in patients with high calcium scores. AJR Am J Roentgenol 2007;189(6):1326-32. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lo KY, Leung KF, Chu CM, et al. Prognostic value of adenosine stress myocardial perfusion by cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease. QJM 2011;104(5):425-32. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Lockie T, Ishida M, Perera D, et al. High-resolution magnetic resonance myocardial perfusion imaging at 3.0-Tesla to detect hemodynamically significant coronary stenoses as determined by fractional flow reserve. J Am Coll Cardiol 2011;57(1):70-5. Full-text exclusion reason(s): Data for women not reported as a subgroup.

Loimaala A, Groundstroem K, Pasanen M, et al. Comparison of bicycle, heavy isometric, dipyridamole-atropine and dobutamine stress echocardiography for diagnosis of myocardial ischemia. Am J Cardiol 1999;84(12):1396-400. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Lokies J. Value of magnetocardiography for the non-invasive diagnosis of coronary artery disease. 30th Annual Congress of the International Society of Electrocardiology, Helsinki (Finland), 11-14 Jun 2003 (World Meeting Number 000 6973); 2003. Full-text exclusion reason(s): Data for women not reported as a subgroup.

Lonnebakken MT, Bleie O, Strand E, et al. Myocardial contrast echocardiography in assessment of stable coronary artery disease at intermediate dobutamine-induced stress level. Echocardiography 2009;26(1):52-60. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Luotolahti M, Saraste M, Hartiala J. Exercise echocardiography in the diagnosis of coronary artery disease. Ann Med 1996;28(1):73-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ma Es, Yang Zg, Li Y., et al. Correlation of calcium measurement with low dose 64-slice CT and angiographic stenosis in patients with suspected coronary artery disease. Int J Cardiol 2010;140(2):249-252. Full-text exclusion reason(s): Data for women not reported as a subgroup.

Maas AHEM, Appelman YEA. Gender differences in coronary heart disease. Netherlands Heart Journal 2010;18(12):598-603. Full-text exclusion reason(s): Not a clinical study report; Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Macaciel RM, Mesquita ET, Vivacqua R., et al. Safety, feasibility, and results of exercise testing for stratifying patients with chest pain in the emergency room. Arq Bras Cardiol 2003;81(2):174-81, 166-73. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Machacollo J, Yam Y, Ruddy TD., et al. Potential clinical and economic consequences of noncardiac incidental findings on cardiac computed tomography. J Am Coll Cardiol 2009;54(16):1533-41. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Maddahi J, Abdulla A, Garcia EV., et al. Noninvasive identification of left main and triple vessel coronary artery disease: improved accuracy using quantitative analysis of regional myocardial stress distribution and washout of thallium-201. J Am Coll Cardiol 1986;7(1):53-60. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Maddahi J, Garcia EV, Berman DS., et al. Improved noninvasive assessment of coronary artery disease by quantitative analysis of regional stress myocardial distribution and washout of thallium-201. Circulation 1981;64(5):924-35. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

J Am Coll Cardiol 1989;14(7):1689-99. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Madu EC. Transesophageal dobutamine stress echocardiography in the evaluation of myocardial ischemia in morbidly obese subjects. Chest 2000;117(3):657-61. Full-text exclusion reason(s): No data for NITs of interest (ECG, ECHO, SPECT, PET, CMR, CT).


Maffei E, Palumbo A, Martini C, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography in a large population of patients without revascularisation: registry data and review of multicentre trials. Radiol Med 2010;115(3):368-84. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Maffei E, Seitun S, Martini C, et al. Prognostic value of CT coronary angiography: focus on obstructive vs. nonobstructive disease and on the presence of left main disease. Radiol Med 2011;116(1):15-31. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Mahajani PS, Vankayala H, et al. Diagnostic accuracy of myocardial perfusion imaging and stress echocardiography for the diagnosis of left main and triple vessel coronary artery disease: a comparative meta-analysis. Heart 2010;96(12):956-66. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Mahenthiran J, Bangalore S, Yao SS, et al. Comparison of prognostic value of stress echocardiography versus stress electrocardiography in patients with suspected coronary artery disease. Am J Cardiol 2005;96(5):628-34. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Maintz D, Ozgun M, Hoffmeier A, et al. Whole-heart coronary magnetic resonance angiography: value for the detection of coronary artery stenoses in comparison to multislice computed tomography angiography. Acta Radiol 2007;48(9):967-73. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Manka R, Vitinis V, Boesiger P, et al. Clinical feasibility of accelerated, high spatial resolution myocardial perfusion imaging. JACC: Cardiovascular Imaging 2010;3(7):710-717. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Marano R, De Cobelli F, Floriani I, et al. Italian multicenter, prospective study to evaluate the negative predictive value of 16- and 64-slice MDCT imaging in patients scheduled for coronary angiography (NIMISCAD-Non Invasive Multicenter Italian Study for Coronary Artery Disease). Eur Radiol 2009;19(5):1114-23. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Marcovitz PA, Armstrong WF. Accuracy of dobutamine stress echocardiography in detecting coronary artery disease. Am J Cardiol 1992;69(16):1269-73. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Martin CM, McConahay DR. Maximal treadmill exercise electrocardiography. Correlations with coronary arteriography and cardiac hemodynamics. Circulation 1972;46(5):956-62. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Martuscelli E, Razzini C, D'Eliseo A, et al. Limitations of four-slice multirow detector computed tomography in the detection of coronary stenosis. Ital Heart J 2004;5(2):127-31. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Martuscelli E, Romagnoli A, D'Eliseo A, et al. Accuracy of thin-slice computed tomography in the detection of coronary stenoses. Eur Heart J 2004;25(12):1043-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Maruyama T, Takada M, Hasuie T, et al. Radiation dose reduction and coronary assessability of prospective electrocardiogram-gated computed tomography coronary angiography: comparison with retrospective electrocardiogram-gated helical scan. J Am Coll Cardiol 2008;52(18):1450-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Marwick TH, Case C, Sawada S, et al. Prediction of mortality using dobutamine echocardiography. J Am Coll Cardiol 2001;37(3):754-60. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Marwick TH, Case C, Sawada S, et al. Use of stress echocardiography to predict mortality in patients with diabetes and known or suspected coronary artery disease. Diabetes Care 2002;25(6):1042-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Marwick TH, Case C, Short L, et al. Prediction of mortality in patients without angina: use of an exercise score and exercise echocardiography. Eur Heart J 2003;24(13):1223-30. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Marwick TH, Case C, Vasey C, et al. Prediction of mortality by exercise echocardiography: a strategy for combination with the duke treadmill score. Circulation 2001;103(21):2566-71. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Marwick TH, Nemec JJ, Stewart WJ,, et al. Diagnosis of coronary artery disease using exercise echocardiography and positron emission tomography: comparison and analysis of discrepant results. J Am Soc Echocardiogr 1992;5(3):231-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Marwick TH, Shaw L, Case C,, et al. Clinical and economic impact of exercise electrocardiography and exercise echocardiography in clinical practice. Eur Heart J 2003;24(12):1153-63. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Mason JR, Palac RT, Freeman ML,, et al. Thallium scintigraphy during dobutamine infusion: nonexercise-dependent screening test for coronary disease. Am Heart J 1984;107(3):481-5. Full-text exclusion reason(s): Population does not include women ≥ age 18; No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Masood Y, Liu YH, Depuey G,, et al. Clinical validation of SPECT attenuation correction using x-ray computed tomography-derived attenuation maps: multicenter clinical trial with angiographic correlation. J Nucl Cardiol 2005;12(6):676-86. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Matsumoto N, Sato Y, Suzuki Y,, et al. Usefulness of rapid low-dose/high-dose 1-day 99mTc-sestamibi ECG-gated myocardial perfusion single-photon emission computed tomography. Circ J 2006;70(12):1585-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Matsumura Y, Hozumi T, Arai K,, et al. Non-invasive assessment of myocardial ischaemia using new real-time three-dimensional dobutamine stress echocardiography: comparison with conventional two-dimensional methods. Eur Heart J 2005;26(16):1625-32. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Matsumura Y, Hozumi T, Watanabe H,, et al. Cut-off value of coronary flow velocity reserve by transthoracic Doppler echocardiography for diagnosis of significant left anterior descending artery stenosis in patients with coronary risk factors. Am J Cardiol 2003;92(12):1389-93. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Matsuo S, Nakajima K, Akhter N,, et al. Clinical usefulness of novel cardiac MDCT/SPECT fusion image. Ann Nucl Med 2009;23(6):579-86. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


18. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Mazeika PK, Nadazdin A, Oakley CM. Dobutamine stress echocardiography for detection and assessment of coronary artery disease. J Am Coll Cardiol 1992;19(6):1203-11. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Data for women not reported as a subgroup.

Mazur W, Rivera JM, Khoury AF, et al. Prognostic value of exercise echocardiography: validation of a new risk index combining echocardiographic, treadmill, and exercise electrocardiographic parameters. J Am Soc Echocardiogr 2003;16(4):318-25. **Full-text exclusion reason(s):** No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

McCarthy RM, Deshpande VS, Beohar N, et al. Three-dimensional breathhold magnetization-prepared TrueFISP: a pilot study for magnetic resonance imaging of the coronary artery disease. Invest Radiol 2007;42(10):665-70. **Full-text exclusion reason(s):** No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

McHenry PL, Phillips JF, Knoebel SB. Correlation of computer-quantitated treadmill exercise electrocardiogram with arteriographic location of coronary artery disease. Am J Cardiol 1972;30(7):747-52. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Data for women not reported as a subgroup.

McKeogh JR. The diagnostic role of stress echocardiography in women with coronary artery disease: evidence based review. Curr Opin Cardiol 2007;22(5):429-33. **Full-text exclusion reason(s):** Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Meijboom WB, Mollet NR, Van Mieghem CA, et al. 64-Slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome. Heart 2007;93(11):1386-92. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Data for women not reported as a subgroup.

Meijboom WB, Van Mieghem CA, Mollet NR, et al. 64-slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. J Am Coll Cardiol 2007;50(15):1469-75. **Full-text exclusion reason(s):** Data for women not reported as a subgroup.


Meijer AB, O YL, Geleijns J, et al. Meta-analysis of 40- and 64-MDCT angiography for assessing coronary artery stenosis. AJR Am J Roentgenol 2008;191(6):1667-75. **Full-text exclusion reason(s):** No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Menon M, Lesser JR, Hara H, et al. Multidetector CT coronary angiography for patient triage to invasive coronary angiography: Performance and cost in ambulatory patients with equivocal or suspected inaccurate noninvasive stress

Merhige ME, Breen WJ, Shelton V, et al. Impact of myocardial perfusion imaging with PET and (82)Rb on downstream invasive procedure utilization, costs, and outcomes in coronary disease management. J Nucl Med 2007;48(7):1069-76. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Merkle N, Wohrle J, Grebe O, et al. Assessment of myocardial perfusion for detection of coronary artery stenoses by steady-state, free-precession magnetic resonance first-pass imaging. Heart 2007;93(11):1381-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Meyer C, Strach K, Thomas D, et al. High-resolution myocardial stress perfusion at 3 T in patients with suspected coronary artery disease. Eur Radiol 2008;18(2):226-33. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Michaelides AP, Andrikopoulos GK, Antoniades C, et al. Duration of treadmill exercise testing combined with QRS score predicts adverse cardiac outcome at long-term follow-up. Coron Artery Dis 2009;20(5):337-42. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Michaelides AP, Fourlas CA, Andrikopoulos GK, et al. QRS score versus ST-segment changes in patients undergoing Tl-201 scintigraphy using dipyridamole infusion. J Nucl Cardiol 2005;12(2):203-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Michaelides AP, Psomadaki ZD, Aigyptiadou MN, et al. Significance of exercise-induced ST changes in leads aVR, V5, and V1. Discrimination of patients with single- or multivessel coronary artery disease. Clin Cardiol 2003;26(5):226-30. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Mieres JH, Shaw LJ, Arai A, et al. Role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease: Consensus statement from the Cardiac Imaging Committee, Council on Clinical Cardiology, and the Cardiovascular Imaging and Intervention Committee, Council on Cardiovascular Radiology and
Intervention, American Heart Association. Circulation 2005;111(5):682-96. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Milavetz JJ, Miller TD, Hodge DO,, et al. Accuracy of single-photon emission computed tomography myocardial perfusion imaging in patients with stents in native coronary arteries. Am J Cardiol 1998;82(7):857-61. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Miller CD, Hwang W, Hoekstra JW,, et al. Stress cardiac magnetic resonance imaging with observation unit care reduces cost for patients with emergent chest pain: a randomized trial. Ann Emerg Med 2010;56(3):209-219 e2. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Miller TD, Chaliki HP, Christian TF,, et al. Usefulness of worsening clinical status or exercise performance in predicting future events in patients with coronary artery disease. Am J Cardiol 2001;88(11):1294-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Miller TD, Hodge DO, Milavetz JJ,, et al. A normal stress SPECT scan is an effective gatekeeper for coronary angiography. J Nucl Cardiol 2007;14(2):187-93. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Milosavljevic J, Ostojic M, Marinkovic J. Dipyridamole-dobutamine stress echocardiography for the detection of myocardial ischemia in patients with hypertension. Herz 2005;30(3):215-222. Full-text exclusion reason(s): All women in the study are known to have CAD.

Min JK, Dunning A, Lin FY,, et al. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the international multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 patients without known coronary artery disease. J Am Coll Cardiol 2011;58(8):849-60. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Min JK, Dunning A, Lin FY,, et al. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings: Results from the international multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 patients without known coronary artery disease. J Am Coll Cardiol 2011;58(8):849-60. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization.


Min JK, Feignoux J, Treutenaere J,, et al. The prognostic value of multidetector coronary CT angiography for the prediction of major adverse cardiovascular events: a multicenter observational cohort study. Int J Cardiovasc Imaging 2010;26(6):721-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Min JK, Robinson M, Shaw LJ,, et al. Differences in episode-based care costs for multidetector computed tomographic coronary angiography versus myocardial perfusion imaging for the diagnosis of coronary artery
Min JK, Shaw LJ, Berman DS, et al. Costs and clinical outcomes in individuals without known coronary artery disease undergoing coronary computed tomographic angiography from an analysis of Medicare category III transaction codes. Am J Cardiol 2008;102(6):672-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Minardi G, Di Segni M, Manzara CC, et al. Diagnostic and prognostic value of dipyridamole and dobutamine stress echocardiography in patients with Q-wave acute myocardial infarction. Am J Cardiol 1997;80(7):847-51. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Mizalski-Jamka T, Kuntz-Hehner S, Schmidt H, et al. Myocardial contrast echocardiography enhances long-term prognostic value of supine bicycle stress two-dimensional echocardiography. J Am Soc Echocardiogr 2009;22(11):1220-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Modena MG. Sex differences in noninvasive diagnosis of multivessel coronary artery disease. 46th Annual Scientific Session of the American College of Cardiology, Anaheim, CA (USA), 16-19 Mar 1997 (World Meeting Number 971 0068) 1997. Full-text exclusion reason(s): Conference abstract or trial registry posting.


Mollet NR, Cademartiri F, Krestin GP, et al. Improved diagnostic accuracy with 16-row multi-slice computed tomography coronary angiography. J Am Coll Cardiol 2005;45(1):128-32. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.
Mollet NR, Cademartiri F, Nieman K, et al. Multislice spiral computed tomography coronary angiography in patients with stable angina pectoris. J Am Coll Cardiol 2004;43(12):2265-70. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Mollet NR, Cademartiri F, Nieman K, et al. Noninvasive assessment of coronary plaque burden using multislice computed tomography. Am J Cardiol 2005;95(10):1165-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Mollet NR, Cademartiri F, van Mieghem CA, et al. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. Circulation 2005;112(15):2318-23. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Morgan-Hughes GJ, Roobottom CA, Owens PE, et al. Highly accurate coronary angiography with submillimetre, 16 slice computed tomography. Heart 2005;91(3):308-13. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Morganroth J, Chen CC, David D, et al. Exercise cross-sectional echocardiographic diagnosis of coronary artery disease. Am J Cardiol 1981;47(1):20-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Morise AP, Beto R, Gupta N, et al. Exercise QT dispersion as an independent predictor of the presence of ischemia on myocardial perfusion imaging. Ann Noninvasive Electrocardiol 2000;5(3):240-247. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.


Mowatt G, Brazzelli M, Gemmell H, et al. Systematic review of the prognostic effectiveness of SPECT myocardial perfusion scintigraphy in patients with suspected or known coronary artery disease and following myocardial infarction. Nucl Med Commun 2005;26(3):217-29. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Mowatt G, Cook JA, Hillis GS, et al. 64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. Heart 2008;94(11):1386-93. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Mowatt G, Cummins E, Waugh N, et al. Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease. Health Technol Assess 2008;12(17):iii-iv, ix-143. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Muller-Suur R, Eriksson SV, Strandberg LE,, et al. Comparison of adenosine and exercise stress test for quantitative perfusion imaging in patients on beta-blocker therapy. Cardiology 2001(2):112-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Muro T, Hozumi T, Watanabe H,, et al. Assessment of myocardial perfusion abnormalities by intravenous myocardial contrast echocardiography with harmonic power Doppler imaging: comparison with positron emission tomography. Heart 2003;89(2):145-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Murphy JC, Scott PJ, Shannon HJ,, et al. ST elevation on the exercise ECG in patients presenting with chest pain and no prior history of myocardial infarction. Heart 2009;95(21):1792-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Musto C, Simon P, Nicol E,, et al. 64-multislice computed tomography in consecutive patients with suspected or proven coronary artery disease: initial single center experience. Int J Cardiol 2007;114(1):90-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Nagata M, Kato S, Kitagawa K,, et al. Diagnostic accuracy of 1.5-T unenhanced whole-heart coronary MR angiography performed with 32-channel cardiac coils: initial single-center experience. Radiology 2011;259(2):384-92. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Nagel E, Klein C, Paetsch L,, et al. Magnetic resonance perfusion measurements for the noninvasive detection of coronary artery disease. Circulation 2003;108(4):432-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Nagurney JT, Bamberg F, Nichols JH., et al. The Disposition Decision on Emergency Department Patients with Chest Pain is Affected by the Results of Multi-Detector Computed Axial Tomography Scan of the Coronary Arteries. J Emerg Med 2010;39(1):57-64. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Napel S, Rubin GD, Jeffrey RB, Jr. STS-MIP: a new reconstruction technique for CT of the chest. J Comput Assist Tomogr 1993;17(5):832-8. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Nemes A, Balazs E, Pinter S., et al. Long-term prognostic significance of coronary flow velocity reserve in patients with significant coronary artery disease not involving the left anterior descending coronary artery (results from the SZEGED study). Echoangiography 2010;27(3):306-10. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Nguyen T, Heo J, Ogilby JD, et al. Single photon emission computed tomography with thallium-201 during adenosine-induced coronary hyperemia; correlation with coronary arteriography, exercise thallium imaging and two-dimensional echocardiography. J Am Coll Cardiol 1990;16(6):1375-83. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Nicol ED, Stirrup J, Reyes E, et al. Comparison of 64-slice cardiac computed tomography with myocardial perfusion scintigraphy for assessment of global and regional myocardial function and infarction in patients with low to intermediate likelihood of coronary artery disease. J Nucl Cardiol 2008;15(4):497-502. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Nicol ED, Stirrup J, Reyes E, et al. Sixty-four-slice computed tomography coronary angiography compared with myocardial perfusion scintigraphy for the diagnosis of functionally significant coronary stenoses in patients with a low to intermediate likelihood of coronary artery disease. J Nucl Cardiol 2008;15(3):311-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Nieman K, Cademartiri F, Lemos PA, et al. Reliable noninvasive coronary angiography with fast submillimeter multislice spiral computed tomography. Circulation 2002;106(16):2051-4. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Nieman K, Rensing BJ, van Geuns RJ, et al. Usefulness of multislice computed tomography for detecting obstructive coronary artery disease. Am J Cardiol 2002;89(8):913-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Nieman K, Rensing BJ, van Geuns RJ, et al. Non-invasive coronary angiography with multislice spiral computed tomography: impact of heart rate. Heart 2002;88(5):470-4. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Nishimura S, Mahmarian JJ, Boyce TM, et al. Quantitative thallium-201 single-photon emission computed tomography during maximal pharmacologic coronary vasodilation with adenosine for assessing coronary artery disease. J Am Coll Cardiol 1991;18(3):736-45. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Nkoulou R, Pazhenkottil AP, Kuest SM, et al. Semiconductor detectors allow low-dose - Low-dose 1-day SPECT myocardial perfusion imaging. J Nucl Med 2011;52(8):1204-1209. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.
Nucifora G, Badano LP, Sarraf-Zadegan N., et al. Comparison of early dobutamine stress echocardiography and exercise electrocardiographic testing for management of patients presenting to the emergency department with chest pain. Am J Cardiol 2007;100(7):1068-73. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Nucifora G, Schuijf JD, van Werkhoven JM., et al. Relation between Framingham risk categories and the presence of functionally relevant coronary lesions as determined on multislice computed tomography and stress testing. Am J Cardiol 2009;104(6):758-63. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Nygaard TW, Gibson RS, Ryan JM., et al. Prevalence of high-risk thallium-201 scintigraphic findings in left main coronary artery stenosis: comparison with patients with multiple- and single-vessel coronary artery disease. Am J Cardiol 1984;53(4):462-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Odagiri K, Uehara A, Kurata C. Vasodilator stress impairs the left ventricular function obtained with gated single-photon emission computed tomography in patients with known or suspected coronary artery disease. Circ J 2010;74(12):2666-73. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Oguzhan A, Kisacik HL, Ozdemir K., et al. Comparison of exercise stress testing with dobutamine stress echocardiography and exercise technetium-99m isonitrile single photon emission computerized tomography for diagnosis of coronary artery disease. Jpn Heart J 1997;38(3):333-44. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


O'Keefe JH, Jr., Barnhart CS, Bateman TM. Comparison of stress echocardiography and stress myocardial perfusion scintigraphy for diagnosing coronary artery disease and assessing its severity. Am J Cardiol 1995;75(11):25D-34D. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

O'Keefe JH, Jr., Bateman TM, Silvestri R., et al. Safety and diagnostic accuracy of adenosine thallium-201 scintigraphy in patients unable to exercise and those with left bundle branch block. Am Heart J 1992;124(3):614-21. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Olson MB, Kelsey SF, Matthews K., et al. Symptoms, myocardial ischaemia and quality of life in women: results from the NHLBI-sponsored WISE Study. Eur Heart J 2003;24(16):1506-14. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Olszowska M, Kostkiewicz M, Tracz W., et al. Assessment of myocardial perfusion in patients with coronary artery disease. Comparison of myocardial contrast echocardiography and 99mTc MIBI single photon emission computed tomography. Int J Cardiol 2003;90(1):49-55. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ong K, Chin SP, Chan WL., et al. Feasibility and accuracy of 64-row MDCT coronary imaging from a centre with early experience: a review and comparison with established centres. Med J Malaysia 2005;60(5):629-36. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ong TK, Chin SP, Liew CK., et al. Accuracy of 64-row multidetector computed tomography in detecting coronary artery disease in 134 symptomatic patients: influence of calcification. Am Heart J 2006;151(6):1323 e1-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ozmen N, Yiginer O, Oz O., et al. ST elevation in the lead aVR during exercise treadmill testing may indicate left main coronary artery disease. Kardiol Pol 2010;68(10):1107-11. Full-text exclusion reason(s): Data for women not reported as a subgroup; No outcomes of interest.

Paetsch I, Jahnke C, Barkhausen J., et al. Detection of coronary stenoses with contrast enhanced, three-dimensional free breathing coronary MR angiography using the gadolinium-based intravascular contrast agent gadocoletic acid
Paetsch I, Jahnke C, Wahl A., et al. Comparison of dobutamine stress magnetic resonance, adenosine stress magnetic resonance, and adenosine stress magnetic resonance perfusion. Circulation 2004;110(7):835-42. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Paladugu N, Shaqra H, Blum S, et al. Positive vasodilator stress ECG with normal myocardial perfusion imaging and its correlation with coronary angiographic findings in African Americans and Hispanics. Clin Cardiol 2010;33(10):638-42. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Park MY, Choi SJ, Kim JK, et al. Use of multidetector computed tomography for evaluating coronary artery disease in patients undergoing dialysis. Nephrology (Carlton) 2011;16(3):285-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Parthenakis FI, Karidis KS, Zuridakis G, et al. Left ventricular diastolic filling changes during dipyridamole-induced ischaemia. An echo-Doppler study. Coron Artery Dis 1997;8(7):449-54. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


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in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Peix A, Garcia EJ, Valiente J., et al. Ischemia in women with angina and normal coronary angiograms. Coron Artery Dis 2007;18(5):361-6. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Penfornis A, Zimmermann C, Boumal D., et al. Use of dobutamine stress echocardiography in detecting silent myocardial ischaemia in asymptomatic diabetic patients: a comparison with thallium scintigraphy and exercise testing. Diabet Med 2001;18(11):900-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Peng NJ, Mar GY, Liu CP., et al. Does inadequate exercise lower the accuracy of myocardial perfusion scintigraphy? Nucl Med Commun 2001;22(6):625-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Peteiro J, Bouzas-Mosquera A, Broullon F., et al. Treadmill exercise echocardiography as a predictor of events in patients with left ventricular hypertrophy. Am J Hypertens 2010;23(7):794-801. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Pflederer T, Marwan M, Schepis T,, et al. Characterization of culprit lesions in acute coronary syndromes using coronary dual-source CT angiography. Atherosclerosis 2010;211(2):437-444. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Pfleger S, Scherhag A, Latsch A,, et al. Safety of dobutamine echocardiography: No signs of myocardial cell damage or activation of the coagulation system. Disease Management and Clinical Outcomes 2001;3(1):15 -19. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Philippe L, Merino B, Blaire T,, et al. Tetrofosmin early time gated post-stress single-photon emission computed tomography imaging: feasibility and potential benefits. J Nucl Cardiol 2011;18(1):62-72. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest


Picano E, Alaimo A, Chubuchny V,, et al. Noninvasive pacemaker stress echocardiography for diagnosis of coronary artery disease: a multicenter study. J Am Coll Cardiol 2002;40(7):1305-10. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Picano E, Bedetti G, Varga A,, et al. The comparable diagnostic accuracies of dobutamine-stress and dipyridamole-stress echocardiographies: a meta-analysis. Coron Artery Dis 2000;11(2):151-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Picano E, Lattanzi F, Masini M,, et al. Comparison of the high-dose dipyridamole-echocardiography test and exercise two-dimensional echocardiography for diagnosis of coronary artery disease. Am J Cardiol 1987;59(6):539-42. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Picano E, Molinaro S, Pasanisi E. The diagnostic accuracy of pharmacological stress echocardiography for the assessment of coronary artery disease: a meta-analysis. Cardiovasc Ultrasound 2008;6:30. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Pilz G, Jeske A, Klos M., et al. Prognostic value of normal adenosine-stress cardiac magnetic resonance imaging. Am J Cardiol 2008;101(10):1408-12. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Pingitore A, Picano E, Colosso MQ., et al. The atropine factor in pharmacologic stress echocardiography. Echo Persantine (EPIC) and Echo Dobutamine International Cooperative (EDIC) Study Groups. J Am Coll Cardiol 1996;27(5):1164-70. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Pizzuto F, Voci P, Bartolomucci F., et al. Usefulness of coronary flow reserve measured by echocardiography to improve the identification of significant left anterior descending coronary artery stenosis assessed by multidetector computed tomography. Am J Cardiol 2009;104(5):657-64. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Plass A, Grunenfelder J, Leschka S., et al. Coronary artery imaging with 64-slice computed tomography from cardiac surgical perspective. Eur J Cardiothorac Surg 2006;30(1):109-16. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Plein S, Greenwood JP, Ridgway JP., et al. Assessment of non-ST-segment elevation acute coronary syndromes with cardiac magnetic resonance imaging. J Am Coll Cardiol 2004;44(11):2173-81. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Plein S, Kozerke S, Suerder D., et al. High spatial resolution myocardial perfusion cardiac magnetic resonance for the detection of coronary artery disease. Euro Heart J 2008;29(17):2148-2155. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Plein S, Radjenovic A, Ridgway JP., et al. Coronary artery disease: myocardial perfusion MR imaging with sensitivity encoding versus conventional angiography. Radiology 2005;235(2):423-30. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Pontone G, Andreini D, Ballerini G., et al. Diagnostic work-up of unselected patients with suspected coronary artery disease: complementary role of multidetector computed tomography, symptoms and electrocardiogram stress test. Coron Artery Dis 2007;18(4):265-74. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


152. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Pouleur AC, le Polain de Waroux JB, Kefer J., et al. Direct comparison of whole-heart navigator-gated magnetic resonance coronary angiography and 40- and 64-slice multidetector row computed tomography to detect the coronary artery stenosis in patients scheduled for conventional coronary angiography. Circ Cardiovasc Imaging 2008;1(2):114-21. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Pozzoli MM, Fioretti PM, Salustri A., et al. Exercise echocardiography and technetium-99m MIBI single-photon emission computed tomography in the detection of coronary artery disease. Am J Cardiol 1991;67(5):350-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Pratt CM, Francis MJ, Divine GW., et al. Exercise testing in women with chest pain. Are there additional exercise characteristics that predict true positive test results? Chest 1989;95(1):139-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; No outcomes of interest.

Previtali M, Lanzarini L, Fetiveau R., et al. Comparison of dobutamine stress echocardiography, dipyridamole stress echocardiography and exercise stress testing for diagnosis of coronary artery disease. Am J Cardiol 1993;72(12):865-70. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Probst C, Kovacs A, Schmitz C., et al. Quantification of coronary artery stenosis with 16-slice MSCT in patients before CABG surgery: comparison to standard invasive coronary angiography. Heart Surg Forum 2005;8(1):E42-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Pugliese F, Mollet NR, Runza G., et al. Diagnostic accuracy of non-invasive 64-slice CT coronary angiography in patients with stable angina pectoris. Eur Radiol 2006;16(3):575-82. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Pundziute G, Schuif JD, Jukema JW., et al. Head-to-head comparison of coronary plaque evaluation between multislice computed tomography and intravascular ultrasound radiofrequency data analysis. JACC Cardiovasc Interv 2008;1(2):176-82. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Pundziute G, Schuif JD, van Werkhoven JM., et al. Head-to-head comparison between bicycle exercise testing and coronary calcium score and coronary stenoses on multislice computed tomography. Coron Artery Dis 2009;20(4):281-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Quinones MA, Verani MS, Haichin RM., et al. Exercise echocardiography versus 201TI single-photon emission computed tomography in evaluation of coronary artery disease. Analysis of 292 patients. Circulation 1992;85(3):1026-31. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Raff GL, Chinnaiyan KM, Share DA., et al. Radiation dose from cardiac computed tomography before and after implementation of radiation dose-reduction techniques. JAMA 2009;301(22):2340-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Rambihar S, Abramson B. Cardiovascular imaging and noninvasive diagnosis for older adults. Geriatrics and Aging 2007;10(1):14-22. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Ravipati G, Aronow WS, Lai H., et al. Comparison of sensitivity, specificity, positive predictive value, and negative predictive value of stress testing versus 64-multislice coronary computed tomography angiography in predicting obstructive coronary artery disease diagnosed by coronary angiography. Am J Cardiol 2008;101(6):774-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Rehn T, Griffith LS, Achuff SC., et al. Exercise thallium-201 myocardial imaging in left main coronary artery disease: sensitive but not specific. Am J Cardiol 1981;48(2):217-23. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Reis G, Marcovitz PA, Leichtman AB., et al. Usefulness of dobutamine stress echocardiography in detecting coronary artery disease in end-stage renal disease. Am J Cardiol 1995;75(10):707-10. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Reynolds HR, Srichai MB, Iqbal SN, et al. Mechanisms of myocardial infarction in women without angiographically obstructive coronary artery disease. Circulation 2011;124(13):1414-25. Full-text exclusion reason(s): All women in the study are known to have CAD.

Rieber J, Huber A, Erhard I, et al. Cardiac magnetic resonance perfusion imaging for the functional assessment of coronary artery disease: a comparison with coronary angiography and fractional flow reserve. Eur Heart J 2006;27(12):1465-71. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Rijneke RD, Ascoop CA, Talmon JL. Clinical significance of upsloping ST segments in exercise electrocardiography. Circulation 1980;61(4):671-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ripswedén J, Brismar TB, Holm J, et al. Impact on image quality and radiation exposure in coronary CT angiography: 100 kVp versus 120 kVp. Acta Radiol 2010;51(8):903-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Rocchi G, Fallani F, Bracchetti G, et al. Non-invasive detection of coronary artery stenosis: a comparison among power-Doppler contrast echo, 99Tc-Šestamibi SPECT and echo wall-motion analysis. Coron Artery Dis 2003;14(3):239-45. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Rodriguez O, Picano E, Fedele S, et al. Noninvasive prediction of coronary artery disease progression by comparison of serial exercise electrocardiography and dipyridamole stress echocardiography. Int J Cardiovasc Imaging 2002;18(2):93-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Rocha-Filho JA, Blankstein R, Shturman LD, et al. Incremental value of adenosine-induced stress myocardial perfusion imaging with dual-source CT at cardiac CT angiography. Radiology 2010;254(2):410-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Rodríguez O, Picano E, Fedele S, et al. Non-invasive prediction of angiographic progression of coronary artery disease by dipyridamole-stress echocardiography. Coron Artery Dis 2001;12(3):197-204. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Roger VL, Jacobsen SJ, Weston SA, et al. Sex differences in evaluation and outcome after stress testing. Mayo Clin Proc 2002;77(7):638-45. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization.


Romanens M, Gradel C, Saner H, et al. Comparison of (99m)Tc-sestamibi lung/heart ratio, transient ischaemic dilatation and perfusion defect size for the identification of severe and extensive coronary artery disease. European Journal of Nuclear Medicine 2001;28(7):907-910. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Romeo F, Leo R, Clementi F, et al. Multislice computed tomography in an asymptomatic high-risk population. Am J Cardiol 2007;99(3):325-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Ropers D, Pohle FK, Kuetten A, et al. Diagnostic accuracy of noninvasive coronary angiography in patients after bypass surgery using 64-slice spiral computed tomography with 330-ms gantry rotation. Circulation 2006;114(22):2334-41; quiz 2334. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ropers D, Rixe J, Anders K, et al. Usefulness of multidetector row spiral computed tomography with 64×0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. Am J Cardiol 2006;97(3):343-8. Full-text exclusion reason(s): Data for women not reported as a subgroup.


Rozanski A, Granars H, Wong ND, et al. Clinical outcomes after both coronary calcium scanning and exercise myocardial perfusion scintigraphy. J Am Coll Cardiol 2007;49(12):1352-61. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Rubinshtein R, Halon DA, Gaspar T,, et al. Impact of 64-slice cardiac computed tomographic angiography on clinical decision-making in emergency department patients with chest pain of possible myocardial ischemic origin. Am J Cardiol 2007;100(10):1522-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Rubinshtein R, Halon DA, Gaspar T,, et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. Circulation 2007;115(13):1762-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Rubinshtein R, Halon DA, Gaspar T,, et al. Cardiac computed tomographic angiography for risk stratification and prediction of late cardiovascular outcome events in patients with a chest pain syndrome. Int J Cardiol 2009;137(2):108-15. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Rubinshtein R, Halon DA, Gaspar T,, et al. Usefulness of 64-slice multidetector computed tomography in diagnostic triage of patients with chest pain and negative or nondiagnostic exercise treadmill test result. Am J Cardiol 2007;99(7):925-9. Full-text exclusion reason(s): Data for women not reported as a subgroup.

Rubinshtein R, Miller TD, Williamson EE,, et al. Detection of myocardial infarction by dual-source coronary computed tomography angiography using quantitated myocardial scintigraphy as the reference standard. Heart 2009;95(17):1419-22. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Rumberger JA, Behrenbeck T, Breen JF,, et al. Coronary calcification by electron beam computed tomography and obstructive coronary artery disease: a model for costs and effectiveness of diagnosis as compared with conventional cardiac testing methods. J Am Coll Cardiol 1999;33(2):453-62. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Rumberger JA, Sheedy PF, 3rd, Breen JF,, et al. Coronary calcium, as determined by electron beam computed tomography, and coronary disease on arteriogram. Effect of patient's sex on diagnosis. Circulation 1995;91(5):1363-7. Full-text exclusion reason(s): All women in the study are known to have CAD; No outcomes of interest.

Russo V, Gostoli V, Lovato L,, et al. Clinical value of multidetector CT coronary angiography as a preoperative screening test before non-coronary cardiac surgery. Heart 2007;93(12):1591-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Russo V, Zavalloni A, Bacchi Reggiani ML,, et al. Incremental prognostic value of coronary CT angiography in patients with suspected coronary artery disease. Circ Cardiovasc Imaging 2010;3(4):351-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Ruzsics B, Lee H, Zwerner PL, et al. Dual-energy CT of the heart for diagnosing coronary artery stenosis and myocardial ischemia-initial experience. Eur Radiol 2008;18(11):2414-24. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ruzsics B, Schwarz F, Schoepf UJ,, et al. Comparison of dual-energy computed tomography of the heart with single photon emission computed tomography for assessment of coronary artery stenosis and of the myocardial blood supply. Am J Cardiol 2009;104(3):318-26. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Ryan T, Segar DS, Sawada SG,, et al. Detection of coronary artery disease with upright bicycle exercise echocardiography. J Am Soc Echocardiogr 1993;6(2):186-97. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sa MI, Nicol ED, Stirrup J, et al. Implications for single phase prospective CT coronary angiography for the diagnosis of significant coronary stenoses in clinical practice. Int J Cardiol 2011;147(3):393-397. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Saad MAM, Azer HY. Dual-source CT coronary angiography: Diagnostic accuracy without the use of B blockers. Egyptian Journal of Radiology and Nuclear Medicine 2011. Full-text exclusion reason(s): Data for women not reported as a subgroup.

Sabharwal NK, Lahiri A. Role of myocardial perfusion imaging for risk stratification in suspected or known coronary artery disease. Heart 2003;89(11):1291-7. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Sahin M, Karakelleoglu S, Alp N, et al. Diagnostic value of dobutamine stress echocardiography in coronary artery disease. Thorac Cardiovasc Surg 1994;42(5):285-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sakakura K, Yasu T, Kobayashi Y, et al. Noninvasive tissue characterization of coronary arterial plaque by 16-slice computed tomography in acute coronary syndrome. Angiology 2006;57(2):155-60. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sakuma H, Ichikawa Y, Chino S, et al. Detection of coronary artery stenosis with whole-heart coronary magnetic resonance angiography. J Am Coll Cardiol 2006;48(10):1946-50. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Salm LP, Schuijf JD, de Roos A, et al. Global and regional left ventricular function assessment with 16-detector row CT: comparison with echocardiography and cardiovascular magnetic resonance. Eur J Echocardiogr 2006;7(4):308-14. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Salustri A, Fioretti PM, McNeill AJ, et al. Pharmacological stress echocardiography in the diagnosis of coronary artery disease and myocardial ischaemia: a comparison between dobutamine and dipyridamole. Eur Heart J 1992;13(10):1356-62. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Samady H, Wackers FJ, Joska TM, et al. Pharmacologic stress perfusion imaging with adenosine: role of simultaneous low-level treadmill exercise. J Nucl Cardiol 2002;9(2):188-96. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in
the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


San Roman JA, Sanz-Ruiz R, Ortega JR., et al. Safety and predictors of complications with a new accelerated dobutamine stress echocardiography protocol. J Am Soc Echocardiogr 2008;21(1):53-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Sandstede JJ, Pabst T, Wacker C., et al. Breath-hold 3D MR coronary angiography with a new intravascular contrast agent (feruglose)—first clinical experiences. Magn Reson Imaging 2001;19(2):201-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Santana CA, Folks RD, Garcia EV., et al. Quantitative (82)Rb PET/CT: development and validation of myocardial perfusion database. J Nucl Med 2007;48(7):1122-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Santana CA, Garcia EV, Faber TL., et al. Diagnostic performance of fusion of myocardial perfusion imaging (MPI) and computed tomography coronary angiography. J Nucl Cardiol 2009;16(2):201-11. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Santana CA, Garcia EV, Vansant JP., et al. Gated stress-only 99mTc myocardial perfusion SPECT imaging accurately assesses coronary artery disease. Nucl Med Commun 2003;24(3):241-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Sarullo FM, Di Pasquale P, Orlando G., et al. Utility and safety of immediate exercise testing of low-risk patients admitted to the hospital with acute chest pain. Int J Cardiol 2000;75(2-3):239-43. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Scandrett RM, Mukherjee SK. Frontiers in women's cardiovascular health prevention: What have we learned so far? World Heart Journal 2008;1(2):141-159. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Schannwell CM. Echocardiographic diastolic function: A sensitive noninvasive approach for the detection of coronary artery disease in women. 46th Annual Scientific Session of the American College of Cardiology, Anaheim, CA (USA), 16-19 Mar 1997 (World Meeting Number 971 0068) 1997. Full-text exclusion reason(s): No outcomes of interest.

Schartl M, Beckmann S, Bocksch W., et al. Stress echocardiography in special groups: In women, in left bundle branch block, in hypertension and after heart transplantation. Euro Heart J 1997;18(SUPPL. D). Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.


Scheffel H, Stolzmann P, Alkadhi H., et al. Low-dose CT and cardiac MR for the diagnosis of coronary artery disease: accuracy of single and combined approaches. Int J Cardiovasc Imaging 2010;26(5):579-90. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Schenker MP, Dorbala S, Hong EC., et al. Interrelation of coronary calcification, myocardial ischemia, and outcomes in patients with intermediate likelihood of coronary artery disease: a combined positron emission tomography/computed tomography study. Circulation 2008;117(13):1693-700. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Scherhag AW, Pfleger S, Schreckenberger AB., et al. Detection of patients with restenosis after PTCA by dipyridamole-atropine-stress-echocardiography. Int J Card Imaging 1997;13(2):115-23. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Schinkel AF, Elhendy A, Van Domburg RT., et al. Long-term prognostic value of dobutamine stress 99mTc-sestamibi SPECT: single-center experience with 8-year follow-up. Radiology 2002;225(3):701-6. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Schinkel AF, Elhendy A, van Domburg RT., et al. Incremental value of exercise technetium-99m tetrofosmin myocardial perfusion single-photon emission computed tomography for the prediction of cardiac events. Am J Cardiol 2003;91(4):408-11. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Schlegel TT, Kulecz WB, Feiveson AH., et al. Accuracy of advanced versus strictly conventional 12-lead ECG for detection and screening of coronary artery disease, left ventricular hypertrophy and left ventricular systolic dysfunction. BMC Cardiovascular Disorders 2010;10(28). Full-text exclusion reason(s): No data for NITs of interest (ECG, ECHO, SPECT, PET, CMR, CTA).
Schlett CL, Banerji D, Siegel E., et al. Prognostic value of CT angiography for major adverse cardiac events in patients with acute chest pain from the emergency department: 2-Year outcomes of the ROMICAT trial. JACC: Cardiovascular Imaging 2011;4(5):481-491. Full-text exclusion reason(s): Data for women not reported as a subgroup; No outcomes of interest.

Schlosser T, Mohrs OK, Magedanz A., et al. Noninvasive coronary angiography using 64-detector-row computed tomography in patients with a low to moderate pretest probability of significant coronary artery disease. Acta Radiol 2007;48(3):300-7. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Schmermund A, Elsasser A, Behl M., et al. Comparison of prognostic usefulness (three years) of computed tomographic angiography versus 64-slice computed tomographic calcium scanner in subjects without significant coronary artery disease. Am J Cardiol 2010;106(11):1574-9. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup

Schmermund A, Stang A, Mohlenkamp S., et al. Prognostic value of electron-beam computed tomography-derived coronary calcium scores compared with clinical parameters in patients evaluated for coronary artery disease. Prognostic value of EBCT in symptomatic patients. Z Kardiol 2004;93(9):696-705. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Schonenberger E, Schnapauff D, Teige F., et al. Patient acceptance of noninvasive and invasive coronary angiography. PLoS One 2007;2(2):e246. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Schroeder K, Voller H, Dingerkus H., et al. Comparison of the diagnostic potential of four echocardiographic stress tests shortly after acute myocardial infarction: submaximal exercise, transesophageal atrial pacing, dipyridamole, and dobutamine-atropine. Am J Cardiol 1996;77(11):909-14. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Schroeder K, Wieckhorst A, Voller H. Comparison of the prognostic value of dipyridamole and dobutamine stress echocardiography in patients with known or suspected coronary artery disease. Am J Cardiol 1997;79(11):1516-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Schroeder S, Kuettnner A, Beck T., et al. Usefulness of noninvasive MSCT coronary angiography as first-line imaging technique in patients with chest pain: initial clinical experience. Int J Cardiol 2005;102(3):469-75. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Schuijf JD, Bax JJ. Noninvasive coronary angiography with multislice computed tomography and myocardial perfusion imaging. Cardiol Rev 2007;24(6):38-41. Full-text exclusion reason(s): Data for women not reported as a subgroup.
Schuijf JD, Bax JJ, Jukema JW., et al. Assessment of left ventricular volumes and ejection fraction with 16-slice multi-slice computed tomography; comparison with 2D-echocardiography. Int J Cardiol 2007;116(2):201-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Schuijf JD, Bax JJ, Jukema JW., et al. Noninvasive angiography and assessment of left ventricular function using multislice computed tomography in patients with type 2 diabetes. Diabetes Care 2004;27(12):2905-10. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Schuijf JD, Bax JJ, Salm LP., et al. Noninvasive coronary imaging and assessment of left ventricular function using 16-slice computed tomography. Am J Cardiol 2005;95(5):571-4. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Schuijf JD, Pundziute G, Bax JJ. Prognostic value of multislice computed tomography coronary angiography. Cardiol Rev 2007;24(12):39-42. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Schuijf JD, van Werkhoven JM, Pundziute G., et al. Invasive versus noninvasive evaluation of coronary artery disease. JACC Cardiovasc Imaging 2008;1(2):190-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Schuijf JD, Wijns W, Jukema JW., et al. Relationship between noninvasive coronary angiography with multi-slice computed tomography and myocardial perfusion imaging. J Am Coll Cardiol 2006;48(12):2508-14. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Schuijf JD, Wijns W, Jukema JW., et al. A comparative regional analysis of coronary atherosclerosis and calcium score on multislice CT versus myocardial perfusion on SPECT. J Nucl Med 2006;47(11):1749-55. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Schwartz JG, Johnson RB, Apfelbacher FC., et al. Sensitivity, specificity and accuracy of stress SPECT myocardial perfusion imaging for detection of coronary artery disease in the distribution of first-order branch vessels, using an anatomical matching of angiographic and perfusion data. Nucl Med Commun 2003;24(5):543-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Schwitter J, Wacker CM, van Rossum AC., et al. MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a
multicentre, multivendor, randomized trial. Eur Heart J 2008;29(4):480-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Segar DS, Brown SE, Sawada SG., et al. Dobutamine stress echocardiography: correlation with coronary lesion severity as determined by quantitative angiography. J Am Coll Cardiol 1992;19(6):1197-202. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Selcoki Y, Yilmaz OC, Kankilic MN., et al. Diagnostic accuracy of 64-slice computed tomography in patients with suspected or proven coronary artery disease. Turk Kardiyol Dern Ars 2010;38(2):95-100. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Senior R, Janardhanan R, Jeetley P., et al. Myocardial contrast echocardiography for distinguishing ischemic from nonischemic first-onset acute heart failure: insights into the mechanism of acute heart failure. Circulation 2005;112(11):1587-93. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Sensky PR, Jivan A, Hudson NM., et al. Coronary artery disease: combined stress MR imaging protocol-one-stop evaluation of myocardial perfusion and function. Radiology 2000;215(2):608-14. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sensky PR, Samani NJ, Reek C., et al. Magnetic resonance perfusion imaging in patients with coronary artery disease: a qualitative approach. Int J Cardiovasc Imaging 2002;18(5):373-83; discussion 385-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Shaw LJ, Gillam L, Feinstein S,, et al. Use of an intravenous contrast agent (Optison) to enhance echocardiography: efficacy and cost implications. Optison Multicenter Study Group. Am J Manag Care 1998;4 Spec No:SP169-76. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Shaw LJ, Hachamovitch R, Redberg RF. Current evidence on diagnostic testing in women with suspected coronary artery disease: choosing the appropriate test. Cardiol Rev 2000;8(1):65-74. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Shaw LJ, Hendel R, Borges-Neto S,, et al. Prognostic value of normal exercise and adenosine (99m)Tc-tetrofosmin SPECT imaging: results from the multicenter registry of 4,728 patients. J Nucl Med 2003;44(2):134-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Shaw LJ, Hendel RC, Cerquiera M,, et al. Ethnic differences in the prognostic value of stress technetium-99m tetrofosmin gated single-photon emission computed tomography myocardial perfusion imaging. J Am Coll Cardiol 2005;45(9):1494-504. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Shaw LJ, Mieres JH. The role of noninvasive testing in the diagnosis and prognosis of women with suspected CAD. J Fam Pract 2005;Suppl:4-5, 7. Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Shaw LJ, Min JK, Narula J,, et al. Sex differences in mortality associated with computed tomographic angiographic measurements of obstructive and nonobstructive coronary artery disease: an exploratory analysis. Circ Cardiovasc Imaging 2010;3(4):473-81. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Shaw LJ, Vasey C, Sawada S,, et al. Impact of gender on risk stratification by exercise and dobutamine stress echocardiography: long-term mortality in 4234 women and 6898 men. Eur Heart J 2005;26(5):447-56. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Shaw LJ, Wilson PW, Hachamovitch R,, et al. Improved near-term coronary artery disease risk classification with gated stress myocardial perfusion SPECT. JACC Cardiovasc Imaging 2010;3(11):1139-48. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Shelley S, Sathymurthy I, Madhavan, et al. Adenosine myocardial SPECT—its efficacy and safety and correlation with coronary angiogram. J Assoc Physicians India 2003;51:557-60. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Sheth TN, Rieber J, Mooyaart EA,, et al. Usefulness of coronary computed tomographic angiography to assess suitability for revascularization in patients with significant coronary artery disease and angina pectoris. Am J Cardiol 2006;98(9):1198-201. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Shi H, Aschoff AJ, Brambs HJ,, et al. Multislice CT imaging of anomalous coronary arteries. Eur Radiol 2004;14(12):2172-81. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Shimoni S, Goland S, Livshitz S,, et al. Accuracy and long-term prognostic value of pacing stress echocardiography compared with dipyridamole Tl emission computed tomography in patients with a permanent pacemaker and known or suspected coronary artery disease. Cardiology 2010;116(3):229-236. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Shimoni S, Zoghbi WA, Xie F,, et al. Real-time assessment of myocardial perfusion and wall motion during bicycle and treadmill exercise echocardiography: comparison with single photon emission computed tomography. J Am Coll Cardiol 2001;37(3):741-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Shin JH, Pokharna HK, Williams KA,, et al. SPECT myocardial perfusion imaging with prone-only acquisitions: correlation with coronary angiography. J Nucl Cardiol 2009;16(4):590-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Shirai N, Yamagishi H, Yoshiyama M,, et al. Incremental value of assessment of regional wall motion for detection of multivessel coronary artery disease in exercise (201)Tl gated myocardial perfusion imaging. J Nucl Med 2002;43(4):443-50. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Shry EA, Eckart RE, Furgerson JL, et al. Addition of right-sided and posterior precordial leads during stress testing. Am Heart J 2003;146(6):1090-4. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Shuman WP, Branch KR, May JM, et al. Whole-chest 64-MDCT of emergency department patients with nonspecific chest pain: Radiation dose and coronary artery image quality with prospective ECG triggering versus retrospective ECG gating. AJR Am J Roentgenol 2009;192(6):1662-7. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Shuman WP, May JM, Branch KR, et al. Negative ECG-gated cardiac CT in patients with low-to-moderate risk chest pain in the emergency department: 1-year follow-up. AJR Am J Roentgenol 2010;195(4):923-7. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Simonetti I, Rezai K, Rossen JD, et al. Physiological assessment of sensitivity of noninvasive testing for coronary artery disease. Circulation 1991;83(5 SUPPL.). Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.

Simova I, Katova T, Denchev S, et al. Flow-mediated dilatation has an additive value to stress ECG for the diagnosis of angiographically significant coronary atherosclerosis. J Am Soc Hypertens 2010;4(4):203-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sinha AM, Mahnken AH, Borghans A, et al. Multidetector-row computed tomography vs. angiography and intravascular ultrasound for the evaluation of the diameter of proximal coronary arteries. Int J Cardiol 2006;110(1):40-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.
Sirol M, Sanz J, Henry P., et al. Evaluation of 64-slice MDCT in the real world of cardiology: a comparison with conventional coronary angiography. Arch Cardiovasc Dis 2009;102(5):433-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sitges M, Azqueta M, Pare C., et al. Dobutamine stress echocardiography and exercise electrocardiography for risk stratification in medically treated unstable angina. J Am Soc Echocardiogr 2000;13(12):1084-90. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sitges M, Azqueta M, Pare C., et al. Dobutamine stress echocardiography and exercise electrocardiography for risk stratification in medically treated unstable angina. J Am Soc Echocardiogr 2000;13(12):1084-90. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Slart RH, Zeebregts CJ, Hillege HL., et al. Myocardial perfusion reserve after a PET-driven revascularization procedure: a strong prognostic factor. J Nucl Med 2011;52(6):873-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Smart SC, Bhatia A, Hellman R., et al. Dobutamine-atropine stress echocardiography and dipyridamole sestamibi scintigraphy for the detection of coronary artery disease: limitations and concordance. J Am Coll Cardiol 2000;36(4):1265-73. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Smart SC, Knickelbine T, Malik F., et al. Dobutamine-atropine stress echocardiography for the detection of coronary artery disease in patients with left ventricular hypertrophy. Importance of chamber size and systolic wall stress. Circulation 2000;101(3):258-63. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Smart SC, Knickelbine T, Stoiber TR., et al. Safety and accuracy of dobutamine-atropine stress echocardiography for the detection of residual stenosis of the infarct-related artery and multivessel disease during the first week after acute myocardial infarction. Circulation 1997;95(6):1394-401. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


So NM, Lam WW, Li D., et al. Magnetic resonance angiography of coronary arteries with a 3-dimensional magnetization-prepared true fast imaging with steady-state precession sequence compared with conventional coronary angiography. Am Heart J 2005;150(3):530-5. Full-text exclusion reason(s): Data for women not reported as a subgroup.


Sommer T, Hackenbroch M, Hofer U., et al. Coronary MR angiography at 3.0 T versus that at 1.5 T: initial results in patients suspected of having coronary artery disease. Radiology 2005;234(3):718-25. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.
Soofi MA, Khan SA. Dobutamine stress echocardiography as a prognostic tool for future cardiac events. Ann Saudi Med 2008;28(5):371-3. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Soon KH, Chaitowitz I, Cox N., et al. Diagnostic accuracy of 16-slice CT coronary angiography in the evaluation of coronary artery disease. Australas Radiol 2007;51(4):365-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Soon KH, Cox N, Chaitowitz I., et al. Determining the proportion of coronary segments assessable on 16-slice CT coronary angiography: a brief report. Australas Radiol 2007;51(2):139-42. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Soon KH, Kelly AM, Cox N., et al. Practicality, safety and accuracy of computed tomography coronary angiography in the evaluation of low TIMI-risk score chest pain patients: a pilot study. Emerg Med Australas 2007;19(2):129-35. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sosnowski M, Pysz P, Gola A., et al. Coronary artery visualization using a 64-row multi-slice computed tomography in unselected patients with definite or suspected coronary artery disease: a comparison with invasive coronary angiography. Cardiol J 2009;16(5):413-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Southard J, Baker L, Schaefer S. In search of the false-negative exercise treadmill testing evidence-based use of exercise echocardiography. Clin Cardiol 2008;31(1):35-40. Full-text exclusion reason(s): All women in the study are known to have CAD.

Soylu O, Celik S, Karakus G., et al. Transthoracic Doppler echocardiographic coronary flow imaging in identification of left anterior descending coronary artery stenosis in patients with left bundle branch block. Echocardiography 2008;25(10):1065-70. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Sozzi FB, Civaia F, Rossi P., et al. Long-term follow-up of patients with first-time chest pain having 64-slice computed tomography. Am J Cardiol 2011;107(4):516-21. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Sozzi FB, Elhendy A, Roelandt JR., et al. Prognostic value of dobutamine stress echocardiography in patients with diabetes. Diabetes Care 2003;26(4):1074-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Sozzi FB, Poldermans D, Bax JJ., et al. Second harmonic imaging improves sensitivity of dobutamine stress echocardiography for the diagnosis of coronary artery disease. Am Heart J 2001;142(1):153-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Srivastava AV, Ananthasubramaniam K, Patel SJ., et al. Prognostic implications of negative dobutamine stress echocardiography in African Americans compared to Caucasians. Cardiovasc Ultrasound 2008;6:20. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Steel K, Broderick R, Gandla V, et al. Complementary prognostic values of stress myocardial perfusion and late gadolinium enhancement imaging by cardiac magnetic resonance in patients with known or suspected coronary artery disease. Circulation 2009;120(14):1390-400. *Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.*

Steeg L, Lipke CS, Kies P, et al. Quantification of left ventricular volumes and ejection fraction from gated 99mTc-MIBI SPECT: validation of an elastic surface model approach in comparison to cardiac magnetic resonance imaging, 4D-MSPECT and QGS. Eur J Nucl Med Mol Imaging 2007;34(6):900-9. *Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.*


Stein PD, Yaekoub AY, Matta F, et al. 64-slice CT for diagnosis of coronary artery disease: a systematic review. Am J Med 2008;121(8):715-25. *Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.*

Steingart RM, Hodnett P, Musso J, et al. Exercise myocardial perfusion imaging in elderly patients. J Nucl Cardiol 2002;9(6):573-80. *Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.*

Stewart RE, Schwaiger M, Molina E, et al. Comparison of rubidium-82 positron emission tomography and thallium-201 SPECT imaging for detection of coronary artery disease. Am J Cardiol 1991;67(16):1303-10. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*


Stratmann HG, Mark AL, Walter KE, et al. Prognostic value of atrial pacing and thallium-201 scintigraphy in patients with stable chest pain. Am J Cardiol 1989;64(16):985-90. *Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.*


Stroebek JE, Shen JT, Singh B, et al. Comparison of a two-lead, computerized, resting ECG signal analysis device, the MultiFunction-CardioGram or MCG (a.k.a. 3DMP), to quantitative coronary angiography for the detection of relevant coronary artery stenosis (>70%) - a meta-analysis of all published trials performed and analyzed in the US. Int J Med Sci 2009;6(4):143-55. *Full-text exclusion reason(s): Not original peer-reviewed data or a secondary analysis of RCT, prospective or retrospective observational study, or registry.*

Sumanen M, Jussila M, Mattila K. Exercise treadmill test may predict clinical outcome among working-aged patients suspected of coronary heart disease in general practice. Scand J Prim Health Care 2005;23(1):47-51. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Sumanen M, Mattila K. A negative finding in an exercise test is reliable among elderly people: a follow-up study. Gerontology 2007;53(3):159-64. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Sun Z, Cao Y. Multislice CT angiography assessment of left coronary artery: Correlation between bifurcation angle and dimensions and development of coronary artery disease. Euro J Radiol 2011;79(2):e90-e95. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; No outcomes of interest.


Sundram F, Notghi A, Smith NB. Pharmacological stress myocardial perfusion scintigraphy: use of a modified adenosine protocol in patients with asthma. Nucl Med Commun 2009;30(3):217-25. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Sunman H, Yorgun H, Canpolat U., et al. Association between family history of premature coronary artery disease and coronary atherosclerotic plaques shown by multidetector computed tomography coronary angiography. Int J Cardiol 2011. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Suratkal V, Shirke M, Lele RD. Treadmill ECG test combined with myocardial perfusion imaging for evaluation of coronary artery disease: analysis of 340 cases. J Assoc Physicians India 2003;51:561-4. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Svane B, Bone D, Holmgren A. Coronary angiography and thallium-201 single photon emission computed tomography in single vessel coronary artery disease. Acta Radiol 1990;31(3):237-44. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Swailam S, Abdel-Salam Z, Emil S., et al. Multi-slice computed tomography: Can it adequately rule out left main coronary disease in patients with an intermediate probability of coronary artery disease? Cardiol J 2010;17(6):594-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


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Takagi T, Takagi A, Yoshikawa J. Detection of coronary artery disease using delayed strain imaging at 5 min after the termination of exercise stress: head to head comparison with conventional treadmill stress echocardiography. J Cardiol 2010;55(1):41-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Takase B, Nagata M, Kihara T,, et al. Whole-heart dipyridamole stress first-pass myocardial perfusion MRI for the detection of coronary artery disease. Jpn Heart J 2004;45(3):475-86. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Takeishi Y, Chiba J, Abe S,, et al. Noninvasive identification of left main and three-vessel coronary artery disease by thallium-201 single photon emission computed tomography during adenosine infusion. Ann Nucl Med 1994;8(1):1-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Tamaki N, Yonekura Y, Mukai T., et al. Stress thallium-201 transaxial emission computed tomography: quantitative versus qualitative analysis for evaluation of coronary artery disease. J Am Coll Cardiol 1984;4(6):1213-21. Full-text exclusion reason(s): Population does not include women ≥ age 18; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Tamarappoo B, Dey D, Shmilovich H., et al. Increased pericardial fat volume measured from noncontrast CT predicts myocardial ischemia by SPECT. JACC Cardiovasc Imaging 2010;3(11):1104-12. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Tamarappoo BK, Dey D, Nakazato R., et al. Comparison of the extent and severity of myocardial perfusion defects measured by CT coronary angiography and SPECT myocardial perfusion imaging. JACC Cardiovasc Imaging 2010;3(10):1010-9. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Tardif JC, Dore A, Chan KL., et al. Economic impact of contrast stress echocardiography on the diagnosis and initial treatment of patients with suspected coronary artery disease. J Am Soc Echocardiogr 2002;15(11):1335-45. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Tejani FH, Thompson RC, Iskandrian AE., et al. Effect of caffeine on SPECT myocardial perfusion imaging during regadenoson pharmacologic stress: rationale and design of a prospective, randomized, multicenter study. J Nucl Cardiol 2011;18(1):73-81. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.
Tepe SM. Imaging of the heart and coronary arteries. Cardiovasc Intervent Radiol 2003;26(SUPPL. 1). Full-text exclusion reason(s): Conference abstract or trial registry posting.

Teresinska A, Wnuk J, Konieczna S., et al. Verification of the left ventricular ejection fraction from gated myocardial perfusion studies (GSPECT). Kardiol Pol 2005;63(5):465-75; discussion 476-7. Full-text exclusion reason(s): Data for women not reported as a subgroup; No outcomes of interest.

Thanigaraj S, Nease RF, Jr., Schechtman KB., et al. Use of contrast for image enhancement during stress echocardiography is cost-effective and reduces additional diagnostic testing. Am J Cardiol 2001;87(12):1430-2. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Thiele H, Plein S, Breeuwer M., et al. Color-encoded semiautomatic analysis of multi-slice first-pass magnetic resonance perfusion: comparison to tetrofosmin single photon emission computed tomography perfusion and X-ray angiography. Int J Cardiovasc Imaging 2004;20(5):371-84; discussion 385-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Thilo C, Schoepf UJ, Gordon L., et al. Integrated assessment of coronary anatomy and myocardial perfusion using a retractable SPECT camera combined with 64-slice CT: Initial experience. Euro Radiol 2009;19(4):845-856. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Thomas D, Meyer C, Strach K., et al. Dobutamine stress tagging and gradient-echo imaging for detection of coronary heart disease at 3 T. Br J Radiol 2011;84(997):44-50. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Thomas GS, Miyamoto MI, Morello AP, 3rd., et al. Technetium 99m sestamibi myocardial perfusion imaging predicts clinical outcome in the community outpatient setting. The Nuclear Utility in the Community (NUC) Study. J Am Coll Cardiol 2004;43(2):213-23. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Thomson HL, Basmadjian AJ, Rainbird AJ., et al. Contrast echocardiography improves the accuracy and reproducibility of left ventricular remodeling measurements: a prospective, randomly assigned, blinded study. J Am Coll Cardiol 2001;38(3):867-75. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.

Toledo E, Jacobs LD, Lodato JA,, et al. Quantitative diagnosis of stress-induced myocardial ischemia using analysis of contrast echocardiographic parametric perfusion images. Eur J Echocardiogr 2006;7(3):217-25. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Tolstrup K, Madsen BE, Ruiz JA,, et al. Non-invasive resting magnetocardiographic imaging for the rapid detection of ischemia in subjects presenting with chest pain. Cardiology 2006;106(4):270-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Tsiflikas I, Brodoefel H, Reimann AJ,, et al. Coronary CT angiography with dual source computed tomography in 170 patients. Eur J Radiol 2010;74(1):161-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Tsiflikas I, Drosch T, Brodoefel H,, et al. Diagnostic accuracy and image quality of cardiac dual-source computed tomography in patients with arrhythmia. Int J Cardiol 2010;143(1):79-85. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Tsutsui JM, Elhendy A, Anderson JR., et al. Prognostic value of dobutamine stress myocardial contrast perfusion echocardiography. Circulation 2005;112(10):1444-50. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Tsutsui JM, Elhendy A, Xie F., et al. Safety of dobutamine stress real-time myocardial contrast echocardiography. J Am Coll Cardiol 2005;45(8):1235-42. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Tsutsui JM, Osorio AF, Lario FA., et al. Comparison of safety and efficacy of the early injection of atropine during dobutamine stress echocardiography with the conventional protocol. Am J Cardiol 2004;94(11):1367-72. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Tsutsui JM, Xie F, Cloutier D., et al. Real-time dobutamine stress myocardial perfusion echocardiography predicts outcome in the elderly. Eur Heart J 2008;29(3):377-85. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Tsutsui JM, Xie F, O'Leary EL., et al. Diagnostic accuracy and prognostic value of dobutamine stress myocardial contrast echocardiography in patients with suspected acute coronary syndromes. Echocardiography 2005;22(6):487-95. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Turner AS, Nathan MC, Watson OF., et al. The correlation of the computer quantitated treadmill exercise electrocardiogram with cinearteriographic assessment of coronary artery disease. N Z Med J 1979;89(630):115-8. Full-text exclusion reason(s): Population does not include women ≥ age 18; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Ueno K, Anzai T, Jinzaki M., et al. Increased epicardial fat volume quantified by 64-multidetector computed tomography is associated with coronary atherosclerosis and totally occlusive lesions. Circ J 2009;73(10):1927-33. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Ugolini P, Pressacco J, Lesperance J., et al. Evaluation of coronary atheroma by 64-slice multidetector computed tomography: Comparison with intravascular ultrasound and angiography. Can J Cardiol 2009;25(11):641-7. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.
Ulimoen GR, Gjonnaess E, Atar D, et al. Noninvasive coronary angiography with 64-channel multidetector computed tomography in patients with acute coronary syndrome. Acta Radiol 2008;49(10):1140-4. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Vacanti LJ, Sposito AC, Sespedes L, et al. In comparison to the myocardial perfusion scintigraphy, a treadmill stress test is a viable, efficient and cost effective option to predict cardiovascular events in elderly patients. Arq Bras Cardiol 2007;88(5):531-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Valeti US, Miller TD, Hodge DO, et al. Exercise single-photon emission computed tomography provides effective risk stratification of elderly men and elderly women. Circulation 2005;111(14):1771-6. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.


van Dijkman PR, Kuijpers DA, Blom BM, et al. Dobutamine stress magnetic resonance imaging: a valuable method in the noninvasive diagnosis of ischemic heart disease. J Electrocardiol 2002;35 Suppl:57-9. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Van Train KF, Maddahi J, Berman DS, et al. Quantitative analysis of tomographic stress thallium-201 myocardial scintigrams: a multicenter trial. J Nucl Med 1990;31(7):1168-79. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


van Werkhoven JM, de Boer SM, Schuijf JD, et al. Impact of clinical presentation and pretest likelihood on the relation between calcium score and computed tomographic coronary angiography. Am J Cardiol 2010;106(12):1675-9. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

van Werkhoven JM, Gaemperli O, Schuijf JD, et al. Multislice computed tomography coronary angiography for risk stratification in patients with an intermediate pretest likelihood. Heart 2009;95(19):1607-11. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


van Werkhoven JM, Schuijf JD, Jukema JW, et al. Anatomic correlates of a normal perfusion scan using 64-slice computed tomographic coronary angiography. Am J Cardiol 2008;101(1):40-5. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Vanhoeacker PK, Decramer I, Bladt O, et al. Detection of non-ST-elevation myocardial infarction and unstable angina in the acute setting: meta-analysis of diagnostic performance of multi-detector computed tomographic angiography. BMC Cardiovasc Disord 2007;7:39. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Society of Echocardiography 2011;24(7):758-767. Full-text exclusion reason(s): No data for NITs of interest (ECG, ECHO, SPECT, PET, CMR, CTA); Data for women not reported as a subgroup.

Vegsundvag J, Holte E, Wiseth R., et al. Transthoracic echocardiography for imaging of the different coronary artery segments: a feasibility study. Cardiovasc Ultrasound 2009;7:58. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Venkat-Kahoud V, Ellins ML, Yang S., et al. Incremental detection of coronary artery disease by assessment of non-calcified plaque on coronary CT angiography. Clin Radiol 2009;64(3):250-5. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Verani MS, Mahmariant JJ, Hixson JB., et al. Diagnosis of coronary artery disease by controlled coronary vasodilatation with adenosine and thallium-201 scintigraphy in patients unable to exercise. Circulation 1990;82(1):80-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.

Verani MS, Marcus ML, Razzak MA., et al. Sensitivity and specificity of thallium-201 perfusion scintigrams under exercise in the diagnosis of coronary artery disease. J Nucl Med 1978;19(7):773-82. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Verna E, Ceriani L, Giovanella L., et al. "False-positive" myocardial perfusion scintigraphy findings in patients with angiographically normal coronary arteries: insights from intravascular sonography studies. J Nucl Med 2000;41(12):1935-40. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Vitarelli A, Conde Y, Luzzi MF., et al. Transesophageal dobutamine stress echocardiography with tissue Doppler imaging for detection and assessment of coronary artery disease. J Investig Med 2001;49(6):534-43. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Vitarelli A, Luzzi MF, Penco M., et al. On-line quantitative assessment of left ventricular filling during dobutamine stress echocardiography: a useful addition to conventional wall motion scoring. Int J Cardiol 1997;59(1):57-69. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Vivekananthan DP, Blackstone EH, Pothier CE., et al. Heart rate recovery after exercise is a predictor of mortality, independent of the angiographic severity of coronary disease. J Am Coll Cardiol 2003;42(5):831-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.


Vural M, Ucar O, Selvi NA., et al. Assessment of global left ventricular systolic function with multidetector. Diagn Interv Radiol 2010;16(3):236-240. Full-text exclusion reason(s): Data for women not reported as a subgroup; No outcomes of interest.

Wagdi P, Alkadhi H. The impact of cardiac CT on the appropriate utilization of catheter coronary angiography. Int J Cardiovasc Imaging 2010;26(3):333-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup; No outcomes of interest.


Wagner M, Rosler R, Lembcke A., et al. Whole-heart coronary magnetic resonance angiography at 1.5 Tesla: does a blood-pool contrast agent improve diagnostic accuracy? Invest Radiol 2011;46(3):152-9. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Wagdi S, Schuster S, Zahn R., et al. Postinfarction stress testing and one year outcome of stable patients after myocardial infarction treated with thrombolytics. Eur J Med Res 1996;1(12):575-81. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Wahl A, Paetsch I, Gollesch A., et al. Safety and feasibility of high-dose dobutamine-atropine stress cardiovascular magnetic resonance for diagnosis of myocardial ischaemia: experience in 1000 consecutive cases. Eur Heart J 2004;25(14):1230-6. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Walimbe V, Jaber WA, Garcia MJ., et al. Multimodality cardiac stress testing: combining real-time 3-dimensional echocardiography and myocardial perfusion SPECT. J Nucl Med 2009;50(2):226-30. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Wallace EL, Morgan TM, Walsh TF., et al. Dobutamine cardiac magnetic resonance results predict cardiac prognosis in women with known or suspected ischemic heart disease. JACC Cardiovasc Imaging 2009;2(3):299-307. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Wallhaus TR, Lacy J, Stewart R., et al. Copper-62-pyruvaldehyde bis(N-methyl-thiosemicarbazone) PET imaging in the detection of coronary artery disease in humans. J Nucl Cardiol 2001;8(1):67-74. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Watanabe H, Hozumi T, Hirata K, et al. Noninvasive coronary flow velocity reserve measurement in the posterior descending coronary artery for detecting coronary stenosis in the right coronary artery using contrast-enhanced transthoracic Doppler echocardiography. Echocardiography 2004;21(3):225-33. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Watkins MW, Hesse B, Green CE, et al. Detection of coronary artery stenosis using 40-channel computed tomography with multi-segment reconstruction. Am J Cardiol 2007;99(2):175-81. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Wehrschtuetz M, Wehrschtuetz E, Schuchlenz H, et al. Accuracy of MSCT coronary angiography with 64 row CT scanner—Facing the facts. Clinical Medicine Insights: Cardiology 2010;4:15-22. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Weininger M, Schoepf UJ, Ramachandra A, et al. Adenosine-stress dynamic real-time myocardial perfusion CT and adenosine-stress first-pass dual-energy myocardial perfusion CT for the assessment of acute chest pain: Initial results. Eur J Radiol 2010. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.


Wertman BM, Cheng VY, Kar S, et al. Characterization of complex coronary artery stenosis morphology by coronary computed tomographic angiography. JACC Cardiovasc Imaging 2009;2(8):950-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Weustink AC, Neefjes LA, Kyrzopoulos S, et al. Impact of heart rate frequency and variability on radiation exposure, image quality, and diagnostic performance in dual-source spiral CT coronary angiography. Radiology 2009;253(3):672-80. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Wexler O, Yoder SR, Elder JL, et al. Effect of gender on cardiovascular risk stratification with ECG gated SPECT left ventricular volume indices and ejection fraction. J Nucl Cardiol 2009;16(1):28-37. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

White CS, Kuo D, Kelemen M, et al. Chest pain evaluation in the emergency department: can MDCT provide a comprehensive evaluation? AJR Am J Roentgenol 2005;185(2):533-40. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Williams KA, Schneider CM. Increased stress right ventricular activity on dual isotope perfusion SPECT: a sign of multivessel and/or left main coronary artery disease. J Am Coll Cardiol 1999;34(2):420-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Wolak A, Gutstein A, Cheng VY, et al. Dual-source coronary computed tomography angiography in patients with atrial fibrillation: initial experience. J Cardiovasc Comput Tomogr 2008;2(3):172-80. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Wolff SD, Schwitter J, Coulden R, et al. Myocardial first-pass perfusion magnetic resonance imaging: a multicenter dose-ranging study. Circulation 2004;110(6):732-7. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.


Wu YW, Huang PJ, Su MY, et al. Myocardium viability assessed by delayed contrast-enhanced magnetic resonance imaging in patients with severe ischemic heart failure: A comparison with thallium SPECT and dobutamine echocardiography. World Heart Journal 2008;1(1):57-68. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Xie F, Tsutsui JM, McGrain AC, et al. Comparison of dobutamine stress echocardiography with and without real-time perfusion imaging for detection of coronary artery disease. Am J Cardiol 2005;96(4):506-11. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Xu L, Yang L, Fan Z, et al. Diagnostic performance of 320-detector CT coronary angiography in patients with atrial fibrillation: preliminary results. Eur Radiol 2011;21(5):936-43. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup; No outcomes of interest.

Xu Y, Fish M, Gerlach J, et al. Combined quantitative analysis of attenuation corrected and non-corrected myocardial perfusion SPECT: Method development and clinical validation. J Nucl Cardiol 2010;17(4):591-599. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Yamada AT, Soares J, Jr., Meneghetti JC., et al. Planar myocardial perfusion imaging for evaluation of patients with acute chest pain. Int J Cardiol 2004;97(3):447-53. Full-text exclusion reason(s): All women in the study are known to have CAD; Data for women not reported as a subgroup.

Yamada K, Hirai M, Abe K., et al. Diagnostic usefulness of postexercise systolic blood pressure response for detection of coronary artery disease in patients with echocardiographic left ventricular hypertrophy. Can J Cardiol 2004;20(7):705-11. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Yamada T, Sawada T, Yamano T., et al. Evaluation of coronary arterial stenoses using 2D magnetic resonance coronary angiography. Minimally Invasive Therapy and Allied Technologies 2002;11(1):7-15. Full-text exclusion reason(s): Women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Yamaguchi M, Shimizu M, Ino H., et al. Diagnostic usefulness of the post-exercise systolic blood pressure response for the detection of coronary artery disease in patients with diabetes mellitus. Jpn Circ J 2000;64(12):949-52. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Yang CW, Carr JC, Francois CJ., et al. Coronary magnetic resonance angiography using magnetization-prepared contrast-enhanced breath-hold volume-targeted imaging (MPCE-VCATS). Invest Radiol 2006;41(8):639-44. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Yang L, Zhang Z, Fan Z., et al. 64-MDCT coronary angiography of patients with atrial fibrillation: influence of heart rate on image quality and efficacy in evaluation of coronary artery disease. AJR Am J Roentgenol 2009;193(3):795-801. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.


Yang PC, Santos JM, Nguyen PK., et al. Dynamic real-time architecture in magnetic resonance coronary angiography—a prospective clinical trial. J Cardiovasc Magn Reson 2004;6(4):885-94. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Yang Q, Li K, Liu X., et al. Contrast-enhanced whole-heart coronary magnetic resonance angiography at 3.0-T: a comparative study with X-ray angiography in a single center. J Am Coll Cardiol 2009;54(1):69-76. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Yang WI, Hur J, Ko YG., et al. Assessment of tissue characteristics of noncalcified coronary plaques by 64-slice computed tomography in comparison with integrated backscatter intravascular ultrasound. Coron Artery Dis 2010;21(3):168-74. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Yang X, Gai LY, Li P., et al. Diagnostic accuracy of dual-source CT angiography and coronary risk stratification. Vasc Health Risk Manag 2010;6:935-41. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.
Yanik A, Yetkin E, Senen K, et al. Value of dobutamine stress echocardiography for diagnosis of coronary artery disease in patients with left bundle branch blockage. Coron Artery Dis 2000;11(7):545-8. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.

Yao SS, Bangalore S, Chaudhry FA. Prognostic implications of stress echocardiography and impact on patient outcomes: An effective gatekeeper for coronary angiography and revascularization. Journal of the American Society of Echocardiography 2010;23(8):832-839. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Yao SS, Qureshi E, Sherrid MV, et al. Practical applications in stress echocardiography: risk stratification and prognosis in patients with known or suspected ischemic heart disease. J Am Coll Cardiol 2003;42(6):1084-90. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Yao SS, Shah A, Bangalore S, et al. Transient ischemic left ventricular cavity dilation is a significant predictor of severe and extensive coronary artery disease and adverse outcome in patients undergoing stress echocardiography. J Am Soc Echocardiogr 2007;20(4):352-8. Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Yao Z, Liu XJ, Shi R, et al. A comparison of 99mTc-MIBI myocardial SPET with electron beam computed tomography in the assessment of coronary artery disease. Eur J Nucl Med 1997;24(9):1115-20. Full-text exclusion reason(s): No assessment of symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.

Yao Z, Liu XJ, Shi RF, et al. A comparison of 99Tcm-MIBI myocardial SPET and electron beam computed tomography in the assessment of coronary artery disease in two different age groups. Nucl Med Commun 2000;21(1):43-8. Full-text exclusion reason(s): No assessment of symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Yap LB, Arshad W, Jain A, et al. Significance of ST depression during exercise treadmill stress and adenosine infusion myocardial perfusion imaging. Int J Cardiovasc Imaging 2005;21(2-3):253-8; discussion 259-60. Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


Yildirir A, Kaynar G, Gulmez O, et al. Is it possible to increase the diagnostic value of exercise electrocardiography by post-exercise B-type natriuretic peptide levels? Acta Cardiol 2007;62(1):39-45. Full-text exclusion reason(s): Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.
Yilmaz MH, Yasar D, Albayram S., et al. Coronary calcium scoring with MDCT: the radiation dose to the breast and the effectiveness of bismuth breast shield. Eur J Radiol 2007;61(1):139-43. *Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization.*


Yorgun H, Kaya EB, Hazirolan T., et al. Prevalence of incidental pulmonary findings and early follow-up results in patients undergoing dual-source 64-slice computed tomography coronary angiography. J Comput Assist Tomogr 2010;34(2):296-301. *Full-text exclusion reason(s): All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.*


Yoshinaga K, Chow BJ, Williams K., et al. What is the prognostic value of myocardial perfusion imaging using rubidium-82 positron emission tomography? J Am Coll Cardiol 2006;48(5):1029-39. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*

Yoshitani H, Takeuchi M, Mor-Avi V., et al. Comparative diagnostic accuracy of multiplane and multislice three-dimensional dobutamine stress echocardiography in the diagnosis of coronary artery disease. J Am Soc Echocardiogr 2009;22(5):437-42. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*

Yoshitani H, Takeuchi M, Sakamoto K., et al. Effect of one or more co-morbid conditions on diagnostic accuracy of coronary flow velocity reserve for detecting significant left anterior descending coronary stenosis. Heart 2005;91(10):1294-8. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*

Younis LT, Byers S, Shaw L., et al. Prognostic importance of silent myocardial ischemia detected by intravenous dipyridamole thallium myocardial imaging in asymptomatic patients with coronary artery disease. J Am Coll Cardiol 1989;14(7):1635-41. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.*

Yuda S, Khoury V, Marwick TH. Influence of wall stress and left ventricular geometry on the accuracy of dobutamine stress echocardiography. J Am Coll Cardiol 2002;40(7):1311-9. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Data for women not reported as a subgroup.*

Zafrir N, Mats I, Solodky A., et al. Prognostic value of stress myocardial perfusion imaging in octogenarian population. J Nucl Cardiol 2005;12(6):671-5. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.*


Zaid G, Tanchilevitch A, Rivlin E., et al. Diagnostic accuracy of serum B-type natriuretic peptide for myocardial ischemia detection during exercise testing with spect perfusion imaging. Int J Cardiol 2007;117(2):157-64. *Full-text exclusion reason(s): No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup; No outcomes of interest.*
Zaid G, Yehudai D, Rosenschein U., et al. Coronary artery disease in an asymptomatic population undergoing a multidetector computed tomography (mdct) coronary angiography. Open Cardiovascular Medicine Journal 2010;4:7-13. **Full-text exclusion reason(s):** No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization.

Zakavi SR, Taherpour M, Saleh F., et al. Electrocardiographic changes after dipyridamole infusion in patients undergoing myocardial perfusion imaging. Nucl Med Commun 2010;31(6):502-505. **Full-text exclusion reason(s):** No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.


Zellweger MJ, Dubois EA, Lai S., et al. Risk stratification in patients with remote prior myocardial infarction using rest-stress myocardial perfusion SPECT: prognostic value and impact on referral to early catheterization. J Nucl Cardiol 2002;9(1):23-32. **Full-text exclusion reason(s):** All women in the study are known to have CAD; Study does not compare one NIT to another or to diagnostic cardiac catheterization; Data for women not reported as a subgroup.

Zerahn B, Jensen BV, Nielsen KD., et al. Increased prognostic value of combined myocardial perfusion imaging and exercise electrocardiography in patients with coronary artery disease. J Nucl Cardiol 2000;7(6):616-22. **Full-text exclusion reason(s):** No women with symptomatic chest pain, or results are not reported separately for symptomatic subgroup; All women in the study are known to have CAD; Data for women not reported as a subgroup.


