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Draft Comparative Effectiveness Review
Number XXX (Provided by AHRQ)

Adjunctive Devices to Remove Thrombi or Protect Against Distal Embolization in Acute Coronary Syndrome Patients: A Comparative Effectiveness Review

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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 State Children's Health Insurance Program (SCHIP).

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

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Structured Abstract

Objectives: This is an evidence report examining the benefits and harms of adjunctive devices to remove thrombi or protect against embolization in patients with acute coronary syndromes (ACS) undergoing percutaneous coronary intervention (PCI) of native vessels.

Data Sources: MEDLINE, Cochrane Database, and abstracts from major cardiology meetings were searched from 1996-March 2010; as was www.clinicaltrials.gov and a manual search of identified references.

Review Methods: Randomized controlled trials (RCTs), controlled observational studies enrolling ≥500 patients, and meta-analyses were eligible for inclusion in this systematic review. Data amenable to meta-analysis were pooled as relative risks (RR) with accompanying 95 percent confidence intervals (CIs) using a random-effects model.

Results: One hundred sixty-five articles were included. Three direct comparative RCTs were identified; comparing catheter aspiration to distal balloon protection devices or other catheter aspiration devices, and showed no significant differences for evaluated outcomes. The data comparing adjunctive devices to control are predominantly in patients with ST-segment elevation myocardial infarction (STEMI).

In RCTs conducted within STEMI patients, catheter aspiration devices decreased the risk of major adverse cardiovascular events (MACE) [RR 0.73 (0.61-0.88)] versus control. Catheter aspiration devices increased the achievement of ST-segment resolution [RR 1.48 (1.30-1.70)], myocardial blush grade of 3 (MBG-3) [RR 1.60 (1.40-1.84)] and thrombolysis in myocardial infarction (TIMI) 3 flow [RR 1.07 (1.03-1.11)], while reducing distal embolization [RR 0.55 (0.39-0.78)], no reflow [RR 0.48 (0.29-0.79)], and coronary dissection [RR 0.30 (0.12-0.75)] versus control. Other final health and intermediate outcomes were not significantly impacted by catheter aspiration devices versus control. In a majority of trials, the use of catheter aspiration devices increased procedural time upon qualitative assessment.

The use of mechanical thrombectomy or embolic protection devices did not significantly impact any of the final health outcomes or harms in RCTs although increased procedural time in qualitative assessment versus control. Distal balloon embolic protection devices increased the achievement of MBG-3 [RR 1.39 (1.15-1.69)], but did not significantly impact other intermediate outcomes versus control. Mechanical thrombectomy or embolic protection devices did not significantly impact any of the intermediate outcomes evaluated versus control. The associations between predetermined factors and outcomes in people receiving adjunctive devices were generally weak.

Conclusions: For most devices, there are few RCTs evaluating final health outcomes over a long period of followup and the data outside of STEMI is scarce. In patients with STEMI, catheter aspiration devices have the most robust trial data and appeared to have a favorable balance of benefits to harms.

Contents

Evidence Report **1**
Chapter 1. Introduction **3**
Background 3
Objective 6
The Key Questions 7
Analytic Framework 8
Chapter 2. Methods **9**
Input from Stakeholders 9
Searching for the Evidence: Literature Search Strategies for Identifying Relevant Studies to Answer the Key Questions 9
Criteria for Inclusion and Exclusion of Studies in the Review 9
Data Extraction and Data Management 10
Assessment of Methodological Quality of Individual Studies 10
Data Synthesis 11
Grading the Evidence for Each Key Question 12
Applicability of Evidence 14
Chapter 3. Results **15**
Results of Literature Search 15
Key Question 1 17
Key Points 17
Detailed Analysis 22
Study Design and Population Characteristics 22
Outcome Evaluations 25
Summary 124
Final health outcomes in patients with STEMI 124
Final health outcomes in patients with other ACSs 126
Intermediate Health Outcomes 127
Key Question 2 129
Key Points 129
Detailed Analysis 131
Study Design and Population Characteristics 131
Outcome Results 131
Summary 146
Key Question 3 147
Key Points 147
Detailed Anlaysis 149
Study Design and Population Characteristics 149
Summary 161
Strength of Evidence and Applicability 163
Strength of Evidence 163
Applicability 165
Chapter 4. Discussion **189**
Future Research 190
Limitations of Current Research 190

Future Avenues for Research 191
References and Included Studies 193
List of Acronyms/Abbreviations 204

Tables

Table 1. Thrombolysis in Myocardial Infarction (TIMI) Flow Grading System 3
Table 2. Myocardial Blush Grade 4
Table 3. Thrombectomy and embolic protection devices used in the randomized controlled trials included in the quantitative synthesis 5
Table 4. Summary ratings of quality of individual studies 11
Table 5. Definitions for grading the strength of evidence 13
Table 6. Applicability PICOTS and data to extract 14
Table 7. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction 69
Table 8. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction 70
Table 9. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction 70
Table 10. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction 70
Table 11. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction 71
Table 12. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating embolic protection devices combined in patients with ST-segment elevation myocardial infarction 71
Table 13. Ejection fraction of direct comparative randomized controlled trials in ST-segment elevation myocardial infarction. 81
Table 14. Ejection fraction in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction. 82
Table 15. Ejection fraction in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction. 84
Table 16. Ejection fraction in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction. 85
Table 17. Ejection fraction in randomized controlled trials evaluating thrombectomy or embolic protection devices in patients with mixed acute coronary syndromes. 85
Table 18. Ejection fraction in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction. 86
Table 19. Ejection fraction in randomized controlled studies with unique comparison in patients with mixed acute coronary syndromes. 87

Table 20. Ejection fraction in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction. 88
Table 21. Intermediate health outcomes in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction.....122
Table 22. Intermediate health outcomes in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction 123
Table 23. Intermediate health outcomes in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction 123
Table 24. Intermediate health outcomes in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction 123
Table 25. Intermediate health outcomes in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction 123
Table 26. Intermediate health outcomes in randomized controlled trials evaluating embolic protection devices combined in patients with ST-segment elevation myocardial infarction 124
Table 27. Adverse events in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction 144
Table 28. Adverse events in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction 145
Table 29. Adverse events in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction 145
Table 30. Adverse events in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction 145
Table 31. Adverse events in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction 145
Table 32. Adverse events in randomized controlled trials evaluating embolic protection devices combined in patients with ST-segment elevation myocardial infarction.....146
Table 33. Results of subgroup analysis from randomized controlled trials evaluating the effect of gender on clinical outcome.....149
Table 34. Results of subgroup analysis from randomized controlled trials evaluating the effect of age on clinical outcome 150
Table 35. Results of subgroup analysis from randomized controlled trials evaluating the effect of diabetes mellitus on clinical outcome.....151
Table 36. Results of subgroup analysis from randomized controlled trials evaluating the effect of smoking on clinical outcome.....151
Table 37. Results of subgroup analysis from randomized controlled trials evaluating the effect of failed thrombolysis on clinical outcome.....152
Table 38. Results of subgroup analysis from randomized controlled trials evaluating the effect of glycoprotein 2B 3A inhibitor use on clinical outcome.....153
Table 39. Results of subgroup analysis from randomized controlled trials evaluating the effect of ischemic time on clinical outcome 155
Table 40. Results of subgroup analysis from randomized controlled trials evaluating the effect of visible thrombus on clinical outcome.....156

Table 41. Results of subgroup analysis from randomized controlled trials evaluating the effect of infarct-related artery on clinical outcome.....157
Table 42. Results of subgroup analysis from randomized controlled trials evaluating the effect of lesion location on clinical outcome 158
Table 43. Results of subgroup analysis from randomized controlled trials evaluating the effect of baseline thrombolysis in myocardial infarction flow on clinical outcome.....160
Table 44. Results of subgroup analysis from randomized controlled trials evaluating the effect of direct stenting on clinical outcome.....160
Table 45. Summary of the strength of evidence for Key Question 1 166
Table 46. Summary of the strength of evidence for Key Question 2 180

Figures

Figure 1. Analytic Framework for Adjunctive Devices to Remove Thrombi and Protect Against Distal Embolization in Patients With ACS Who Are Undergoing PCI of Native Vessels.....8
Figure 2. PRISMA flow diagram for the search for KQs 1-3.....16
Figure 3. Impact of catheter aspiration devices versus control on mortality using the maximal duration of followup. 30
Figure 4. Impact of mechanical thrombectomy devices versus control on mortality using the maximal duration of followup. 31
Figure 5. Impact of distal filter embolic protection devices versus control on mortality using the maximal duration of followup. 32
Figure 6. Impact of distal balloon embolic protection devices versus control on mortality using the maximal duration of followup versus control in patients with ST-segment elevation myocardial infarction. 33
Figure 7. Impact of distal balloon embolic protection devices versus control on mortality using the maximal duration of followup in patients with mixed acute coronary syndromes. 34
Figure 8. Impact of embolic protection devices combined versus control on mortality using the maximal duration of followup in patients with ST-segment elevation myocardial infarction. 35
Figure 9. Impact of embolic protection devices combined versus control on mortality using the maximal duration of followup in patients with other acute coronary syndromes.....36
Figure 10. Impact of catheter aspiration devices versus control on myocardial infarction using the maximal duration of followup. 41
Figure 11. Impact of mechanical thrombectomy devices versus control on myocardial infarction using the maximal duration of followup. 42
Figure 12. . Impact of distal filter embolic protection devices versus control on myocardial infarction using the maximal duration of followup. 43
Figure 13. Impact of distal balloon embolic protection devices versus control on myocardial infarction using the maximal duration of followup. 44
Figure 14. . Impact of embolic protection devices combined versus control on myocardial infarction using the maximal duration of followup. 45
Figure 15. Impact of catheter aspiration devices versus control on stroke using the maximal duration of followup. 49
Figure 16. Impact of mechanical thrombectomy devices versus control on occurrence of stroke using the maximal duration of followup. 50

Figure 17. Impact of embolic protection devices combined versus control on stroke using the maximal duration of followup. 51
Figure 18. Impact of catheter aspiration devices versus control on target revascularization using the maximal duration of followup.....56
Figure 19. Impact of mechanical thrombectomy devices versus control on target revascularization using the maximal duration of followup.....57
Figure 20. Impact of distal filter embolic protection devices versus control on target revascularization using the maximal duration of followup.....58
Figure 21. Impact of distal balloon embolic protection devices versus control on target revascularization using maximal duration of followup. 59
Figure 22. Impact of embolic protection devices combined versus control on target revascularization using the maximal duration of followup.....60
Figure 23. Impact of catheter aspiration devices versus control on MACE of maximal duration of followup. 65
Figure 24. Impact of mechanical thrombectomy devices versus control on MACE using the maximal duration of followup. 66
Figure 25. Impact of distal filter embolic protection devices versus control on MACE using the maximal duration of followup. 67
Figure 26. Impact of distal balloon embolic protection devices versus control on MACE using the maximal duration of followup.....68
Figure 27. Impact of embolic protection devices combined versus control on MACE using the maximal duration of followup. 69
Figure 28. Impact of catheter aspiration devices versus control on ST-segment resolution. 76
Figure 29. Impact of mechanical thrombectomy devices versus control on ST-segment resolution.....77
Figure 30. Impact of distal filter embolic protection devices versus control on ST-segment resolution.....78
Figure 31. Impact of distal balloon embolic protection devices versus control on ST-segment resolution.....79
Figure 32. . Impact of embolic protection devices combined versus control on ST-segment resolution.....80
Figure 33. Impact of catheter aspiration devices versus control on myocardial blush grade of 3.92
Figure 34. Impact of mechanical thrombectomy devices versus control on myocardial blush grade of 3. 93
Figure 35. . Impact of distal filter embolic protection devices versus control on myocardial blush grade of 3. 94
Figure 36. . Impact of distal balloon embolic protection devices versus control on myocardial blush grade of 3 in patients with ST-segment elevation myocardial infarction. 95
Figure 37. Impact of distal balloon embolic protection devices versus control on myocardial blush grade of 3 in patients with mixed acute coronary syndrome.....96
Figure 38. Impact of embolic protection devices combined versus control on myocardial blush grade of 3. 97
Figure 39. Impact of catheter aspiration devices versus control on TIMI-3 blood flow in patients with ST-segment elevation myocardial infarction. 102
Figure 40. Impact of catheter aspiration devices versus control on TIMI-3 blood flow in patients with mixed acute coronary syndrome. 103

Figure 41. Impact of mechanical thrombectomy devices versus control on TIMI- 3 blood flow.104
Figure 42. Impact of distal filter embolic protection devices versus control on TIMI-3 blood flow. 105
Figure 43. Impact of distal balloon embolic protection devices versus control on TIMI- 3 blood flow in patients with ST-segment elevation myocardial infarction. 106
Figure 44. Impact of distal balloon embolic protection devices versus control on TIMI- 3 blood flow in patients with mixed acute coronary syndrome. 107
Figure 45. Impact of embolic protection devices combined versus control on TIMI-3 blood flow in patients with ST-segment elevation myocardial infarction. 108
Figure 46. Impact of embolic protection devices combined versus control on TIMI-3 blood flow in patients with mixed acute coronary syndrome. 109
Figure 47. Impact of catheter aspiration devices versus control on distal embolization. 112
Figure 48. Impact of mechanical thrombectomy devices versus control on distal embolization.113
Figure 49. Impact of distal balloon embolic protection devices versus control on distal embolization.....114
Figure 50. Impact of embolic protection devices combined versus control on distal embolization.115
Figure 51. Impact of catheter aspiration devices versus control on no reflow. 118
Figure 52. Impact of mechanical thrombectomy devices versus control on no reflow. 119
Figure 53. Impact of distal filter embolic protection devices versus control on no reflow. 120
Figure 54. Impact of distal balloon embolic protection devices versus control on no reflow. 121
Figure 55. Impact of embolic protection devices combined versus control on no reflow. 122
Figure 56. Impact of catheter aspiration devices on coronary dissection versus control. 134
Figure 57. Impact of mechanical thrombectomy devices on coronary perforation versus control.137
Figure 58. Impact of catheter aspiration devices on side branch occlusion versus control. 142
Figure 59. Impact of distal balloon embolic protection devices on side branch occlusion versus control. 143
Figure 60. Impact of embolic protection devices combined on side branch occlusion versus control. 144

Appendixes

Appendix A: Exact search strategy
Appendix B: Data extraction form
Appendix C: Excluded studies
Appendix D: Characteristics and qaulity assessment of included trials, studies and meta-analyses
Appendix E: Baseline and procedural characteristics of included trials and studies
Appendix F: Additional evidence tables and reference list
Appendix G: Strength of evidence for outcomes
Appendix H: Applicability of individual studies and of the body of evidence
Appendix I: Forest plots for results of final health outcomes analyzed at individual time points
Appendix J: Glossary

Appendixes and Evidence Tables for this report are provided electronically at http://www.ahrq.gov/downloads/pub/evidence/pdf/XXX/XXX.pdf.

Evidence Report

Chapter 1. Introduction

Background

Coronary heart disease (CHD) is a leading cause of morbidity and mortality in the United States. According to the American Heart Association statistics, >650,000 deaths were attributed to CHD in 2003. Moreover, treatment costs for CHD represent the largest healthcare expenditure for a single disease in the United States.[1] Acute coronary syndromes (ACSs), which include the clinical entities of unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), account for more than 1.5 million hospital admissions annually in the United States alone. Approximately 1 million of these admissions are classified as UA/NSTEMI and approximately 500,000 are STEMI.[2]

Percutaneous coronary intervention (PCI) has revolutionized the management of angina and myocardial infarction (MI), frequently negating the need for coronary bypass surgery and permitting a more rapid return to normal activities. The clinical use of PCI is reflected in the number of patients who undergo this procedure. In the United States alone, 664,000 procedures were performed in 652,000 patients in 2003, representing a 326 percent increase from the number of procedures performed in 1987.[1]

Coronary stents and adjunctive pharmacologic agents—including glycoprotein IIb/IIIa receptor inhibitors and thienopyridines—have improved the effect of PCI establishing near normal antegrade blood flow in the vast majority of patients.[1,3-5] However, dislodgement of atherothrombotic material from coronary lesions during PCI can result in distal embolization that leads to what is commonly referred to as the "no-reflow phenomenon." This phenomenon, characterized by inadequate flow at the cardiac tissue level despite patent coronary vessels is often defined as (1) a thrombolysis in myocardial infarction (TIMI) flow grade$\leq$2 (Table 1) despite vessel patency and the absence of dissection, spasm or distal macroembolus, (2) a myocardial blush grade (MBG) of 0 or 1 (Table 2), or (3) a contrast perfusion defect observed upon myocardial contrast echocardiography. Depending on the exact clinical definition used, the incidence of no-reflow has been found to range from 12 to 39 percent,[1,3] and may be associated with advanced age, presence of diabetes mellitus, left ventricular systolic dysfunction, longer ischemic times, poor initial TIMI flow grades, and anterior myocardial infarction.[6]

Table 1. Thrombolysis in Myocardial Infarction (TIMI) Flow Grading System[7]

Grade 0	Complete occlusion of the infarct-related artery
Grade 1	Some penetration of contrast material beyond the point of obstruction but without perfusion of the distal coronary bed
Grade 2	Perfusion of the entire infarct vessel into the distal bed but with delayed flow compared with a normal artery
Grade 3	Full perfusion of the infarct vessel with normal flow

Table 2. Myocardial Blush Grade[8]

Grade 0	Failure of dye to enter the microvasculature. Either minimal or no ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit artery indicating lack of tissue level perfusion.
Grade 1	Dye slowly enters but fails to exit the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that fails to clear from the microvasculature, and dye staining is present on the next injection (approximately 30 seconds between injections).
Grade 2	Delayed entry and exit of dye from the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that is strongly persistent at the end of the washout phase (i.e. dye is strongly persistent after 3 cardiac cycles of the washout phase and either does not or only minimally diminishes in intensity during washout).
Grade 3	Normal entry and exit of dye from the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that clears normally, and is either gone or only mildly/moderately persistent at the end of the washout phase (i.e. dye is gone or is mildly/moderately persistent after 3 cardiac cycles of the washout phase and noticeably diminishes in intensity during the washout phase), similar to that in an uninvolved artery. Blush that is of only mild intensity throughout the washout phase but fades minimally is also classified as grade 3.

A higher rate of adverse outcomes has been noted in patients with no-reflow, including larger infarcts, more significant left ventricular systolic dysfunction, and an increased risk of major adverse cardiovascular events (MACE) or death.

Numerous adjunctive devices have been developed in an attempt to improve clinical outcomes by removing thrombi and to protect against distal embolization during PCI.[9] These devices utilize different technologies and can be broadly classified as catheter aspiration, mechanical thrombectomy, or embolic protection devices (i.e., distal embolic balloon or filter protection devices or proximal embolic balloon protection devices) (Table 3).[10]

Although such devices (mainly embolic protection devices) have previously been demonstrated to reduce MACE in patients undergoing PCI for degenerative saphenous vein grafts,[1,3] their use during ACSs—particularly, STEMI—has been less well supported mainly because of underpowered clinical trials that evaluated intermediate markers.[3] More recently, larger randomized controlled trials (RCTs) of patients with STEMI have evaluated MACE as an end point and followed patients beyond hospital discharge (typically 3 to 12 months) but have given conflicting results.[11-21] Thus, the comparative effectiveness and safety of these devices is unclear and needs to be systematically evaluated.

Table 3. Thrombectomy and embolic protection devices used in the randomized controlled trials included in the quantitative synthesis

Device Type (Mechanism)	Device Name	Manufacturer	FDA Approved Indication(s)
Catheter Aspiration	Diver	Invatec	Not/no longer available for sale in US
	Diver CE	Invatec	Not/no longer available for sale in US
	Export	Medtronic	Removal/aspiration of embolic material (thrombus/debris) from vessels of the arterial system, and to sub-selectively infuse/deliver diagnostic or therapeutic agents with or without vessel occlusion
	Pronto	Vascular solutions	Removal of emboli and thrombi from vessels in the arterial or deep venous system and to infuse diagnostic or therapeutic agents
	Rescue	Boston Scientific	Not/no longer available for sale in US
	Thrombobuster	Kaneka Medix	No FDA approved indication
	TransVascular Aspiration Catheter (TVAC)	Nipro	No FDA approved indication
Mechanical Thrombectomy	AngioJet	MEDRAD Interventional / Possis	Removal of thrombus in the treatment of patients with symptomatic coronary artery or saphenous vein graft lesions in vessels ≥ 2 mm in diameter prior to balloon angioplasty or stent placement
	X-Sizer	ev3	Removal of thrombus in synthetic hemodialysis access grafts
Distal Filter Embolic Protection	FilterWire EX	Boston Scientific	Use as a guidewire and embolic protection system to contain and remove embolic material (thrombus/debris) while performing percutaneous transluminal coronary angioplasty or stenting procedures in coronary saphenous vein bypass grafts with reference vessel diameters of 3.5 to 5.5 mm
	FilterWire EZ	Boston Scientific	Use as a guidewire and embolic protection system to contain and remove embolic material (thrombus/debris) while performing angioplasty and stenting procedures in coronary saphenous vein bypass grafts and carotid arteries
	SpideRX	ev3	No longer available for sale in US
	AngioGuard	Cordis	No longer available for sale in US
	AngioGuard XP	Cordis	Use as a guidewire and embolic protection system to contain and remove embolic material (thrombus/debris) while performing angioplasty and stenting procedures in carotid arteries
Distal Balloon Embolic Protection	PercuSurge GuardWire	Medtronic	Not/no longer available for sale in US

Table 3. Thrombectomy and embolic protection devices used in the randomized controlled trials included in the quantitative synthesis (continued)

Device Type (Mechanism)	Device Name	Manufacturer	FDA Approved Indication(s)
	PercuSurge GuardWire Plus	Medtronic	Use to contain and aspirate embolic material (thrombus/debris) while performing percutaneous transluminal coronary angioplasty or stenting procedures
Proximal Balloon Embolic Protection	Proxis	St. Jude Medical	Use as a proximal embolic protection system to prevent distal release of and to aspirate embolic material (thrombus/debris) in saphenous vein coronary bypass graft(s) during percutaneous transluminal coronary angioplasty and/or stenting procedures and to control the flow of fluids in the coronary and peripheral vasculature

Objective

To perform a comparative effectiveness review examining the benefits and harms associated with using adjunctive devices to remove thrombi or protect against distal embolization in patients with ACS who are undergoing PCI of native vessels.

The Key Questions

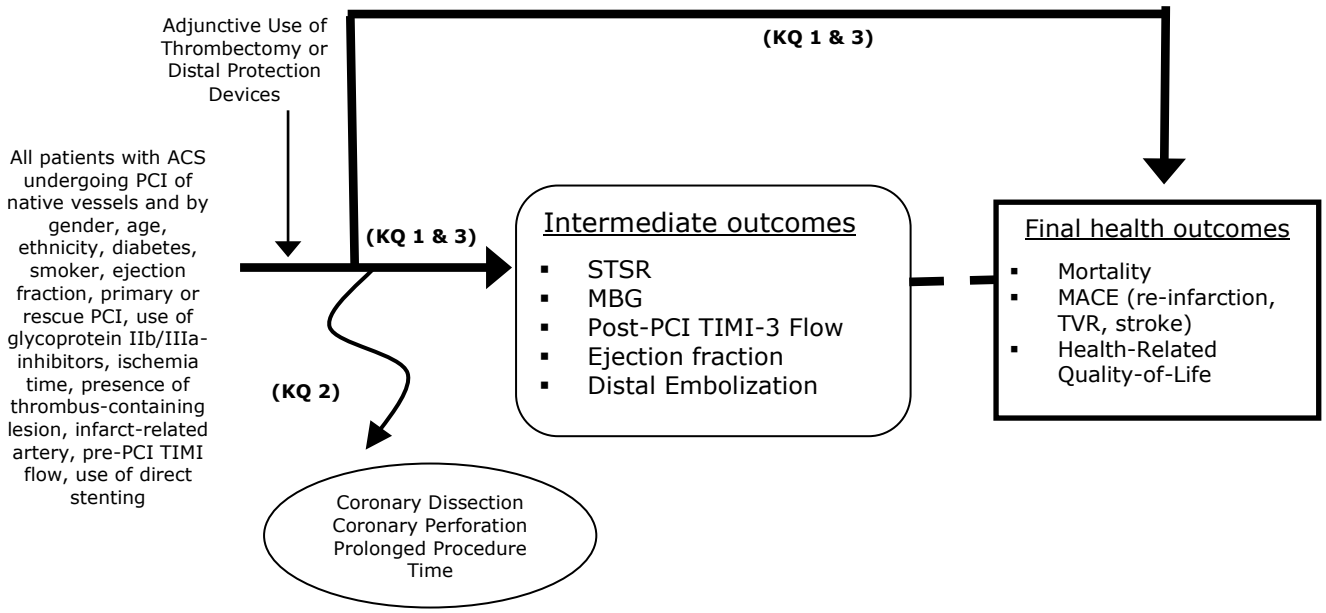
Question 1. In patients with ACS who are undergoing PCI of native vessels, what are the comparative effects of adjunctive devices from different classes (e.g., catheter aspiration, mechanical thrombectomy, distal balloon embolic protection, distal filter embolic protection, proximal balloon embolic protection) on intermediate outcomes (e.g., ST-segment resolution, MBG, TIMI-3 flow, ejection fraction and distal embolization) and final health outcomes (mortality, MACE, health-related quality-of-life)?

Question 2. In patients with ACS who are undergoing PCI of native vessels, how does the rate and type of adverse events (e.g., coronary dissection, coronary perforation, prolonged procedure time) differ between device types when compared to PCI alone?

Question 3. In patients with ACS who are undergoing PCI of native vessels, which patient characteristics (e.g., gender, age, ethnicity, diabetes, smoker, ejection fraction, primary or rescue PCI, use of glycoprotein IIb/IIIa inhibitors, ischemia time, presence of a thrombus-containing lesion, infarct-related artery and pre-PCI TIMI flow, use of direct stenting) affect outcomes?

Analytic Framework

Figure 1. Analytic Framework for Adjunctive Devices to Remove Thrombi and Protect Against Distal Embolization in Patients With ACS Who Are Undergoing PCI of Native Vessels



Chapter 2. Methods

Input from Stakeholders

The EPC drafted a topic refinement document with proposed key questions after consult with Key Informants. Our Key Informants included six physicians: two provided methods expertise, two represented the payor's perspective, one provided the local interventional cardiologist's perspective, and the last provided both an interventional cardiologist and American College of Cardiology perspective. Our Key Informants did not have financial or other declared conflicts. The public was invited to comment on the topic refinement document and key questions. After reviewing the public commentary, responses to public commentary, proposed revisions to the key questions, and a preliminary protocol was generated and reviewed with the Technical Expert Panel. The aforementioned Key Informants constituted our Technical Expert Panel and provided feedback on the feasibility and importance of our approach and provided their unique insight. Again, no conflict of interest was identified. The draft CER report will undergo peer review and public commentary and revisions will be made before being finalized.

Searching for the Evidence: Literature Search Strategies for Identifying Relevant Studies to Answer the Key Questions

The following statement describing the population, intervention, comparator and outcomes (PICO) was used to design the literature search: Does the use of adjunctive devices in ACS patients (i.e. catheter aspiration, mechanical thrombectomy, distal balloon embolic protection, distal filter embolic protection, proximal balloon embolic protection, embolic protection devices combined) in combination with PCI of native vessels affect surrogate outcomes (e.g., ST-segment resolution, MBG, TIMI-3 flow, ejection fraction and distal embolization), health (mortality, MACE, health-related quality-of-life) or safety outcomes (coronary dissection, coronary perforation, prolonged procedure time) as compared to PCI alone? We conducted a computerized literature search of the Cochrane Library and MEDLINE databases for both RCTs and observational studies that were published from January 1996 through March 2010. The search was restricted to 1996 and later to reflect contemporary practice. The complete search strategy is included in Appendix A. We did not apply any language restrictions. Additionally, in an attempt to locate unpublished studies and increase the sensitivity of our search, references from identified studies, systematic reviews, and meta-analyses were reviewed. Abstracts from major cardiology meetings (American Heart Association, American College of Cardiology, European Society of Cardiology, and the Transcatheter Cardiovascular Therapeutics (TCT) Conference of the Cardiovascular Research Foundation) and from the TCTMD (http://www.tctmd.com), the CardioSource Plus (http://www.cardiosource.com), and ClinicalTrials.gov (http://www.clinicaltrials.gov) web sites were searched and reviewed.

Criteria for Inclusion and Exclusion of Studies in the Review

Two independent reviewers assessed studies for inclusion in a parallel manner by using criteria defined a priori. RCTs or controlled observational studies that enrolled a total of ≥500

patients were eligible for inclusion if they (1) compared the use of adjunctive devices (i.e., catheter aspiration, mechanical thrombectomy, distal balloon embolic protection, distal filter embolic protection, proximal balloon embolic protection) to remove thrombi or protect against distal embolization versus a control (active or nonactive) before PCI, (2) included only patients with ACS, (3) enrolled only patients with a target lesion(s) in native vessels (studies with less than five percent of patients with target vessel lesions in saphenous vein grafts were included), and (4) reported data on at least one prespecified patient morbidity (ST-segment resolution, MBG, TIMI-3 blood flow, ejection fraction, distal embolization, MACE), mortality, safety (coronary dissection, coronary perforation, prolonged procedure time), or health-related quality-of-life outcome. Observational studies that enrolled <500 subjects total were excluded from Key Questions 1 and 2 because this range contains small initial experiences not representative of current practice and with numerous RCTs already in existence within this smaller sample size range, small studies were thought to be less helpful in defining the applicability of evidence in a tangible way. Observational studies that enrolled <500 subjects total were used to address Key Question 3 if they reported multivariable adjusted results depicting the effect of prespecified patient characteristics on intermediate or terminal outcomes. Meta-analyses which met the inclusion criteria were manually reviewed for additional references.

Data Extraction and Data Management

Two reviewers used a standardized data extraction tool to independently extract study data. (Appendix B) Data extracted from each study included interventions, study design, inclusion and exclusion criteria, methodological quality criteria, study population, baseline patient characteristics, use of concurrent standard medical therapies, data needed to assess for applicability (as specified in Applicability of Evidence below), and prespecified benefits and harms (as specified in the Key Questions). Previous systematic reviews and meta-analyses addressing the same or similar topic and identified during our literature search are described in Appendix D for completeness.

Assessment of Methodological Quality of Individual Studies

Validity assessment was performed using the recommendations in the Methods Guide for Effectiveness and Comparative Effectiveness Reviews[22].Each study was assessed for the following individual criteria: comparable study groups at baseline, detailed description of study outcomes, blinding of outcome assessors, intent-to-treat analysis, description of participant withdrawals (percent followup), and potential conflict of interest. Additionally, RCTs were assessed for randomization technique. Observational studies were assessed for sample size, participant selection method, exposure measurement method, potential design biases, and appropriate analyses to control for confounding. Studies were then given an overall quality score of good, fair, or poor (Table 4).

Table 4. Summary ratings of quality of individual studies

Quality Rating	Definition
Good (low risk of bias)	These studies have the least bias and results are considered valid. A study that adheres mostly to the commonly held concepts of high quality include the following: a formal randomized, controlled study; clear description of the population, setting, interventions, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytic methods and reporting; no reporting errors; less than 30 percent dropout; and clear reporting of dropouts.
Fair	These studies are susceptible to some bias, but it is not sufficient to invalidate results. They do not meet all the criteria required for a rating of good quality because they have some deficiencies, 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)	These studies have significant flaws that imply biases of various types that may invalidate the results. They have serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Data Synthesis

We qualitatively examined data from all identified studies. For each outcome, we conducted separate analyses of studies that compare each individual adjunctive device type (e.g., catheter aspiration, mechanical thrombectomy, distal filter embolic protection, distal balloon embolic protection, proximal balloon embolic protection) with control and studies in which different adjunctive device types were compared to each other. We conducted separate analyses for studies that enrolled patients experiencing only STEMI, studies that enrolled patients experiencing NSTEMI or UA, and studies that enrolled patients with mixed ACS (STEMI or NSTEMI or UA). We conducted meta-analyses when two or more RCTs that were adequate for data pooling were available for any outcome. Observational studies were not pooled with RCTs and were assessed in a qualitative fashion only. For dichotomous outcomes, weighted averages are reported as relative risks (RR) and risk differences (RD) with associated 95 percent confidence intervals. As pooled RD may provide unstable estimates when control rates are heterogeneous, we report the control rate range to aid in interpretation. For intermediate outcomes depicting the extent of myocardial reperfusion (MBG, TIMI blood flow and ST-segment resolution), we defined attainment of optimal myocardial reperfusion as a MBG-3 or TIMI-3 blood flow (or a MBG or TIMI blood flow of at least two in studies not reporting the other endpoint) and complete ST-segment resolution as 70 percent resolution in peak ST-segments (or at least 50 percent resolution in studies not reporting the other endpoint). When possible we used results for ST-segment resolution reported at 60 minutes, although when unavailable, we utilized data reported immediately after the procedure or up to 90 minutes after. For studies with multiple time points, we used the time closest to 60 minutes.

For final health outcomes, we used the maximum duration of followup, defined as the longest time point from the procedure where the occurrence of a final health outcome is reported, as the base case analysis. As heterogeneity between included studies was expected, a DerSimonian and Laird random-effects model was used when pooling data and calculating RR, RD, and 95 percent confidence intervals.[23] Automatic 'zero cell' correction was used for studies with no events for a particular outcome occurring in one group. Studies with no events occurring in both treatment

and control groups were excluded from meta-analysis. When pooling continuous outcomes, weighted mean differences along with 95 percent confidence intervals were calculated using a DerSimonian and Laird random-effects model.[23]

Statistical heterogeneity was addressed by using the I^2 statistic, which assesses the degree of inconsistency not due to chance across studies and ranges from 0-100 percent with the higher percentage representing a higher likelihood of the existence of heterogeneity. Whereas categorization of I^2 values may not be appropriate in all situations, an I^2 value of >50 percent has been regarded as representative of important statistical heterogeneity. Egger's weighted regression statistic was used to assess for the presence of publication bias.[24] Statistics were performed using StatsDirect statistical software, version 2.7.8 (StatsDirect Ltd., Cheshire, England). For all analyses, a *p*-value of <0.05 was considered statistically significant.

To assess the effect of heterogeneity (both clinical and methodological) on the conclusions of our meta-analysis, we conducted multiple subgroup and sensitivity analyses. These analyses were conducted to assess the methodological study quality (analyses limited to "good" studies only) and duration of followup on the efficacy of adjunctive devices. More specifically for duration of followup, data representing the maximal extent of clinical followup and at different extents of clinical followup (in-hospital, ≥ 30 days but <180 days, ≥ 180 days but < 365 days, and ≥ 365 days), were pooled in separate analyses.

For Key Question 3, patient demographics (age, sex, and ethnicity), baseline patient health status (smoking history, history of diabetes, ejection fraction, ischemia time, pre-PCI TIMI flow, presence of thrombus-containing lesion, and location infarct-related artery), and concomitant treatment characteristics (rescue PCI, administration of glycoprotein IIb/IIIa inhibitors, and direct stenting) were assessed for their impact on the efficacy of adjunctive devices. Data from RCTs, controlled observational studies and individual patient data meta-analyses were utilized. For RCTs or controlled observational studies, data from subgroup analyses were abstracted, and when not reported, p-values for statistical heterogeneity between subgroups were calculated to aid in interpretation. Data from single-arm (all patients receiving an adjunctive device) observational study reports were only included if they conducted multivariate analysis to identify independent predictor of pre-specified outcomes.

Grading the Evidence for Each Key Question

We used the Grading of Recommendations Assessment, Development and Evaluation system to assess the strength of evidence for each outcome of interest separately. This system uses four required domains—risk of bias, consistency, directness, and precision. Additional domains were not assessed because they were deemed irrelevant to this review. All assessments were made by two investigators, with disagreements resolved through discussion. The evidence pertaining to each key question was classified into four broad categories: high, moderate, low grade or insufficient (Table 5). Below we describe in more detail the features that determined the strength of evidence for the different outcomes evaluated in this report.

Table 5. Definitions for grading the strength of evidence

Grade	Definition
High	There is 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 our confidence in the estimate of effect and is likely to change the estimate.
Insufficient	Evidence either is unavailable or does not permit estimation of an effect.

Risk of Bias

Risk of bias is the degree to which the included studies for any given outcome or comparison has a high likelihood of adequate protection against bias. This can be assessed through the evaluation of both design and study limitations. Whether the study was designed as an RCT or an observational study will be recorded. Studies were ranked as having no limitations, serious limitations, or very serious limitations.

Consistency

Consistency refers to the degree of similarity in the direction of the effect sizes from included studies within an evidence base. We assessed whether or not the effect sizes were on the same side of unity; whether the range of effect sizes was narrow, and the degree of statistical heterogeneity in evaluating consistency. We ranked this domain as no inconsistency, serious inconsistency, and very serious inconsistency. When only a single study was included, consistency was not judged.

Directness

Directness refers to whether the evidence links the compared interventions directly with health outcomes, and compares two or more interventions in head-to-head trials. Indirectness implies that more than one body of evidence is required to link interventions to the most important health outcomes. We ranked this domain as no indirectness, serious indirectness, and very serious indirectness.

Precision

Precision refers to the degree of certainty surrounding an effect estimate with respect to a given outcome. For example, when a meta-analysis is performed, we will evaluate the confidence interval around the summary effect size. A precise estimate is an estimate that would allow a clinically useful conclusion. An imprecise estimate is one for which the confidence interval is wide enough to include clinically distinct conclusions (e.g. both clinically important superiority and inferiority), a circumstance that will preclude a conclusion.

Applicability of Evidence

To be designated an effectiveness study, it had to meet five of the following seven criteria: used a primary care population, used less-stringent eligibility criteria, assessed final health outcomes, had an adequate study duration with clinically relevant treatment modalities, assessed adverse events, had an adequate sample size, and used intention-to-treat analysis.[25]

Studies meeting fewer than five criteria were classified as efficacy studies and deemed to have less applicability. Table 6 identifies the factors that are important for determining applicability; those factors that were extracted into evidence tables for every study we evaluated. By using all of the applicable studies to answer a key question, the applicability of the body of evidence was then determined and reported separately and qualitatively for each outcome of interest.

Table 6. Applicability PICOTS and data to extract

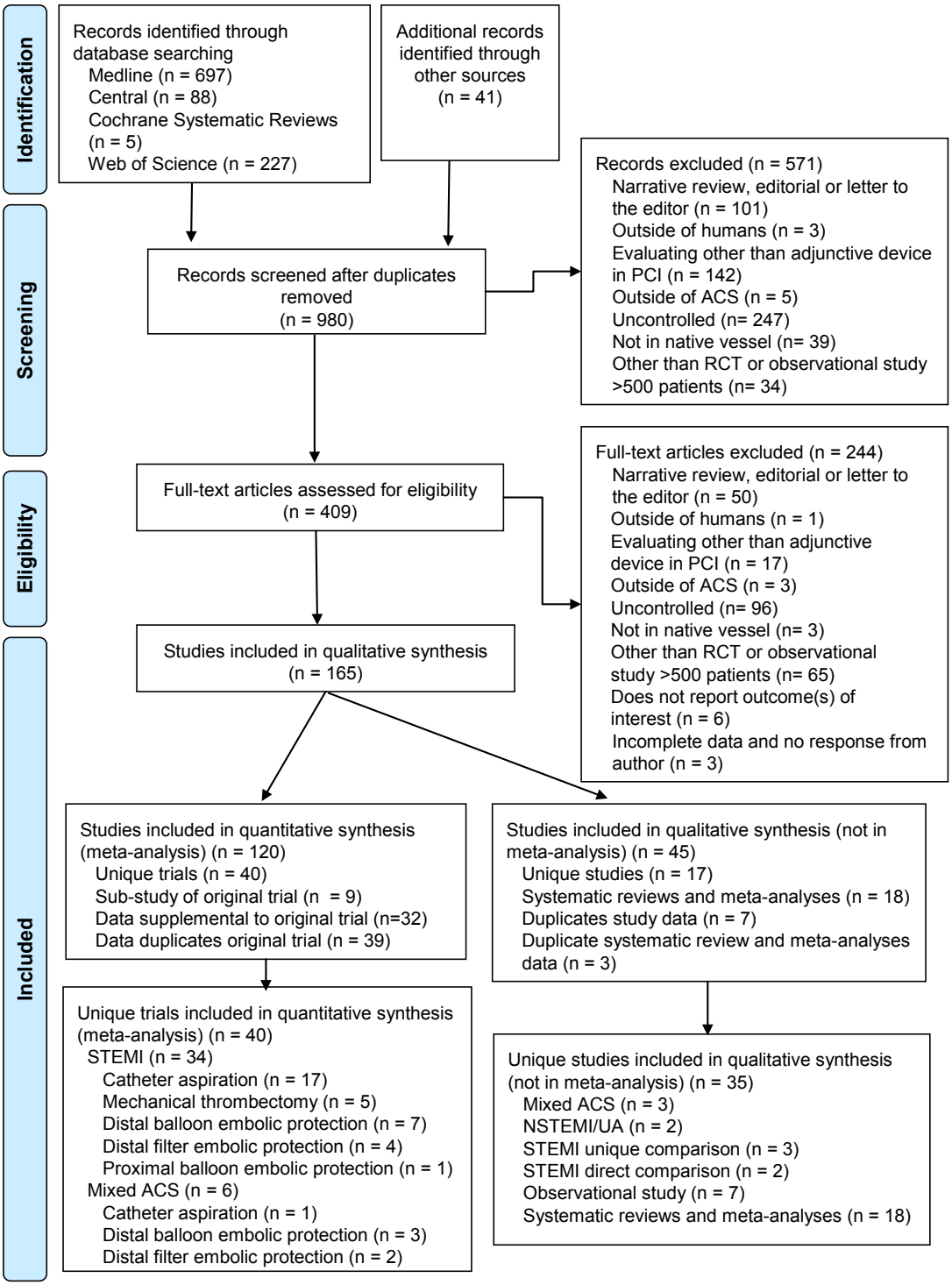
Feature	Condition that limits applicability	Features to be extracted into evidence table
Population	Differences between patients in the study and the community	Eligibility criteria, demographics
Population	Events rates markedly different than in the community	Event rates in treatment and control groups
Intervention	Treatment not reflective of current practice	Type of device, device name
Comparator	Use of substandard alternative therapy	Type of comparator
Outcomes	Intermediate end points, brief followup periods, improper definitions for outcomes, composite end points	Outcomes (benefits and harms) and how they were defined
Settings	Settings where standards of care differ markedly from setting of interest	Clinical setting and geographic setting

Chapter 3. Results

Results of Literature Search

Upon conducting the literature search to identify articles that evaluated the impact of thrombectomy or embolic protection devices on final health or intermediate outcomes, we retrieved 1056 unique citations. Nine hundred and seventy-eight articles remained after duplicates were removed. Five hundred and seventy one articles were excluded during the title and abstract review and 244 were excluded during the full text review (Appendix C). A total of 165 articles were found to match our inclusion criteria. A summary of search results is presented in Figure 2.

Figure 2. PRISMA flow diagram for the search for KQs 1-3



Legend: ACS=acute coronary syndrome; n=number; NSTEMI= non-ST segment elevation myocardial infarction; PCI=percutaneous coronary intervention; PRISMA=preferred reporting items for systematic reviews and meta-analyses; RCT=randomized controlled trial; STEMI=ST segment elevation myocardial infarction; UA=unstable angina

Key Question 1

In patients with ACS who are undergoing PCI of native vessels, what are the comparative effects of adjunctive devices from different classes (e.g., catheter aspiration, mechanical thrombectomy, distal balloon embolic protection, distal filter embolic protection, proximal balloon embolic protection, embolic protection devices combined) on intermediate outcomes (e.g., ST-segment resolution, MBG-3, TIMI-3 blood flow, ejection fraction, distal embolization and no reflow) and terminal outcomes (mortality, myocardial infarction, stroke, target revascularization, MACE, and health-related quality-of-life)?

Key Points

Forty seven RCTs and 5 controlled observational studies were included.

Direct Comparative Trials Assessing Final Health Outcomes in ACS

- Two direct comparative randomized trials and no direct observational studies were available that assessed final health outcomes in ACS.
  - One direct comparative randomized trial compared the use of catheter aspiration devices to distal balloon embolic protection devices in patients undergoing STEMI and evaluated for final health outcomes. In this controlled trial, no significant differences in mortality, myocardial infarction, stroke, target revascularization, or MACE were found at the longest duration of followup.
  - One direct comparative randomized trial compared the use of one catheter aspiration device to another catheter aspiration device in patients with STEMI and evaluated for final health outcomes. In this controlled trial, no significant differences in myocardial infarction, target revascularization, or MACE were found at the longest duration of followup with the other final health outcomes not being evaluated.

Direct Comparative Trials Assessing Intermediate Health Outcomes in ACS

- Three direct comparative randomized trials and no direct observational studies were available that assessed intermediate health outcomes in ACS.
  - Two direct comparative randomized trials compared the use of catheter aspiration devices to distal balloon embolic protection devices in patients undergoing STEMI and evaluated for intermediate health outcomes. In these RCTs, no significant differences were found between groups for ST-segment resolution (one trial), ejection fraction (two trials), MBG-3 (one trial), TIMI-3 blood flow (one trial), or no reflow (one trial) with insufficient data for other intermediate endpoints.
  - One direct comparative randomized trial compared the use of one catheter aspiration device to another catheter aspiration device in patients with STEMI and evaluated for intermediate health outcomes. In this controlled trial, no significant differences in ST segment resolution, MBG-3, or TIMI- 3 blood flow occurred with insufficient data for other intermediate endpoints.

RCTs / Controlled Observational Studies in Patients with STEMI Assessing Final Health Outcomes

- Thirty-four RCTs and three controlled observational studies evaluated patients with STEMI undergoing PCI and compared a thrombectomy or embolic protection device versus control using the maximal duration of followup. Five final health outcomes [mortality, myocardial infarction, stroke, target revascularization and MACE] were evaluated.
    - In RCTs, the use of catheter aspiration devices significantly decreased the risk of MACE but did not significantly impact mortality, myocardial infarction, stroke, or target revascularization versus control using the maximal duration of followup.
        - When the clinical trials eligible for pooling were limited to higher quality trials, the risk for mortality and MACE were significantly reduced when catheter aspiration devices were used versus control but the other endpoints were still nonsignificantly impacted.
        - When the clinical trials eligible for pooling were evaluated at different time periods, mortality and MACE were significantly reduced at 365 days and 180 days, respectively, but no other significant effects were seen for these or other final health outcomes at other time periods.
        - A controlled observational study found a nonsignificantly increased rate of MACE but the other final health outcome results were supportive of findings from RCTs.
    - In RCTs, the use of mechanical thrombectomy devices did not significantly impact mortality, myocardial infarction, stroke, target revascularization or MACE versus control using the longest duration of followup.
        - When the clinical trials eligible for pooling were limiting to higher quality trials, no significant impact on mortality, myocardial infarction, stroke, target revascularization or MACE occurred versus control.
        - When the clinical trials eligible for pooling were evaluated at different time periods, target revascularization and MACE was significantly reduced at 180 days and 365 days (one trial), respectively, but no other significant effects were seen for these or other final health outcomes at other time periods.
        - A controlled observational study was supportive of the myocardial infarction, stroke, target revascularization, and MACE findings.
    - In RCTs, the use of distal filter, distal balloon, proximal balloon, or the use of any one of these embolic protection devices did not significantly impact mortality, myocardial infarction, stroke, target revascularization or MACE versus control.
        - Limiting the trials to higher quality trials did not result in any significant findings for any final health outcome.
        - When clinical trials eligible for pooling were evaluated at different time periods, myocardial infarction was significantly reduced at 180 days (one trial) with the use of distal filter embolic protection devices and stroke was significantly reduced at 30 days (one trial) with the use of a distal balloon embolic protection device versus control, but no other significant effects were seen for these or other final health outcomes at other time periods.

        - In one controlled observational study the use of an embolic protection device did not significantly impact MACE versus control.

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RCTs / Controlled Observational Studies in Patients with STEMI Assessing Intermediate Health Outcomes

- Thirty-four RCTs and two controlled observational studies evaluated patients with STEMI undergoing PCI and compared a thrombectomy or embolic protection device versus control. Six intermediate health outcomes (ST-segment resolution, MBG-3, TIMI-3 blood flow, ejection fraction, distal embolization and no reflow) were evaluated.
    - In RCTs, the use of catheter aspiration devices significantly increased the occurrence of ST-segment resolution, achievement of a MBG-3 and TIMI-3 blood flow while significantly reducing the risk of distal embolization and the occurrence of no reflow versus control. In RCTs, ejection fraction was not impacted by catheter aspiration use versus control.
        - When the clinical trials eligible for pooling were limited to higher quality trials, significant benefits were again seen for the aforementioned intermediate outcomes. No impact on ejection fraction was seen versus control.
        - A controlled observational study was supportive of the findings for distal embolization although the use of a catheter aspiration device did not significantly impact the risk of resolving ST-segment elevation.
    - In RCTs, the use of mechanical thrombectomy devices did not significantly impact ST-segment resolution, MBG-3, TIMI-3 blood flow, distal embolization, or no reflow versus control. In RCTs, ejection fraction was not impacted by mechanical thrombectomy devices versus control.
        - When the clinical trials eligible for pooling were limiting to higher quality trials, no significant impact was seen on any of the aforementioned intermediate health outcomes versus control.
        - In a controlled observational study the use of a mechanical thrombectomy device was associated with a significantly reduced rate of TIMI-3 blood flow versus control.
    - In RCTs, the use of distal filter embolic protection devices did not significantly impact ST-segment resolution, MBG-3, TIMI-3 blood flow, distal embolization, or no reflow versus control. In RCTs, ejection fraction was not impacted by distal filter embolic protection devices versus control.
        - When the clinical trials eligible for pooling were limiting to higher quality trials, no significant impact was seen on any of the aforementioned intermediate health outcomes versus control.
    - In RCTs, the use of distal balloon embolic protection devices significantly increased the occurrence of a MBG-3 but did not significantly impact ST-segment resolution, TIMI-3 blood flow, distal embolization, or no reflow versus control. In RCTs, ejection fraction was not impacted by distal balloon embolic protection devices versus control.
        - When the clinical trials eligible for pooling were limiting to higher quality trials, significant increases in the occurrence of achieving a MBG-3 were

still seen but no significant impact was seen on any of the other aforementioned intermediate health outcomes versus control.

- In RCTs, the use of proximal balloon embolic protection devices did not significantly impact ST-segment resolution, MBG-3, TIMI-3 blood flow, or distal embolization versus control with no data on the other intermediate health outcomes.
    - Only one trial was available for the aforementioned intermediate health outcomes versus control and it was determined to be of good methodological quality.
- In RCTs, the use of embolic protection devices combined significantly increased the occurrence of a MBG-3 but did not significantly impact ST-segment resolution, TIMI-3 blood flow, distal embolization, or no reflow versus control. In RCTs, ejection fraction was not impacted by embolic protection devices.
    - When the clinical trials eligible for pooling were limiting to higher quality trials, significant increases in the occurrence of achieving a MBG-3 were still seen but no significant impact was seen on any of the other aforementioned intermediate health outcomes versus control.

RCTs / Controlled Observational Studies in Mixed or Other ACS populations Assessing Final Health Outcomes

- Five RCTs and two controlled observational studies evaluated patients with mixed ACS (STEMI or NSTEMI or UA) undergoing PCI and compared a thrombectomy or embolic protection device versus control. Five final health outcomes [mortality, myocardial infarction, stroke, target revascularization and MACE] were evaluated.
    - In a RCT, the use of catheter aspiration devices did not significantly impact the risk of in-hospital mortality.
        - In a controlled observational study, the use of a catheter aspiration device significantly reduced the risk of 30-day mortality compared to control.
        - No trials or studies evaluated myocardial infarction, stroke, target revascularization, or MACE at any time period or mortality at additional time periods versus control.
    - In RCTs, the use of mechanical thrombectomy devices did not impact the risk of 30-day mortality (one trial), 30-day target revascularization (one trial), or 30-day MACE (one trial).
        - In an controlled observational study, the use of a mechanical thrombectomy device has no impact on the risk of 180-day mortality, myocardial infarction, target revascularization or MACE.
        - No trials or studies evaluated stroke or other aforementioned final health outcomes at other time points versus control.
    - In RCTs, the use of a distal filter embolic protection device did not impact the risk of 30-day mortality (one trial) or 180-day MACE (one trial) and there was insufficient data to analyze other final health outcomes. No additional trials or studies evaluated final health outcomes at additional time periods.
    - In RCTs, the use of distal balloon embolic protection devices did not impact the risk of mortality using the maximal duration of followup. Neither trial was determined to be of higher methodological quality.

        - Evaluating the clinical trials at different time periods of followup did not result in any significant findings for mortality, although each analysis was based on a single trial.
        - In a single trial, the risk of 180-day MACE was not impacted by the use of a distal balloon embolic protection device versus control.
        - No trials or studies evaluated stroke, target revascularization or aforementioned final health outcomes at individual time points.
    - In RCTs, the use of an embolic protection device (distal or proximal; filter or balloon) did not impact the risk of mortality using the longest duration of followup.
        - Limiting the pooled analysis to trials of higher methodological quality resulted in one trial and therefore pooling was not possible.
        - Evaluating the trials at ≤ 30 days did not significantly impact mortality.
        - No additional data for embolic protection devices combined was available in addition to what was reported in the individual embolic protection device categories.
- Two RCTs and no controlled observational studies evaluated patients with other ACSs (NSTEMI or UA) undergoing PCI and compared a thrombectomy or embolic protection device versus control. Five final health outcomes [mortality, myocardial infarction, stroke, target revascularization and MACE] were evaluated.
    - In RCTs, the use of a distal filter embolic protection device did not impact the risk of 30-day mortality (one trial), in-hospital (one trial) or 30-day MACE (one trial) versus control.
    - No trials or studies evaluated stroke and there was insufficient data to analyze myocardial infarction or target revascularization.
    - No other device categories were evaluated.

RCTs / Controlled Observational Studies in Mixed or Other ACS populations Assessing Intermediate Health Outcomes

- Six RCTs and one controlled observational study evaluated patients with mixed ACS (STEMI or NSTEMI or UA) undergoing PCI and compared a thrombectomy or embolic protection device versus control on intermediate health outcomes. Six intermediate health outcomes (ST-segment resolution, MBG-3, TIMI-3 blood flow, ejection fraction, distal embolization and no reflow) were evaluated.
    - In RCTs, the use of catheter aspiration devices did not significantly impact the risk of attaining TIMI-3 blood flow.
        - In a RCT, the use of a catheter aspiration device significantly increased the risk of attaining a MBG-3.
        - No trials or studies evaluated ST-segment elevation, ejection fraction, distal embolization or no reflow.
    - In RCTs, the use of mechanical thrombectomy devices significantly increased the risk of resolving ST-segment elevation (one trial) and had no impact on attaining TIMI-3 blood flow (one trial) versus control.
        - In an controlled observational study, the use of a mechanical thrombectomy device was associated with a significantly lower rate of TIMI-3 blood flow versus control.

        - No trials or studies evaluated ejection fraction, MBG-3, distal embolization or no reflow.
    - In RCTs, the use of distal filter embolic protection devices did not impact ejection fraction (one trial) or TIMI-3 blood flow (one trial) versus control.
        - No trials or studies evaluated resolution of ST-segment elevation, MBG-3, distal embolization or no reflow.
    - In RCTs, the use of a distal balloon embolic protection device significantly increased the risk of attaining a MBG-3 and did not impact the risk of attaining TIMI-3 blood flow. The trials included were not determined to be of higher methodological quality therefore sensitivity analysis was not possible.
        - In RCTs, the use of a distal balloon embolic protection device led to a significantly increased risk of resolving ST-segment elevation (one trial), significantly higher ejection fraction (one trial) and a significantly reduced risk of no reflow (one trial).
        - No trials or studies evaluated distal embolization.
    - No studies or trials evaluated the use of proximal balloon embolic protection devices in patients with mixed ACS.
    - In RCTs, the use of an embolic protection device did not impact the risk of attaining TIMI-3 blood flow.
        - In RCTs, the use of embolic protection devices increased ejection fraction in one trial and had no impact on ejection fraction in another trial.
        - For the resolution of ST-segment elevation, MBG-3, distal embolization, and no reflow no additional data the results are presented in the respective embolic protection device group and no additional data for embolic protection devices combined was available in addition to what was reported in the individual embolic protection device categories.
- Two RCTs and no controlled observational studies evaluated patients with other ACSs (NSTEMI or UA) undergoing PCI and compared a thrombectomy or embolic protection device versus control. Six intermediate health outcomes (ST-segment resolution, MBG-3, TIMI-3 blood flow, ejection fraction, distal embolization and no reflow) were evaluated.
    - In RCTs, the use of a distal filter embolic protection device did not impact the risk of attaining TIMI-3 blood flow (one trial) versus control.
        - In a RCT, the use of a distal filter embolic protection device did not impact the risk of distal embolization (one trial) versus control.
        - There was insufficient data to evaluate no reflow and no trials or studies evaluated resolution of ST-segment elevation, ejection fraction, MBG-3 or distal embolization.
    - No other device categories were evaluated within this population.

Detailed Analysis

Study Design and Population Characteristics

Overall, 50 RCTs and 7 controlled observational studies have evaluated the impact of thrombectomy or embolic protection devices in ACS. Catheter aspiration, mechanical

thrombectomy, distal filter embolic protection, distal balloon embolic protection and proximal balloon embolic protection devices have been evaluated for at least one endpoint but no studies evaluating proximal filter embolic protection devices met our inclusion and exclusion criteria.

One-hundred and twenty publications of RCTs, which represent 40 unique trials (n=7949) met the inclusion criteria [11-21,26-133] for the quantitative analysis. Of the 120 publications, 43 were full articles[11-18,26,28,39,43,61-63,65,67,68,70,71,73,74,82,83,87-89,94,97,102,106,110,111,113,114,118,122,124,132,133] 48 were abstracts,[20,21,27,29-32,51-59,69,75-78,84-86,90,92,95,98-101,103,104,107,108,115,116,119,121,123,126-131,133] and 29 were slide presentations.[15,19,33-36,38,40-42,44-49,60,66,72,79-81,91,92,96,109,117,120] Of the 40 unique trials, 34 were in patients with STEMI and six were in patients with mixed ACS. The trial characteristics, trail quality assessment, and baseline and procedural characteristics can be found in Appendix D and Appendix E.

Thirty-four unique RCTs evaluated the impact of thrombectomy or embolic protection devices versus control on final, intermediate, or adverse health outcomes when used as an adjunct to PCI as compared to PCI alone in patients with STEMI. Of the 34 trials, 17 trials[12-16,19-21,61,67,68,70,73,82,84-86] (n=3355) evaluated the impact of catheter aspiration devices, five trials[11,26,28,39,43] (n=1374) evaluated the impact of mechanical thrombectomy devices, four trials[88,94,97,100] (n=926) evaluated the impact of distal filter embolic protection devices, seven trials[17,102,106,110,111,118,132] (n=1279) evaluated the impact of distal balloon embolic protection devices and one trial [18] (n=284) evaluated the impact of proximal balloon embolic protection devices.

Amongst the 34 trials, the earliest trial was published in 2003[43] and the latest was published in 2010.[11] The duration of followup of the trials ranged from "in-hospital"[84,85,110,118] to 365 days.[11] One trial reported a followup duration of 240 days, two trials reported a followup duration of 270 days, 12 trials reported a followup duration of 180 days, one trial reported a followup duration of 90 days, 10 trials reported a followup duration of 30 days, and two trials reported a followup duration of 5-8 days. Fourteen trials received funding from industry, of which three reported additional funding from a university or clinical research grant. One trial reported a hospital as the funding source while 19 trials did not report a funding source.

The mean age of patients enrolled in the 34 trials ranged from 55 to 69 years presenting within 6 to 48 hours of symptom onset. Twenty of the 34 trials included patients presenting within 12 hours of symptom onset. Males constituted at least half of the patients in the trials, ranging from 55.1 to 95 percent of the total population. The mean ischemic time reported in the 34 trials ranged from 120 to 510 minutes. The percent of patients presenting with TIMI 0/1 at baseline ranged from 54.8 to 100 percent. Of the 34 trials, 22 trials included patients with no prior fibrinolysis before the index PCI. Five trials included patients with prior fibrinolysis as well as primary PCI and seven trials did not report whether patients who received prior fibrinolysis were included or not.

Six unique trials evaluated the impact of thrombectomy or embolic protection devices versus control on final or intermediate health outcomes when used as an adjunct to PCI as compared to PCI alone in patients with mixed ACS.[124-127,129,130] Of these six trials, two evaluated catheter aspiration devices,[126,127] one evaluated a distal filter embolic protection device,[125] and three evaluated distal balloon embolic protection devices.[124,129,131] The earliest trial was published in 2003[131] and the most recent trial was published in 2008.[124] The duration of followup ranged from in-hopsital[127] to 730 days .[124] Three trials reported followup duration of in-hospital, two

trials reported followup duration of 180 days, and one trial reported followup duration of 730 days. One trial received funding from industry while the other 5 trials did not report a funding source.

The mean age of patients enrolled in the six trials ranged from 55.17 years to 65.9 years. The percentage of males ranged from 76.79 to 95 percent. Two trials reported mean ischemic time which ranged from 372 to 474 minutes. One trial reported the percent of patients with TIMI 0/1 blood flow at baseline which ranged from 57 to 64 percent. Two trials did not include patients who previously failed fibrynoltyic therapy while the other four trials did not report this statistic.

Forty-five publications met inclusion criteria for the qualitative synthesis.[134-178] Of these publications, thirty-five publications represent 17 unique studies (n=13079) [134-157] and twenty-one publications represent eighteen unique meta-analyses (n=80181). [158-178] Of the 17 unique studies, 15 were full articles,[134,135,137,138,142,143,145,147,149-155] eight were abstracts,[136,139-141,146,148,156,157] and one was a slide presentation.[144] Of the 17 unique studies, one study was a RCTs evaluating thrombectomy or embolic protection devices in patients with mixed ACS,[155] seven studies were controlled observational studies,[134-136,138,141-143] two studies were RCTs evaluating thrombectomy or embolic protection devices in patients with UA or NSTEMI,[144,145] two studies were direct comparative RCTs,[147,149] two studies were RCTs with selective inclusion/exclusion criteria in patients with STEMI,[151,152] one study was a RCT with unique comparison in patients with STEMI,[154] and two studies were RCTs with unique comparison in patients with mixed ACS.[153,157] The characteristics of the studies, study quality assessment, and baseline and procedural characteristics can be found in Appendix D and Appendix E.

Amongst the 17 unique studies, the earliest study was published in 2002 and the latest was published in 2009. The duration of followup of the studies ranged from "in-hospital" to 365 days. The mean age group of the patients in the 23 studies ranged from 49.3 to 68 years presenting within 3 hours to 12 hours of symptom onset. Males constituted at least half of the patients in the studies, ranging from 50 to 100 percent of the total population. Two studies used an active control as a comparator. One trial compared the use of the catheter aspiration device Thrombuster along with the use of mutant tissue plasminogen activator versus the use of the catheter aspiration device alone.[154] The other trial compared the use of thrombectomy, distal protection and stenting versus thrombectomy and stenting alone.[157] These two studies are therefore not discussed any further.

Of the 18 unique meta-analyses (n=80181), 11 of the 18 meta-analyses were full text articles[158-160,165-168,178] and seven were abstracts.[169-176] Amongst the 18 systematic review the earliest systematic review was published in 2006 and the latest was published in 2010. The number of studies included in the meta-analyses ranged from seven to 90 studies. The characteristics, quality assessment and results of these meta-analyses can be found in Appendix D. Although several meta-analyses have been conducted recently, the majority are limited to patients with STEMI and do not evaluate adjunctive devices in other ACS, few included the analysis of adverse events which are further limited to procedure time and coronary perforation, and the most recent analyses did not evaluate embolic protection devices. Therefore, an updated analysis will more accurately reflect contemporary practice.

Specifically for key question 1, we present direct comparative data between agents first and subsequently present the comparisons of each type of device versus control for each endpoint.

Numerous endpoints of interest are evaluated at different time points and several trials report the endpoints at multiple time points. We present data for each endpoint at numerous time points as specified: maximum duration of followup (data using the longest reported time point evaluating that endpoint in the trial), ≤30 days (data using the shortest reported time point evaluating the endpoint in the trial up to and including 30 days), 365 days (data from a trial evaluating the endpoint for ≥365 days), 180 days (data from a trial evaluating the endpoint for 180 to 364 days), 30-days (data from a trial evaluating the endpoint for 30 to 179 days), and in-hospital (data from a trial evaluating the endpoint during the initial hospitalization).

Outcome Evaluations

A summary of the results for final heatlh outcomes evaluated at the maximal duration of followup for each device category versus control can be found in Table 7 -Table 12 while the results for evaluations of intermediate outcomes in each device category versus control can be found in Table 13-Table 26.

Mortality

Direct Comparative Trials

Catheter aspiration device versus distal balloon embolic protection device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on mortality.[149] In this trial, there was no difference in the risk of 30-day mortality [RR 1.00 (0.18, 5.54)].

Trials versus Control

Catheter aspiration devices in patients with STEMI

Eleven RCTs evaluated the impact of catheter aspiration devices versus control on mortality using the maximal duration of followup.[14-16,19,61,67,68,70,73,82,84] One trial was excluded from the pooled analysis of relative risk because no events occurred in either group during the prespecified time period.[73] In the 10 trials suitable for pooling, the use of catheter aspiration devices nonsignificantly reduced the risk of mortality [RR 0.69 (0.47, 1.02)] (Figure 3). The weighted-mean followup for mortality using the maximal duration of followup was 7.92 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.64).

When limiting the pooled analysis to only trials of good methodological quality[14-16,61,67,68,70,73,82] the risk of mortality using the maximal duration of followup was significantly decreased in the catheter aspiration device group compared to control [RR 0.67 (0.45, 0.997)]. The weighted mean duration of followup for this analysis was 8.08 months. Statistical heterogeneity (I^2 = 0 percent) was not detected. Using the risk difference for the analysis of trials of higher methodological quality [RD -0.01 (-0.02, 0.01), control rate (0, 0.14)], 100 patients would need to be treated to prevent one death.[14-16,61,67,68,70,73,82]

When the impact of catheter aspiration devices versus control was assessed in hospital [RR 0.81 (0.23, 2.86)], ≤30 days [RR 0.65 (0.39, 1.10)], 30-days [RR 0.61 (0.35, 1.07)], and 180-days [RR 0.89 (0.31, 2.51)] (Appendix Figures 1-4); nonsignificant reductions in the risk of mortality were seen in each analysis. In the 365-day analysis, there was a significant reduction in the risk of mortality with the use of catheter aspiration devices versus control in the two trials with available data [RR 0.62 (0.39, 0.98)] (Appendix Figure 5). Using the risk difference for the analysis [RD -0.03 (-0.06, -0.002), control rate (0.08, 0.14)], 33 patients would need to be treated to prevent one death.

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and 30-day mortality.[141] The names of the catheter aspiration devices included in this study were not reported. There was no difference in the 30-day mortality rate with use of a catheter aspiration device during PCI versus PCI without catheter aspiration (2.6 percent versus 2.4 percent, p = 0.74).

Catheter aspiration devices in other ACS populations

One RCT evaluated the impact of the catheter aspiration device Rescue PT versus control on mortality in patients with acute myocardial infarction.[127] The risk of in-hospital mortality was not significantly different between the catheter aspiration device group and control [RR 1.00 (0.18, 5.60)].

One controlled observational study of patients with acute myocardial infarction evaluated the association between the use of catheter aspiration devices and 30-day mortality.[138] The following catheter aspiration devices were included in this study: RESCUE catheter, Thrombuster catheter, Transvascular aspiration catheter and Export PercuSurge system. In univariate analysis, the use of a catheter aspiration device was associated with a significantly lower rate of 30-day mortality compared to PCI without catheter aspiration [HR 0.64 (0.45, 0.93)] although upon adjustment for baseline characteristics, there was no longer a significant benefit associated with catheter aspiration devices [HR 0.66 (0.36, 1.19)].

Mechanical thrombectomy devices in patients with STEMI

Five RCTs evaluated the impact of mechanical thrombectomy devices versus control on mortality using the maximal duration of followup.[11,26,28,39,43] One trial was excluded from the pooled analysis of relative risk because no deaths occurred within the prespecified time period in either group.[26] In the four trials eligible for pooling, the use of a mechanical thrombectomy device nonsignificantly increased the risk of mortality [RR 1.19 (0.51, 2.76)][11,28,39,43] (Figure 4). The weighted-mean followup for mortality using the maximal duration of followup was 7.80 months. A higher level of statistical heterogeneity was detected (I^2 = 54.9 percent) and publication bias was not be detected (Egger's P = 0.736). All trials were determined to be of good methodological quality.[11,26,28,39,43]

When the impact of mechanical thrombectomy devices versus control was assessed during hospitalization, no difference in mortality [RR 1.00 (0.24, 4.16)] was seen; the risk of mortality was nonsignificantly increased at ≤30 days [RR 1.25 (0.47, 3.32)], 30-days [same results as the ≤ 30 days analysis], and 180-days [RR 1.35 (0.53, 3.44)] (Appendix Figures 6-7); and was

nonsignificantly reduced at 365-days [RR 0.50 (0.21, 1.17)], although the in-hospital and 365-day analyses were each based on a single trial.

One controlled observational study evaluated the association between the use of a mechanical thrombectomy device and mortality.[134] Patients undergoing PCI with a mechanical thrombectomy device, either the AngioJet XMI or XVG catheter, were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a nonsignificantly lower rate of in-hospital mortality compared to PCI without a mechanical thrombectomy device (2.9 percent versus 5.4 percent, p = 0.11). After adjustment for baseline and angiographic characteristics, the use of a mechanical thrombectomy device was associated with a nonsignificantly lower odds of in-hospital mortality [OR 0.58 (0.26, 1.32)] compared to PCI without a mechanical thrombectomy device.

Mechanical thrombectomy devices in other ACS populations

One RCT evaluated the impact of mechanical thrombectomy devices versus control on mortality in patients with STEMI or UA.[155] In this trial, the X-Sizer device was compared to control. The use of a mechanical thrombectomy device nonsignificantly increased the risk of 30-day mortality [RR 2.00 (0.27, 14.89)] compared to control.

One controlled observational study evaluated the association between the use of mechanical thrombectomy devices and mortality.[142] The types of ACSs included in this study were not reported. Patients undergoing PCI with the mechanical thrombectomy device AngioJet were compared to patients undergoing PCI without mechanical thrombectomy and mortality was evaluated at 270 days. The use of a mechanical thrombectomy device was associated with a nonsignificantly lower rate of 180-day mortality compared to PCI without a mechanical thrombectomy device (5.0 percent versus 6.5 percent, p = 0.53).

Distal filter embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal filter embolic protection devices versus control on mortality using the maximal duration of followup.[88,94,97,100] In these trials, the use of distal filter embolic protection devices nonsignificantly increased the risk of mortality [RR 1.17 (0.57, 2.40)] (Figure 5). The weighted-mean followup for mortality using the maximal duration of followup was 1.76 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.388).

Limiting the pooled analysis to only trials of good methodological quality,[88,94,97] the risk of mortality using the maximal duration of followup remained nonsignificantly increased [RR 1.19 (0.57, 2.52)]. The weighted mean duration of followup was 1.81 months. Statistical heterogeneity was not detected (I^2 = 0 percent).

When the impact of distal filter embolic protection devices versus control was assessed at ≤30 days [RR 1.09 (0.52, 2.27)], 30-days [same results as the ≤30 days analysis], and 180-days [RR 1.25 (0.38, 4.16)] (Appendix Figure 8); nonsignificant increases in the risk of mortality were seen in each analysis, although the 180-day analysis was based on a single trial.

No controlled observational trials were conducted that evaluated the impact of distal filter embolic protection devices on mortality.

Distal filter embolic protection devices in other ACS populations

Two RCTs evaluated the impact of distal filter embolic protection devices versus control on mortality in other ACS populations using the maximal duration of followup. However, the trials were not suitable for pooling because one trial was conducted in patients with either STEMI or NSTEMI[125] and the other trial was conducted in patients with either NSTEMI or UA.[145] In the first trial, the impact of a distal filter embolic protection device (FilterWire EX) on 30-day mortality versus control[125] in patients with STEMI or NSTEMI was evaluated. The use of a distal filter embolic protection device nonsignificantly decreased the risk of 30-day mortality [RR 0.67 (0.14, 3.27)] compared to control. This trial was determined to be of good methodological quality. In the second trial, the impact of a distal filter embolic protection device (AngioGuard) on 30-day mortality[145] in patients with NSTEMI or UA was evaluated. The risk of 30-day mortality was not significantly different between the distal filter embolic protection device group and control [RR 1.00 (0.24, 2.45)]. This trial was determined to be of fair methodological quality.

No controlled observational studies of distal filter embolic protection devices assessed this outcome.

Distal balloon embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal balloon embolic protection devices versus control on mortality using the maximal duration of followup.[17,102,111,132] The use of a distal balloon embolic protection device nonsignificantly decreased the risk of mortality using the maximal duration of followup [RR 0.82 (0.45, 1.51)] (Figure 6). The weighted-mean followup for mortality using the maximal duration of followup was 6 months. A lower level of statistical heterogeneity was found (I^2=2.5 percent) and publication bias was detected (Egger's P = 0.023). All trials were determined to be of good methodological quality.[17,102,111,132]

When the impact of distal balloon embolic protection devices versus control was assessed at in-hospital [RR 0.69 (0.24, 2.03)], ≤30 days [RR 0.64 (0.30, 1.39)], 30-days [same results as the ≤30 day analysis], and 180-days [RR 0.86 (0.48, 1.57)] (Appendix Figures 9-10); nonsignificant decreases in the risk of mortality were seen in each analysis, although the in-hospital analysis is based on a single trial.

No controlled observational studies of distal balloon embolic protection devices assessed this outcome.

Distal balloon embolic protection devices in other ACS populations

Two RCTs evaluated the impact of distal balloon embolic protection devices versus control on mortality in patients with acute myocardial infarction using the maximal duration of followup.[124,130] The use of a distal balloon embolic protection device nonsignificnatly reduced the risk of mortality using the maximal duration of followup [RR 0.31 (0.10, 1.77)] (Figure 7). The weighted mean duration of followup was 10.99 months for this analysis. Neither trial was determined to be of good methodological quality.[124,131]

When the impact of distal balloon embolic protection devices versus control was assessed during hospitalization [RR 0.33 (0.00, 2.79)][131] and at 365-days [RR 0.31 (0.05, 1.91)],[124] nonsignficnat decreases were seen, although each analysis was based on a single trial.

One RCT evaluated the impact of distal balloon embolic protection devices versus abciximab therapy on 180-day mortality in patients with acute myocardial infarction.[153] In this trial, the PercuSurge device was used. The risk of 180-day mortality could not be calculated because no events occurred in either group within the prespecified time period.

No controlled observational studies of distal balloon embolic protection devices assessed this outcome.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on mortality.[18] The use of a proximal balloon embolic protection device nonsignificantly increased the risk of 30-day mortality [RR 1.01 (0.18, 5.69)] versus control.

Proximal balloon embolic protection devices in other ACS populations

No studies or trials were available that were evaluating the impact of proximal balloon embolic protection devices versus control on mortality in the population.

Embolic protection devices combined in patients with STEMI

Nine RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on the occurrence of mortality using the maximal duration of followup.[17,18,88,94,97,100,102,111,132] In these trials, the use of embolic protection devices combined nonsignificantly reduced the risk of mortality [RR 0.96 (0.61, 1.49)] (Figure 8). The weighted-mean followup for mortality using the maximal duration of followup was 3.54 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.434).

When limiting the pooled analysis to only trials of good methodological quality,[17,18,88,94,97,102,111,132] the risk of mortality using the maximal duration of followup remained nonsignificantly decreased in the embolic protection devices combined group compared to control [RR 0.96 (0.61, 1.50)]. The weighted mean followup for mortality using the maximal duration of followup was 3.61 months. No statistical heterogeneity was found (I^2 = 0 percent).

When the impact of embolic protection devices combined versus control was assessed at in-hospital mortality [RR 0.69 (0.24, 2.03)], ≤30 days [RR 0.86 (0.52, 1.44)], 30-days [same results as the ≤30 day analysis], and 180-days [RR 0.92 (0.54, 1.58)] (Appendix Figures 11-12); nonsignificant decreases in the risk of mortality was seen in each analysis, although the in-hospital analysis was based on a single trial.

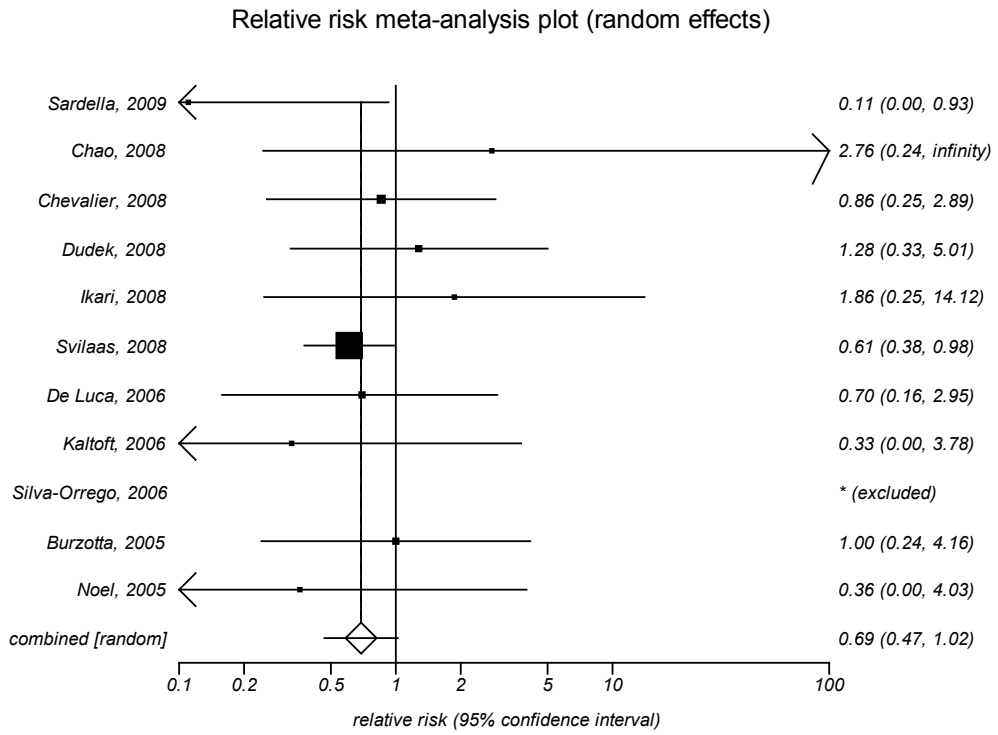
Embolic protection devices combined in other ACS populations

Three RCTs evaluated the impact of embolic protection device (distal or proximal; filter or balloon) versus control in patients with mixed ACS on mortality using the maximal duration of

followup.[124,125,131] The use of an embolic protection device nonsignificantly reduced the risk of mortality [RR 0.59 (0.18, 1.89)] versus control (Figure 9). The weighted mean duration of followup was 8.12 months for this analysis. Statistical heterogeneity was not detected ($I^2 = 0$ percent) but publication bias could not be evaluated. One trial was determined to be of good methodological quality,[133] therefore a pooled analysis limited to trials of higher methodological quality was not possible.

When the impact of embolic protection devices combined versus control was evaluated at ≤30days, a nonsignificant decrease in mortality was found [RR 0.55 (0.12, 2.50)]. (Appendix Figure 13).

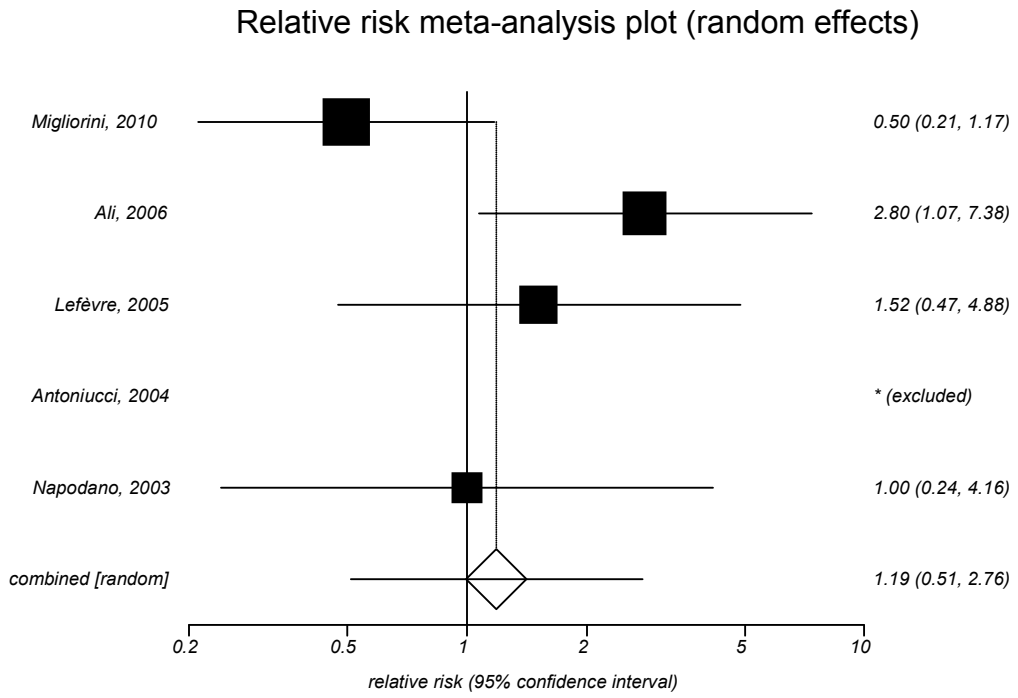
Figure 3. Impact of catheter aspiration devices versus control on mortality using the maximal duration of followup.



Cochran Q: P = 0.870
I²: 0%
Egger: P = 0.638

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

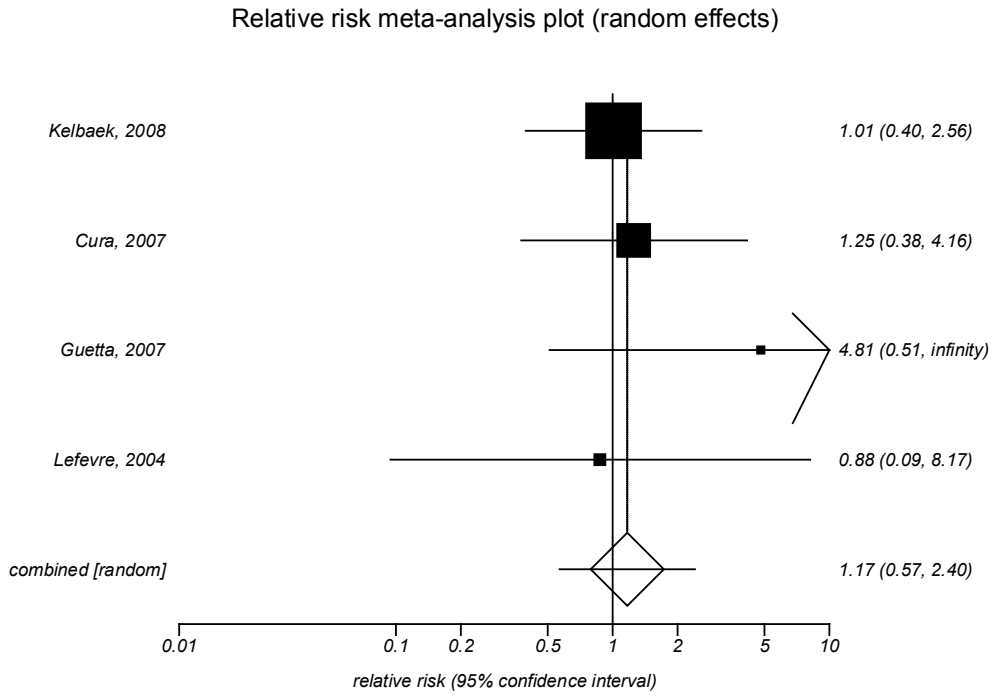
Figure 4. Impact of mechanical thrombectomy devices versus control on mortality using the maximal duration of followup.



Cochran Q: P = 0.084
I^2: 54.9%
Egger: P = 0.736

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

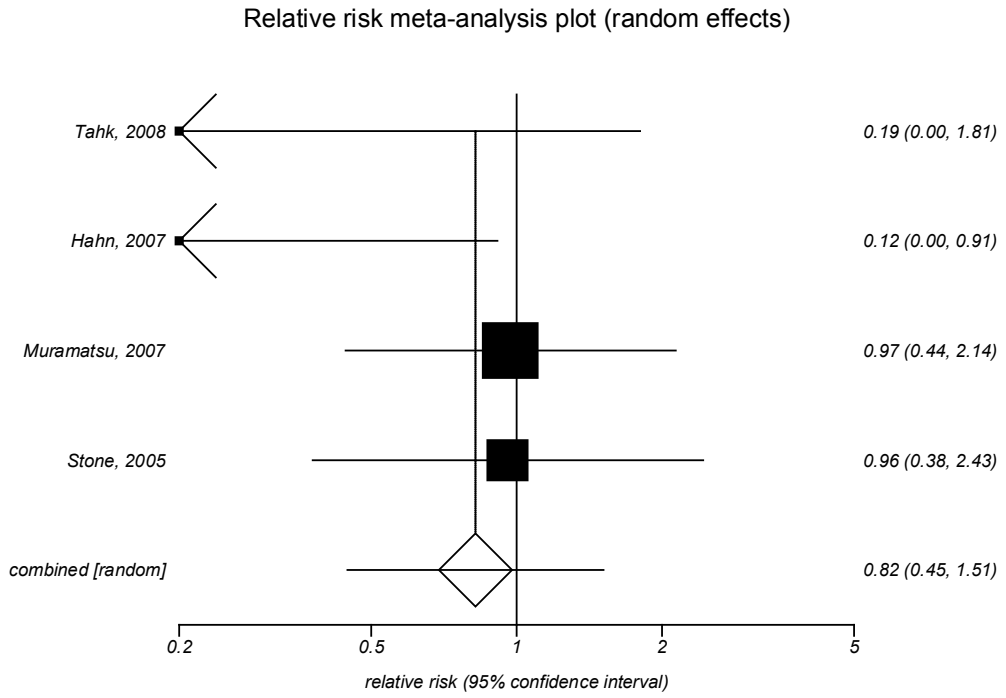
Figure 5. Impact of distal filter embolic protection devices versus control on mortality using the maximal duration of followup.



Cochran Q: P = 0.800
I^2: 0%
Egger: P = 0.388

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

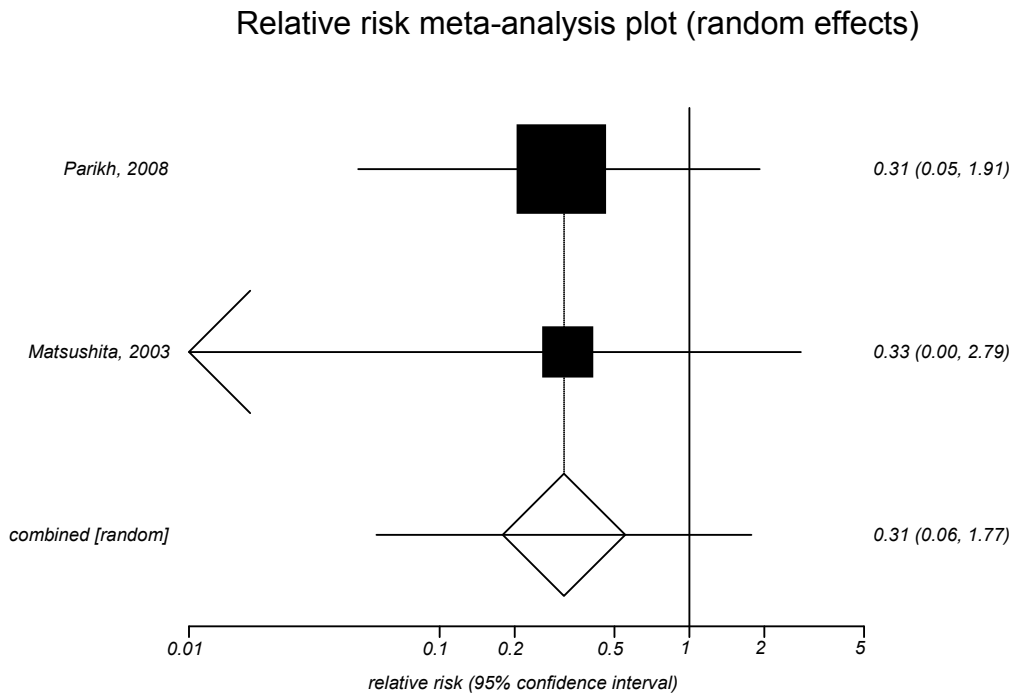
Figure 6. Impact of distal balloon embolic protection devices versus control on mortality using the maximal duration of followup versus control in patients with ST-segment elevation myocardial infarction.



Cochran Q: P = 0.380
I^2: 2.5%
Egger: P = 0.023

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

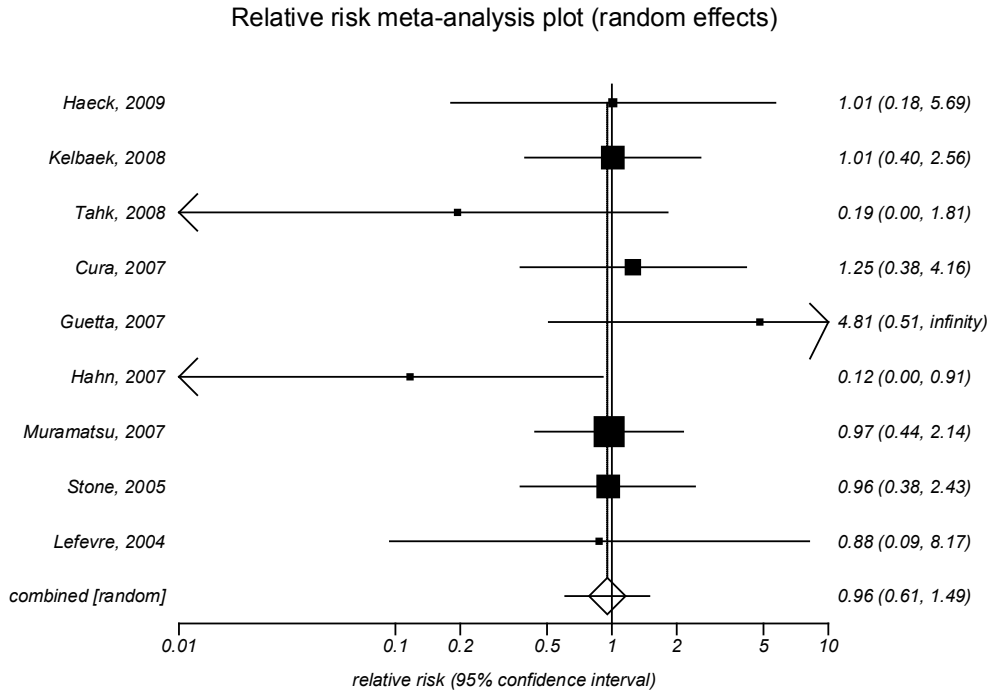
Figure 7. Impact of distal balloon embolic protection devices versus control on mortality using the maximal duration of followup in patients with mixed acute coronary syndromes.



Cochran Q: P = 0.976
I^2: Too few strata
Egger: P = too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

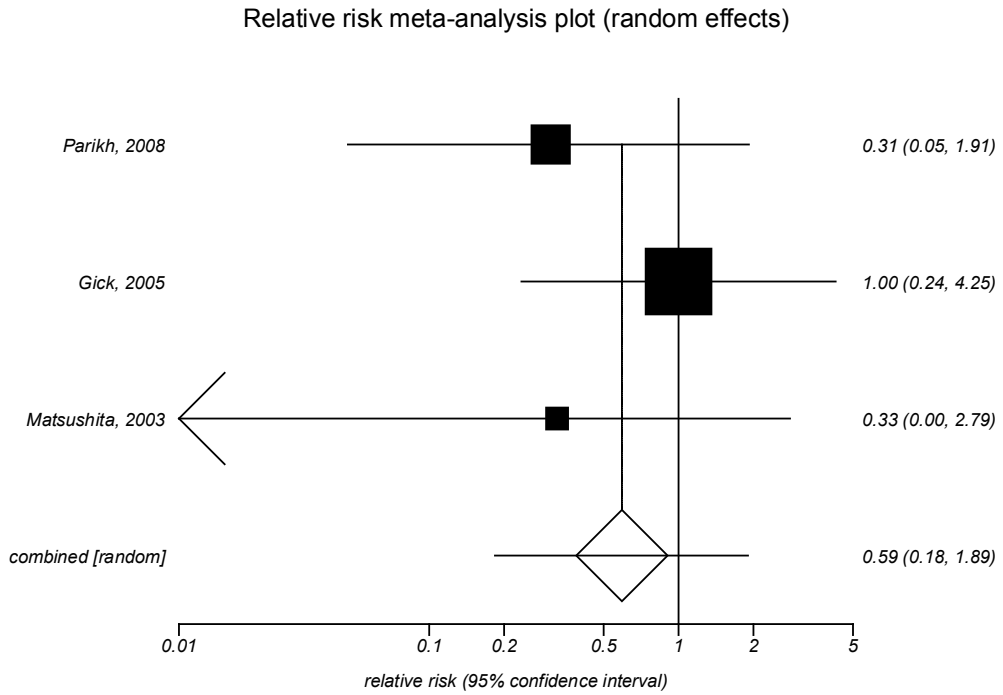
Figure 8. Impact of embolic protection devices combined versus control on mortality using the maximal duration of followup in patients with ST-segment elevation myocardial infarction.



Cochran Q: P = 0.808
I^2: 0%
Egger: P = 0.434

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 9. Impact of embolic protection devices combined versus control on mortality using the maximal duration of followup in patients with other acute coronary syndromes.



Cochran Q: P = 0.619
I^2: 0%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Myocardial Infarction

Direct Comparative Trials

Catheter aspiration device versus distal balloon embolic protection device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on myocardial infarction using the maximum duration of followup which in this case was 365 days.[147] Patients with either Q-wave or non-Q-wave myocardial infarctions were evaluated. In this trial, the use of Diver-Invatec nonsignificantly increased the risk of 365-day Q-wave myocardial infarction [RR 2.88 (0.25 to infinity)] and nonsignificantly decreased the risk of 365-day non-Q-wave myocardial infarction [RR 0.32 (0.00, 3.63)] compared to Export-Medtronic. This trial was determined to be of good methodological quality.

Catheter aspiration device versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on 30-day myocardial infarction.[149] In this trial, the use of Diver CE nonsignificantly increased the risk of 30-day myocardial infarction [RR 3.00 (0.26, infinity)] compared to Guardwire Plus.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Ten RCTs evaluated the impact of catheter aspiration devices versus control on the occurrence of myocardial infarction over the maximal duration of followup.[12,14-16,19,61,68,70,73,82] In these trials, the use of catheter aspiration devices nonsignificantly reduced the risk of myocardial infarction using the maximal duration of followup [RR 0.61 (0.36, 1.04)] (Figure 10). The weighted-mean followup for myocardial infarction in this analysis was 8.80 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.651).

When limiting the pooled analysis to only trials of good methodological quality[12,14-16,61,68,70,73,82] the risk of myocardial infarction using the maximal duration of followup remained nonsignificantly decreased in the catheter aspiration device group compared to control [RR 0.64 (0.37, 1.09)]. The weighted mean duration of followup was 9.02 months. Statistical heterogeneity (I^2 = 0 percent) was not detected.

When the impact of catheter aspiration device use versus control was assessed at in-hospital [RR 0.32 (0.03, 3.06)], <30 days [RR 0.55 (0.24, 1.25)], 30 days [RR 0.60 (0.25, 1.45)], 180 days [RR 0.70 (0.24, 1.99)], and 365 days [RR 0.51 (0.26, 1.00)] (Appendix Figures 14-18); nonsignificant decreases in the risk of myocardial infarction were seen versus control in each analysis.

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and 30-day myocardial infarction.[141] The catheter aspiration devices included in this study were not reported. The use of a catheter aspiration device was associated with a nonsignficantly lower rate of 30-day myocardial infarction compared to control (1.3 percent versus 1.9, p = 0.44).

Catheter aspiration devices in other ACS population

No trials or studies evaluated the impact of catheter aspiration devices versus control in non-STEMI ACS populations.

Mechanical thrombectomy devices in patients with STEMI

Five RCTs evaluated the impact of mechanical thrombectomy devices versus control on myocardial infarction using the maximal duration of followup.[11,26,28,39,43] Two trials were excluded from the pooled analysis of relative risk because no myocardial infarctions occurred within the prespecified time period in either treatment group.[26,39] In the three trials eligible for pooling, the use of a mechanical thrombectomy device nonsignificantly decreased the risk of myocardial infarction [RR 0.71 (0.27, 1.85)][11,28,43] (Figure 11). The weighted-mean followup for

myocardial infarction using the maximal duration of followup was 8.98 months. Statistical heterogeneity was not detected (I^2 = 0 percent) and publication bias could not be evaluated. All of the trials in the pooled analysis were determined to be of good methodological quality.[11,28,43]

When the impact of mechanical thrombectomy device use versus control was assessed at ≤30 days [RR 0.63 (0.21, 1.96)], 30 days [same results as the ≤30 days analysis], 180-days [RR 0.57 (0.17, 1.92)], and 365-days [RR 0.66 (0.13, 3.29)] (Appendix Figures 19-20); nonsignificant decreases in the risk of myocardial infarction were seen in each analysis, although the 365-day analysis was based on a single trial. The use of a mechanical thrombectomy device had no effect on the risk of in-hospital myocardial infarction [RR 1.00 (0.11, 9.41)] versus control based on a single trial.

One controlled observational study evaluated the association between the use of a mechanical thrombectomy device and in-hospital myocardial infarction.[134] Patients undergoing PCI with a mechanical thrombectomy device, either the AngioJet XMI or XVG catheter, were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a nonsignificantly lower rate of in-hospital myocardial infarction compared to PCI without a mechanical thrombectomy device (1.0 percent versus 2.5 percent, p = 0.10).

Mechanical thrombectomy devices in other ACS populations

One controlled observational study evaluated the association between the use of mechanical thrombectomy devices and myocardial infarction.[142] The types of ACSs included in this study were not reported. Patients undergoing PCI with the AngioJet mechanical thrombectomy device were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a nonsignificantly higher rate of 180-day myocardial infarction compared to PCI without a mechanical thrombectomy device (4.0 percent versus 2.1 percent, p = 0.14).

Distal filter embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal filter embolic protection devices versus control on the occurrence of myocardial infarction using the maximal duration of followup versus control.[88,94,97,100] In these trials, the use of distal filter embolic protection devices nonsignificantly reduced the risk of myocardial infarction using the maximal duration of followup [RR 0.73 (0.12, 4.44)] (Figure 12). The weighted-mean followup for myocardial infarction using the maximal duration of followup was 1.76 months. A lower level of statistical heterogeneity was detected (I^2 = 44.3 percent) but publication bias was not detected (Egger's P = 0.128).

Limiting the pooled analysis to only trials of good methodological quality[88,94,97] the risk of myocardial infarction using the maximal duration of followup remained nonsignificantly reduced [RR 0.62 (0.05, 8.12)]. The weighted mean duration of followup was 1.81 months. A higher level of statistical heterogeneity was detected (I^2 = 62.9 percent).

For three of the four trials used in the maximum duration of followup analysis, the results at ≤30 days were all 30 day analyses and represented the maximum duration of followup in those trials.[88,97,100] The other trial reported both 30 days and 180 days results but the number of events

at both time periods in the two groups were the same.[94] As such, the impact of distal filter embolic protection devices on myocardial infarction at ≤30 days and 30 days versus control were the same as the maximum duration of followup results [RR 0.63 (0.21, 1.96)]. In the single trial evaluating results at 180 days, a significant reduction in the risk of myocardial infarction occurred in the distal filter embolic protection device group versus the control group [RR 0.09 (0.00, 0.74)].[94]

There were no available controlled observational studies evaluating this endpoint.

Distal filter embolic protection devices in other ACS populations

Two RCTs evaluated the impact of distal filter embolic protection devices versus control in patients with other ACSs on myocardial infarction using the maximal duration of followup.[125,145] These trials were not suitable for pooling because one trial evaluated patients with either STEMI or NSTEMI[125] and the other trial evaluated patients with UA.[145] Additionally, the risk of myocardial infarction could not be calculated in either case because no events occurred in either trial during the specified time period.

There were no available controlled observational studies evaluating this endpoint.

Distal balloon embolic protection devices in patients with STEMI

Five RCTs evaluated the impact of distal balloon embolic protection devices versus control on myocardial infarction using the maximal duration of followup.[17,102,106,111,132] The use of a distal balloon embolic protection device nonsignificantly decreased the risk of myocardial infarction [RR 0.67 (0.29, 1.57)] (Figure 13). The weighted-mean followup for myocardial infarction using the maximal duration of followup was 6 months. Statistical heterogeneity and publication bias were not detected ($I^2 = 0$ percent, Egger's P = 0.820). All trials were determined to be of good methodological quality.[17,102,106,111,132]

When the impact of distal balloon protection device use versus control was assessed at in-hospital [RR 0.32 (0.00, 3.71)], ≤30 days [RR 0.85 (0.32, 2.23)], 30 days [same results as the ≤30 days analysis], and 180 days [same results as maximal duration of followup analysis] (Appendix Figure 21-22); nonsignificant decreases in the risk of myocardial infarction were seen in each analysis, although the in-hospital analysis is based on a single trial.

There were no available controlled observational studies that evaluated this endpoint.

Distal balloon embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal balloon embolic protection device PercuSurge versus abciximab therapy on myocardial infarction in patients with acute myocardial infarction.[153] The use of a distal balloon embolic protection device nonsignificantly increased the risk of 180-day myocardial infarction [RR 1.66 (0.34, 8.10)] compared to abciximab therapy.

There were no controlled observational studies that evaluated this endpoint.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on myocardial infarction.[18] The use of a proximal balloon embolic protection device nonsignificantly reduced the risk of having a myocardial infarction over the next 30 days [RR 0.68 (0.14, 3.34)].

Proximal balloon embolic protection devices in other ACS populations

No trials or studies were available that evaluated the impact of proximal balloon embolic protection devices versus control on myocardial infarction in this population.

Embolic protection devices combined in patients with STEMI

Ten RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on the occurrence of myocardial infarction using the maximal duration of followup.[17,18,88,94,97,100,102,106,111,132] In these trials, the use of embolic protection devices combined nonsignificantly reduced the risk of myocardial infarction [RR 0.72 (0.37, 1.40)] (Figure 14). The weighted-mean followup for myocardial infarction using the maximal duration of followup was 3.70 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.865).

When limiting the pooled analysis to only trials of good methodological quality,[17,18,88,94,97,102,106,111,132] the risk of myocardial infarction using the maximal duration of followup remained nonsignificantly decreased in the embolic protection devices combined group compared to control [RR 0.71 (0.36, 1.41)]. The weighted-mean followup for myocardial infarction using the maximal duration of followup was 3.77 months. No statistical heterogeneity was found (I^2 = 0 percent).

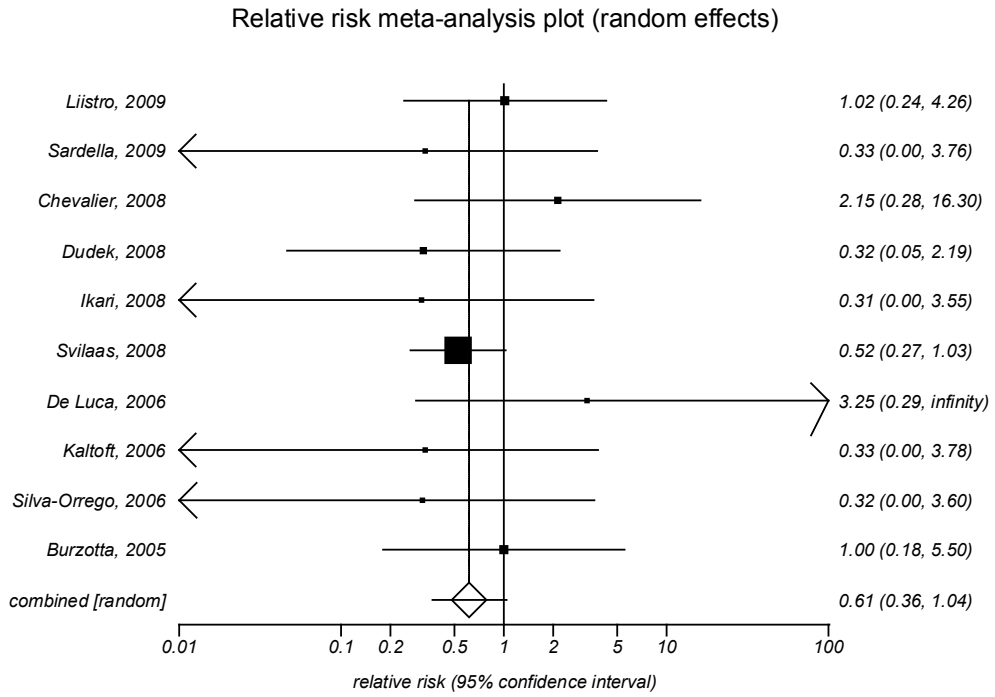
When the impact of embolic protection devices combined versus control was assessed at in-hospital [RR 0.32 (0.00, 3.71)], ≤30 days [RR 0.83 (0.41, 1.69)], 30-days [same results as the ≤30 days analysis], and 180-days [RR 0.57 (0.25, 1.29)] (Appendix Figures 23-24); nonsignificant decreases in the risk of myocardial infarction were seen in each analysis, although the in-hospital analysis is based on a single trial.

There were no available controlled observational studies that evaluated this endpoint.

Embolic protection devices combined in other ACS populations

No trials or studies were available that evaluated the impact of any embolic protection device versus control on myocardial infarction in addition to the three trials reported above. Pooling was not suitable because each trial evaluated a different ACS.

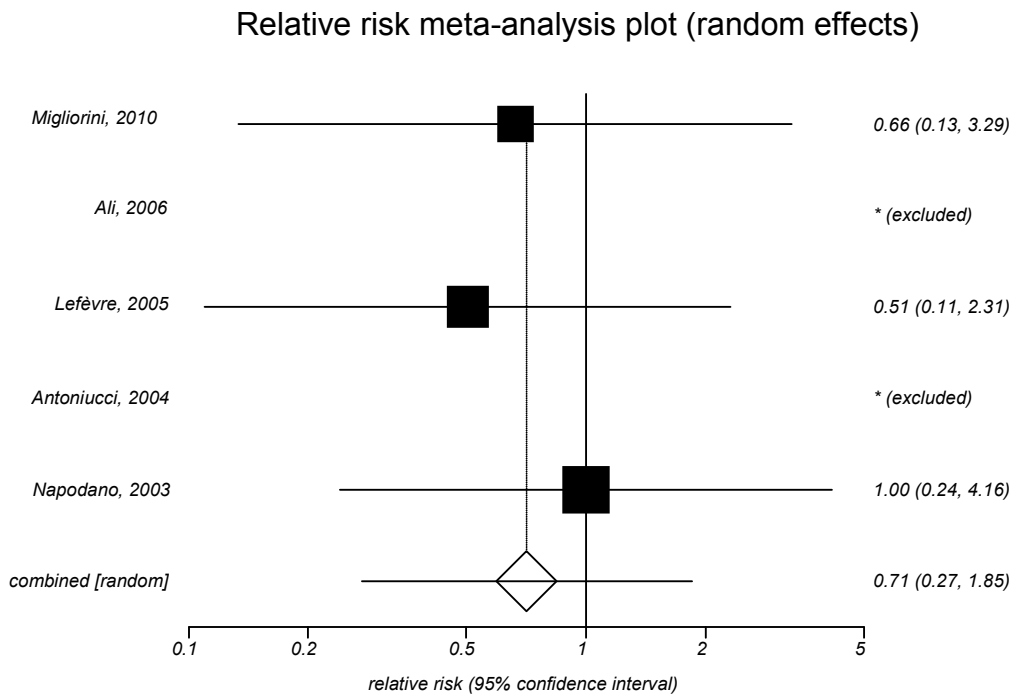
Figure 10. Impact of catheter aspiration devices versus control on myocardial infarction using the maximal duration of followup.



Cochran Q: P = 0.915
I^2: 0%
Egger: P = 0.651

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

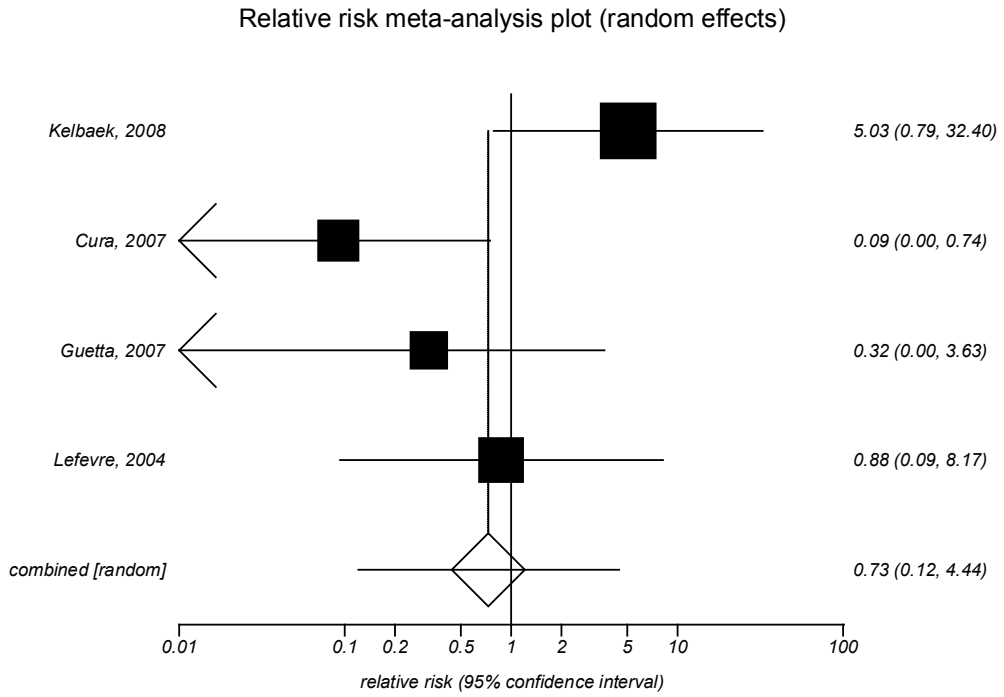
Figure 11. Impact of mechanical thrombectomy devices versus control on myocardial infarction using the maximal duration of followup.



Cochran Q: P = 0.838
I^2: 0%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

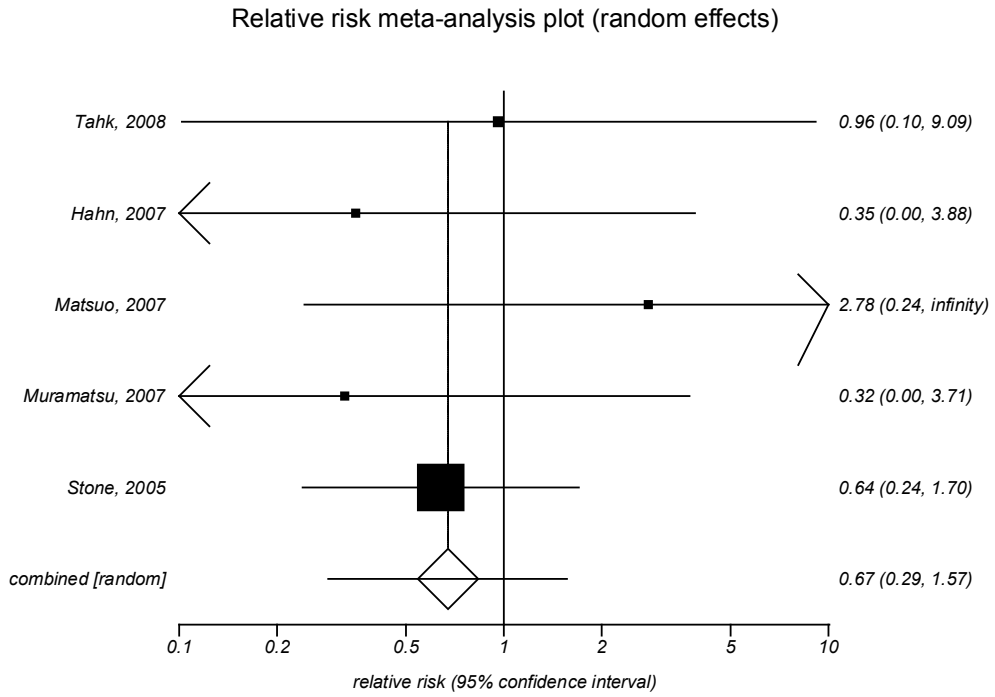
Figure 12. Impact of distal filter embolic protection devices versus control on myocardial infarction using the maximal duration of followup.



Cochran Q: P = 0.146
I^2: 44.3%
Egger: P = 0.128

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

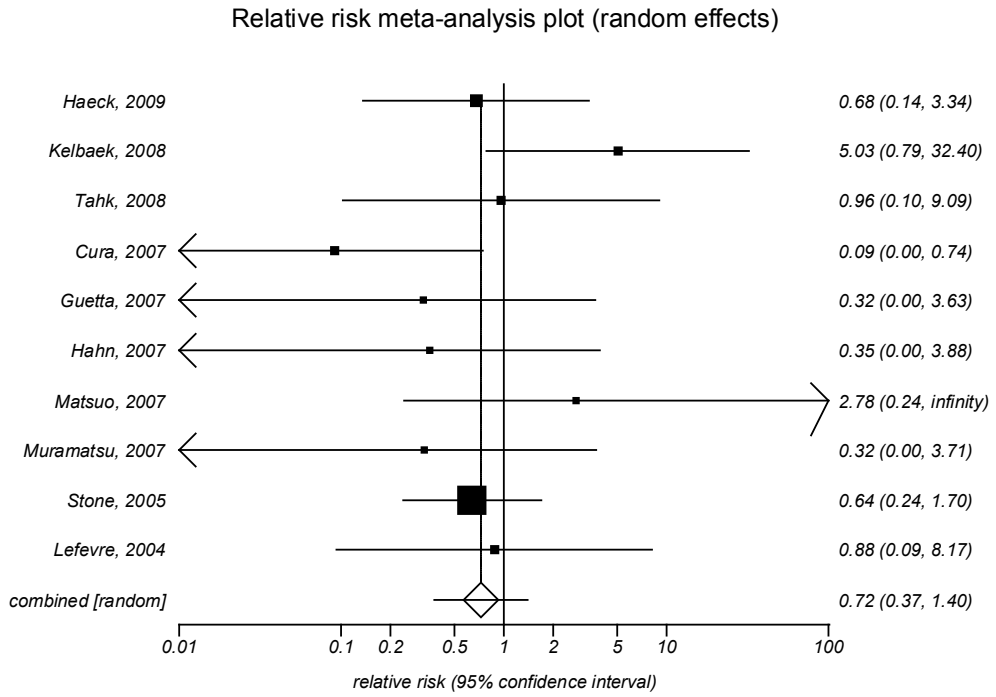
Figure 13. Impact of distal balloon embolic protection devices versus control on myocardial infarction using the maximal duration of followup.



Cochran Q: P = 0.877
I^2: 0%
Egger: P = 0.820

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 14. Impact of embolic protection devices combined versus control on myocardial infarction using the maximal duration of followup.



Cochran Q: P = 0.672
I^2: 0%
Egger: P = 0.865

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Stroke

Direct Comparative Trials

Catheter aspiration devices versus distal balloon embolic protection devices in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on stroke.[149] The risk of 30-day stroke could not be calculated because no events occurred in either group during the specified time period.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Five RCTs evaluated the impact of catheter aspiration devices versus control on stroke using the maximal duration of followup.[14,15,70,73,82] One trial was excluded from the pooled analysis because no events occurred in either group during the prespecified time period.[73] In the four

trials eligible for pooling, the use of catheter aspiration devices nonsignificantly increased the risk of stroke [RR 3.18 (0.73, 13.88)] (Figure 15). The weighted-mean followup for stroke using the maximal duration of followup was 0.79 months. There was no statistical heterogeneity ($I^2 = 0$ percent) but publication bias was detected (Egger's P = 0.001). All of the trials included in the pooled analysis were determined to be of good methodological quality.[14,15,70,73,82]

The four trials which evaluated stroke using the maximal duration of followup are the same trials and data included in the analysis of ≤ 30 day stroke above[14,15,70,82] because the maximal duration of followup for stroke in the four trials was ≤ 30 days. The use of a catheter aspiration device nonsignificantly increased the risk of in-hospital stroke [RR 4.94 (0.52, infinity)] versus control in a single trial and 30 days stroke occurrence in three others [RR 2.77 (0.51, 14.98)] (Appendix Figure 25). One trial evaluated the impact of catheter aspiration devices on 180-day stroke.[73] In this trial, the use of the Pronto extraction catheter was compared to control. No stroke events occurred in either treatment arm, therefore a relative risk and risk difference could not be evaluated.

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and 30-day stroke.[141] The catheter aspiration devices included in this study were not reported. The use of a catheter aspiration device was associated with a significantly higher rate of 30-day stroke compared to control (1.3 percent versus 0.4 percent, p = 0.03).

Catheter aspiration devices in other ACS populations

There were no trials or studies that evaluated catheter aspiration devices in other ACS populations.

Mechanical thrombectomy in patients with STEMI

Five RCTs evaluated the impact of mechanical thrombectomy devices versus control on stroke using the maximal duration of followup.[11,26,28,39,43] One trial was excluded from the pooled analysis of relative risk because no strokes occurred within the prespecified time period in either treatment group.[43] In the four trials eligible for pooling, the use of a mechanical thrombectomy device nonsignificantly increased the risk of stroke [RR 2.42 (0.75, 7.78)][11,26,28,39] (Figure 16). The weighted-mean followup for this analysis was 5.79 months. Statistical heterogeneity and publication bias were not detected ($I^2 = 0$ percent, P= 0.227). All of the pooled trials were determined to be of good methodological quality.[11,26,28,39]

When the impact of mechanical thrombectomy versus control was assessed at ≤30 days [RR 1.89 (0.55, 6.48)], 30-days [same results as the ≤30 days analysis], 180-days [RR 2.05 (0.27, 15.78)], and 365-days [RR 1.99 (0.26, 15.14)] (Appendix Figures 26-27); nonsignificant increases in the risk of stroke were seen in each analysis, although the 365-day analysis is based on a single trial.

One controlled observational study evaluated the association between the use of a mechanical thrombectomy device and in-hospital stroke.[134] Patients undergoing PCI with a mechanical thrombectomy device, either the AngioJet XMI or XVG catheter, were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy

device was associated with a nonsignificantly higher rate of in-hospital stroke compared to PCI without a mechanical thrombectomy device (0.5 percent versus 0.4 percent, p = 1.00).

Mechanical thrombectomy devices in other ACS populations

No trials or studies assessed the use of mechanical thrombectomy devices in other ACS populations.

Distal filter embolic protection devices in patients with STEMI

One RCT evaluated the impact of a distal filter embolic protection device versus control on the occurrence of stroke using the maximal duration of followup.[88] In this trial, the use of a distal filter embolic protection device nonsignificantly increased the risk of long-term occurrence of stroke [RR 1.51 (95 percent CI = 0.30 to 7.52)]. The duration of followup for stroke was 1 month. The trial was determined to be of good methodological quality.[88]

Distal filter embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal filter embolic protection device FilterWire versus control on stroke[125] in patients with NSTEMI or STEMI. The risk of 30-day stroke could not be calculated because no events occurred in either group during the specified time period.

No controlled observational studies assessed for this endpoint.

Distal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of distal balloon embolic protection devices versus control on stroke using the maximal duration of followup.[111] In this trial, the use of the GuardWire Plus was compared to control therapy. The use of a distal balloon embolic protection device nonsignificantly decreased the risk of stroke at 180 days [RR 0.48 (0.10, 2.22)].[111] The impact of distal balloon embolic protection devices on stroke was also evaluated in this trial at 30 days.[111] The use of a distal balloon embolic protection device significantly decreased the risk of ≤30-day stroke [RR 0.11 (0.00, 0.94)] and 30-day stroke [same results as the ≤30 day analysis] versus control. This trial was determined to be of good methodological quality.

No controlled observational studies assessed for this endpoint.

Distal balloon embolic protection devices in other ACS populations

No trials or studies were available that evaluated the impact of distal balloon embolic protection devices versus control on stroke in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on stroke.[18] The use of a proximal balloon embolic protection device nonsignificantly reduced the risk of having a stroke over the next 30-days [RR 0.34 (0.01, 3.81)].

Proximal balloon embolic protection devices inother ACS populations

No trials or studies were available that evaluated the impact of proximal balloon embolic protection devices versus control on stroke in this population.

Embolic protection devices combined in patients with STEMI

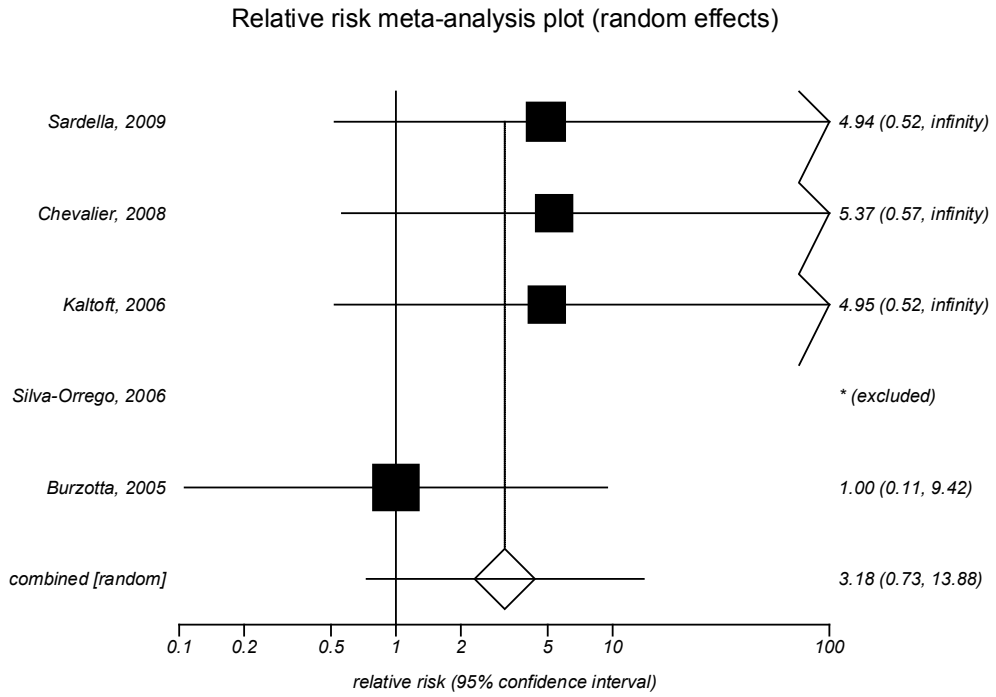
Three RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on the occurrence of stroke using the maximal duration of followup.[18,88,111] In these trials, the use of embolic protection devices combined nonsignificantly reduced the risk of stroke [RR 0.74 (0.23, 2.31)] (Figure 17). The weighted mean followup for stroke using the maximal duration of followup was 2.72 months. Statistical heterogeneity was not detected ($I^2 = 0$ percent) and publication bias could not be calculated due to the number of studies available. All of the trials were determined to be of good methodological quality.[18,88,111]

When the impact of embolic protection devices combined was assessed at ≤30 days [RR 0.56 (0.11, 2.84)] and 180-days [RR 0.48 (0.10, 2.22)] (Appendix Figure 28); nonsignificant decreases in the risk of stroke were seen versus control, although the 180-day analysis is based on a single trial.

Embolic protection devices combined in other ACS populations

No trials or studies were available that evaluated the impact of any embolic protection device versus control on stroke in this population in addition to the one trial reported above, and therefore pooling was not possible.

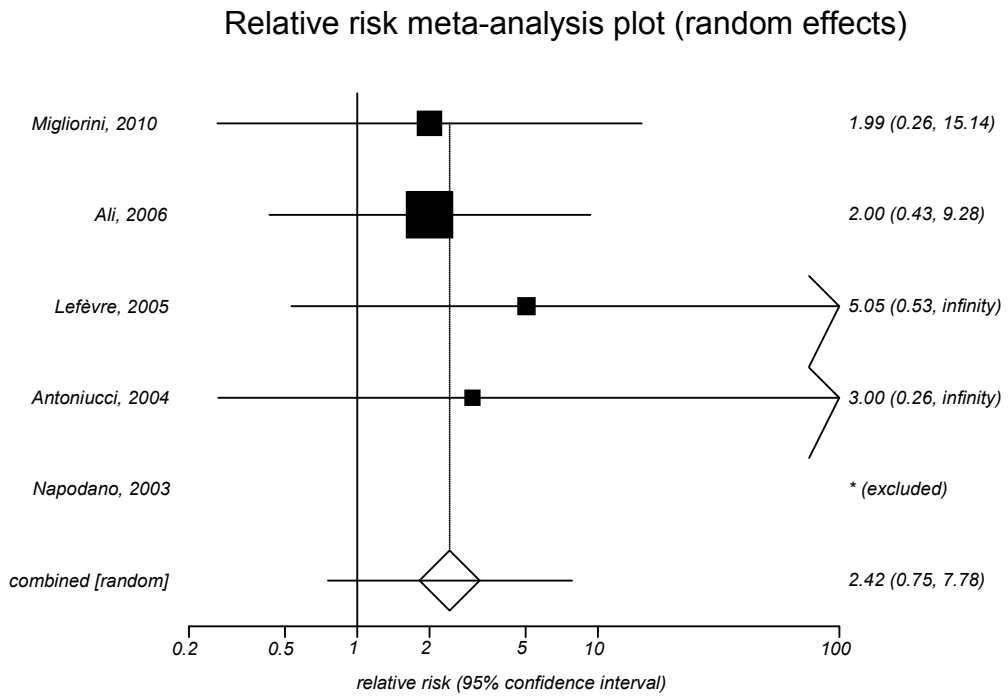
Figure 15. Impact of catheter aspiration devices versus control on stroke using the maximal duration of followup.



Cochran Q: P = 0.807
I^2: 0%
Egger: P = 0.001

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

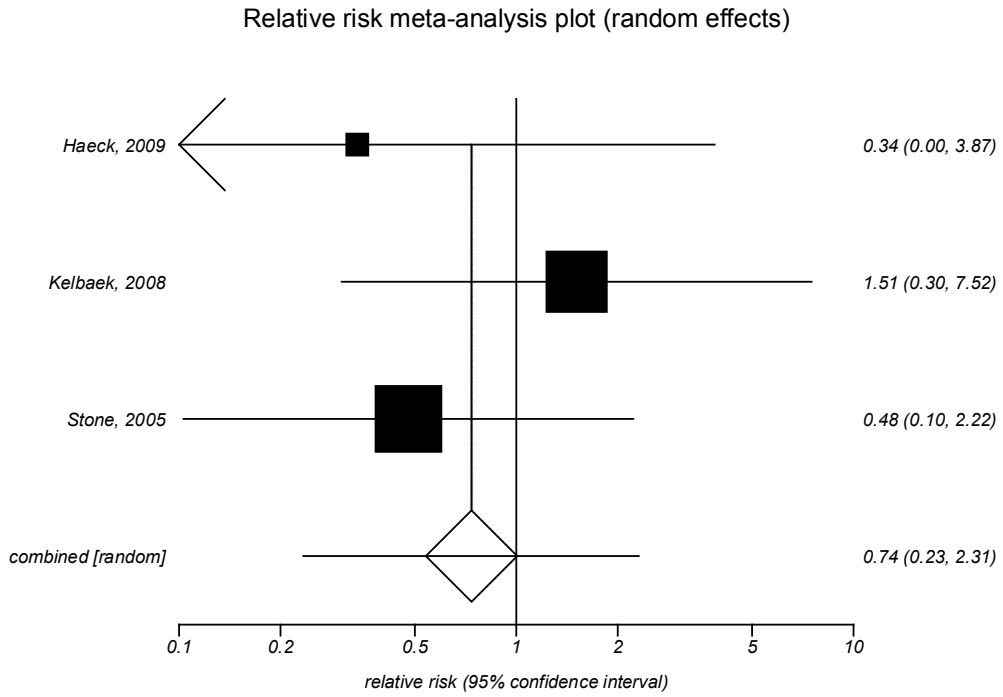
Figure 16. Impact of mechanical thrombectomy devices versus control on occurrence of stroke using the maximal duration of followup.



Cochran Q: P = 0.956
I^2: 0%
Egger: P = 0.227

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 17. Impact of embolic protection devices combined versus control on stroke using the maximal duration of followup.



Cochran Q: P = 0.577
I^2: 0%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Target Revascularization

Direct Comparative Trials

Catheter aspiration device versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on 365-day target revascularization.[147] In this trial, the use of Diver-Invatec nonsignificantly increased the risk of 365-day target revascularization [RR 1.44 (0.30, 7.00)] compared to Export-Medtronic. In this trial, no events occurred in either group at 30-days.

Catheter aspiration device versus distal balloon embolic protection device in patients with STEMI

One direct comparative trial evaluated the impact of the catheter aspiration device Diver CE versus the distal balloon embolic protection device Guardwire Plus on 30-day target revascularization.[149] In this trial, there was no difference in the risk of 30-day target revascularization [RR 1.00 (0.11, 9.45)].

Trials versus Control

Catheter aspiration devices in patients with STEMI

Nine RCTs evaluated the impact of catheter aspiration devices versus control on target revascularization using the maximal duration of followup.[12,14-16,19,61,67,73,82] In these trials, the use of catheter aspiration devices nonsignificantly reduced the risk of target revascularization [RR 0.81 (0.62, 1.04)] (Figure 18). The weighted-mean followup for target revascularization using the maximal duration of followup was 9.01 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.534).

When limiting the pooled analysis to only trials of good methodological quality[12,14-16,61,67,73,82] the risk of target revascularization using the maximal duration of followup remained nonsignificantly reduced in the catheter aspiration device group compared to control [RR 0.80 (0.62, 1.03)]. The weighted mean duration of followup was 9.78 months. Statistical heterogeneity was not detected (I^2 = 0 percent).

When the impact of catheter aspiration devices versus control was assessed at 180 days [RR 0.62 (0.40, 0.96)] (Appendix Figure 29) a significant reduction in the risk of target revascularization versus control was seen. Using the risk difference for the analysis [RD –0.04 (-0.07, -0.01), control rate (0.03, 0.20)] 25 patients would need to be treated to prevent one target revascularization. However, at ≤30 days [RR 0.85 (0.53, 1.38)], 30 days [RR 0.82 (0.50, 1.35)] and 365 days [RR 0.87 (0.63, 1.19)] (Appendix Figures 30-32); nonsignificant decreases in the risk of target revascularization were seen versus control in each analysis. The in-hospital risk for target revascularization was nonsignificantly increased with catheter aspiration device use versus control [RR 1.35 (0.26, 6.94)]. (Appendix Figure 33)

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and 30-day target revascularization.[141] The catheter aspiration devices included in this study were not reported. The use of a catheter aspiration device was associated with a nonsignficantly lower rate of 30-day target revascularization compared to control (1.9 percent versus 2.5 percent, p = 0.46).

Catheter aspiration devices in other ACS populations

No trials or studies assessed target revascularization in other ACS populations.

Mechanical thrombectomy in patients with STEMI

Five RCTs evaluated the impact of mechanical thrombectomy devices versus control on target revascularization using the maximal duration of followup.[11,26,28,39,43] Two trials were excluded from the pooled analysis of relative risk because no target revascularizations occurred within the prespecified time period in either treatment group.[26,43] In the three trials eligible for pooling, the use of a mechanical thrombectomy device nonsignificantly decreased the risk of target revascularization [RR 0.87 (0.36, 2.10)][11,28,39] (Figure 19). The weighted-mean followup for target revascularization using the maximal duration of followup was 6.22 months. A lower level of statistical heterogeneity was detected (I^2 = 39.2 percent) and publication bias could not be evaluated. All of the pooled trials were determined to be of good methodological quality.[11,28,39]

When the impact of mechanical thrombectomy devices versus control was assessed at ≤30 days [RR 1.62 (0.21, 12.55)] and 30 days [same results as the ≤30 days analysis] (Appendix Figure 34); nonsignificant increases in the risk of target revascularization were seen versus control in each analysis but a significant decrease was seen at 180 days [RR 0.55 (0.33, 0.92)] and a nonsignificant decrease was seen at 365 days [RR 0.68 (0.41, 1.13)] (Appendix Figure 35), although the 365-day analysis is based on a single trial.

One controlled observational study evaluated the association between the use of a mechanical thrombectomy device and in-hospital target revascularization.[134] Patients undergoing PCI with a mechanical thrombectomy device, either the AngioJet XMI or XVG catheter, were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a nonsignificantly higher rate of in-hospital target revascularization compared to PCI without a mechanical thrombectomy device (2.7 percent versus 2.1 percent, p = 0.57).

Mechanical thrombectomy devices in other ACS populations

One RCT evaluated the impact of the X-Sizer mechanical thrombectomy device versus control on 30-day target revascularization in patients with STEMI or UA.[155]. The use of a mechanical thrombectomy device nonsignificantly decreased the risk of 30-day target revascularization [RR 0.33 (0.00, 3.75)] compared to control.

One controlled observational study evaluated the association between the use of mechanical thrombectomy devices and 180-day target revascularization.[142] The types of ACSs included in this study were not reported. Patients undergoing PCI with the mechanical thrombectomy device AngioJet were compared to patients undergoing PCI without mechanical thrombectomy and target revascularization was evaluated at 270 days. The use of a mechanical thrombectomy device was associated with a nonsignificantly higher rate of 180-day target revascularization compared to PCI without a mechanical thrombectomy device (5.5 percent versus 4.8 percent, p = 0.72).

Distal filter embolic protection devices in patients with STEMI

Two RCTs evaluated the impact of distal filter embolic protection devices versus control on target revascularization using the maximal duration of followup.[88,94] In these trials, the use of distal filter embolic protection devices nonsignificantly increased the risk target revascularization using the maximal duration of followup [RR 1.48 (0.52, 4.21)] (Figure 20). The weighted-mean followup for target revascularization using the maximal duration of followup was 1.91 months. Both trials were determined to be of good methodological quality.[88,94]

One RCT evaluated the impact of a distal filter embolic protection device versus control on the occurrence of target revascularization at 30 days.[88] In this trial, the use of a distal filter embolic protection device nonsignificantly increased the risk of ≤30 day target revascularization [RR 3.02 (0.70, 13.01)]. The other trial evaluated the impact of a distal filter embolic protection device on the risk of 180-day target revascularization versus control.[94] In this trial, the use of a distal filter embolic protection device did not impact the risk of target revascularization over 180 days [RR 1.00 (0.35, 2.82)].

No controlled observational studies were available that assessed for this endpoint.

Distal filter embolic protection devices in other ACS populations

Two RCTs evaluated the impact of distal filter embolic protection devices versus control on target revascularization in patients with other ACSs using the maximal duration of followup.[125,145] These trials were not suitable for pooling because the first trial evaluated patients with either NSTEMI or STEMI[125] and the second trial evaluated patients with UA.[145] Both trials evaluated target revascularization at 30-days although the risk could not be calculated because no events occurred in either trial during the specified time period.[125,145]

Distal balloon embolic protection devices in patients with STEMI

Five RCTs evaluated the impact of distal balloon embolic protection devices versus control on target revascularization using the maximal duration of followup.[17,102,106,111,132] The use of a distal balloon embolic protection device nonsignificantly decreased the risk of target revascularization [RR 0.93 (0.61, 1.42)] (Figure 21). The weighted-mean followup for target revascularization using the maximal duration of followup was 6 months. Statistical heterogeneity and publication bias were not detected ($I^2 = 0$ percent, Egger's P = 0.369). All of the trials were determined to be of good methodological quality [17,102,106,111,132] did not change the results.

When the impact of distal balloon embolic protection devices versus control was assessed at in-hospital [RR 0.32 (0, 3.71)].≤30 days [RR 1.38 (0.55, 3.50)], 30 days [same results as the ≤30 days analysis], and 180 days [RR 0.93 (0.61, 1.42)] (Appendix Figures 36-37); nonsignificant decreases in the risk of target revascularization were seen versus control in each analysis, although the in-hospital analysis is based on a single trial.

No controlled observational studies assessed for this outcome.

Distal balloon embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal balloon embolic protection device PercuSurge versus abciximab therapy on target revascularization in patients with acute myocardial infarction.[153] The use of a distal balloon embolic protection device nonsignificantly increased the risk of 180-day target revascularization [RR 1.11 (0.46, 2.67)] compared to abciximab therapy.

No controlled observational studies assessed for this outcome in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on target revascularization.[18] The use of a proximal balloon embolic protection device nonsignificantly reduced the risk of having target revascularization over the next 30 days [RR 0.51 (0.14, 1.81)].

Proximal balloon embolic protection devices in other ACS populations

No trials or studies were available that evaluated the impact of proximal balloon embolic protection devices versus control on target revascularization in the population.

Embolic protection devices combined in patients with STEMI

Eight RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on target revascularization using the maximal duration of followup.[17,18,88,94,102,106,111,132] In these trials, the use of embolic protection devices combined nonsignificantly reduced the risk of long-term occurrence of target revascularization [RR 0.96 (0.66, 1.38)] (Figure 22). The weighted mean followup for target revascularization using the maximal duration of followup was 3.90 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.653). All of the trials were determined to be of good methodological quality.[17,18,88,94,102,106,111,132]

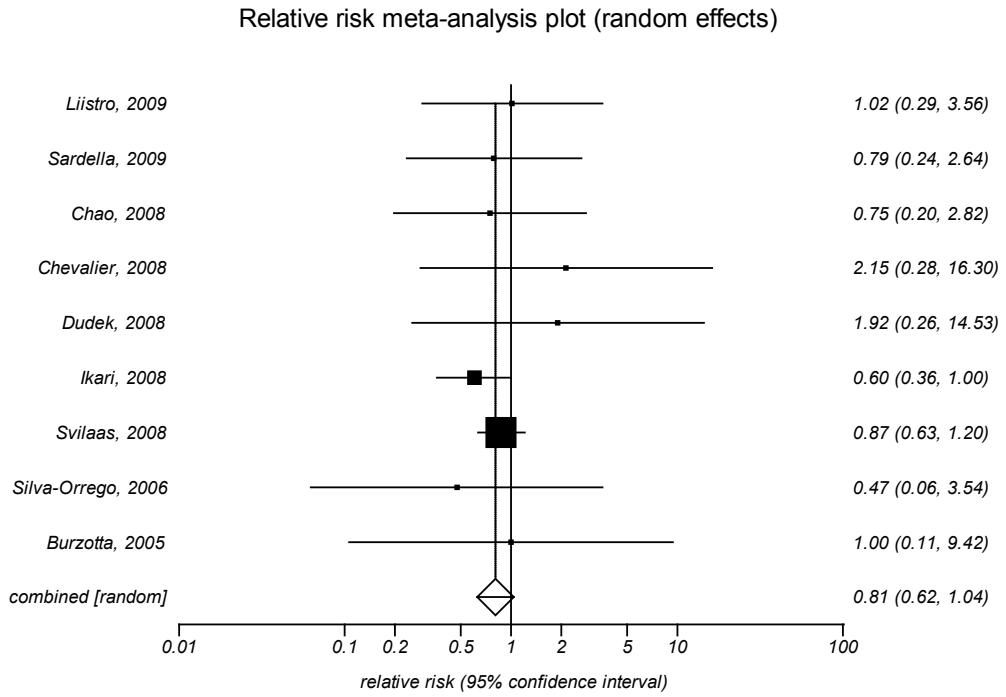
When the impact of embolic protection devices combined versus control was assessed at in-hospital [RR 0.32 (0.00 to 3.71)] and 180 days [RR 0.94 (0.64, 1.39)]; nonsignificant decreases in risk of target revascularization were seen versus control but at ≤30 days [RR 1.24 (0.62, 2.48)] and 30 days [same results as the ≤30 days analysis] (Appendix Figures 38-39); nonsignificant increases in risk were seen versus control, although the in-hospital analysis is based on a single trial.

No controlled observational studies assessed for this endpoint.

Embolic protection devices combined in other ACS populations

No trials or studies were available that evaluated the impact of any embolic protection device versus control on target revascularization in addition to the 3 trails reported above. Pooling was not suitable because each trial evaluated a different ACS.

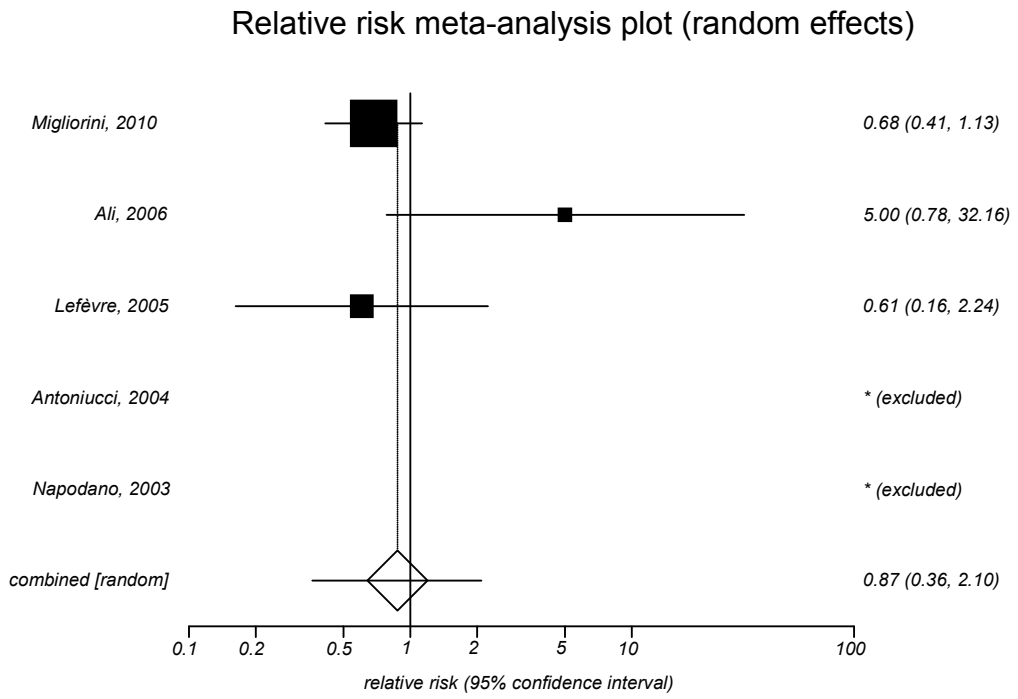
Figure 18. Impact of catheter aspiration devices versus control on target revascularization using the maximal duration of followup.



Cochran Q: P = 0.936
I^2: 0%
Egger: P = 0.534

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

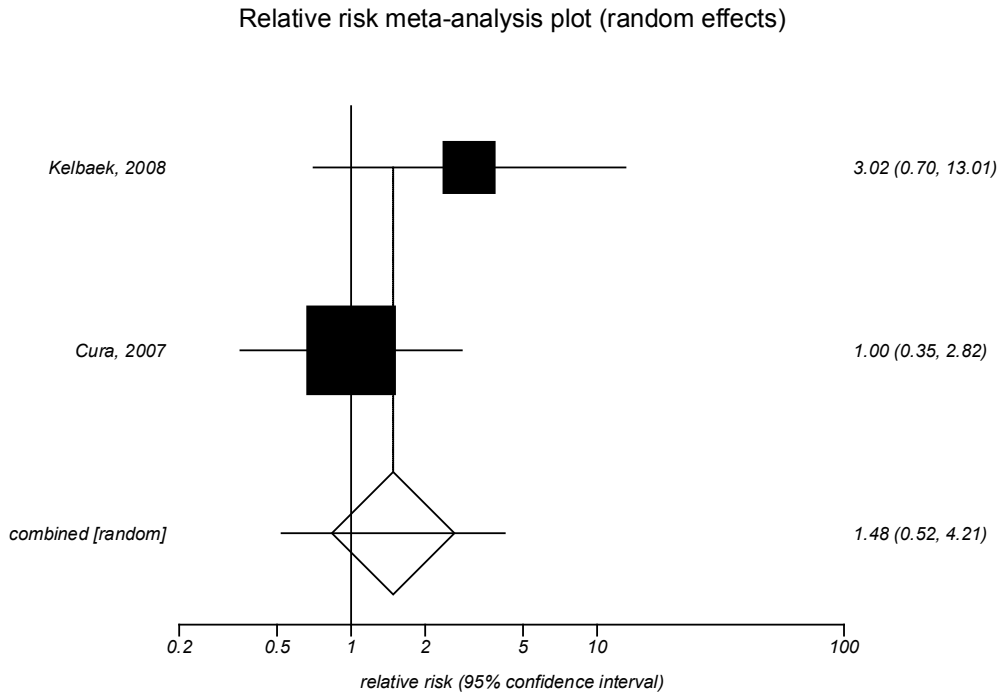
Figure 19. Impact of mechanical thrombectomy devices versus control on target revascularization using the maximal duration of followup.



Cochran Q: P = 0.193
I^2: 39.2%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

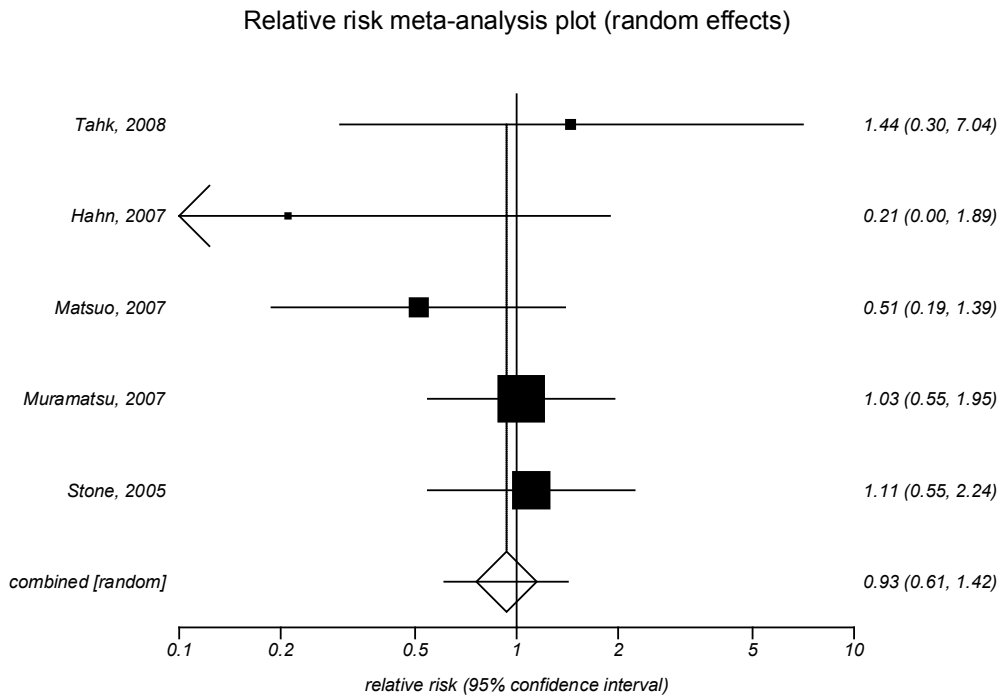
Figure 20. Impact of distal filter embolic protection devices versus control on target revascularization using the maximal duration of followup.



Cochran Q: P = 0.258
I^2: Too few strata
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

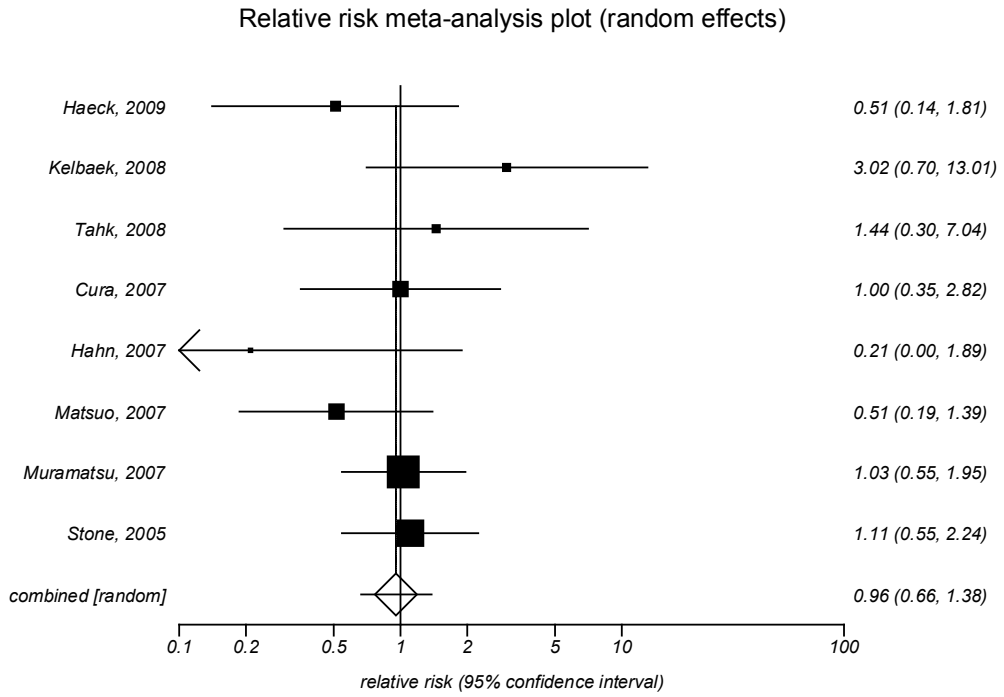
Figure 21. Impact of distal balloon embolic protection devices versus control on target revascularization using maximal duration of followup.



Cochran Q: P = 0.597
I^2: 0%
Egger: P = 0.369

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 22. Impact of embolic protection devices combined versus control on target revascularization using the maximal duration of followup.



Cochran Q: P = 0.586
I^2: 0%
Egger: P = 0.653

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Combined MACE

Direct Comparative Trials

Catheter aspiration device versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on 365-day MACE.[147] In this trial, the use of Diver-Invatec nonsignificantly increased the risk of 365-day MACE [RR 2.40 (0.57, 10.41)] compared to Export-Medtronic. This same trial evaluated the impact of the Diver-Invatec versus the Export-Medtronic device on 30-day MACE.[147] The use of Diver-Invatec nonsignificantly decreased the risk of 30-day MACE [RR 0.65 (0.13, 3.16)] compared to Export-Medtronic.

Catheter aspiration device versus distal balloon embolic protection device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on 30-day MACE.[149] In this trial, the use of Diver CE nonsignificantly increased the risk of 30-day MACE [RR 1.33 (0.35, 5.16)] compared to Guardwire Plus.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Eleven RCTs evaluated the impact of catheter aspiration devices versus control on MACE of maximal duration of followup. [12,14-16,19,61,67,68,70,82,84] In these trials, the use of a catheter aspiration device significantly reduced the occurrence of MACE using the maximal duration of followup [RR 0.73 (0.61, 0.88)] (Figure 23). The weighted-mean followup for MACE using the maximal duration of followup was 12.43 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.965). Given the risk difference [RD -0.03 (-0.01, 0.001), control rate (0.02, 0.35)], 33 people would need to be treated with a catheter aspiration device to prevent one MACE.

When limiting the pooled analysis to only trials of good methodological quality[12,14-16,61,67,68,70,82] the risk of MACE using the maximal duration of followup remained significantly reduced in the catheter aspiration device group compared to control [RR 0.73 (0.61, 0.88)]. The weighted mean duration of followup was 13.20 months. Statistical heterogeneity was not detected (I^2 = 0 percent). Given the risk difference [RD -0.04 (-0.08, 0.01), control rate (0.02, 0.35)], 25 people would need to be treated with a catheter aspiration device to prevent one MACE.

When the impact of catheter aspiration devices versus control was assessed at in-hospital [RR 0.97 (0.36, 2.58)], ≤30 days [RR 0.80 (0.57, 1.12)], 30 days [RR 0.79 (0.56, 1.13)], and 365 days [RR 0.61 (0.26, 1.41)] (Appendix Figures 40-43); nonsignificant decreases in the risk of MACE were seen versus control in each analysis with a significant decrease in risk at 180 days [RR 0.66 (0.47, 0.94)] (Appendix Figure 44). Given the risk difference [RD -0.04 (-0.10, -0.003), control rate (0.06, 0.27)], 25 people would need to be treated with a catheter aspiration device to prevent one MACE.

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and 30-day MACE and 365-day MACE.[141] The catheter aspiration devices included in this study were not reported. The use of a catheter aspiration device was associated with a nonsignficantly lower rate of 30-day MACE compared to control (5.5 percent versus 5.3 percent, p = 0.81). The use of a catheter aspiration device was associated with a nonsignificantly decreased rate of 30-day MACE [HR 0.96 (0.56, 1.52)] and a nonsignficantly higher rate of 365-day MACE [HR 1.03 [0.68, 1.55)].

Catheter aspiration devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Mechanical thrombectomy in patients with STEMI

Four RCTs evaluated the impact of mechanical thrombectomy devices versus control on MACEs using the maximal duration of followup.[11,26,28,39] One trial was excluded from the pooled analysis of relative risk because there were no MACE at the prespecified time-point in either treatment groups.[26] In the three trials eligible for pooling, the use of a mechanical thrombectomy device nonsignificantly increased the risk of MACE using the maximal duration of followup [RR 1.23 (0.50, 3.01)][11,28,39] (Figure 24). The weighted mean followup for MACE was 6.22 months. A higher level of statistical heterogeneity was found (I^2 = 79.9 percent) and publication bias could not be evaluated. The three pooled trials were all determined to be of good methodological quality.[11,28,39]

When the impact of mechanical thrombectomy devices versus control was assessed at ≤30 days [RR 1.28 (0.37, 4.38)] and 30 days [same results as the ≤30 days analysis], nonsignificant increases in the risk of MACE were seen versus control while nonsignificant reductions in risk were seen at 180 days [RR 0.71 (0.41, 1.20)]. (Appendix Figures 45-46). One trial evaluated the impact of mechanical thrombectomy devices on 365-day MACE versus control.[11] In this trial, the use of the AngioJet rheolytic thrombectomy system was compared to control therapy. The use of a mechanical thrombectomy device significantly decreased the risk of 365-day MACE [RR 0.66 (0.44, 0.97)]. Given the risk difference for 365-day MACE [RD -0.10 (-0.15, -0.01), control rate = 0.23], 10 people would need to be treated with a catheter thrombectomy device in order to prevent one occurrence of MACE.

One controlled observational study evaluated the association between the use of a mechanical thrombectomy device and in-hospital MACE.[134] Patients undergoing PCI with a mechanical thrombectomy device, either the AngioJet XMI or XVG catheter, were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a nonsignificantly lower rate of in-hospital MACE compared to PCI without a mechanical thrombectomy device (7.5 percent versus 9.0 percent, p = 0.47). After adjustment for baseline and angiographic characteristics, the use of a mechanical thrombectomy device was associated with a nonsignificantly lower odds of in-hospital MACE [OR 0.83 (0.48, 1.42)] compared to PCI without a mechanical thrombectomy device.

Mechanical thrombectomy devices in other ACS populations

One RCT evaluated the impact of the mechanical thrombectomy device X-Sizer versus control on 30-day MACE in patients with STEMI or UA.[155] The risk of 30-day MACE was not significantly different between the mechanical thrombectomy device group and control [RR 1.00 (0.18, 5.43)].

One controlled observational study evaluated the association between the use of mechanical thrombectomy devices and 180-day MACE.[142] The types of ACSs included in this study were not reported. Patients undergoing PCI with the mechanical thrombectomy device AngioJet were compared to patients undergoing PCI without mechanical thrombectomy and MACE was evaluated at 270 days. The use of a mechanical thrombectomy device was associated with a nonsignificantly higher rate of 180-day MACE compared to PCI without a mechanical thrombectomy device (14.0 percent versus 11.6 percent, p = 0.35).

Distal filter embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal filter embolic protection devices versus control on the occurrence of MACE using the maximal duration of followup.[88,94,97,100] In these trials, the use of distal filter embolic protection devices nonsignificantly increased the risk of MACE using the maximal duration of followup [RR 1.13 (0.72, 1.78)] (Figure 25). The weighted-mean followup for MACE was 6.49 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.701).

When limiting the pooled analysis to only trials of good methodological quality[88,94,97] the risk of MACE remained nonsignificantly increased in the distal filter embolic protection device group compared to control [RR 1.15 (0.72, 1.83)]. The weighted mean duration of followup was 6.87 months. Statistical heterogeneity was not detected (I^2 = 0 percent).

When the impact of distal filter embolic protection devices versus control was assessed ≤30 days [RR 1.34 (0.80, 2.26)], 30 days [same results as the ≤30 day analysis], and 180 days [RR 1.10 (0.68, 1.78)] (Appendix Figures 47-48); nonsignificant increases in the risk of MACE were seen versus control in each analysis.

No controlled observational studies were available that assessed for this endpoint.

Distal filter embolic protection devices in other ACS populations

Two RCTs evaluated the impact of distal filter embolic protection devices versus control in patients with other ACSs on MACE using the maximal duration of followup.[125,144] These trials were not suitable for pooling because the first trial evaluated patients with either NSTEMI or UA[144] and the second trial evaluated patients with either STEMI or NSTEMI.[125] In the trial evaluating patients with NSTEMI or UA,[144] the FilterWire EZ device was compared to control. The use of a distal filter embolic protection device was associated with a nonsignficant increase in the risk of MACE at in-hospital [RR 1.24 (0.50, 3.06)] and at 30-days [RR 1.08 (0.45, 2.59)] compared to control.[144] In the trial evaluating patients with either STEMI or NSTEMI,[125] the FilterWire EX device was compared to control. The use of a distal filter embolic protection device nonsignificantly increased the risk of 180-day MACE [RR 1.08 (0.53, 2.23)] compared to control.

Distal balloon embolic protection devices in patients with STEMI

Six RCTs evaluated the impact of distal balloon embolic protection devices versus control on MACE using the maximal duration of followup.[17,102,106,110,111,132] One study was excluded from the pooled analysis of relative risk because there were no MACE at the prespecified time point in either treatment group.[110] In the five studies eligible for pooling, the use of a distal embolic protection device nonsignificantly decreased the risk of MACE [RR 0.87 (0.64, 1.19)][17,102,106,111,132] (Figure 26). The weighted-mean followup for MACE was 6 months. Statistical heterogeneity was not detected (I^2=0 percent) but publication bias was detected (Egger's P = 0.032). All of the trials were determined to be of good methodological quality.[17,102,106,110,111,132]

When the impact of distal embolic protection devices was assessed at ≤30 days [RR 0.74 (0.44, 1.23)], 30 days [same results as the ≤30 day analysis], and 180 days [RR 0.87 (0.64, 1.19)]

(Appendix Figures 49-50); nonsignificant decreases in the risk of MACE were seen versus control in each analysis.

No controlled observational studies assessed for this endpoint.

Distal balloon embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal balloon embolic protection device GuardWire percuSurge versus control on MACE in patients with acute myocardial infarction.[131] The use of a distal filter embolic protection device nonsignificantly decreased the risk of 180-day MACE [RR 0.33 (0.05, 1.87)] compared to control.

No controlled observational studies evaluated this endpoint in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on MACE.[18] The use of a proximal balloon embolic protection device nonsignificantly reduced the risk of experiencing a MACE endpoint over the next 30 days [RR 0.34 (0.01, 8.23)].

Proximal balloon embolic protection devices in other ACS populations

No trials or studies were available that evaluated the impact of proximal balloon embolic protection devices versus control on MACE in this population.

Embolic protection devices combined in patients with STEMI

Eleven RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on MACE using the maximal duration of followup.[17,18,88,94,97,100,102,106,110,111,132] The trial by Zhou et al was excluded from the pooled analysis of relative risk because no events occurred within the prespecified time period in either control or treatment group. In the 10 trials suitable for pooling, the use of embolic protection devices combined nonsignificantly reduced the risk of long-term occurrence of MACE [RR 0.92 (0.72, 1.18)] (Figure 27). The weighted mean followup for MACE using the maximal duration of followup was 5.58 months. Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.367). The analysis was then limited to only trials of good methodological quality[17,18,88,94,97,102,106,110,111,132] although one trial was excluded from the analysis because no events occurred in either group during the prespecified time period.[110] In the nine trials of good methodological quality suitable for pooling, the risk of MACE remained nonsignificantly decreased in the combined embolic protection device group compared to control [RR 0.92 (0.72, 1.18)]. The weighted mean followup for MACE using the maximal duration of followup was 5.71 months. Statistical heterogeneity was not detected (I^2 = 0 percent).

When the impact of distal embolic protection devices versus control was assessed at ≤30 days [RR 0.94 (0.66, 1.32)], 30 days [same results as the ≤30 day analysis], and 180 days [RR

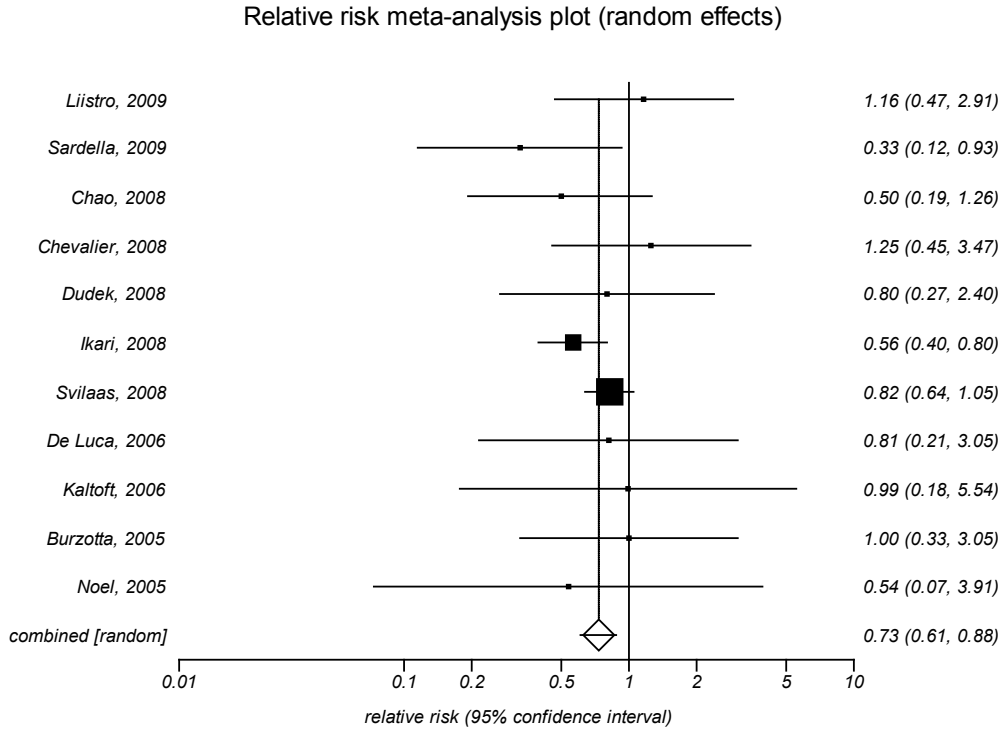
0.93 (0.72, 1.21)] (Appendix Figures 51-52); nonsignificant decreases in the risk of MACE were seen versus control in each analysis.

One controlled observational study evaluated the association between the use of a distal protection device and 365-day MACE in patients with STEMI.[136] In this study, the device name was not reported nor was the distinction between distal balloon and distal filter. There was no significant difference in the adjusted rate of 365-day MACE when comparing the distal protection group with those who did not receive distal protection during PCI [HR 0.85 (0.59, 3.48)].

Embolic protection devices combined in other ACS populations

No trials or studies were available that evaluated the impact of any embolic protection device versus control on MACE in addition to the three trials reported above, and pooling was not suitable because each trial evaluated a different ACS.

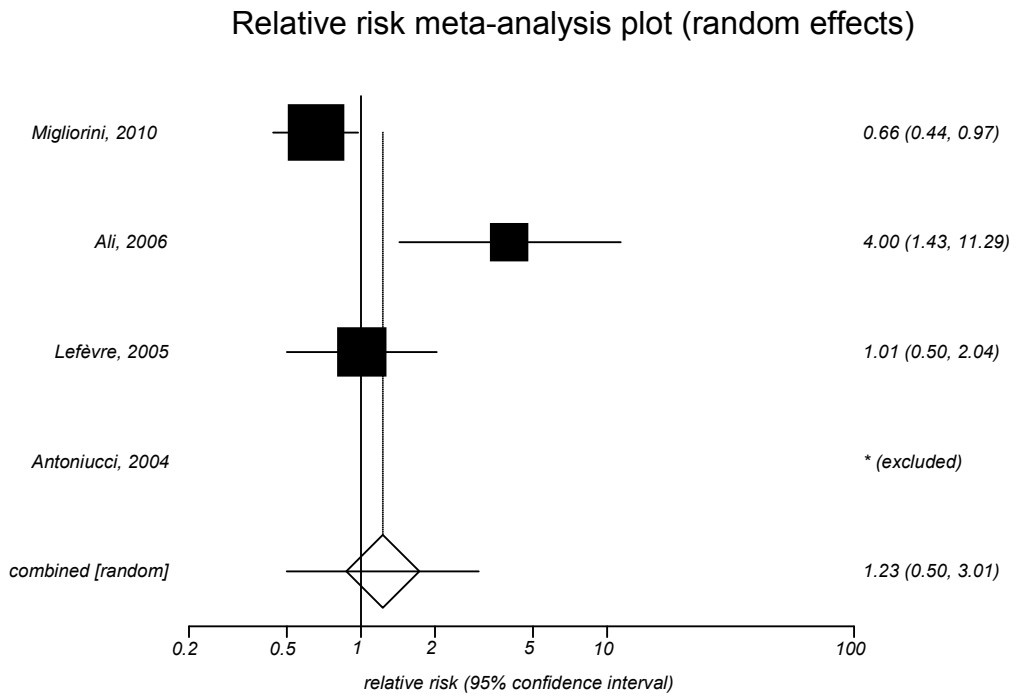
Figure 23. Impact of catheter aspiration devices versus control on MACE of maximal duration of followup.



Cochran Q: P = 0.645
I^2: 0%
Egger: P = 0.965

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

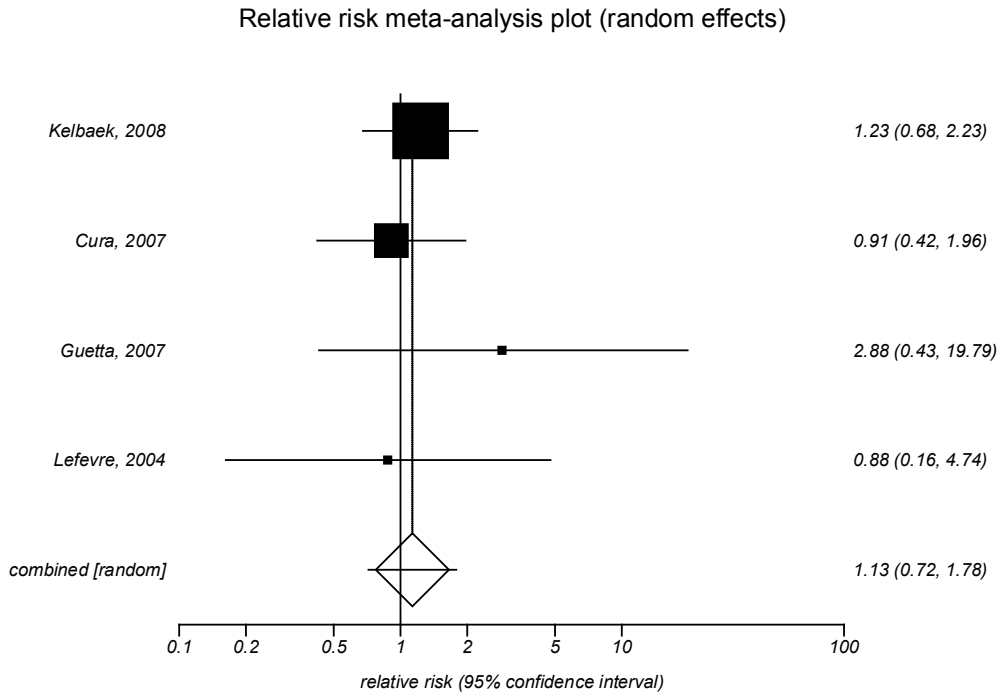
Figure 24. Impact of mechanical thrombectomy devices versus control on MACE using the maximal duration of followup.



Cochran Q: P = 0.007
I^2: 79.9%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

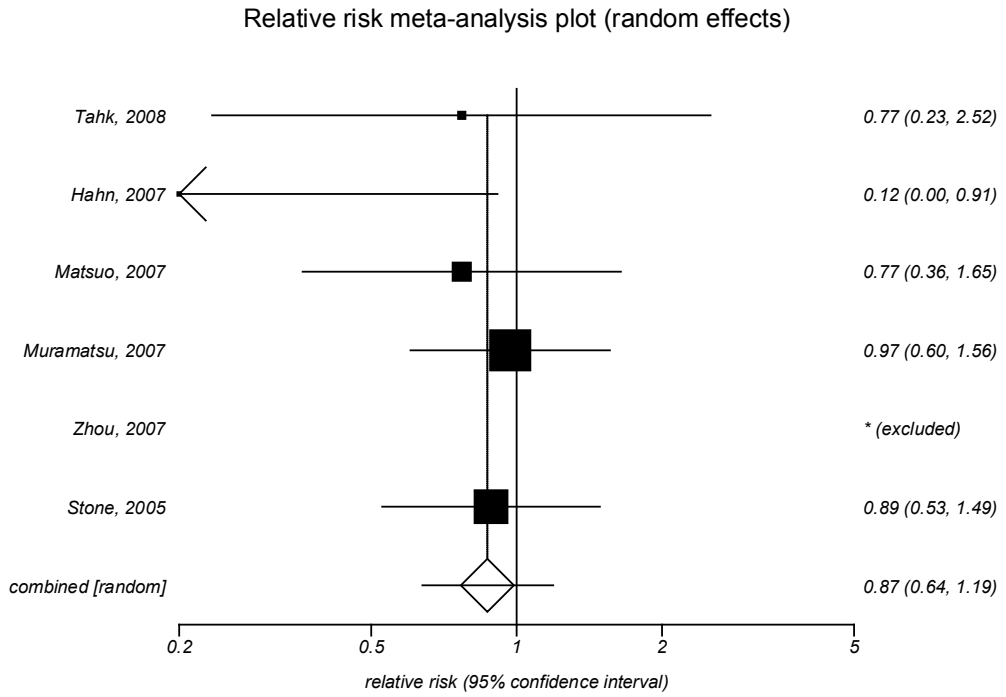
Figure 25. Impact of distal filter embolic protection devices versus control on MACE using the maximal duration of followup.



Cochran Q: P = 0.772
I^2: 0%
Egger: P = 0.701

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

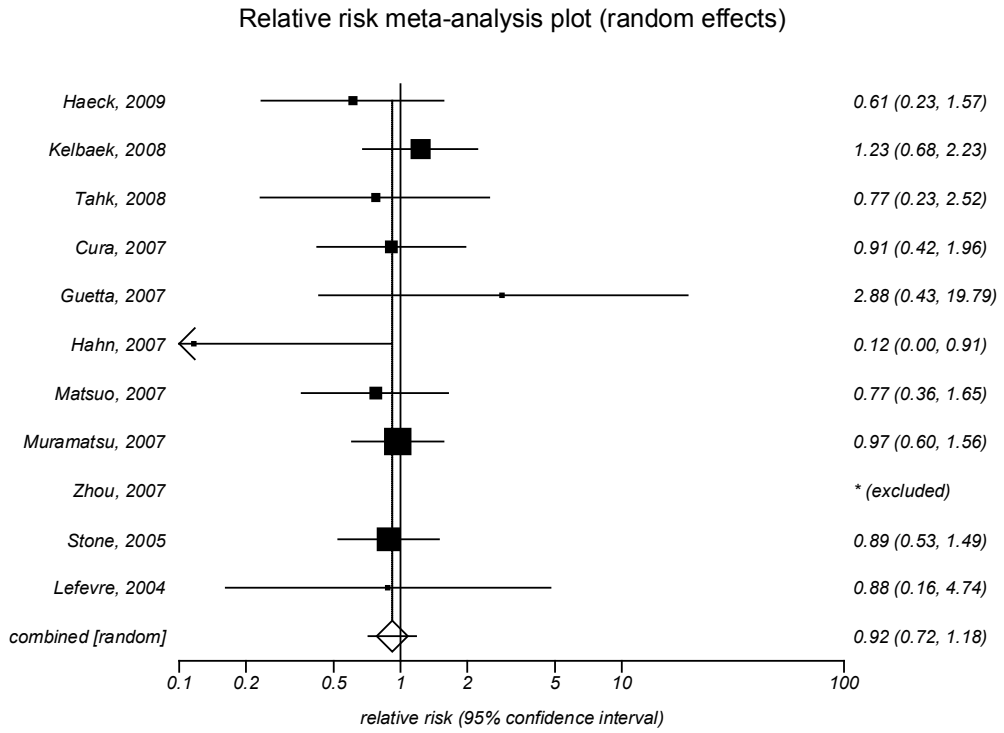
Figure 26. Impact of distal balloon embolic protection devices versus control on MACE using the maximal duration of followup.



Cochran Q: P = 0.685
I^2: 0%
Egger: P = 0.032

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 27. Impact of embolic protection devices combined versus control on MACE using the maximal duration of followup.



Cochran Q: P = 0.839
I²: 0%
Egger: P = 0.367

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Table 7. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction

Final Health Outcome	Weighted Mean Followup (months)	Relative Risk (95% CI)	I^2 for Relative Risk
Mortality	7.92	0.69 (0.47 to 1.02)	0%
Myocardial infarction	8.80	0.61 (0.36 to 1.04)	0%
Stroke	0.79	3.18 (0.73 to 13.88)	0%
Target revascularization	9.01	0.81 (0.62 to 1.04)	0%
MACE	12.43	0.73 (0.61 to 0.88)	0%

Abbreviations: CI=confidence interval; MACE=major adverse cardiac events

Table 8. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction

Final Health Outcome	Weighted Mean Followup (months)	Relative Risk (95% CI)	I^2 for Relative Risk
Mortality	7.80	1.19 (0.51 to 2.76)	54.9
Myocardial infarction	8.98	0.71 (0.27 to 1.85)	0%
Stroke	5.79	2.42 (0.75 to 7.78)	0%
Target revascularization	6.22	0.87 (0.36 to 2.10)	39.2%
MACE	6.22	1.23 (0.50 to 3.01)	79.9%

Abbreviations: CI=confidence interval; MACE=major adverse cardiac events

Table 9. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction

Final Health Outcome	Weighted Mean Followup (months)	Relative Risk (95% CI)	I^2 for Relative Risk
Mortality	1.76	1.17 (0.57 to 2.40)	0%
Myocardial infarction	1.76	0.73 (0.12 to 4.44)	44.3%
Stroke	1	1.51 (0.30 to 7.52)*	NA
Target revascularization	1.91	1.48 (0.52 to 4.21)	NA
MACE	6.49	1.13 (0.72 to 1.78)	0%

*Result is based on a single trial

Abbreviations: CI=confidence interval; MACE=major adverse cardiac events; NA=not applicable

Table 10. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction

Final Health Outcome	Weighted Mean Followup (months)	Relative Risk (95% CI)	I^2 for Relative Risk
Mortality	6	0.82 (0.45 to 1.51)	2.5%
Myocardial infarction	6	0.67 (0.29 to 1.57)	0%
Stroke	6	0.48 (0.10 to 2.22)*	NA
Target revascularization	6	0.93 (0.61 to 1.42)	0%
MACE	6	0.87 (0.64 to 1.19)	0%

*Result is based on a single trial

Abbreviations: CI=confidence interval; MACE=major adverse cardiac events; NA=not applicable

Table 11. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction

Final Health Outcome	Weighted Mean Followup (months)	Relative Risk (95% CI)	I^2 for Relative Risk
Mortality	1	1.01 (0.18 to 5.69)*	NA
Myocardial infarction	1	0.68 (0.14 to 3.34)*	NA
Stroke	1	0.34 (0 to 3.87)*	NA
Target revascularization	1	0.51 (0.14 to 1.81)*	NA
MACE	1	0.61 (0.23 to 1.57)*	NA

*Result is based on a single trial

Abbreviations: CI=confidence interval; MACE=major adverse cardiac events; NA=not applicable

Table 12. Final health outcomes using the maximal duration of followup in randomized controlled trials evaluating embolic protection devices combined in patients with ST-segment elevation myocardial infarction

Final Health Outcome	Weighted Mean Followup (months)	Relative Risk (95% CI)	I^2 for Relative Risk
Mortality	3.54	0.96 (0.61 to 1.49)	0%
Myocardial infarction	3.70	0.72 (0.37 to 1.40)	0%
Stroke	2.72	0.74 (0.23 to 2.31)	0%
Target revascularization	3.90	0.96 (0.66 to 1.38)	0%
MACE	5.58	0.92 (0.72 to 1.18)	0%

Abbreviations: CI=confidence interval; MACE=major adverse cardiac events

Health-Related Quality Of Life

Direct Comparative Trials

No direct comparative trials evaluated the impact of catheter aspiration, mechanical thrombectomy or embolic protection devices on this endpoint.

Trials versus Control

Catheter aspiration devices

No trials or studies evaluated the impact of catheter aspiration devices on this endpoint.

Mechanical thrombectomy devices

No trials or studies evaluated the impact of catheter aspiration devices on this endpoint.

Distal Balloon Embolic Protection Devices

No trials or studies evaluated the impact of distal balloon embolic protection devices on this endpoint.

Proximal Balloon Embolic Protection Devices

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this endpoint.

Embolic Protection Devices Combined

No trials or studies evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on this endpoint.

ST-Segment Resolution

ST-segment resolution was defined in different ways in different trials. We defined ST-segment resolution as ≥70 percent resolution at 60 minutes if reported, ≥50 percent resolution at 60 minutes if ≥70 percent resolution at 60 minutes data was not reported, or ≥70 percent resolution post-PCI or at 90 minutes if 60 minute data was unavailable.

Direct Comparative Trials

Catheter aspiration device versus catheter aspiration device in STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on ST-segment resolution.[147] In this trial, ST-segment resolution was defined as resolution great than or equal to 70 percent at 90 minutes. The use of Diver-Invatec nonsignificantly decreased the risk of resolving ST-segment elevation [RR 0.79 (0.61, 1.00)] compared to Export-Medtronic.

Catheter aspiration device versus distal balloon protection device in ACS

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on ST-segment resolution.[149] In this trial, ST-segment resolution was defined as greater than or equal to 70 percent up to 6 hours post-procedure (measured immediately after the procedure and at 90 minutes and 6 hours post-procedure). The use of Diver CE nonsignificantly decreased the risk of resolving ST-segment elevation [RR 0.97 (0.72, 1.32)] compared to Guardwire Plus.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Fifteen RCTs evaluated the impact of catheter aspiration devices versus control on ST-segment resolution and were included in the pooled analysis.[12,14-16,19,20,61,68,70,73,82,84-86] The use of a catheter aspiration device significantly increased the risk of resolving ST-segment elevation

versus control [RR 1.48 (1.30, 1.70)] (Figure 28). A higher level of statistical heterogeneity was found (I^2=64.4) and a trend towards publication bias was detected (Egger's P = 0.055). Given the risk difference [RD 0.22 (0.14, 0.29), control rate (0.11, 0.65)], five people would need to be treated with a catheter aspiration device to allow one person to experience ST-segment resolution.

When limiting the pooled analysis to only trials of good methodological quality[12,14-16,61,68,70,73,82] the risk of resolving ST-segment elevation remained significantly increased in the catheter aspiration device group compared to control [RR 1.39 (1.21, 1.61)]. A higher level of statistical heterogeneity was detected (I^2 = 60.4 percent). Given the risk difference [RD 0.18 (0.10, 0.26), control rate (0.27, 0.65)], six people would need to be treated with a catheter aspiration device to allow one person to experience ST-segment resolution.

One RCT evaluated the impact of the catheter aspiration device Diver CE versus control on ST-segment resolution although was not included in the pooled analysis. In this trial patients were only included in if they attained TIMI-3 blood flow post-procedure, therefore it was not included in the pooled analysis of ST-segment resolution. The use of a catheter aspiration device nonsignificantly decreased the risk of resolving ST-segment elevation [RR 0.93 (0.52, 1.62)] compared to control.

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and resolution of ST-segment elevation.[141] The catheter aspiration devices included in this study were not reported. The use of a catheter aspiration device was associated with a nonsignificantly lower rate of resolution of ST-segment elevation (48.2 percent versus 50.3 percent, p = 0.51).

Catheter aspiration devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in patients with STEMI

Five RCTs evaluated the impact of mechanical thrombectomy devices versus control on ST-segment resolution.[11,26,28,39,43] The use of a mechanical thrombectomy device nonsignificantly increased the risk of resolving ST-segment elevation [RR 1.16 (0.99, 1.36)] (Figure 29). A higher level of statistical heterogeneity was found (I^2 = 75.1 percent) but publication bias was not detected (Egger's P = 0.402). All of the trials in the pooled analysis were determined to be of good methodological quality.[11,26,28,39,43]

No controlled observational studies assessed for this endpoint.

Mechanical thrombectomy devices in other ACS populations

One RCT evaluated the impact of the mechanical thrombectomy device X-Sizer versus control on ST-segment resolution in patients with STEMI or UA.[155] ST-segment resolution was defined as resolution greater than 50 percent after the procedure. The use of a mechanical thrombectomy device significantly increased the risk of resolving ST-segment elevation [RR 1.58 (1.05, 2.57)] compared to control. Given the risk difference for ST-segment resolution [RD

0.30 (0.03, 0.54), control rate 0.52], three people would need to be treated with a mechanical thrombectomy device in order to have one person experience ST-segment resolution. This trial was determined to be of good methodological quality.

No controlled observational studies assessed for this endpoint in this population.

Distal filter embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal filter embolic protection devices versus control on ST-segment resolution.[88,94,97,100] In these trials, the use of distal filter embolic protection devices nonsignificantly increased the risk of resolving ST-segment elevation [RR 1.05 (0.97, 1.14)] (Figure 30). Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.791).

When limiting the pooled analysis to only trials of good methodological quality[88,94,97] the risk of resolving of ST-segment elevation remained nonsignificantly increased [RR 1.04 (0.96, 1.14)]. Statistical heterogeneity was not detected (I^2 = 0 percent).

No controlled observational studies assessed for this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal balloon embolic protection devices versus control on ST-segment resolution.[102,106,111,132] The use of a distal balloon embolic protection device nonsignificantly increased the risk of resolving ST-segment elevation [RR 1.08 (0.91, 1.29)] (Figure 31). A lower level of statistical heterogeneity was found (I^2 = 41.2 percent) but publication bias was not detected (Egger's P = 0.311). All of the trials were determined to be of good methodological quality.[102,106,111,132]

No controlled observational studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal balloon embolic protection device Guardwire Plus versus control on early resolution of ST-segment elevation in patients with acute myocardial infarction.[129] The use of a distal balloon embolic protection device significantly increased the risk of resolving ST-segment elevation compared to control [RR 1.58 (1.10, 2.46)]. Given the risk difference [RD 0.29 (0.10, 0.50), control rate 0.50], three people would need to be treated with a distal balloon embolic protection device to have one patient experience an ST segment resolution. This trial was determined to be of poor methodological quality.[129]

One RCT evaluated the impact of the distal balloon embolic protection device PercuSurge versus abciximab therapy on ST-segment resolution in patients with acute myocardial infarction.[153] ST-segment resolution was defined as ≥70 percent at 60 minutes. The use of a

distal balloon embolic protection device nonsignificantly increased the risk of resolving ST-segment elevation [RR 1.28 (0.86, 1.92)] compared to abciximab therapy.

No controlled observational studies assessed for this endpoint in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on ST-segment resolution.[18] The use of a proximal balloon embolic protection device nonsignificantly increased the risk of resolving ST-segment elevation [RR 1.11 (0.97, 1.28)]. The trial was determined to be of good methodological quality.[18]

Proximal balloon embolic protection devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Embolic protection devices combine in patients with STEMI

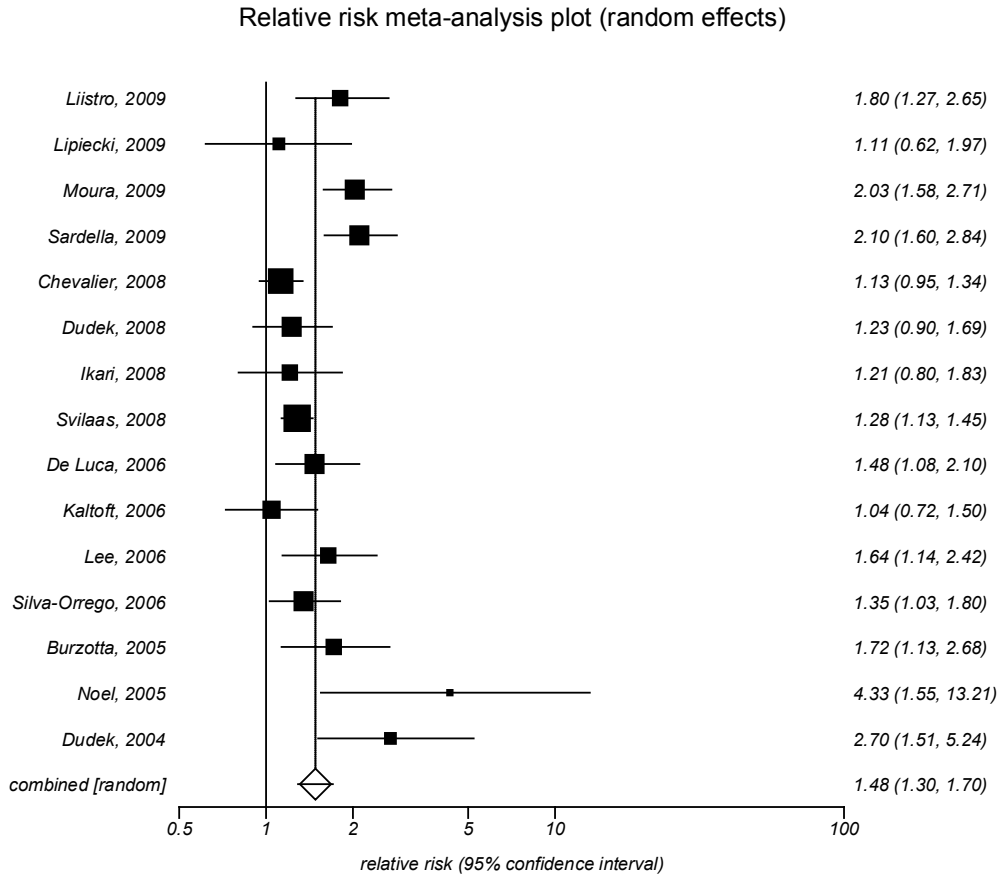
Nine RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on ST-segment resolution.[18,88,94,97,100,102,106,111,132] In these trials, the use of embolic protection devices combined nonsignificantly increased the risk of resolving ST-segment elevation [RR 1.06 (1.00, 1.13)] (Figure 32). Statistical heterogeneity and publication bias were not detected (I^2 = 0 percent, Egger's P = 0.295).

When limiting the analysis to only trials of good methodological quality[18,88,94,97,102,106,111,132] the risk of resolving ST-segment elevation remained nonsignificantly increased in the combined embolic protection device group compared to control [RR 1.06 (1.00, 1.12)]. Statistical heterogeneity was not detected (I^2 = 0 percent).

Embolic protection devices combine in other ACS populations

No trials or studies were available in addition to the two trials reported above that evaluated the impact of any embolic protection device versus control on ST-segment resolution in this patient population. Pooling was not suitable because a different comparator was used in each trial.

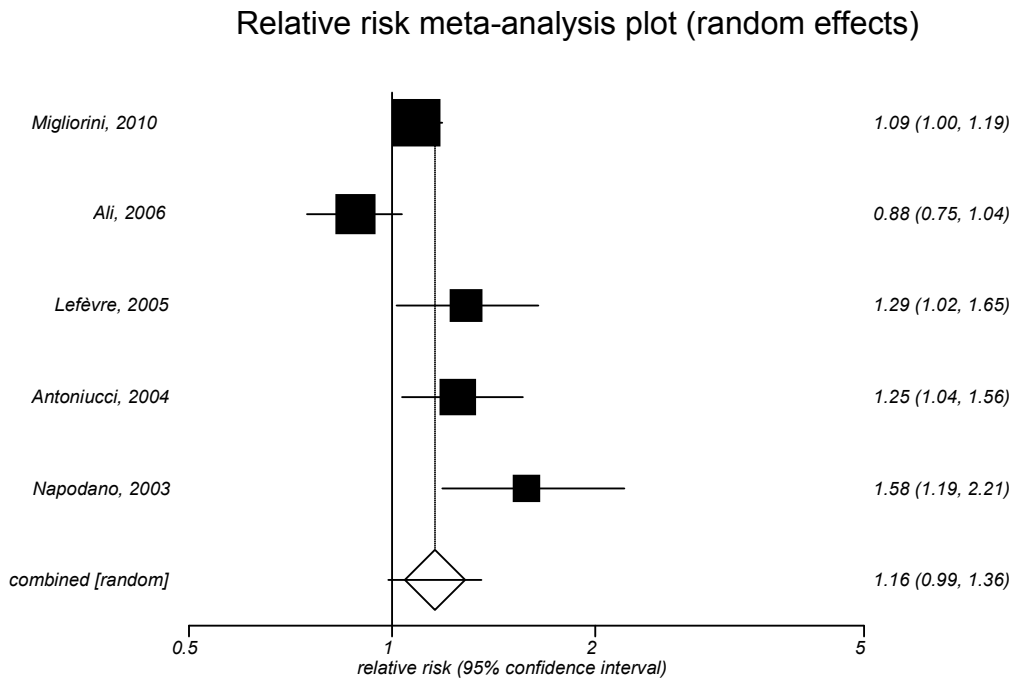
Figure 28. Impact of catheter aspiration devices versus control on ST-segment resolution.



Cochran Q: P < 0.001
I^2: 64.4%
Egger: P = 0.056

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

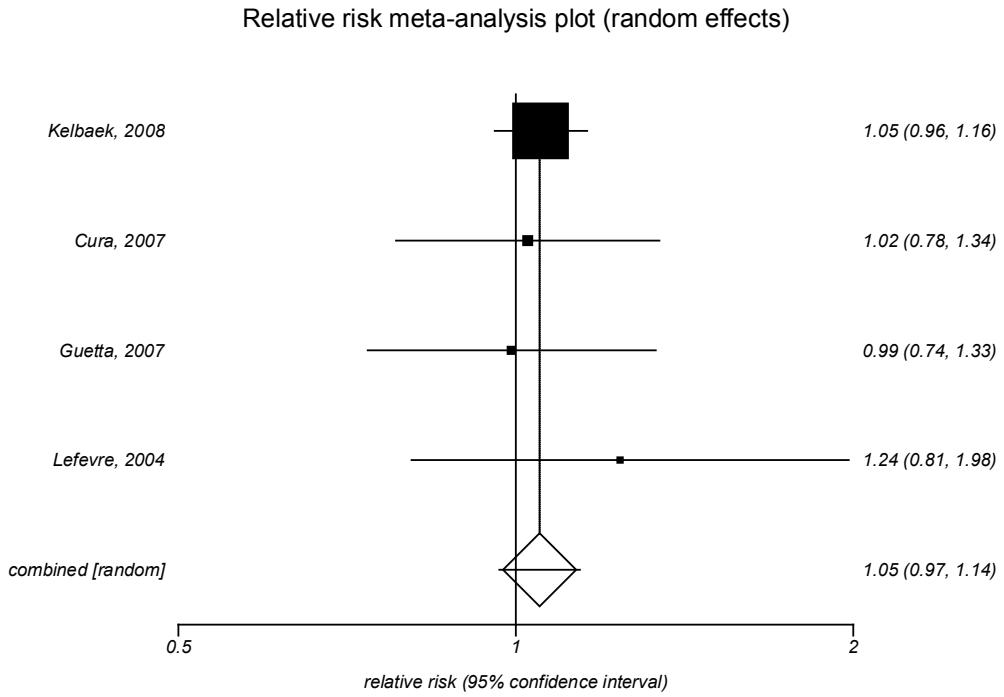
Figure 29. Impact of mechanical thrombectomy devices versus control on ST-segment resolution.



Cochran Q: P = 0.003
I^2: 75.1%
Egger: P = 0.402

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

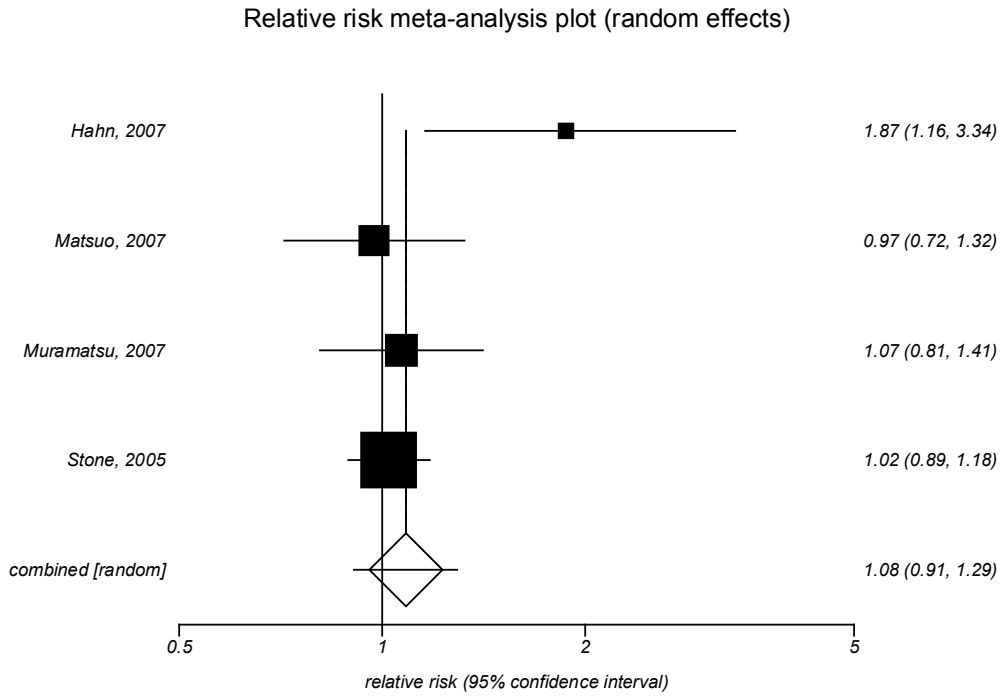
Figure 30. Impact of distal filter embolic protection devices versus control on ST-segment resolution.



Cochran Q: P = 0.864
I^2: 0%
Egger: P = 0.791

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

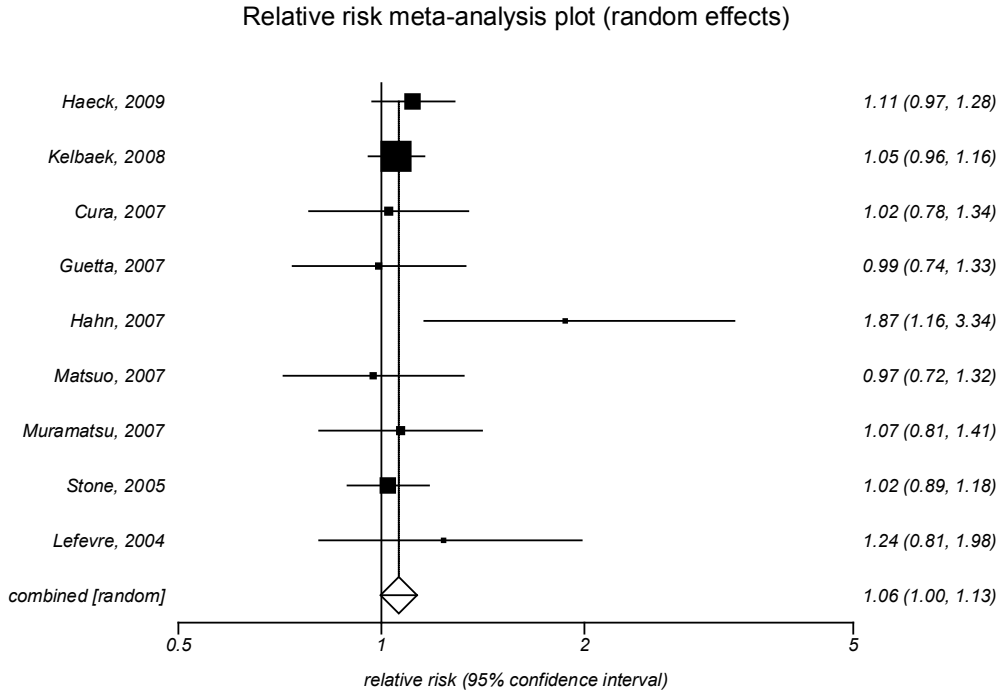
Figure 31. Impact of distal balloon embolic protection devices versus control on ST-segment resolution.



Cochran Q: P = 0.164
I^2: 41.2%
Egger: P = 0.311

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 32. Impact of embolic protection devices combined versus control on ST-segment resolution.



Cochran Q: P = 0.606
I^2: 0%
Egger: P = 0.295

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Ejection Fraction

Direct Comparative Trials

Catheter aspiration device versus distal balloon embolic protection device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on left-ventricular ejection fraction (Table 13).[149] There was no difference in the mean left-ventricular ejection fraction between Diver CE and Guardwire Plus groups at baseline (45 percent ± 11 versus 46 percent ± 10, p = 0.56) or at 30 days post-procedure (54 percent ± 12 versus 54 percent ± 11, p = 0.60), respectively.

Catheter aspiration device versus distal balloon embolic protection device versus control in patients with STEMI

One direct comparative randomized trial evaluated the impact of catheter aspiration devices and distal balloon embolic protection devices on 6-month ejection fraction (Table 13).[152] In this trial, patients were randomized to one of three groups, catheter aspiration with Rescue or Thrombuster devices, distal balloon embolic protection with PercuSurge or GuardWire devices, or to control therapy. Patients were excluded from the trial if they had coronary no reflow or slow flow. Ejection fraction at 180-days did not differ significantly amongst the three groups (50 percent ± 8 versus 54 percent ± 11 versus 52 percent ± 12, p = NS).

Table 13. Ejection fraction of direct comparative randomized controlled trials in ST-segment elevation myocardial infarction.

Study, Year	Device Category	Group	n	Time EF Measured	Mean EF (SD)	P-value
Sardella, 2008	Catheter Aspiration	Diver Invatec catheter	---	---	---	---
	Catheter Aspiration	Export Medtronic	---		---	
Yan, 2007	Catheter Aspiration	Diver CE catheter	61	30d	54 (12)	0.60
	Distal Balloon Embolic Protection	GuardWire Plus	61		54 (11)	
Ozaki, 2006	Catheter Aspiration	Rescue or Thrombuster systems	25	180d	52 (12)	>0.05
	Distal Balloon Embolic Protection	PercuSurge GuardWire	24		54 (11)	
		Control	28		50 (8)	

Abbreviations: d=days; EF=ejection fraction; n=number of participants included in the analysis of ejection fraction; SD=standard deviation

Trials versus Control

Catheter aspiration devices in patients with STEMI

Eleven RCTs evaluated the impact of catheter aspiration devices versus control on ejection fraction but were not amenable for statistical pooling therefore results are reported qualitatively (Table 14).[12-14,16,21,67,68,70,82,86,151]

In the first trial the mean left ventricular ejection fraction at baseline did not differ between the two groups (p = 0.60).[12] When baseline mean LVEF values were compared to mean LVEF at 6 months, a greater improvement was noted in the catheter aspiration group compared to control (48 percent ± 6 to 55 percent ± 6 versus 48 percent ± 7 to 49 percent ± 8, P<0.001), respectively. [12] In the second trial there was no significant difference in the left ventricular ejection fraction at 7 days between the catheter aspiration group and control (48 percent ± 12 versus 45 ± 11, p = 0.04).[13] In the third trial a subset of patients with anterior myocardial infarction from the original trial were randomized to evaluate ejection fraction.[14] No difference in the mean ejection fraction was found at 3-5 days post-procedure (46.3 ± 8.6 versus 44.3 ± 9.5, P=0.06) or at 3 months (49.0 ± 9.3 versus 46.7 ± 10.6, P=0.30) between the catheter aspiration

and control groups, respectively.[14] In the fourth trial, patients were only included in the trial if they achieved a TIMI-3 blood flow post-procedure.[151] In this trial, the mean left ventricular ejection fraction was not significantly different at 7 days post-procedure between the catheter aspiration device group and control (50.1 percent ± 8.4 versus 46.5 percent ± 7.9, p = NS). In the fifth trial there was no significant difference in the left ventricular ejection fraction at 5-8 days between the catheter aspiration device group and control (46.7 percent ± 11 versus 42.5 percent ± 10, p = 0.16).[21] In the sixth trial there was no significant difference between the catheter aspiration group and control in mean left ventricular ejection fraction at baseline (51.3 ± 11.9 versus 51.3 ± 11.9, P=0.99) or at 6 months (57.1 ± 12.5 versus 56.7 ± 12.3, p=0.77).[16] In the seventh trial there was no significant difference in the mean left ventricular ejection fraction at 28 days between the catheter aspiration device group and control (56 percent ± 10 versus 57 percent ± 10, p= 0.51).[67] In the eighth trial the mean ejection fraction was reported in a figure and with use of Engauge Digitizier Version 2.0 to read the figure the values for ejection fraction were obtained.[68] There was no significant difference between the catheter aspiration group and control in mean left ventricular ejection fraction immediately post-procedure (37.29 ± 9.97 versus 36.67 ± 3.03, p=NS) and at 6 months (42.97 ± 9.97 versus 41.28 ± 3.37, p=NS).[68] In the ninth trial there was no significant difference in the median left ventricular ejection fraction at 30 days between the catheter aspiration device group and control (51 percent (43-57) versus 53 percent (47-58), p = 0.13). In a substudy of 50 participants from the trial by Burzotta et al. ejection fraction was reported in a figure.[82,83] Enguage Digitizer, Version 2.0 was used to read the figure and obtain values for ejection fraction. Mean ejection fraction was significantly greater in the catheter aspiration group compared to control at 24 hours (50.36 ± 8.76 versus 45.75 ± 7.49, p<0.05), 1 week (53.34 ± 10.99 versus 48.09 ± 9.4, p<0.05), and 6 months (53.28 ± 10.04 versus 47.72 ± 8.28, p<0.05). Mean ejection fraction at 1 week and at 6 months was significantly greater than mean ejection fraction at 24 hours in the catheter aspiration group (p<0.05).[82] In the eleventh trial the mean left ventricular ejection fraction did not differ significantly between the catheter aspiration group and control in-hospital (56.5 percent ± 9.1 versus 52.8 ± 12.8, p= NS) or at 3 months (60.3 ± 9.2 versus 55.3 ± 14.7, p=NS).[86]

No controlled observational studies assessed for this endpoint in this population.

Catheter aspiration devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Table 14. Ejection fraction in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction.

Study, Year	Group	n	Time EF Measured	Mean EF (SD)	P-value
Liistro, 2009	Export Thrombectomy Catheter	55	180d	55 (6)	<0.0001
	Control	56		49 (8)	
Lipiecki, 2009	Export Catheter	20	7d	48 (12)	0.4
	Control	24		45 (11)	
Moura, 2009	TAC	---	---	---	---
	Control	---		---	
Sardella, 2009*	Export Medtronic (EM)	38	3-5d	46.3 (8.6)	0.30
	Control	37		44.3 (9.5)	

Table 14. Ejection fraction in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction.

Study, Year	Group	n	Time EF Measured	Mean EF (SD)	P-value
Sardella, 2009*	Export Medtronic (EM)	36	90d	49.0 (9.3)	0.3
	Control	36		46.7 (10.6)	
Wita, 2009	Catheter Aspiration	Diver CE	19	7d	50.1 (8.4)
		Control	23		46.5 (7.9)
Chao, 2008	Export Aspiration Catheter	37	28d	56 (10)	0.51
	Control	37		57 (10)	
Chevalier, 2008	Export Aspiration Catheter	---	---	---	---
	Control	---		---	
Ciszewski, 2008	Rescue/Diver	32	5-8d	46.7 (11.0)	0.16
	Control	31		42.5 (10.0)	
Dudek, 2008	Diver CE	---	---	---	---
	Control	---		---	
Ikari, 2008	TVAC	103	180d	57.1 (12.5)	0.77
	Control	113		56.7 (12.3)	
Svilaas, 2008	6F Export Aspiration Catheter	---	---	---	---
	Control	---		---	
DeLuca, 2006*	Diver CE	38	Post-PCI	37.29 (9.97)	>0.05
	Control	38		36.67 (3.03)	
DeLuca, 2006*	Diver CE	35	180d	42.97 (9.97)	>0.05
	Control	36		41.28 (3.37)	
Kaltoft, 2006	Rescue Catheter	108	30d	51 (43-57)[†]	0.13
	Control	107		53 (47-58)[†]	
Lee, 2006	Export Aspiration Catheter	---	---	---	---
	Control	---		---	
Silva-Orrego, 2006	Pronto Extraction Catheter	---	---	---	---
	Control	---		---	
Burzotta, 2005*	Diver CE	25	1d	50.36 (8.76)	<0.05
	Control	25		45.75 (7.49)	
Burzotta, 2005*	Diver CE	25	7d	53.34 (10.99)	<0.05
	Control	25		48.09 (9.4)	
Burzotta, 2005*	Diver CE	25	180d	53.28 (10.04)	<0.05
	Control	25		47.72 (8.28)	
Noel, 2005	Export	---	---	---	---
	Control	---		---	
Dudek, 2004*	Rescue	35	In-hospital	56.5 (9.1)	>0.05
	Control	32		52.8 (12.8)	
Dudek, 2004*	Rescue	35	90d	60.3 (9.2)	>0.05
	Control	32		55.3 (14.7)	

*Data from a single study; [†]Median (interquartile range)

Abbreviations: d=days; EF=ejection fraction; n= number of participants included in the analysis of ejection fraction; PCI = percutaneous coronary intervention, SD=standard deviation; TAC= Thrombectomy Aspiration Catheter; TVAC=Transvascular aspiration catheter

Mechanical thrombectomy in patients with STEMI

Two RCTs evaluated the impact of mechanical thrombectomy devices versus control on ejection fraction but were not amenable for statistical pooling therefore results are reported qualitatively (Table 15).[39,43] In the first trial there was no significant difference in ejection fraction at 14 to 28 days post-procedure between the mechanical thrombectomy device group and control (51.3 percent ± 11.53 versus 52.3 ± 10.89, p=0.38).[39] In the second trial the mean ejection fraction significantly improved in the mechanical thrombectomy device group (49.3 percent ± 7.6 to 51.9 percent ±7.9, p = 0.02) and in control (48.8 percent ± 5.9 to 49.9 percent ± 8.9, p = 0.04) from baseline to 30 days.[43] There was no significant difference in ejection fraction between the mechanical thrombectomy device group and control at baseline (p = 0.50) or at 30 days (p = 0.26). Ejection fraction was also measured at discharge and did not differ significantly between the mechanical thrombectomy device group and control (51.0 percent ± 7.7 versus 48.7 percent ± 10.9, p = 0.29).[43]

Mechanical thrombectomy devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Table 15. Ejection fraction in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction.

Study, Year	Group	n	Time EF Measured	Mean EF (SD)	P-value
Migliorini, 2010	AngioJet Rheolytic Thrombectmy Control	--- ---	---	--- ---	---
Ali, 2006	AngioJet Catheter Control	197 205	14-28d	51.3 (11.53) 52.3 (10.89)	0.38
Lefèvre, 2005	X-Sizer Catheter Control	--- ---	---	--- ---	---
Antoniucci, 2004	AngioJet Control	--- ---	---	--- ---	---
Napodano,* 2003	X-Sizer Catheter Control	46 46	In hospital	51.0 (7.7) 48.7 (10.9)	0.29
Napodano, * 2003	X-Sizer Catheter Control	46 46	30d	51.9 (7.9) 49.9 (8.9)	0.26

*Data from a single study

Abbreviations: d=days; EF=ejection fraction; n=number of participants included in the analysis of ejection fraction; SD=standard deviation

Distal filter embolic protection devices in patients with STEMI

Two RCTs evaluated the impact of distal filter embolic protection devices versus control on ejection fraction but were not amenable for statistical pooling therefore results are reported qualitatively (Table 16).[94,97] In the first trial there was no significant difference in ejection fraction measured at 48 to 72 hours post-procedure between the distal filter embolic protection device group and control (47.4 percent ± 9.9 versus 45.3 percent ± 7.3, p=0.29).[94] In the second trial left ventricular ejection fraction measured after the procedure did not differ significantly

between the distal filter embolic protection device group and control (47 percent versus 44 percent, p=0.56).[97]

No controlled observational studies assessed for this endpoint in this population.

Table 16. Ejection fraction in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction.

Study, Year	Group	n	Time EF Measured	Mean EF (SD)	P-value
Kelbæk, 2008	FilterWire-EZ or SpiderX protection device	---	---	---	---
	Control	---		---	
Cura, 2007	SpideRX	70	2-3d	47.4 (9.9)	0.29
	Control	70		45.3 (7.3)	
Guetta, 2007	FilterWire EZ	51	Post PCI	47 (---)	0.56
	Control	49		44 (---)	
Lefèvre, 2004	AngioGuardXP	---	---	---	---
	Control	---		---	

Abbreviations: d=days; EF=ejection fraction; n=number of participants included in the analysis of ejection fraction; PCI=percutaneous coronary intervention; SD=standard deviation

Distal filter embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal filter embolic protection device FilterWire EX versus control on ejection fraction in patients with either NSTEMI or STEMI (Table 17).[125] In this trial, ejection fraction values were reported in a figure, therefore Engauge Digitizer, Version 2.0 was used to read the figure and obtain values for ejection fraction. There was no significant difference in the ejection fraction measured at 3 days post-procedure between the distal filter embolic protection device group and control (47.57 percent ± 10.94 versus 51.22 percent ± 11.75, p = 0.26).

No controlled observational studies assessed for this endpoint in this population.

Table 17. Ejection fraction in randomized controlled trials evaluating thrombectomy or embolic protection devices in patients with mixed acute coronary syndromes.

Study, Year	Device Category	Group	n	Time EF Measured	Mean EF (SD)	P-value
Parikh, 2008	Distal Balloon Embolic Protection	GuardWire	---	---	---	---
		Control	---		---	
Gick, 2005	Distal Filter Embolic Protection	FilterWire	100	3d	47.57 (10.94)	0.26
		Control	100		51.22 (11.75)	
Sardella, 2005	Catheter Aspiration	Diver CE	---	---	---	---
		Control	---		---	
Kunii, 2004	Catheter Aspiration	Rescue PT	---	---	---	---
		Control	---		---	
Nanasato, 2004	Distal Balloon Embolic Protection	GuardWire	34	Post PCI	51.2 (14.5)	0.02
		Control	30		46.7 (12.2)	
Matsushita, 2003	Distal Balloon Embolic Protection	PercuSurge GuardWire	---	---	---	---
		Control	---		---	
Beran, 2002	Mechanical Thrombectomy	X-sizer	---	---	---	---
		Control	---		---	

Abbreviations: d=days; EF=ejection fraction; n=number of participants included in the analysis of ejection fraction; PCI=percutaneous coronary intervention; SD=standard deviation

Distal balloon embolic protection devices in patients with STEMI

Five RCTs evaluated the impact of distal balloon embolic protection devices versus control on ejection fraction but were not amenable for statistical pooling therefore results are reported qualitatively (Table 18).[17,102,106,118,132] In the first trial there was no significant difference in the mean ejection fraction at baseline (52.1 percent ± 9.4 versus 49.0 percent ± 11.2, p = 0.10) or at 6 months (58.1 percent ± 11.4 versus 54.6 percent ± 10.3 p = 0.24) between the distal balloon embolic protection device group and control.[17] The change in left ventricular ejection fraction from baseline to 6 months did not differ significantly between the distal balloon embolic protection device group and control (6.18 percent ± 9.46 versus 5.65 percent ± 8.64, p = 0.83), respectively.[17] In the second trial there was no significant difference in left ventricular ejection fraction at 3 days post-procedure (50 percent ± 9 versus 49 ± 13, p = 0.60) or at 6 months (48 ± 16 versus 50 ± 9, p = 0.74) between the distal balloon embolic protection device group and control.[102] In the third trial there was no significant difference in left ventricular ejection fraction after the procedure (46.1 percent ± 9.5 versus 55.4 percent ± 13.9, p = 0.99) or at 6 months (61.9 percent versus 62.7 percent, p = 0.36) between the distal balloon embolic protection device group and control.[106] In the fourth trial there was no significant difference in left ventricular ejection fraction post-procedure (54.0 percent versus 53.8 percent, p =0.90), at 1 month (55.3 percent versus 55.4 percent, p = NS) or at 6 months (57.1 percent versus 57.1 percent, p = NS) between the distal balloon embolic protection device group and control.[132] In the fifth trial there was no significant difference in mean left ventricular ejection fraction at discharge (47 ± 9 versus 48 ± 8, p = 0.89) between the distal balloon embolic protection device group and control.[118]

No controlled observational studies assessed for this endpoint in this population.

Table 18. Ejection fraction in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction.

Study, Year	Group	n	Time EF Measured	Mean EF (SD)	P-value
Tahk, 2008	PercuSurge GuardWire Control	48 47	180d	58.1 (11.4) 54.6 (10.3)	0.24
Hahn, 2007*	GuardWire Control	19 20	3d	50 (9) 49 (13)	0.60
Hahn, 2007*	GuardWire Control	15 14	180d	48 (16) 50 (9)	0.74
Matsuo, 2007*	GuardWire Distal Protection System Control	80 74	Post-PCI	46.1 (9.5) 55.4 (13.9)	0.99
Matsuo, 2007*	GuardWire Distal Protection System Control	80 74	180d	61.9 (---) 62.7 (---)	0.36
Muramatsu, 2007*	GuardWire Plus System Control	173 168	Post -PCI	54.0 (---) 53.8 (---)	0.90
Muramatsu, 2007*	GuardWire Plus System Control	133 123	30d	55.3 (---) 55.4 (---)	>0.05
Muramatsu, 2007*	GuardWire Plus System Control	108 117	180d	57.1 (---) 57.1 (---)	>0.05
Zhou, 2007	PercuSurge GuardWire Control	--- ---	---	--- ---	---

Table 18. Ejection fraction in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction. (continued)

Study, Year	Group	n	Time EF Measured	Mean EF (SD)	P-value
Okamura, 2005	PercuSurge GuardWire	8	Hospital discharge (mean 22±4 d)	47 (9)	0.89
	Control	8		48 (8)	
Stone, 2005	GuardWire Plus	---	---	---	---
	Control	---		---	

*Data from a single study

Abbreviations: d=days; EF=ejection fraction; n=number of participants included in the analysis of ejection fraction; PCI=percutaneous coronary intervention; SD=standard deviation

Distal balloon embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal balloon embolic protection device Guardwire plus versus control on ejection fraction in patients with acute myocardial infarction (Table 17).[129] The distal balloon embolic protection device group had a significantly higher post procedural mean left ventricular ejection fraction compared to control (51.2±14.5 percent versus 46.7±12.2 percent, p = 0.02).

One RCT evaluated the impact of the distal balloon embolic protection device PercuSurge versus abciximab therapy on ejection fraction in patients with acute myocardial infarction (Table 19).[153] There was no significant difference in median left ventricular ejection fraction upon admission between the distal balloon embolic protection device group and the abciximab group [43 percent (39-45) versus 40 (38-44), p = NS], respectively. Left ventricular ejection fractions increased in both groups at 6 months (46 percent (45-49) versus 46 percent (44-50), p = NS), although the changes were not significantly different between groups.

No controlled observational studies assessed for this endpoint in this population.

Table 19. Ejection fraction in randomized controlled studies with unique comparison in patients with mixed acute coronary syndromes.

Study, Year	Device Category	Group	n	Time EF Measured	Mean EF (SD)	P-value
Ochala, 2007	Distal Balloon Embolic Protection	PercuSurge Guardwire	57	6m	46 (45-49)*	NS
		Abciximab	63		46 (44-50)*	
Kanaya, 2003	Thrombectomy+ Distal Protection Device	Thrombectomy + Stenting + Distal Protection Device	---	---	---	---
		Thrombectomy + Stenting	---		---	

Abbreviations: EF=ejection fraction; m=months; n=number of participants included in the analysis of ejection fraction; NS=not significant; SD=standard deviation

Proximal balloon embolic protection devices

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this endpoint in STEMI or other ACS populations (Table 20).

Table 20. Ejection fraction in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction.

Study, Year	Group	n	Time EF Measured	Mean EF (SD)	P-value
Haeck, 2009	Proxis Control	--- ---	---	--- ---	---

Abbreviations: EF=ejection fraction; n=number of participants included in the analysis of ejection fraction; SD=standard deviation

Embolic protection devices combined

No additional studies evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) aside from those reported in their respective device categories.

Myocardial Blush Grade

Direct Comparative Trials

Catheter aspiration device versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on MBG.[147] The use of Diver-Invatec nonsignificantly decreased the risk of attaining a MBG-3 [RR 0.71 (0.42, 1.18)] compared to Export-Medtronic.

Catheter aspiration device versus distal balloon embolic protection device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the catheter aspiration device Diver CE versus the distal balloon embolic protection device Guardwire Plus on MBG.[149] The use of Diver CE nonsignificantly decreased the risk of attaining a MBG of 2 [RR 0.97 (0.77, 1.23)] compared to Guardwire Plus.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Thirteen RCTs evaluated the impact of catheter aspiration devices versus control on MBG and were included in the pooled analysis.[12-16,19,20,61,68,73,82,85,86] The use of a catheter aspiration device significantly increased the risk of attaining a MBG-3 [RR 1.60 (1.40, 1.84)] (Figure 33). A higher level of statistical heterogeneity was found (I^2 = 57.4 percent) but publication bias was not detected (Egger's P = 0.106). Give the risk difference [RD 0.22 (0.15, 0.28), control rate (0.12, 0.71)], five people would need to receive the catheter aspiration device to cause one person to experience a MBG-3.

When limiting the pooled analysis to trials of only good methodological quality,[12,14-16,61,68,73,82] the risk of attaining a MBG-3 remained significantly increased [RR 1.75 (1.44, 2.14). A higher level of statistical heterogeneity was detected (I^2 = 69.2) and a trend towards publication bias was detected (Egger's P = 0.07). The risk difference for MBG-3 was significantly increased. A high level of statistical heterogeneity was found (I^2 = 67.3 percent) and publication bias was not detected (Egger's P = 0.457). Given the risk difference for attaining a MBG-3 [RD 0.25 (0.16, 0.33), control rate (0.13, 0.71)], four people would need to receive the catheter aspiration device to cause one person to experience a MBG-3.

One RCT evaluated the impact of the catheter aspiration device Diver CE versus control on MBG although was not included in the pooled analysis.[151] In this trial, patients were only included if they attained TIMI-3 blood flow post-procedure, therefore it was not included in the pooled analysis of MBG. The use of a catheter aspiration device nonsignificantly increased the risk of attaining a MBG-3 [RR 1.04 (0.62, 1.69)] compared to control.

No controlled observational studies assessed for this endpoint in this population.

Catheter aspiration devices in other ACS populations

One RCT evaluated the impact of the catheter aspiration device Diver-Invatec versus control on MBG in patients with acute myocardial infarction.[126] The use of a catheter aspiration device significantly increased the risk of attaining a MBG-3 [RR 4.45 (1.51, 13.88] compared to control. Given the risk difference for MBG-3 [RD 0.30 (0.10, 0.51), control rate 0.09], three people would need to be treated with a catheter aspiration device to cause one person to achieve a MBG-3. This trial was determined to be of poor methodological quality.

No controlled observational studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in patients with STEMI

Four RCTs evaluated the impact of mechanical thrombectomy devices versus control on MBG.[11,28,39,43] The use of a mechanical thrombectomy device nonsignificantly increased the risk of attaining a MBG-3 [RR 1.07 (0.80, 1.43)] (Figure 34). A higher level of statistical heterogeneity was found (I^2=76.5 percent) but publication bias was not detected (Egger's P = 0.408). All trials were determined to be of good methodological quality.[11,28,39,43]

No controlled observational studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Distal filter embolic protection devices in patients with STEMI

Two RCTs evaluated the impact of distal filter embolic protection devices versus control on MBG.[94,97] In these trials, the use of distal filter embolic protection devices nonsignificantly decreased the risk of attaining a MBG-3 [RR 0.97 (0.81, 1.15)] (Figure 35). Publication bias

could not be evaluated. Both of the trials were determined to be of good methodological quality.[94,97]

No controlled observational studies assessed for this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in patients with STEMI

Six RCTs evaluated the impact of distal balloon embolic protection devices versus control on MBG.[17,102,106,110,111,132] The use of a distal balloon embolic protection device significantly increased the risk of attaining MBG-3 [RR 1.39 (1.15, 1.69)] (Figure 36). A lower level of statistical heterogeneity was found (I^2 = 43.5 percent) but publication bias was not detected (Egger's P = 0.203). Given the risk difference [RD 0.15 (0.10, 0.24), control rate (0.20, 0.53)], seven people would need to be treated with a distal balloon embolic protection device to cause one person to experience a MBG-3. All of the trials were determined to be of good methodological quality.[17,102,106,110,111,132]

No controlled observational studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in other ACS populations

Two RCTs evaluated the impact of distal balloon embolic protection devices versus control on MBG in patients with acute myocardial infarction.[124,129] The use of a distal balloon embolic protection device significantly increased the risk of attaining a MBG-3 [RR 3.22 (1.03, 10.10)] compared to control (Figure 37). Given the risk difference [RD 0.51 (0.18, 0.84) control rate (0.14, 0.37)], two people would need to be treated with a distal balloon embolic protection device in order to cause one to achieve a MBG-3. Neither trial was determined to be of good methodological quality.[124,129]

One RCT evaluated the impact of the distal balloon embolic protection device PercuSurge versus abciximab therapy on MBG in patients with acute myocardial infarction.[153] The use of a distal balloon embolic protection device nonsignificantly decreased the risk of attaining a MBG-3 [RR 0.94 (0.71, 1.25)] versus abciximab therapy.

No controlled observational studies assessed for this endpoint in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on MBG.[18] The use of a proximal balloon embolic protection device nonsignificantly reduced the risk of attaining MBG-3 [RR 0.98 (0.88, 1.10)]. Limiting the analysis to trials of good methodological quality[18] did not change the results.

No controlled observational studies assessed for this endpoint in this population.

Proximal balloon embolic protection devices in other ACS

No trials or studies assessed for this endpoint in this population.

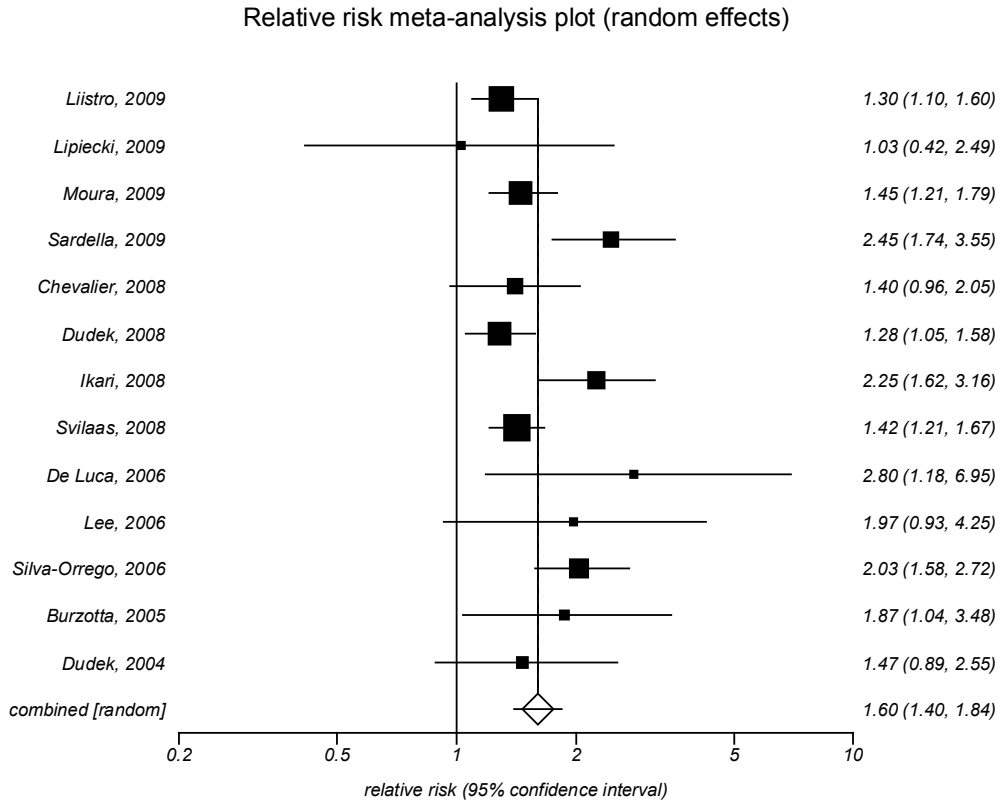
Embolic protection devices combined in patients with STEMI

Nine RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on MBG.[17,18,94,97,102,106,110,111,132] In these trials, the use of embolic protection devices combined significantly increased the risk of attaining a MBG-3 [RR 1.20 (1.02, 1.40)] (Figure 38). A high level of statistical heterogeneity was detected (I^2 = 68.2 percent) but publication bias was not detected (Egger's P = 0.055). Given the risk difference [RD 0.09 (0.02, 0.17), control rate (0.20, 0.82)], eleven people would need to be treated with an embolic protection device to cause one person to achieve a MBG-3. All of the trials were determined to be of good methodological quality.[17,18,94,97,102,106,110,111,132]

Embolic protection devices combined in other ACS populations

No trials or studies were available that evaluated the impact of an embolic protection device versus control on MBG-3 in this patient population in addition to the two trials pooled and reported in the distal balloon embolic protection device section above.

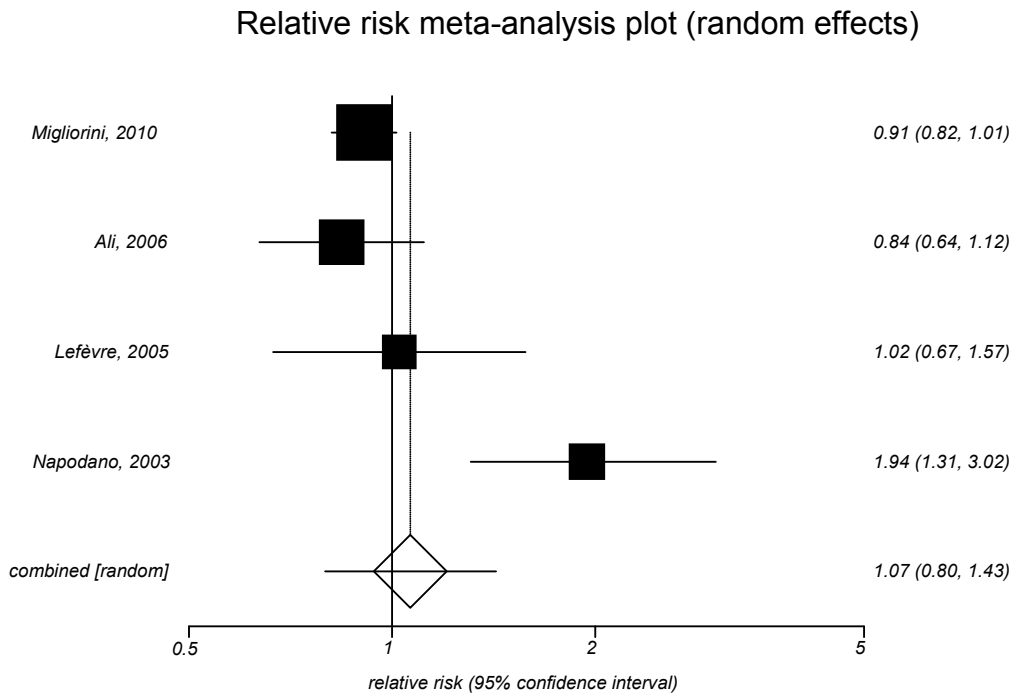
Figure 33. Impact of catheter aspiration devices versus control on myocardial blush grade of 3.



Cochran Q: P = 0.005
I^2: 57.4%
Egger: P = 0.106

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

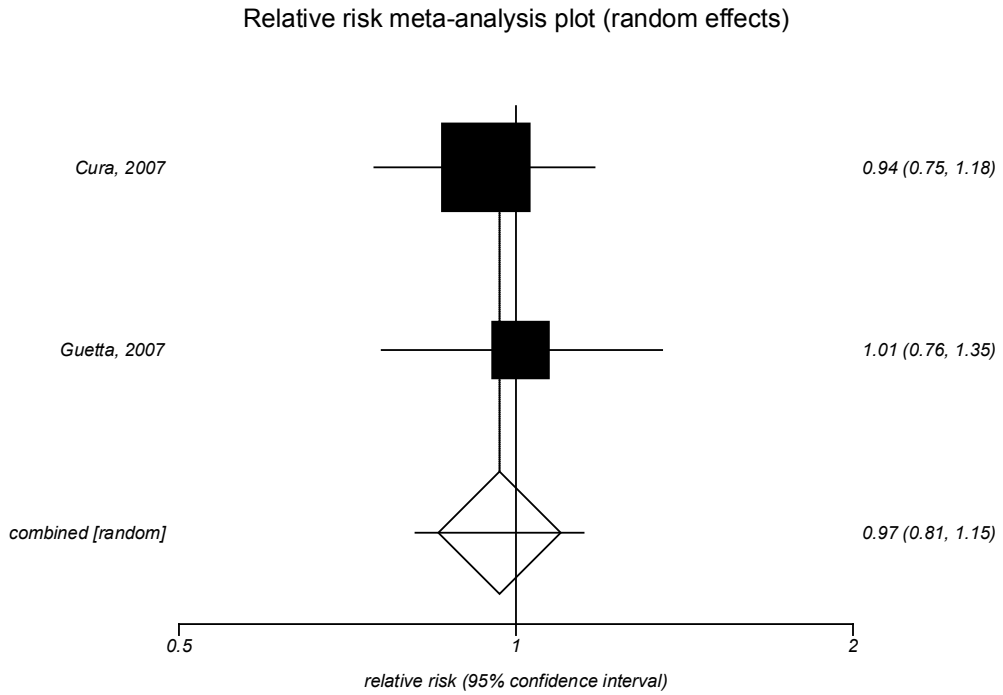
Figure 34. Impact of mechanical thrombectomy devices versus control on myocardial blush grade of 3.



Cochran Q: P = 0.005
I^2: 76.5%
Egger: P = 0.408

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

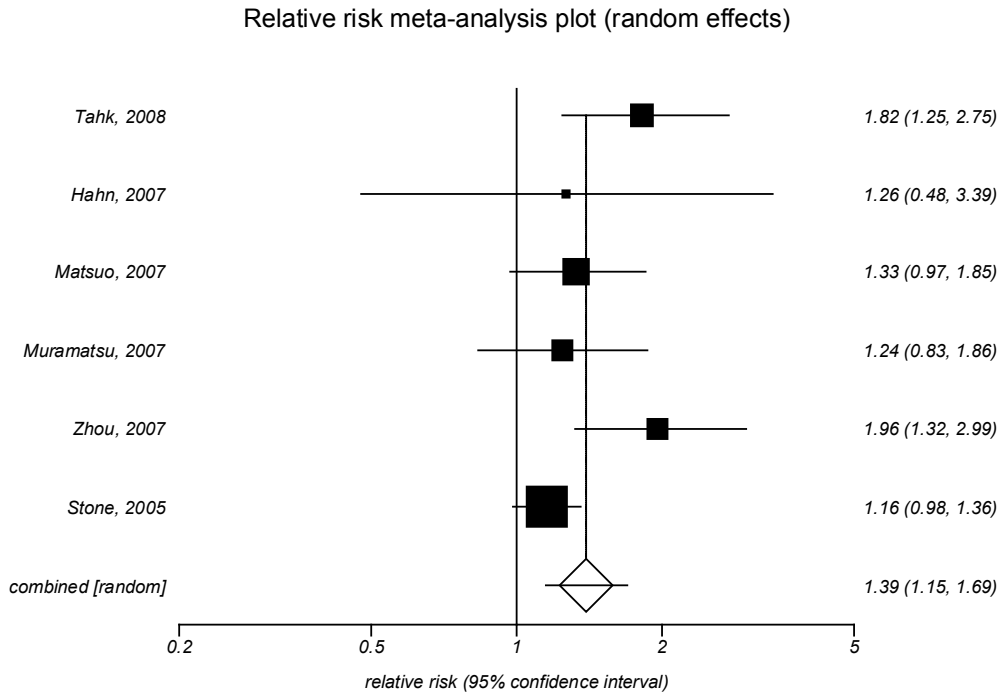
Figure 35. Impact of distal filter embolic protection devices versus control on myocardial blush grade of 3.



Cochran Q: P = 0.692
I^2: Too few strata
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

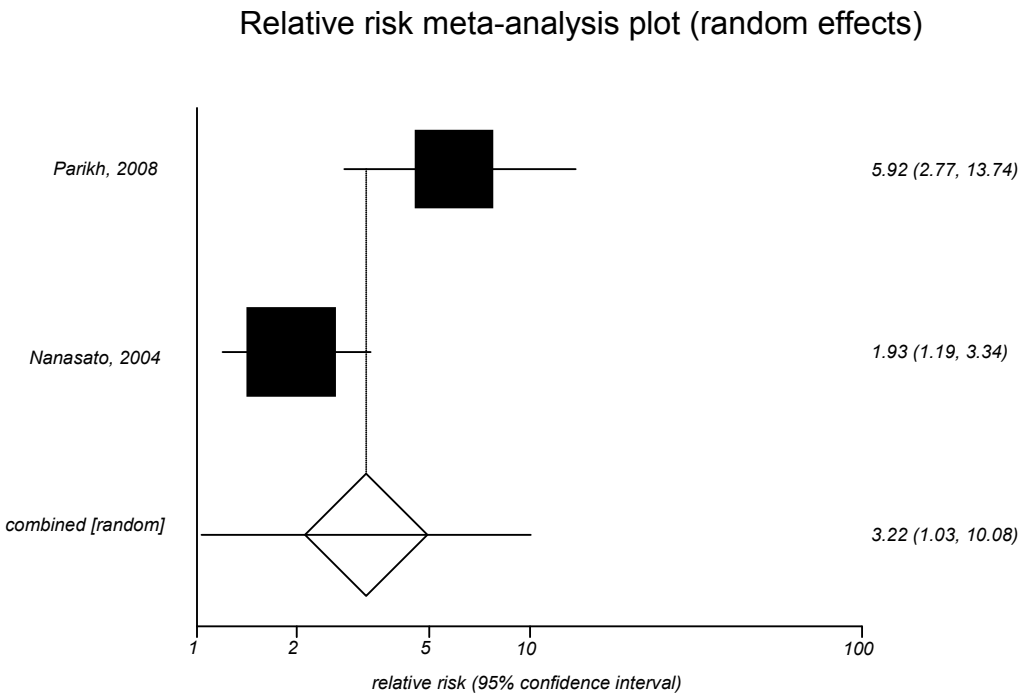
Figure 36. Impact of distal balloon embolic protection devices versus control on myocardial blush grade of 3 in patients with ST-segment elevation myocardial infarction.



Cochran Q: P = 0.115
I^2: 43.5%
Egger: P = 0.203

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

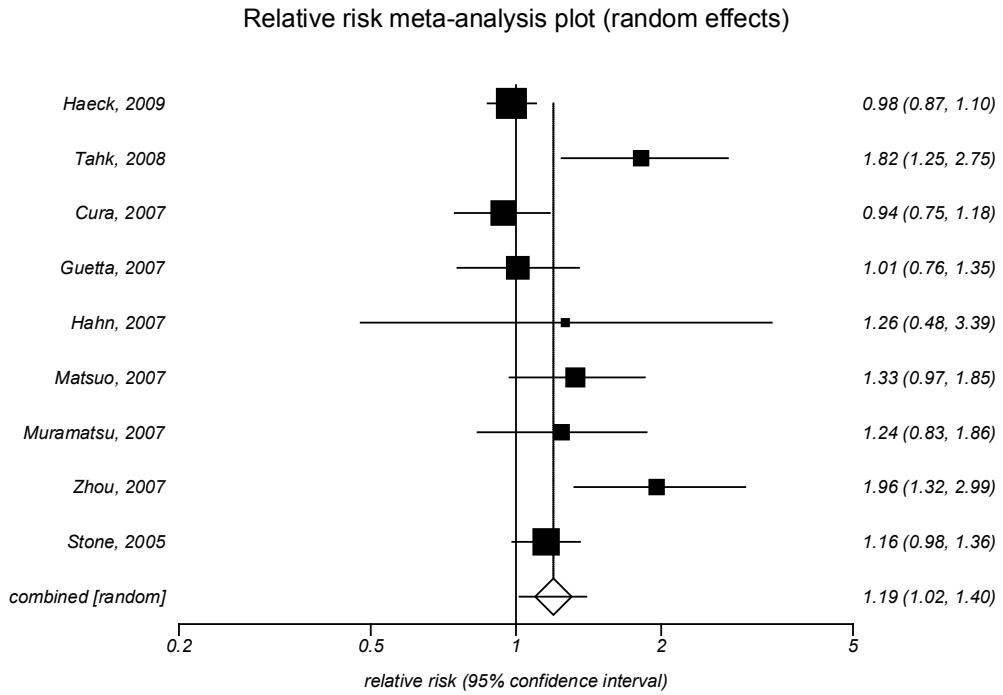
Figure 37. Impact of distal balloon embolic protection devices versus control on myocardial blush grade of 3 in patients with mixed acute coronary syndrome.



Cochran Q: P = 0.020
I^2: Too few strata
Egger: P = To few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 38. Impact of embolic protection devices combined versus control on myocardial blush grade of 3.



Cochran Q: P = 0.002
I^2: 68.2%
Egger: P = 0.055

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

TIMI-3 Blood Flow

Direct Comparative Trials

Catheter aspiration device versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on TIMI-3 blood flow.[147] The use of Diver-Invatec nonsignificantly decreased the risk of attaining TIMI-3 blood flow [RR 0.89 (0.71, 1.10)] compared to Export-Medtronic.

Catheter aspiration device versus distal balloon embolic protection device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the catheter aspiration device Diver CE versus the distal balloon embolic protection device Guardwire Plus on TIMI-3 blood flow.[149] The use of Diver CE nonsignificantly decreased the risk of attaining TIMI-3 blood flow [RR 0.98 (0.89, 1.08)] compared to Guardwire Plus.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Thirteen RCTs evaluated the impact of catheter aspiration devices versus control on TIMI-3 blood flow.[12-16,19,61,68,70,73,82,84,86] The use of a catheter aspiration device significantly increased the risk of attaining TIMI-3 blood flow [RR 1.07 (1.03, 1.11)] (Figure 39). A lower level of statistical heterogeneity was found (I^2 = 11.4 percent) but no publication bias was detected (Egger's P = 0.593). Given the risk difference [RD 0.06 (0.03, 0.10), control rate (0.68, 0.88)], 17 people would need to be treated with a catheter aspiration device to cause one person to achieve TIMI-3 blood flow.

Limiting the pooled analyses to trials of good methodological quality still resulted in a significantly increased risk of attaining TIMI-3 blood flow [RR 1.07 (1.04, 1.11)]. A lower level of statistical heterogeneity was found (I^2 = 0 percent). Given the risk difference [RD 0.06 (0.03, 0.10), control rate (0.68, 0.88)], 17 people would need to be treated with a catheter aspiration device to cause one person to achieve TIMI-3 blood flow.[12,14-16,61,68,70,73,82]

No controlled observational studies assessed for this endpoint in this population.

Catheter Aspiration Devices in other ACS populations

Two RCTs evaluated the impact of catheter aspiration devices versus control on TIMI-3 blood flow in patients with acute myocardial infarction.[126,127] The use of a catheter aspiration device nonsignificantly increased the risk of attaining TIMI-3 blood flow [RR 1.15 (0.82, 1.62)] compared to contro[126,127] (Figure 40). Both trials were determined to be of poor methodological quality.

No controlled observational studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in patients with STEMI

Four RCTs evaluated the impact of mechanical thrombectomy devices versus control on TIMI-3 blood flow.[11,28,39,43] The use of a mechanical thrombectomy device nonsignificantly decreased the risk of attaining TIMI-3 blood flow [RR 0.98 (0.92, 1.04)] (Figure 41). A high level of statistical heterogeneity was found (I^2=67.5 percent) but publication bias was not detected (Egger's P = 0.464). All of the trials were determined to be of good methodological quality.[11,28,39,43]

One controlled observational study evaluated the association between the use of a mechanical thrombectomy device and TIMI-3 blood flow.[134] Patients undergoing PCI with a mechanical thrombectomy device, either the AngioJet XMI or XVG catheter, were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a significantly lower rate of TIMI-3 blood flow compared to PCI without a mechanical thrombectomy device (86 percent versus 90 percent, p = 0.04).

Mechanical Thrombectomy Devices in other ACS populations

One RCT evaluated the impact of the mechanical thrombectomy device X-Sizer versus control on TIMI-3 blood flow in patients with STEMI or UA.[155] The use of a mechanical thrombectomy device nonsignificantly increased the risk of attaining TIMI-3 blood flow [RR 1.07 (0.86, 1.36)] compared to control. This trial was determined to be of good methodological quality.

One controlled observational study evaluated the association between the use of mechanical thrombectomy devices and TIMI-3 blood flow.[142] The types of ACSs included in this study were not reported. Patients undergoing PCI with the mechanical thrombectomy device AngioJet were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a significantly lower rate of TIMI-3 blood flow compared to PCI without a mechanical thrombectomy device (85 percent versus 93 percent, p = 0.0003). However, there were significantly more patients with TIMI-3 blood flow in the mechanical thrombectomy device group at baseline compared to the group without mechanical thrombectomy (15 percent versus 27 percent, p = 0.0001).

Distal Filter Embolic Protection Devices in patients with STEMI

Four RCTs evaluated the impact of distal filter embolic protection devices versus control on TIMI-3 blood flow.[88,92,97,100] In these trials, the use of distal filter embolic protection devices nonsignificantly decreased the risk of attaining TIMI-3 blood flow [RR 0.98 (0.88, 1.10)] (Figure 42). A higher level of statistical heterogeneity was detected (I^2 = 76.4 percent) and publication bias was detected (Egger's P = 0.005).

When limiting the pooled analysis to only trials of good methodological quality,[88,94,97] the risk of attaining TIMI-3 blood flow remained nonsignificantly decreased in the distal filter embolic protection device group versus control [RR 0.996 (0.87, 1.15)]. A higher level of statistical heterogeneity was detected (I^2 = 79.5 percent).

No controlled observational studies assessed for this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

Three RCTs evaluated the impact of distal filter embolic protection devices versus control in patients with other ACSs on TIMI-3 blood flow although were not suitable for pooling because each trial evaluated a different ACS.[125,144,145] In the first trial, the FilterWire EZ device was compared to control in patients with NSTEMI.[144] The use of a distal filter embolic protection device nonsignificantly decreased the risk of attaining TIMI-3 blood flow [RR 0.99 (0.90, 1.09)]. In the second trial the Angioguard device was compared to control in patients with UA.[145] The risk of attaining TIMI-3 blood flow could not be calculated because all patients in both groups attained TIMI-3 blood flow after the procedure. In the third trial, the FilterWire EX was compared to control in patients with either NSTEMI or STEMI.[125] The risk of attaining TIMI-3 blood flow was not different between the distal filter embolic protection device group and control [RR 1.00 (0.92, 1.09)]. Of the three trials, this one trial was determined to be of good methodological quality.

No controlled observational studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in patients with STEMI

Seven RCTs evaluated the impact of distal balloon embolic protection devices versus control on TIMI-3.[17,102,106,110,111,118,132] One study was excluded from the pooled analysis of relative risk because all patients in both groups achieved TIMI-3 blood flow with the same number of participants in each group.[118] In the six trials eligible for pooling, the use of a distal balloon embolic protection device nonsignificantly increased the risk of attaining TIMI-3 blood flow [RR 1.07 (1.00, 1.16)][17,102,106,110,111,132] (Figure 43). A higher level of statistical heterogeneity was found (I^2=56.1 percent) but publication bias was not detected (Egger's P = 0.355). All of the trials were determined to be of good methodological quality.[17,102,106,110,111,132]

No controlled observational studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in other ACS populations

Two RCTs evaluated the impact of distal balloon embolic protection devices versus control on TIMI-3 blood flow in patients with acute myocardial infarction.[124,129] The use of a distal balloon embolic protection device nonsignificantly increased the risk of attaining TIMI-3 blood flow [RR 1.36 (0.65, 2.86)] compared to control (Figure 44). Neither trial was determined to be of good methodological quality.

One RCT evaluated the impact of the distal balloon embolic protection device PercuSurge versus abciximab therapy on TIMI-3 blood flow in patients with acute myocardial infarction.[153] The use of a distal balloon embolic protection device nonsignificantly increased the risk of attaining TIMI-3 blood flow [RR 1.01 (0.87, 1.15)] versus abciximab therapy.

No controlled observational studies assessed for this endpoint in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on TIMI-3 blood flow.[18] The use of a proximal balloon embolic protection device nonsignificantly increased the risk of attaining TIMI-3 blood flow [RR 1.06 (0.98, 1.16)]. This trial was determined to be of good methodological quality.[18]

Proximal balloon embolic protection devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Embolic protection devices combined in patients with STEMI

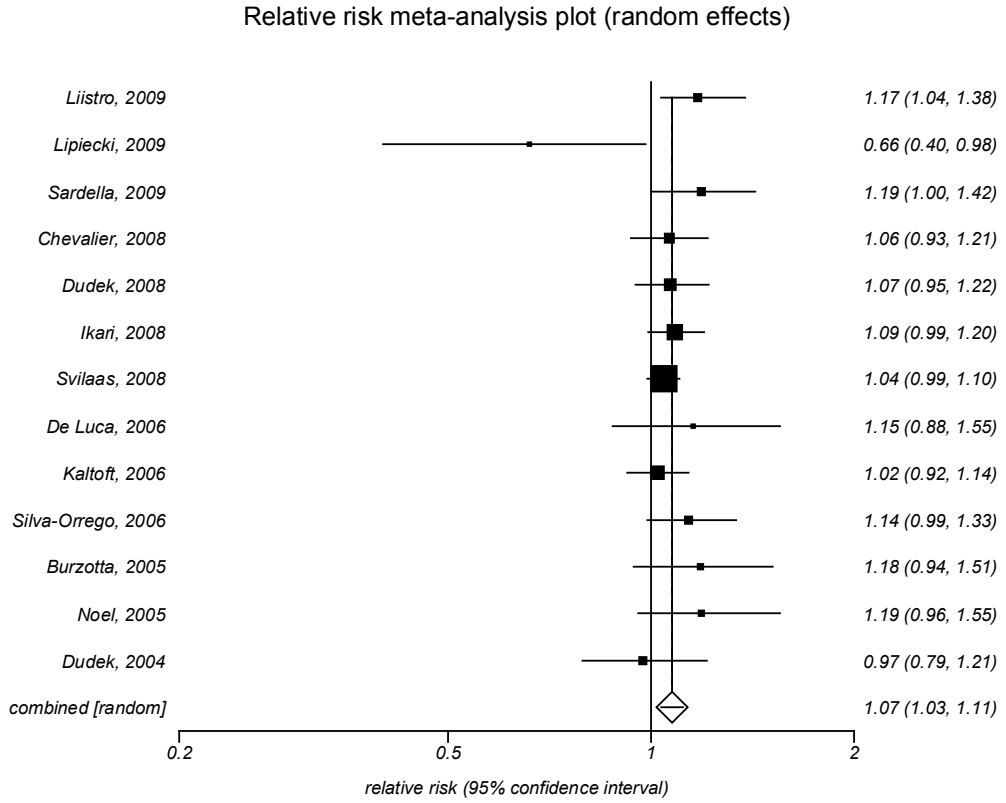
Twelve RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on TIMI-3 blood flow.[17,18,88,94,97,100,102,106,110,111,118,132] The trial by Okamura et al was excluded from the pooled analysis of relative risk because no events occurred within the prespecified time period in either control or treatment group. In the trials 11 suitable for pooling, the use of embolic protection devices combined nonsignificantly increased the risk of attaining TIMI-3 blood flow [RR 1.04 (0.99, 1.10)] (Figure 45). A high level of statistical heterogeneity was detected (I^2 = 58.6 percent) but publication bias was not detected (Egger's P = 0.458).

When the pooled analysis was limited to only trials of good methodological quality,[17,18,88,94,97,102,106,110,111,132] the risk of attaining TIMI-3 blood flow remained nonsignificantly increased in the combined embolic protection device group compared to control [RR 1.05 (1.00, 1.11)]. A higher level of statistical heterogeneity was detected (I^2 = 57.5 percent).

Embolic protection devices combined in other ACS populations

Three RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control in patients with mixed ACS (acute myocardial infarction, not otherwise specified) on attaining TIMI-3 blood flow.[124,125,129] The use of an embolic protection device nonsignificantly increased the risk of attaining TIMI-3 blood flow versus control [RR 1.15 (0.93, 1.41)] (Figure 46). One trial was determined to be of higher methodological quality[125] therefore sensitivity analysis was not possible based on trial quality.

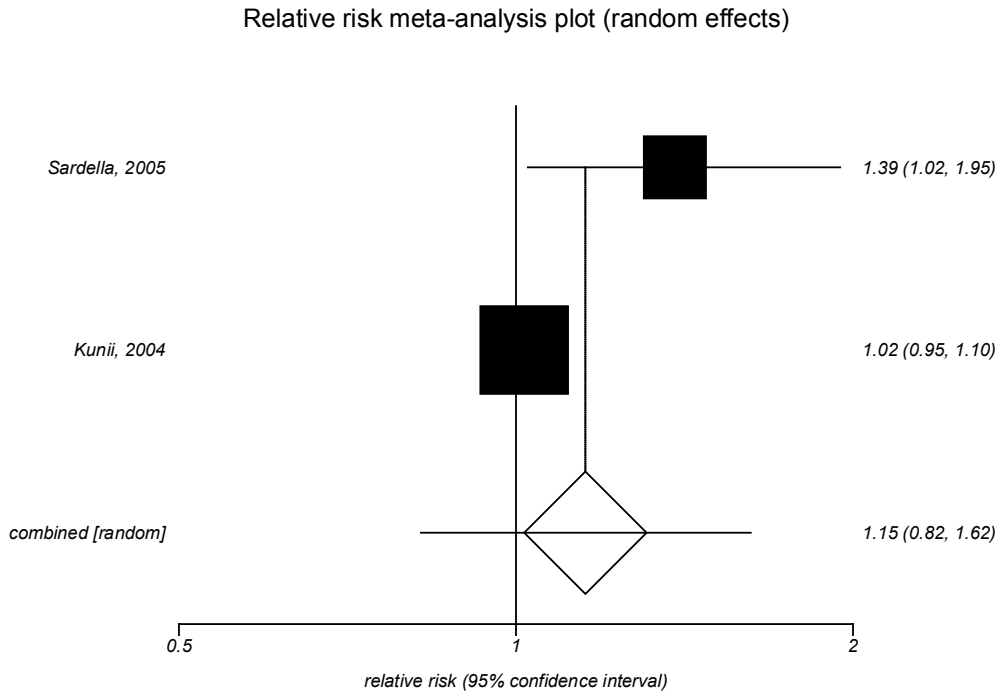
Figure 39. Impact of catheter aspiration devices versus control on TIMI-3 blood flow in patients with ST-segment elevation myocardial infarction.



Cochran Q: P = 0.331
I^2: 11.4%
Egger: P = 0.593

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

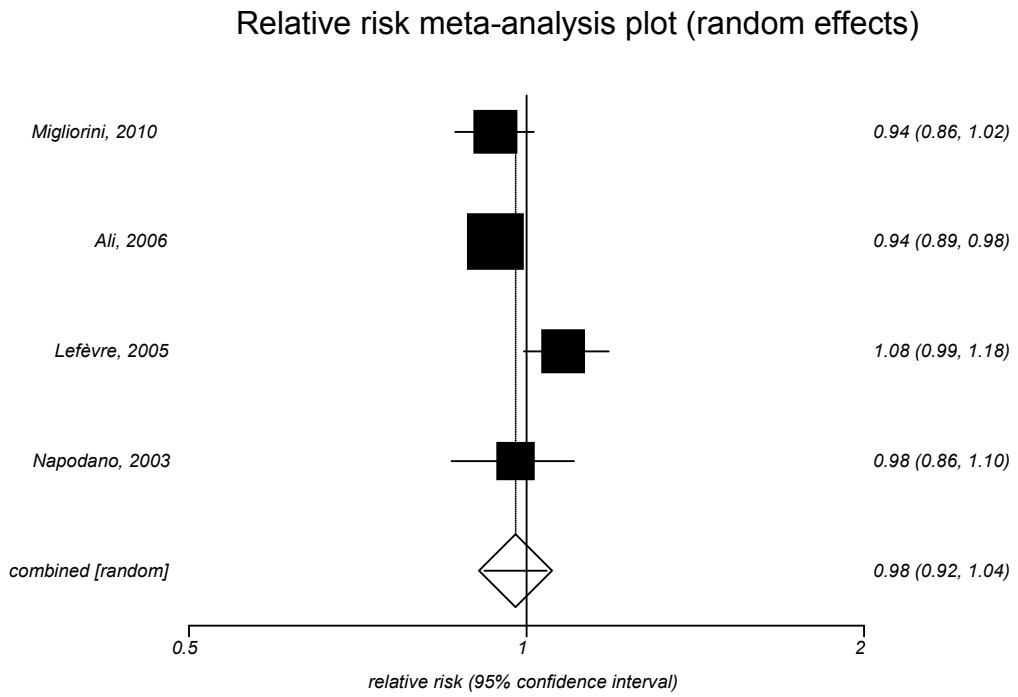
Figure 40. Impact of catheter aspiration devices versus control on TIMI-3 blood flow in patients with mixed acute coronary syndrome.



Cochran Q: P = 0.027
I^2: Too few strata
Egger: P = Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

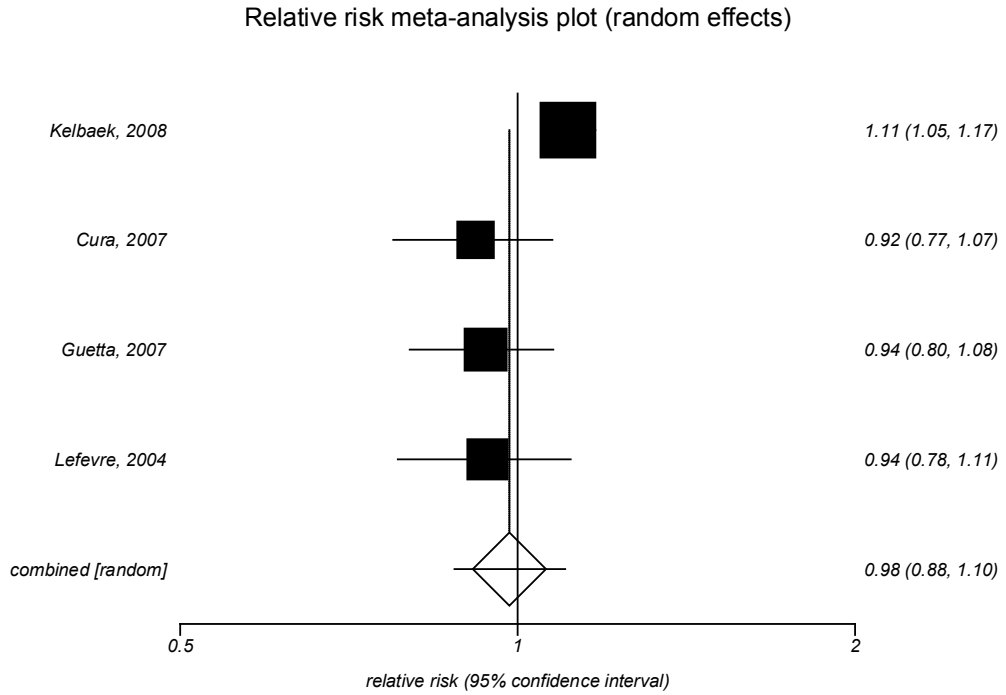
Figure 41. Impact of mechanical thrombectomy devices versus control on TIMI- 3 blood flow.



Cochran Q: P = 0.026
I^2: 67.5%
Egger: P = 0.464

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

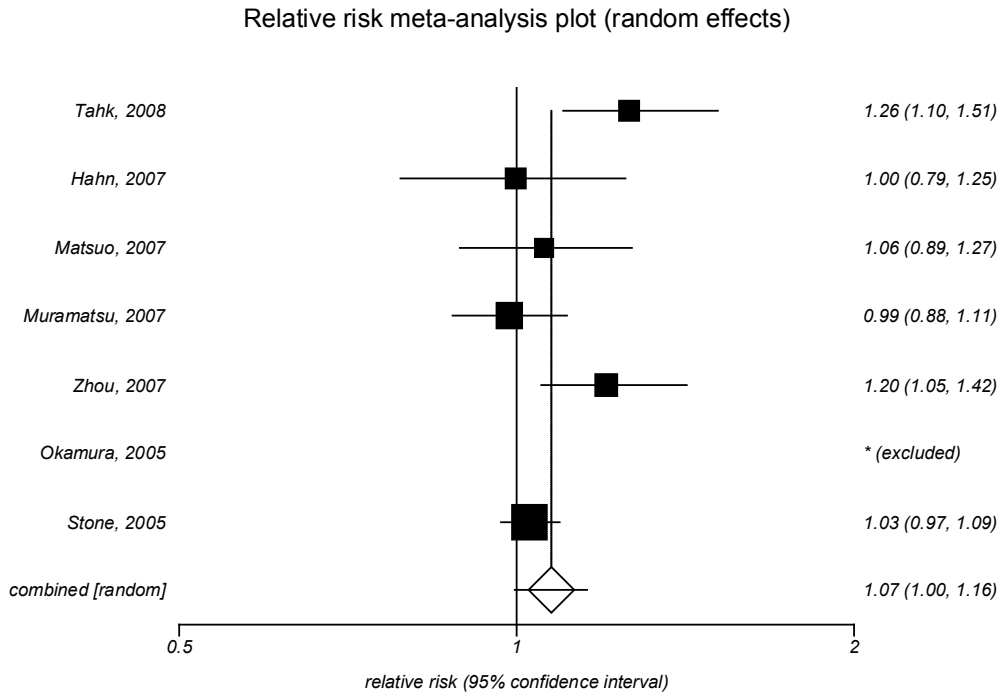
Figure 42. Impact of distal filter embolic protection devices versus control on TIMI-3 blood flow.



Cochran Q: P = 0.005
I^2: 76.4%
Egger: P = 0.005

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

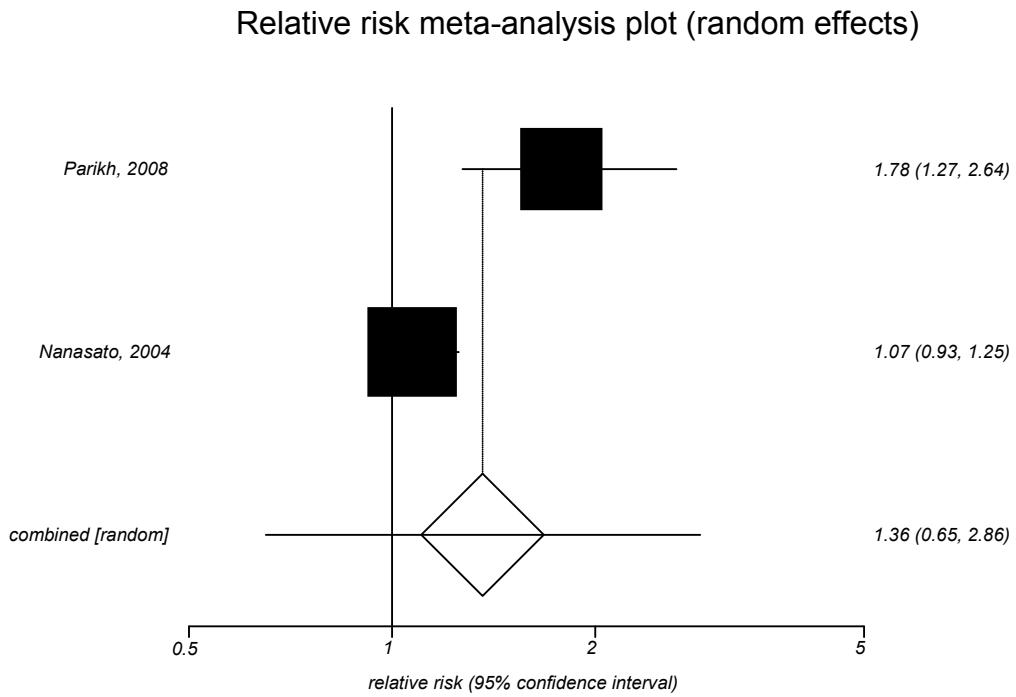
Figure 43. Impact of distal balloon embolic protection devices versus control on TIMI- 3 blood flow in patients with ST-segment elevation myocardial infarction.



Cochran Q: P = 0.044
I^2: 56.1%
Egger: P = 0.355

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 44. Impact of distal balloon embolic protection devices versus control on TIMI- 3 blood flow in patients with mixed acute coronary syndrome.



Cochran Q: P <0.0001
I^2: Too few strata
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

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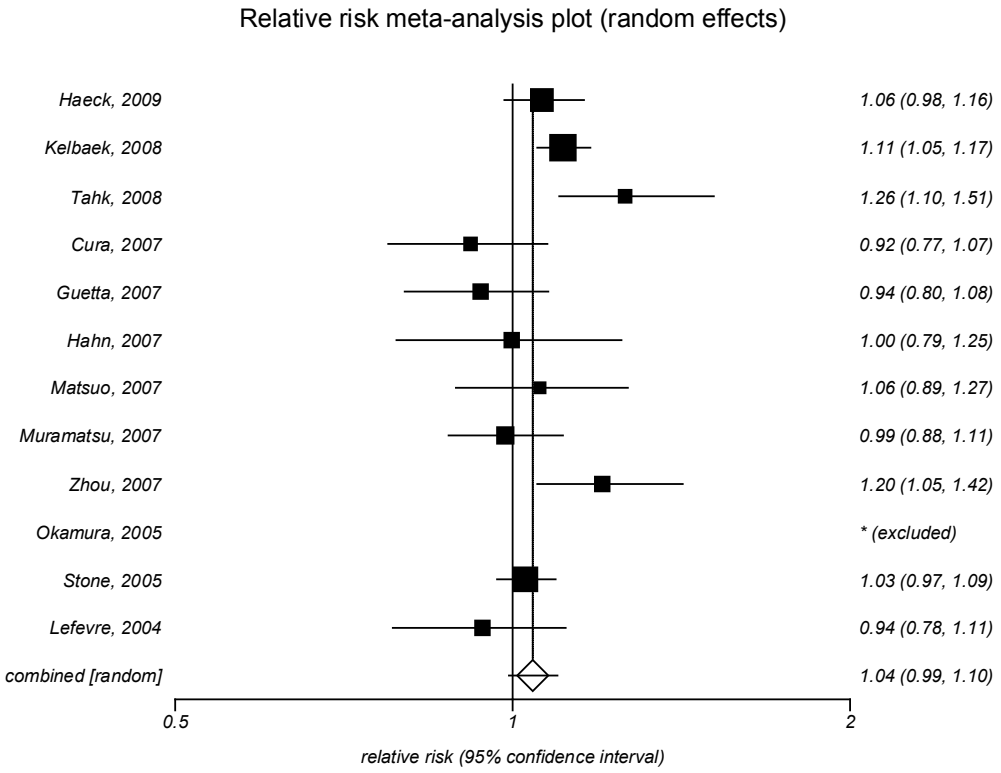
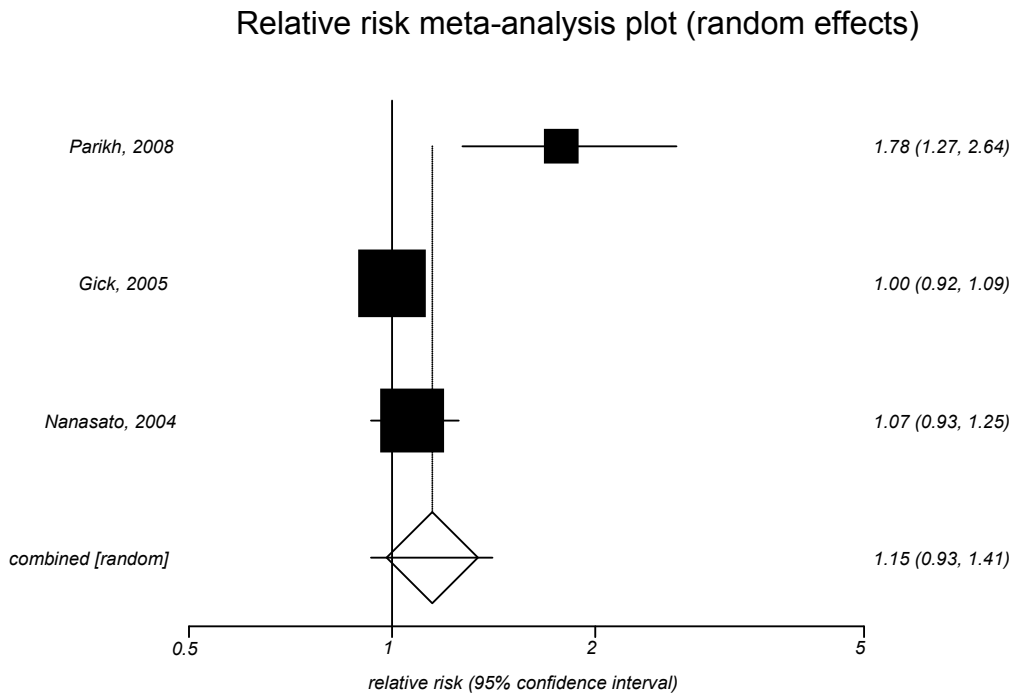
Figure 45. Impact of embolic protection devices combined versus control on TIMI-3 blood flow in patients with ST-segment elevation myocardial infarction.



Cochran Q: P = 0.007
I^2: 58.6%
Egger: P = 0.476

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 46. Impact of embolic protection devices combined versus control on TIMI-3 blood flow in patients with mixed acute coronary syndrome.



Cochran Q: P = 0.001
I²: 85.5%
Egger: P = Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

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Distal Embolization

Direct Comparative Trials

No direct comparative trials evaluated the impact of catheter aspiration, mechanical thrombectomy or embolic protection devices on this endpoint.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Ten RCTs evaluated the impact of catheter aspiration devices versus control on distal embolization.[12-16,19,70,73,82,85] The use of a catheter aspiration device significantly decreased the risk of distal embolization [RR 0.55 (0.39, 0.78)] (Figure 47). A lower level of statistical heterogeneity was found (I^2 = 42.5 percent) but no publication bias was detected (Egger's P = 0.166). Given the risk difference [RD -0.10 (-0.17, -0.10), control rate (0.03, 0.66)], 10 people would need to be treated with a catheter aspiration device to prevent one person from experiencing distal embolization.

When limiting the pooled analysis to only trials of good methodological quality, [12,14-16,70,73,82] the risk of distal embolization remained significantly decreased in the catheter aspiration device group compared to control [RR 0.48 (0.34, 0.66)]. A lower level of statistical heterogeneity was detected (I^2 = 33.7 percent). Given the risk difference [RD -0.14 (-0.23, -0.04), control rate (0.06, 0.66)], seven people would need to be treated with a catheter aspiration device to prevent one person from experiencing distal embolization.

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and distal embolization.[141]. The catheter aspiration devices included in this study were not reported. The use of a catheter aspiration device was associated with a significantly higher rate of distal embolization (9.0 percent versus 3.2 percent, p<0.0001).

Catheter aspiration devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in patients with STEMI

Three RCTs evaluated the impact of mechanical thrombectomy devices versus control on distal embolization.[28,39,43] The use of a mechanical thrombectomy device nonsignificantly decreased the risk of distal embolization [RR 0.44 (0.17, 1.12)] (Figure 48). A lower level of statistical heterogeneity was found (I^2 = 41.6 percent) and publication bias could not be evaluated. All of the trials were determined to be of good methodological quality. [28,39,43]

No controlled observational studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Distal filter embolic protection devices in patients with STEMI

One RCT evaluated the impact of a distal filter embolic protection device versus control on distal embolization.[94] In this trial, the use of a distal filter embolic protection device nonsignificantly decreased the risk of distal embolization [RR 0.63 (0.22, 1.73)]. This trial was determined to be of good quality.[94]

No controlled observational studies assessed for this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal filter embolic protection device FilterWire EX versus control on distal embolization in patients with either NSTEMI or STEMI.[125] The use of a distal filter embolic protection device nonsignificantly decreased the risk of distal embolization [RR 0.38 (0.11, 1.26)] compared to control. This trial was determined to be of good methodological quality.

No controlled observational studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal balloon embolic protection devices versus control on distal embolization.[102,106,111,132] The use of a distal balloon embolic protection device nonsignificantly increased the risk of distal embolization [RR 1.10 (0.67, 1.81)] (Figure 49). A lower level of statistical heterogeneity was found (I^2 = 5.8 percent) and publication bias was not detected (Egger's P = 0.176). All of the trials were determined to be of good methodological quality[102,106,111,132] did not change the results.

No controlled observational studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of the proximal balloon embolic protection device Proxis versus control on distal embolization.[18] The use of a proximal balloon embolic protection device nonsignificantly reduced the risk of having distal embolization [RR 0.71 (0.37, 1.35)]. This single trial was determined to be of good quality.[18]

No controlled observational studies assessed for this endpoint in this population.

Proximal balloon embolic protection devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

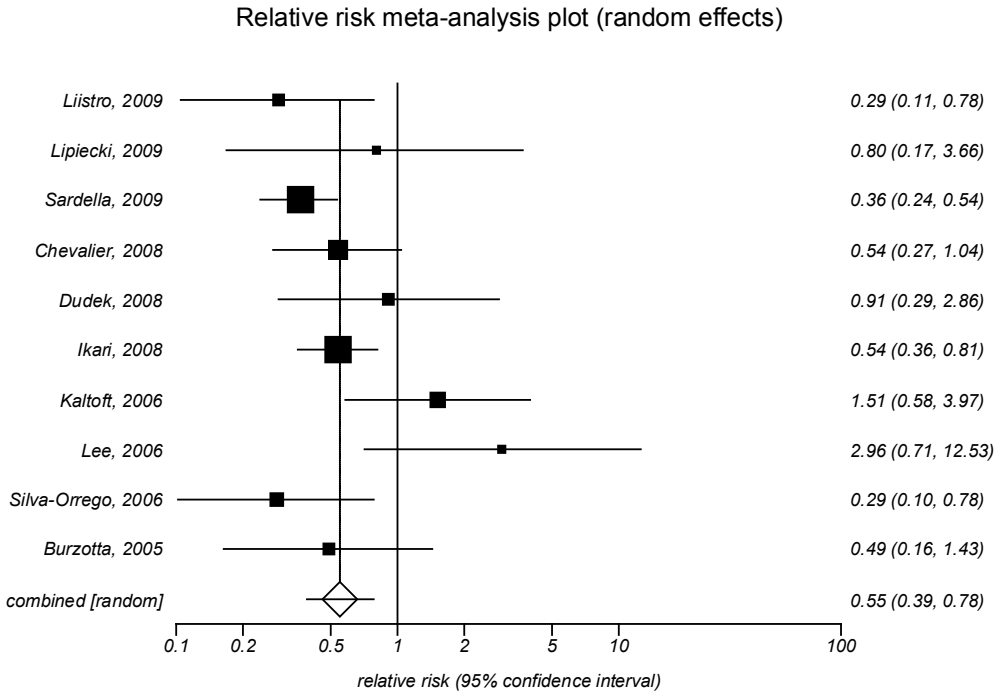
Embolic protection devices combined in patients with STEMI

Six RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on distal embolization.[18,94,102,106,111,132] In these trials, the use of embolic protection devices combined nonsignificantly decreased the risk of distal embolization [RR 0.91 (0.64, 1.30)] (Figure 50). A low level of statistical heterogeneity was detected (I^2 = 0.2 percent) but publication bias was not detected (Egger's P = 0.409). All of the trials were determined to be of good methodological quality.[18,94,102,106,111,132]

Embolic protection devices combined in other ACS populations

No trials or studies were available that evaluated the impact of any embolic protection device versus control on distal embolization in addition to the one trial reported above, and therefore pooling was not possible.

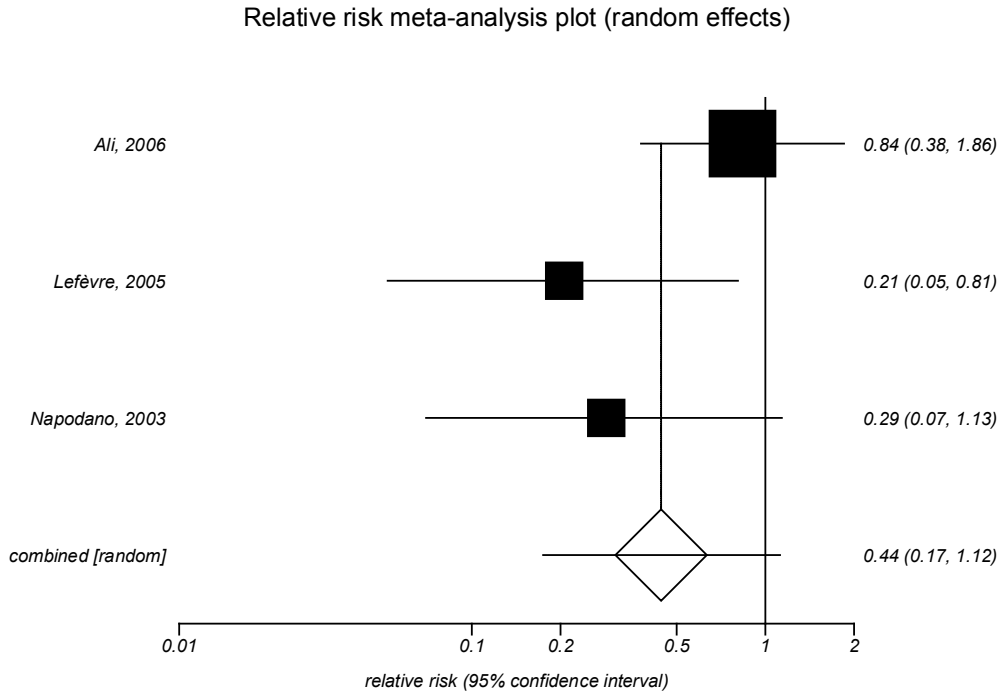
Figure 47. Impact of catheter aspiration devices versus control on distal embolization.



Cochran Q: P = 0.075
I^2: 42.5%
Egger: P = 0.166

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

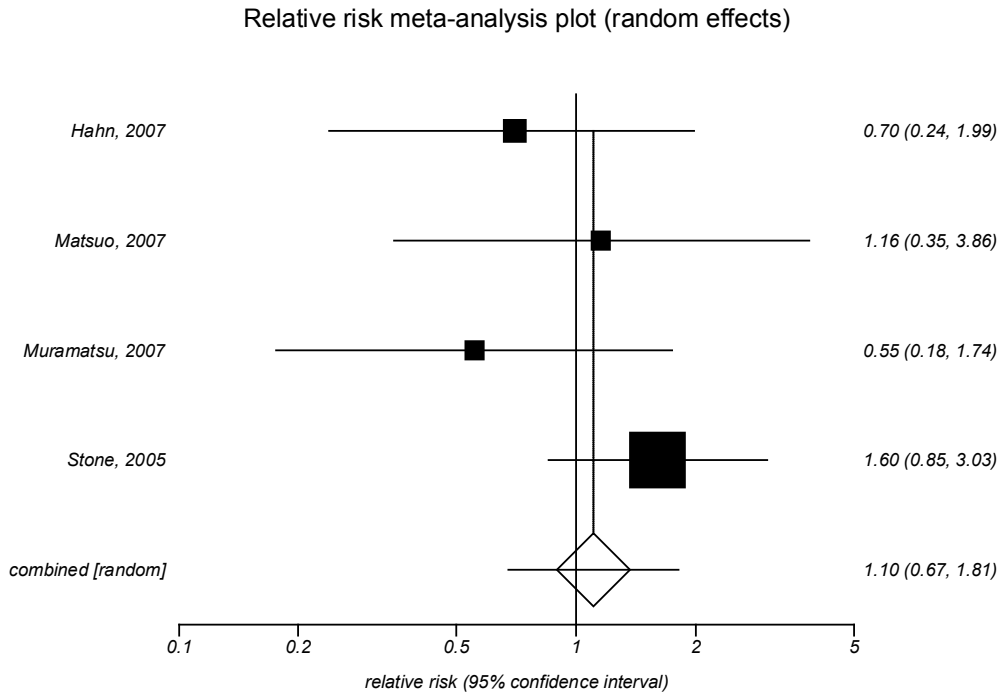
Figure 48. Impact of mechanical thrombectomy devices versus control on distal embolization.



Cochran: P = 0.181
I^2: 41.6%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

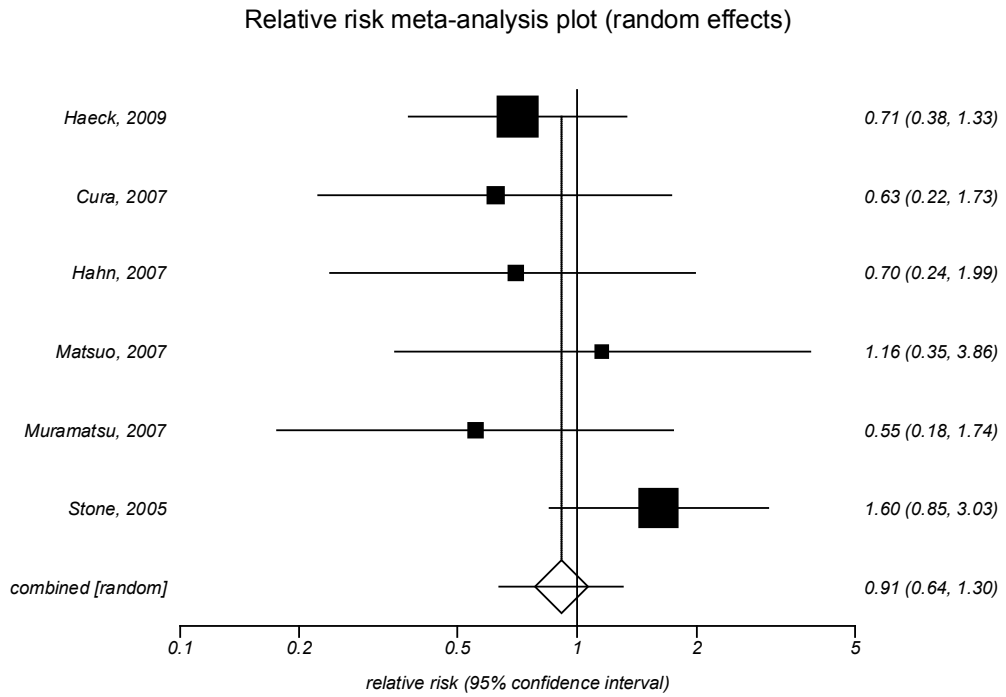
Figure 49. Impact of distal balloon embolic protection devices versus control on distal embolization.



Cochran Q: P = 0.364
I^2: 5.8%
Egger: P = 0.176

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 50. Impact of embolic protection devices combined versus control on distal embolization.



Cochran Q: P = 0.415
I²: 0.2%
Egger: P = 0.409

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

No Reflow

Direct Comparative Trials

Catheter aspiration device versus distal balloon protection device in STEMI

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on no reflow.[149] In this study, a composite of no reflow / slow reflow was reported. The use of Diver CE nonsignificantly increased the risk of no reflow / slow reflow [RR 1.25 (0.38, 4.14)] compared to Guardwire Plus.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Seven RCTs evaluated the impact of catheter aspiration devices versus control on no reflow.[12,15,16,73,82,84,85] The use of a catheter aspiration device significantly decreased the risk of no reflow [RR 0.48 (0.29, 0.79)] (Figure 51). A low level of statistical heterogeneity was found

(I^2 = 27.4 percent) but no publication bias was detected (Egger's P = 0.332). Given the risk difference [RD -0.10 (-0.12, -0.02), control rate (0.05, 0.27)], ten people would need to be treated with a catheter aspiration device in order to prevent one no reflow event from occurring.

When limiting the pooled analysis to only trials of good methodological quality,[15,16,47,73,82] the risk of having no reflow remained significantly decreased in the catheter aspiration device group compared to control [RR 0.45 (0.27, 0.75)]. A lower level of statistical heterogeneity was detected (I^2 = 22.3 percent). Given the risk difference [RD -0.08 (-0.12, -0.05), control rate (0.10, 0.19)], thirteen people would have to be treated with a catheter aspiration device to prevent one no reflow event from occurring.

No controlled observational studies assessed for this endpoint in this population.

Catheter aspiration devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in patients with STEMI

Three RCTs evaluated the impact of mechanical thrombectomy devices versus control on no reflow.[28,39,43] The use of a mechanical thrombectomy device nonsignificantly decreased the risk of no reflow [RR 0.50 (0.17, 1.48)] (Figure 52). A lower level of statistical heterogeneity was found (I^2=41.7 percent). All of the trials were determined to be of good methodological quality.[28,39,43]

No controlled observational studies assessed for this endpoint in this population.

Mechanical thrombectomy devices in other ACS populations

No controlled observational studies assessed for this endpoint in this population.

Distal filter embolic protection devices in patients with STEMI

Two RCTs evaluated the impact of distal filter embolic protection devices versus control on no reflow.[94,100] In these trials, the use of distal filter embolic protection devices nonsignificantly decreased the risk of having no reflow [RR 0.59 (0.14, 2.51)] (Figure 53). Only one of these trials were determined to be of good methodological quality.[94] In that trial there was no difference in the risk of no reflow with the use of a distal filter embolic protection device versus control [RR 1.00 (0.18, 5.55)].

No controlled observational studies assessed for this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

One RCT evaluated the impact of distal filter embolic protection devices on no reflow[145] in patients with NSTEMI or UA. In this trial, the Angioguard device was compared to control. The risk of no reflow could not be calculated because no events occurred in either group.

No controlled observational studies assessed for this endpoint in this population.

Distal balloon embolic protection devices in patients with STEMI

Four RCTs evaluated the impact of distal balloon embolic protection devices versus control on no reflow.[102,106,109,111] The use of a distal balloon embolic protection device nonsignificantly decreased the risk of no reflow [RR 0.51 (0.19, 1.33)] (Figure 54). Statistical heterogeneity and publication bias were not detected ($I^2 = 0$ percent, Egger's P = 0.880). All of the trials were determined to be of good methodological quality.[102,106,109,111]

Distal balloon embolic protection devices in other ACS populations

One RCT evaluated the impact of the distal balloon embolic protection device PercuSurge GuardWire Plus Temporary Occlusion and Aspiration System versus control on no reflow in patients with acute myocardial infarction.[124] The use of a distal balloon embolic protection device significantly decreased the risk of no reflow compared to control [RR 0.36 (0.20, 0.59)]. Given the risk difference for no reflow [RD -0.54 (-0.71, -0.31), control rate (0.02, 0.05)], two people would need to be treated with a distal balloon embolic protection device to prevent one person from experiencing no reflow. This trial was determined to be of good methodological quality.

No controlled observational studies assessed for this endpoint in this population.

Proximal balloon embolic protection devices in patients with STEMI

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this endpoint.

Proximal balloon embolic protection devices in other ACS populations

No trials or studies assessed for this endpoint in this population.

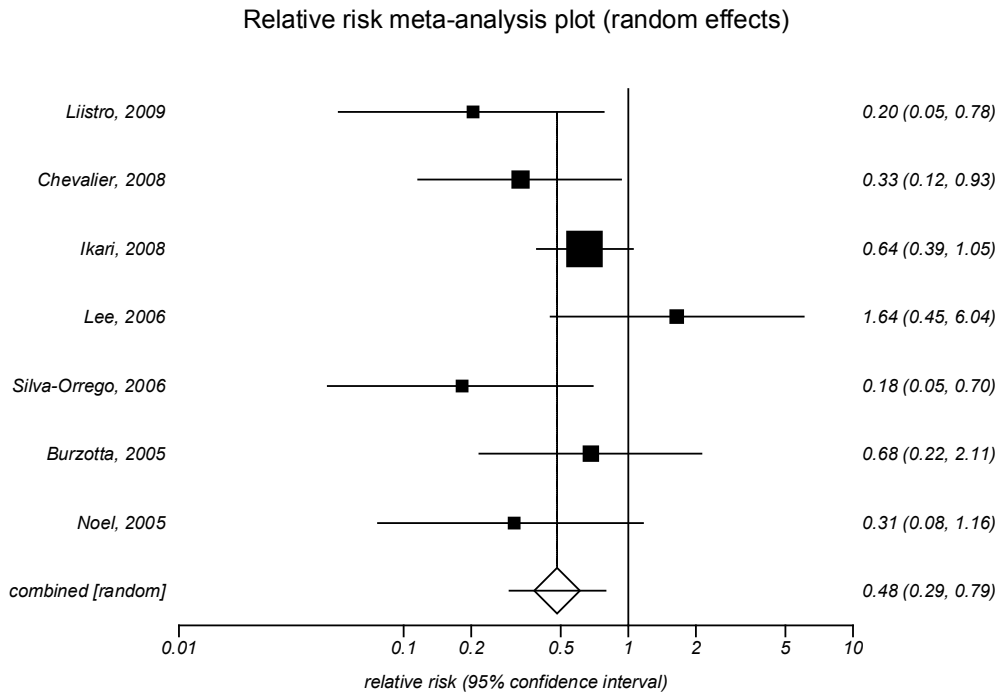
Embolic protection devices combined in patients with STEMI

Six RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) versus control on no reflow.[94,100,102,106,111,132] In these trials, the use of embolic protection devices combined nonsignificantly decreased the risk of having no reflow [RR 0.53 (0.24, 1.18)] (Figure 55). Statistical heterogeneity and publication bias were not detected ($I^2 = 0$ percent, Egger's P = 0.969). When limiting the analysis to only trials of good methodological quality[94,102,106,111,132] the risk of no reflow remain nonsignificantly decreased in the embolic protection devices combined group versus control [(RR 0.58 (0.25, 1.37)]. No statistical heterogeneity was found ($I^2 = 0$ percent).

Embolic protection devices combined in other ACS populations

No trials or studies were available that evaluated the impact of any embolic protection device versus control on no reflow in this population in addition to the two trials reported above. Pooling was not suitable because the trials evaluated different ACS.

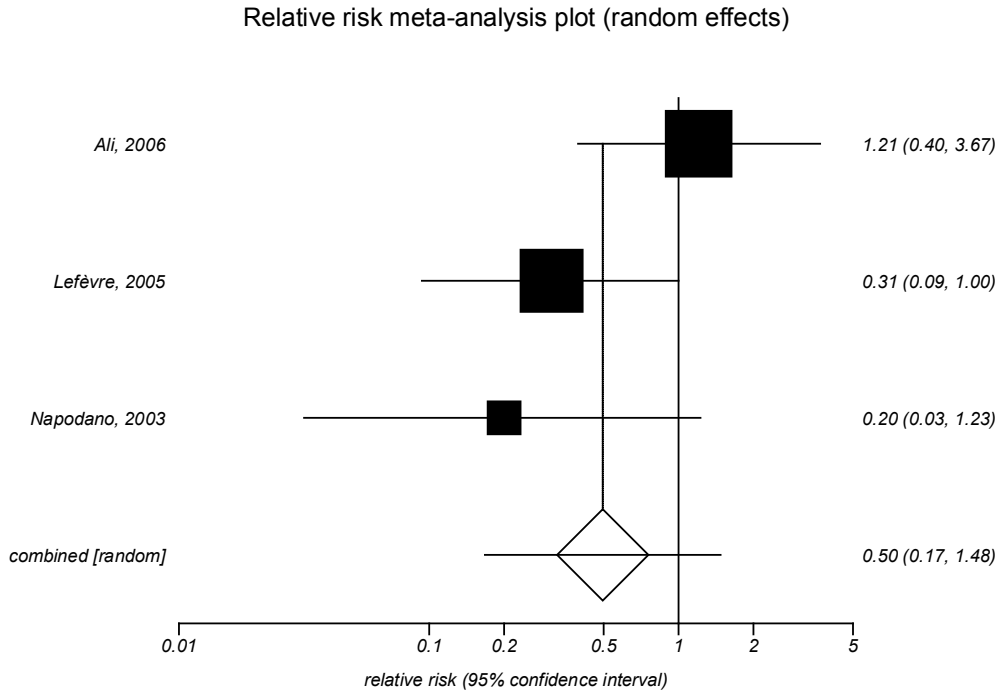
Figure 51. Impact of catheter aspiration devices versus control on no reflow.



Cochran Q: P = 0.219
I^2: 27.4%
Egger: P = 0.332

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

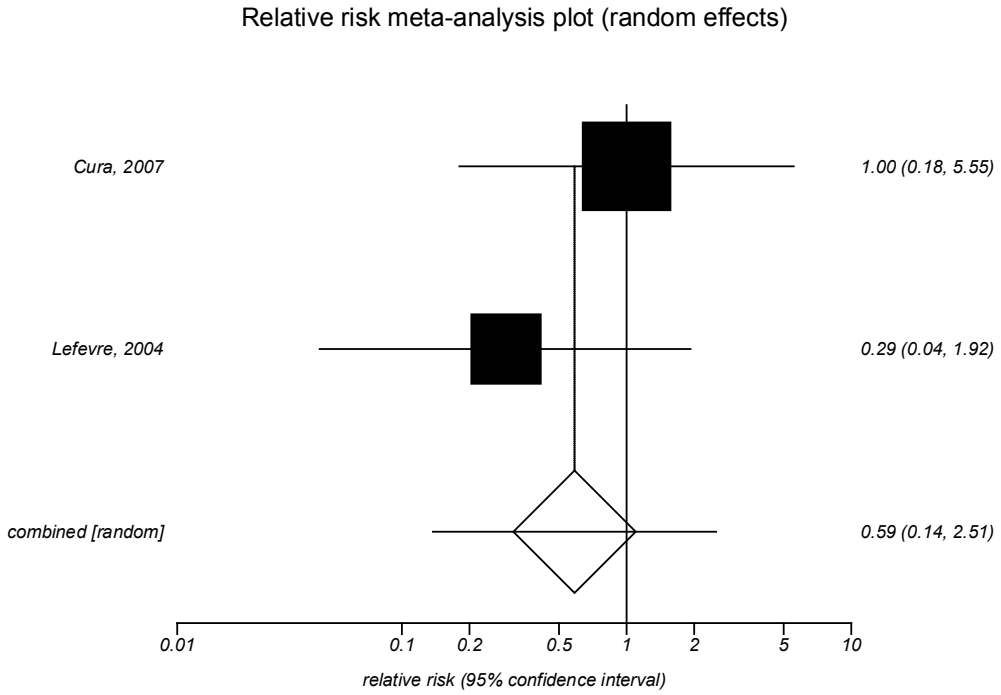
Figure 52. Impact of mechanical thrombectomy devices versus control on no reflow.



Cochran Q: P = 0.180
I^2: 41.7%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

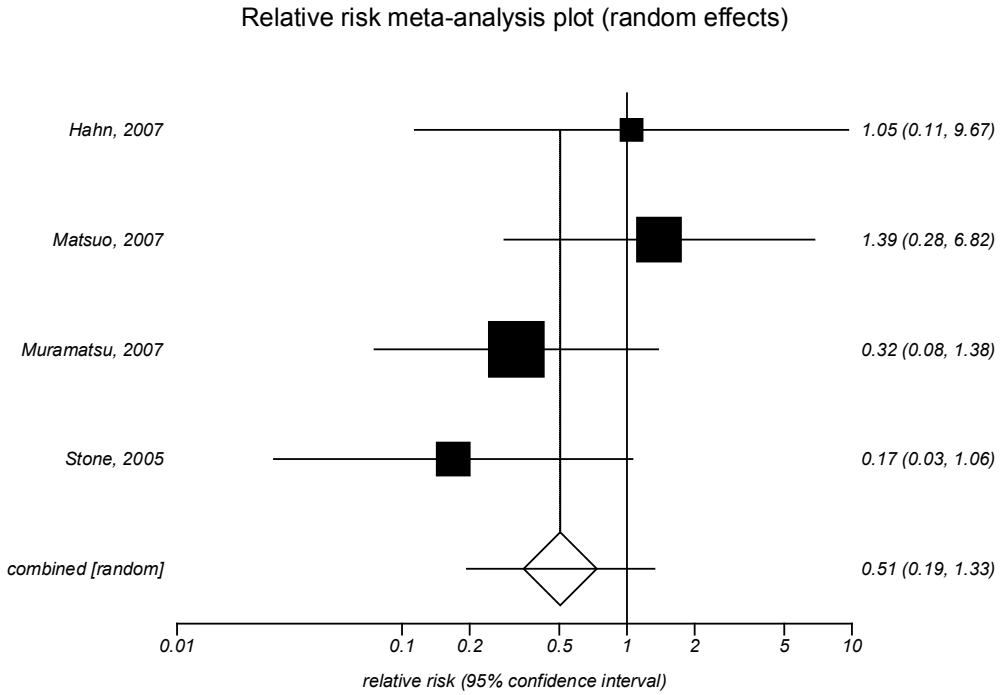
Figure 53. Impact of distal filter embolic protection devices versus control on no reflow.



Cochran Q: P = 0.409
I^2: Too few strata
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

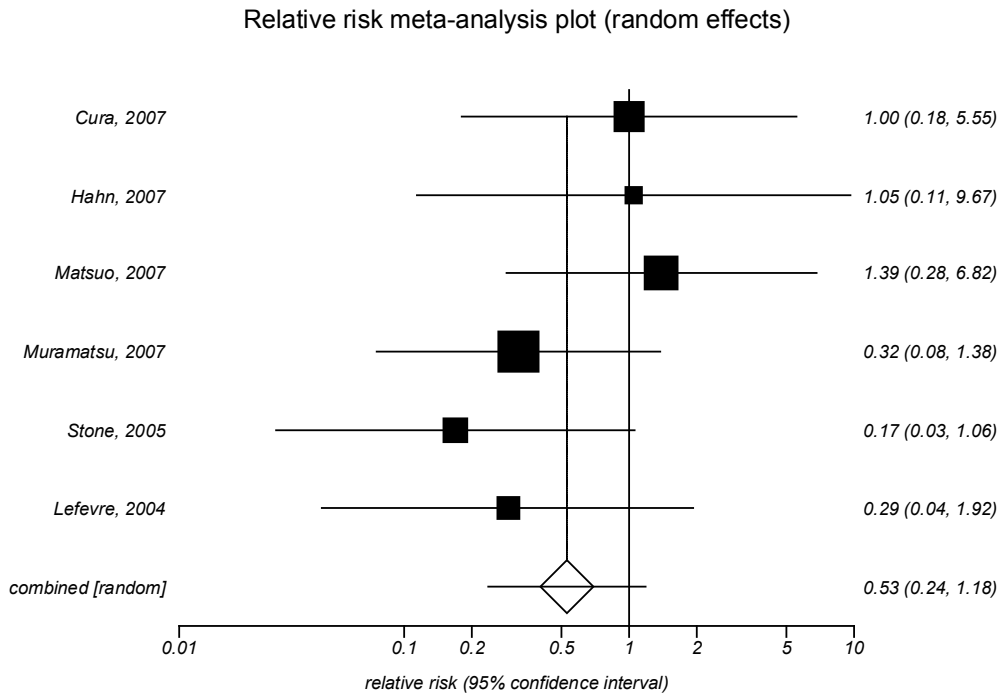
Figure 54. Impact of distal balloon embolic protection devices versus control on no reflow.



Cochran Q: P = 0.403
I^2: 0%
Egger: P = 0.880

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 55. Impact of embolic protection devices combined versus control on no reflow.



Cochran Q: P = 0.603
I²: 0%
Egger: P = 0.969

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Table 21. Intermediate health outcomes in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction

Intermediate health outcomes	Relative Risk (95% CI)	I^2 for Relative Risk
MBG-3	1.60 (1.40 to 1.84)	57.4%
TIMI-3	1.07 (1.03 to 1.11)	11.4%
Distal embolization	0.55 (0.39 to 0.78)	42.5%
No reflow	0.48 (0.29 to 0.79)	27.4%
ST-segment resolution	1.48 (1.30 to 1.70)	64.4%

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; TIMI=thrombolysis in myocardial infarction

Table 22. Intermediate health outcomes in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction

Intermediate health outcomes	Relative Risk (95% CI)	I^2 for Relative Risk
MBG-3	1.07 (0.80 to 1.43)	76.5%
TIMI-3	0.98 (0.92 to 1.04)	67.5%
Distal embolization	0.44 (0.17 to 1.12)	41.6%
No reflow	0.50 (0.17 to 1.48)	41.7%
ST-segment resolution	1.16 (0.99 to 1.36)	75.1%

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; TIMI=thrombolysis in myocardial infarction

Table 23. Intermediate health outcomes in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction

Intermediate health outcomes	Relative Risk (95% CI)	I^2 for Relative Risk
MBG-3	0.97 (0.81 to 1.15)	NA
TIMI-3	0.98 (0.88 to 1.10)	76.4%
Distal embolization	0.63 (0.22 to 1.82)*	NA
No reflow	0.59 (0.14 to 2.51)	NA
ST-segment resolution	1.05 (0.97 to 1.14)	0%

*Result is based on a single trial

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; NA=not applicable; TIMI=thrombolysis in myocardial infarction

Table 24. Intermediate health outcomes in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction

Intermediate health outcomes	Relative Risk (95% CI)	I^2 for Relative Risk
MBG-3	1.39 (1.15 to 1.69)	43.5%
TIMI-3	1.07 (0.995 to 1.16)	56.1%
Distal embolization	1.10 (0.67 to 1.81)	5.8%
No reflow	0.51 (0.19 to 1.33)	0%
ST-segment resolution	1.08 (0.91 to 1.29)	41.2%

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; TIMI=thrombolysis in myocardial infarction

Table 25. Intermediate health outcomes in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction

Intermediate health outcomes	Relative Risk (95% CI)	I^2 for Relative Risk
MBG-3	0.98 (0.88 to 1.10)*	NA
TIMI-3	1.06 (0.98 to 1.15)*	NA
Distal embolization	0.71 (0.37 to 1.35)*	NA
No reflow	---†	---†
ST-segment resolution	1.11 (0.97 to 1.28)*	NA

*Result is based on a single trial; †Risk could not be calculated because no trials evaluated this outcome

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; NA=not applicable; TIMI=thrombolysis in myocardial infarction

Table 26. Intermediate health outcomes in randomized controlled trials evaluating embolic protection devices combined in patients with ST-segment elevation myocardial infarction

Intermediate health outcomes	Relative Risk (95% CI)	I^2 for Relative Risk
MBG-3	1.20 (1.02 to 1.40)	68.2%
TIMI-3	1.04 (0.99 to 1.10)	58.6%
Distal embolization	0.91 (0.64 to 1.30)	0.2%
No reflow	0.53 (0.24 to 1.18)	0%
ST-segment resolution	1.06 (0.999 to 1.13)	0%

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; TIMI=thrombolysis in myocardial infarction

Summary

While there were a number of controled trials where patients undergoing PCI were treated with a thrombectomy or embolic protection device plus standard of care therapy or standard of care therapy alone, the duration of followup, the time points at which they evaluated events and the number of times they evaluated events also varied considerably between trials. For our base case analysis, we used the maximum duration of followup to allow the pooling of a greater number of individual studies. However, we also evaluated for the shortest duration of followup within a trial and at several durational ranges specified a priori. As such, we sought to determine if the effects seen during the maximal duration of followp was representative of the results derived using other time frames. Although several meta-analyses have been conducted in the past, the majority are limited to patients with STEMI and did not evaluate adjunctive devices in other ACS and the most recent analyses did not evaluate embolic protection devices. Therefore, applicability of those results to contemporary practice is limited.

Final health outcomes in patients with STEMI

In patients with STEMI, the impact of catheter aspiration devices was directly compared to distal balloon embolic protection devices on final health outcomes in only one direct comparative RCT. In this trial, no significant differences in mortality, myocardial infarction, stroke, target revascularization, or MACE were found at the longest duration of followup. A nonsignificant trend towards an increased risk of MACE was noted in those receiving the catheter aspiration device. Given limited direct comparative trial data, the superiority of one device over another cannot be directly determined.

In patients with STEMI, the use of catheter aspiration devices significantly reduced the occurrence of MACE versus standard of care by 27 percent using the maximum duration of followup (12.43 months). To prevent one major adverse cardiovascular events, 33 patients would need to be treated with a catheter aspiration device. Using other time cut-offs, the directionality of effect for MACE was similar but statisitcal significance was only maintained at the 180-days evaluation (studies reporting MACE outcomes from in-hospital to 365 days after the procedure). When we assessed individual components of MACE (mortality, myocardial infarction, or target revascularization) using the maximal duration of followup, no significant reductions were found although the direction of effect was in favor of catheter aspiration device benefit. When limiting the pooled analyses of final health outcomes to only trials of good methodological quality, the risk of mortality became significantly reduced by 33 percent using

the maximal duration of followup (8.08 months) while the remaining final health outcome results were unchanged in the direction and significance of effect. When other time periods were assessed, mortality was significantly reduced by 38 percent at the 365-day time point and target revascularization was significantly reduced by 38 percent at 180-day time point but not at other evaluated time points. While there is a significant reduction in MACE with catheter aspiration devices versus control, there is a nonsigificant three-fold increase in the risk of develping stroke using the maximum duration of followup (0.79 months). The direction of effect suggests an increased risk of stroke with catheter aspiration devices regardless of the time point chosen.

In patients with STEMI, the use of mechanical thrombectomy devices did not significantly impact the risk of mortality, myocardial infarction, stroke, target revascularization or MACE at the maximal duration of followup although a higher level of statisitcal heterogeneity was found in the mortality, target revascularization, and MACE analyses. Like with the catheter aspiration analyses at various time periods, a signficant reduction in the risk of 365-day MACE and 180-day target revascularization was found with mechanical aspiration device use versus control. All of the trials included in the pooled analyses were determined to be of higher methodological quality therefore sensitivity analyses based on trial methodological quality did not reduce the observed heterogeneity or impact the overall results. When evaluating each final health outcome by individual time point; statistical heterogeneity could not longer be evaluated in most cases because too few studies were left to evaluate. Therefore it is diffucilt to say whether the inclusion of various time points in the pooled analysis of final health outcomes contributed to the higher level of statistical heterogeneity when evaluating mechanical thrombectomy devices.

Given this data, we cannot make any determinations as to whether catheter aspiration or mechanical thrombectomy are superior strategies versus standard of care or whether one type of device is superior to another.

In patients with STEMI, the use of distal filter, distal balloon, proximal balloon or embolic protection devices combined (distal or proximal; filter or balloon) did not significantly impact the risk of mortality, myocardial infarction, stroke, target revascularization or MACE at the maximal duration of followup versus control. The overall direction of effect of pooled results evaluating the impact of distal filter embolic protection devices on final health outcomes using the maximal duration of followup versus control generally opposed the direction of effect observed with both the distal balloon embolic protection devices and the embolic protection devices combined (distal or proximal; filter or balloon). Myocardial infarction was one excpetion in which all embolic protection device categories (distal or proximal, fitler or ballon, or combined) demonstrated a direction of effect in favor of embolic protection devices versus control. Pooled analyses of final health outcomes at individual time points were limited within the distal filter and balloon embolic protection device categories because of the few number of trials reporting these outcomes and the rare occurance of events in the trials which did report results. Therefore, the majority of individual time points could not be evaluated in these device categories or risk was based on a single trial. No significnat findings were observed, with the exception of the impact of distal filter embolic protection devices versus control on 180-day myocardial infarction (one trial) and distal balloon embolic protection devices on $\leq$ 30 day stroke, in which a signficant reduction in risk was seen in each analysis. Pooling of results for proximal balloon embolic protection devices was not possible since only one trial was available with reported outcomes. The overall direction of effect of proximal balloon embolic protection devices on final health outcomes using the maximal duration of followup was consistent with

distal balloon embolic protection devices and embolic protection devices combined, with exception of mortality, which did not favor the use of a proximal embolic protection device versus control. However, the single trial reported final health outcomes at 30 days, while the mean duration of followup for pooled results in the distal embolic protection device categories ranged from 1.76 to 6.49 months. Within any embolic protection device category (distal or proximal; filter or balloon), limiting the pooled analyses to trials determiend to be of higher methodological quality did not change the direction or significance of the results pertaining to any of the final health outcomes.

Given this data, we can not make any determinations as to whether one embolic protection device category is a superior strategy versus standard of care or whether one type of device is superior to another, or to catheter aspiration or mechanical thrombectomy devices.

Final health outcomes in patients with other ACSs

In patients with mixed ACS (ST-segment elevation or non-elevation myocardial infarction, or UA) trials were identified evaluating the impact of four device categories (catheter aspiration, mechanical thrombectomy, distal filter and distal balloon embolic protection devices) on final health outcomes. Using the maximal duration of followup, both distal filter, distal balloon and embolic protection devices combined demonstrated a trend towards reduction in mortality while the mechanical thrombectomy devices demonstrated an increase in mortality. Catheter aspiration devices appeared to have no impact on mortality using the maximal duration of followup. None of the results reached statistical significance, and only the trials evaluating distal balloon and embolic protection devices combined were amenable to pooling. Additionally, the range of time points at which mortality was reported was from in-hospital to 2 years, therefore comparing across the device categories is difficult. Two controlled observational studies provided differing results regarding mortality. A single controlled observational study evaluating catheter aspiration devices demonstrated a nonsignificant reduction in risk of mortality versus control, as did a single controlled observational study evaluating the impact of mechanical thrombectomy devices versus control. Mixed results were observed when evaluating the impact of device use versus control on MACE. Only three trials in different device categories were indentified and were not amenable to pooling. In the trial evaluating the impact of mechanical thrombectomy devices on MACE, no difference was found. The trial evaluating distal balloon embolic protection devices showed a trend towards reduction in MACE risk while the trial evaluating distal filter embolic protection devices showed a trend towards an increase in MACE risk. With limited data available spanning various time points, it is difficult to compare the impact of any device use on the risk of MACE. In RCTs, the use of a mechanical thrombectomy, distal filter or distal balloon embolic protection devices did not significantly impact the risk of MACE versus control. In a controlled observational study, the use of a mechanical thrombectomy device was associated with a trend towards increased risk of MACE, although not statistically significant. One RCT evaluated the impact of mechanical thrombectomy devices and a nonsignificant reduction in the risk of target revascularization was demonstrated although a controlled observational study demonstrated the opposite trend of a reduction in the risk of target revascularization. One controlled observational study evaluated the impact of mechanical thrombectomy devices on myocardial infarction and demonstrated a nonsignificant increase in the risk of myocardial infarction. Overall, making comparisons across device categories or

within device categories comparing various time points for a single outcome is difficult given the limited number of trials and studies in patients with mixed ACS.

In patients with NSTEMI or UA a limited number of studies which evaluated thrombectomy or embolic protections devices were identified. Two RCTs which evaluated the impact distal filter embolic protection devices versus control on final health outcomes using the maximal duration of followup were identified although were not amenable to pooling. Of the five final health outcomes, MACE and mortality were reported with results which could be evaluated. The use of a distal filter embolic protection device demonstrated a trend towards increased mortality at both in-hospital and 30-days while no effect was seen in 30-day mortality versus control. No other studies or trials were found in this patient pipulation for the other device categories.

Intermediate Health Outcomes

In patients with STEMI, the impact of catheter aspiration devices was directly compared to distal balloon embolic protection devices on intermediate health outcomes in a single direct comparative RCT. In this trial, results of intermediate health outcomes appeared to favor distal balloon embolic protection devices over catheter aspiration device although none of the results were significant. A trend towards greater resolution of ST-segment elevation, attainment of MBG-3, TIMI-3 blood flow and reduced risk of no reflow was noted with the use if a distal balloon embolic protection device. No other trials or studies were found to directly compare device categories on their impact on final health outcomes.

In patients with STEMI, the use of a catheter aspiration device significantly improved intermediate health outcomes, including resolution of ST-segment elevation, achievement of MBG-3 and TIMI-3 blood flow, and reduction in distal embolization and no reflow. However, the use of a catheter aspiration device does not appear to significantly impact ejection fraction versus control. Although not amenable to pooling, the majority of trials which evaluated ejection fraction showed no significant differences (9 of the 11 trials) and these trials evaluated ejection fraction within a wide range of time points including immediately post-PCI up to 6 months post-PCI. The use of mechanical thrombectomy devices did not significantly impact any of the intermediate health outcomes. A trend towards a beneficial effect was seen in resolution of ST-segment elevation, attainment of MBG-3, reduction in distal embolization and no reflow; however, a trend towards reduced attainment of TIMI-3 blood flow was seen. In an controlled observational study, the use of a mechanical thrombectomy device significantly decreased the rate of TIMI-3 blood flow versus control. Although not amenable to pooling, in the two trials which evaluated the impact of mechanical thrombectomy devices on ejection fraction versus control, no significant differences were seen. Overall, it appears that the use of catheter aspiration devices more favorably impacts intermediate health outcomes than the use of mechanical thrombectomy devices, although this is based on indirect comparisons.

Distal filter embolic protection devices, distal balloon embolic protection devices, and embolic protection devices combined had an overall favorable impact on intermediate health outcomes versus control, although most results did not reach statistical significance. A single trial evaluating the impact of proximal balloon embolic protection devices versus control was identified therefore pooling was not possible, although the overall impact was favorable on intermediate health outcomes. All embolic protection device categories demonstrated a trend towards increased resolution of ST-segment elevation versus control. All embolic protection

device categories demonstrated a trend towards increased attainment of TIMI-3 blood flow with the exception of distal filter embolic protection devices which showed opposite trends. Both distal balloon embolic protection devices and embolic protection devices combined significantly increased the risk of attaining MBG-3 whereas distal filter ad proximal balloon embolic protection devices demonstrated a trend towards reduced risk in attaining MBG-3. All embolic protection device categories demonstrated a trend towards reduced risk of distal embolization with exception of the distal balloon embolic protection devices which showed an opposite trend. Distal balloon, distal filter and combined embolic protection devices demonstrated a trend towards reduced no reflow. In the evaluation of ejection fraction, data was not amenable to pooling. The impact of distal balloon and distal filter embolic protection device on ejection fraction versus control was reported, although no significant differences between the device group and control were found.

In patients with mixed ACS (ST-segment elevation or non-elevation myocardial infarction, or UA) RCTs sparsely reported intermediate health outcomes comparing thrombectomy or embolic protection devices versus control and most data was not amenable to pooling. One RCT demonstrated a significant increased in the risk of resolving ST-segment resolution with the use of mechanical thrombectomy devices versus control. No other trials evaluated any device categories on ST-segment resolution. Mixed results were observed in the evaluation of the risk of attaining TIMI-3 blood flow. Pooled results evaluating the impact of catheter aspiration devices, distal balloon embolic protection devices, or embolic protection devices combined demonstrated a trend towards improvement versus control. In RCTs, one trial showed no difference in the impact of distal filter embolic protection devices versus control while one trial showed a nonsignificant increase in the impact of mechanical thrombectomy devices versus control. Both in the evaluation of catheter aspiration device and distal balloon embolic protection devices, a significant increase in the risk of attaining MBG-3 was seen, although only the analysis of distal balloon embolic protection devices was based on a pooled analysis. A nonsignificant decrease in the risk of distal embolization was observed in the distal filter embolic protection device versus control while a significant reduction in the risk of no reflow in the distal balloon embolic protection device versus control was noted. One trial reported the impact of distal filter embolic protection devices on ejection fraction at 3 days versus control, and no significant change was seen.

In patients with NSTEMI or UA, limited data was available regarding the impact of thrombectomy or embolic protection devices versus control on intermediate health outcomes. Although not eligible for pooling, the use of distal filter embolic protection devices nonsignificantly reduced the risk of attaining TIMI-3 blood flow. No other trials or studies evaluated other device categories or other intermediate health outcomes, therefore the impact of thrombectomy or embolic protection devices versus control on intermediate health outcomes in this population is difficult to evaluate.

Key Question 2

In patients with ACS who are undergoing PCI of native vessels, how does the rate and type of adverse events (e.g., coronary dissection, coronary perforation, prolonged procedure time) differ between device types when compared to PCI alone?

Key Points

Twenty three RCTs and two controlled observational studies were included.

Direct Comparative Trials in ACS Patients Assessing Adverse Outcomes

- Two direct comparative randomized trials in patients with STEMI undergoing PCI evaluated adverse outcomes.
    - One direct comparative randomized trial compared a catheter aspiration device to another catheter aspiration device. In this trial, the use of one catheter aspiration device versus another did not significantly impact the risk of coronary dissection. No patients experienced coronary perforation in either group.
    - One direct comparative randomized trial compared a catheter aspiration device to a distal balloon embolic protection device. In this trial, the use of a catheter aspiration device did not impact procedure time compared to a distal balloon embolic protection device.
    - No direct comparative trials evaluated side branch occlusion.

RCTs / Controlled Observational Studies in Patients with STEMI Assessing Adverse Outcomes

- Twenty RCTs and two controlled observational studies evaluated patients with STEMI undergoing PCI and compared a thrombectomy or embolic protection device versus control. Four adverse events (coronary dissection, coronary perforation, prolonged procedure time, and side branch occlusion) were evaluated.
    - In RCTs eligible for pooling, the use of catheter aspiration devices versus control significant reduced the risk of coronary dissection and did not significantly impact the risk of side branch occlusion. In the one trial in which coronary perforation was assessed, no events occurred in either group. Nine trials evaluated procedure time although were ineligible for pooling. In eight of the nine trials the use of catheter aspiration devices versus control did not significantly prolong procedure time.
        - When limited to good quality trials, catheter aspiration device use still reduced the risk of coronary dissection with nonsignificant effects on the other aforementioned adverse events.
        - One controlled observational study found no significant impact of catheter aspiration devices on the risk of coronary dissection versus control.
    - In RCTs, the use of mechanical thrombectomy devices versus control did not significantly impact the risk of coronary dissection, coronary perforation, or side branch occlusion. Three trials evaluated the impact of mechanical thrombectomy devices versus control on procedure time although were ineligible for pooling. In

all three trials the procedure time was significantly prolonged in the mechanical thrombectomy device group versus control.
    - When limited to good quality trials, significant increases in procedural time and nonsignificant effects on the risk of coronary dissection, coronary perforation, or side branch occlusion occurred.
    - One controlled observational study found no significant impact of mechnical thrombectomy devices on the risk of coronary perfusion versus control.
  - In RCTs, the use of distal filter embolic protection devices versus control did not significantly impact the risk of side branch occlusion. No coronary dissections and coronary perforations occurred in either group in the one trial reporting these outcomes. Use of a distal filter embolic protection device increased the procedure time versus control in the one trial evaluating this outcome.
    - Limiting to good quality trials yielded the same results.
    - No controlled observational studies were available.
  - In RCTs, the use of distal balloon embolic protection devices versus control did not significantly impact the risk of coronary perforation or side branch occlusion. One trial evaluated the impact of distal balloon embolic protection devices versus control on coronary dissection although no events occurred in either group. Three trials evaluated the impact of distal balloon embolic protection devices versus control on procedure time although were not amenable to pooling. In two of the three trials, procedure time was significantly prolonged with the use of a distal balloon embolic protection device versus control.
    - Limiting to good quality trials yielded the same results.
    - No controlled observational studies were available.
  - In a RCT, the use of a proximal balloon embolic protection device versus control significantly prolonged procedure time. No other trials or studies evaluated the impact of proximal balloon embolic protection devices versus control on adverse events of interest.
    - Limiting to good quality trials yielded the same results.
    - No controlled observational studies were available.
  - In RCTs eligible for pooling, the use of an embolic protection device (distal or proximal; filter or balloon) did not significantly impact the risk of side branch occlusion. In a single trial, the use of an embolic protection device did not significantly impact the risk of coronary perforation versus control. The risk of coronary dissection could not be calculated in the single trial which reported this outcome. Five RCTs evaluated the impact of an embolic protection device on procedure time although were ineligible for pooling. In four of the five trials procedure time was significantly prolonged with the use of an embolic protection device versus control.

RCTs / Controlled Observational Studies in Mixed or Other ACS Populations Assessing Adverse Outcomes

- One RCT evaluated patients with mixed ACS (ST-segment elevation or non-elevation myocardial infarction, or UA) undergoing PCI and comparing thrombectomy or embolic protection devices versus control on adverse events.

- In a RCT, the use of a distal balloon embolic protection device versus control significantly prolonged the procedure time.
- No other trials or studies evaluated other device categories or adverse events.

- No trials or studies evaluating patients with NSTEMI or UA undergoing PCI and comparing catheter aspiration, mechanical thrombectomy, or embolic protection devices versus control on adverse events were identified.

Detailed Analysis

Study Design and Population Characteristics

The study design and population characteristic have been previously described in key question one. Although several meta-analyses have been conducted in the past, the majority are limited to patients with STEMI and did not evaluate adjunctive devices in other ACS, only two were identified to evaluate adverse events limited to procedure time and coronary perforation, and the most recent analyses did not evaluate embolic protection devices. Therefore, applicability of those results to contemporary practice is limited.

Specific to key question two, we present direct comparative data between agents first and subsequently present the comparisons of each type of device versus control for each endpoint.

Outcome Results

A summary of the results for adverse events comparing each device category to control can be found in Table 27-Table 32.

Coronary Dissection

Direct Comparative Trials

Catheter aspiration device versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on coronary dissection.[147] In this trial, the use of Diver-Invatec nonsignificantly decreased the risk of coronary dissection [RR 0.33 (0.00, 3.71)] compared to Export-Medtronic. This trial was determined to be of good methodological quality.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Five RCTs evaluated the impact of catheter aspiration devices on coronary dissection versus control.[16,61,67,68,73] The use of catheter aspiration devices significantly decreased the risk of coronary dissection [RR 0.30 (0.12, 0.75)] (Figure 56). No statistical heterogeneity or publication bias was found (I^2 = 0 percent, Egger's P = 0.626). All of the trials were determined to be of good methodological quality.[16,61,67,68,73] Given the risk difference [RD -0.02 (-0.12,

0.10), control rate (0.0, 0.1)], fifty people would need to be treated with a catheter aspiration device to prevent one person from experiencing a coronary dissection.

One controlled observational study evaluated the association between the use of catheter aspiration devices during PCI and coronary dissection versus control.[141] The names of the catheter aspiration devices included in this study were not reported. The use of a catheter aspiration device during PCI was associated with a nonsignficantly higher rate of coronary dissection compared to PCI without the use of a catheter aspiration device (6.6 percent versus 5.3 percent, p = 0.32).

Catheter aspiration devices in other ACS populations

No trials or studies evaluated the impact of catheter aspiration devices on this outcome.

Mechanical thrombectomy devices in patients with STEMI

One RCT evaluated the impact of a mechanical thrombectomy device on coronary dissection versus control.[39] The use of a mechanical thrombectomy device nonsignificantly increased the risk of coronary dissection [RR 1.51 (0.57, 4.01)]. This trial was determined to be of good methodological quality. [39]

No controlled observational studies evaluated this endpoint in this population.

Mechanical thrombectomy devices in other ACS populations

No trials or studies evaluated the impact of mechanical thrombectomy devices on this outcome.

Distal filter embolic protection devices in patients with STEMI

One RCT evaluated the impact of distal filter embolic protection devices on coronary dissection versus control.[94] The risk of coronary dissection could not be calculated because no events occurred in either control or treatment group. This trial was determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

No trials or studies evaluated the impact of distal filter embolic protection devices on this outcome.

Distal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of distal balloon embolic protection devices on coronary dissection versus control.[110] The risk of coronary dissection could not be calculated because no events occurred in either control or treatment group. This trial was determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Distal balloon embolic protection devices in other ACS populations

No trials or studies evaluated the impact of distal balloon embolic protection devices on this outcome.

Proximal balloon embolic protection devices in patients with STEMI

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this outcome.

Proximal balloon embolic protection devices in other ACS populations

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this outcome.

Embolic protection devices combined in patients with STEMI

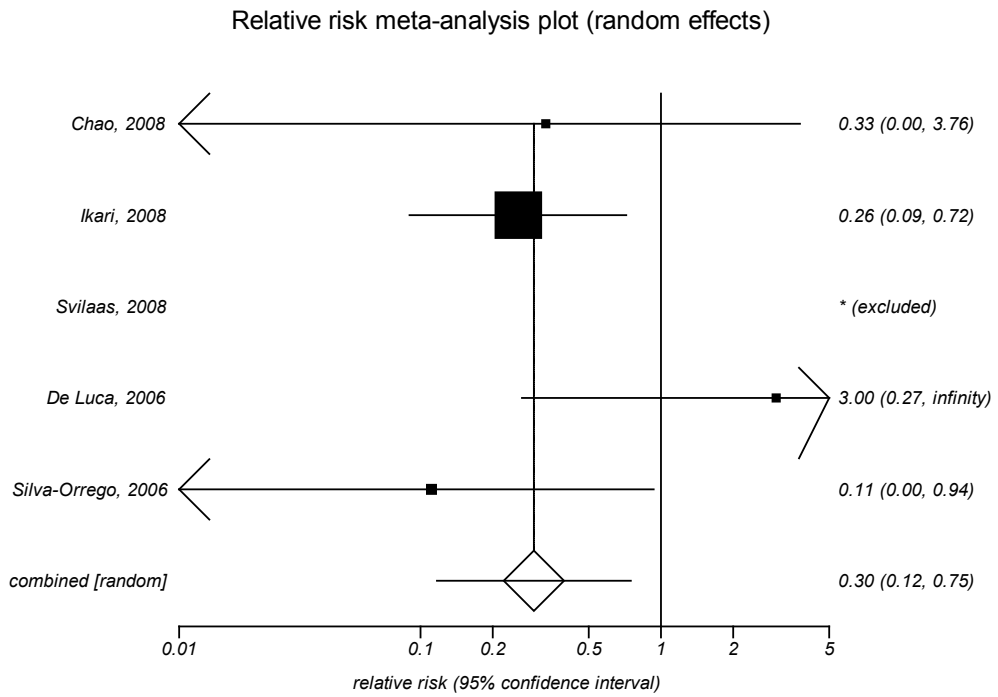
Two RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on coronary dissection versus control.[94,110] In these two trials, the risk could not be calculated because no events occurred in either control or treatment group. Both trials were determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Embolic protection devices combined in other ACS populations

No trials or studies evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on this outcome.

Figure 56. Impact of catheter aspiration devices on coronary dissection versus control.



Cochran Q: P = 0.464
I^2: 0%
Egger: P = 0.626

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Coronary Perforation

Direct Comparative Trials

Catheter aspiration devices versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver-Invatec catheter aspiration device versus the Export-Medtronic catheter aspiration device on coronary perforation.[147] The risk of coronary perforation could not be calculated because no events occurred in either group during this trial. This trial was determined to be of good methodological quality.

Trails versus Control

Catheter aspiration devices in patients with STEMI

One RCT evaluated the impact of using a catheter aspiration device on coronary perforation versus control.[16] The risk of coronary perforation could not be calculated because no events occurred in either control or treatment group.

No controlled observational studies evaluated this endpoint in this population.

Catheter aspiration devices in other ACS populations

No trials or studies evaluated the impact of catheter aspiration devices on this outcome.

Mechanical thrombectomy devices in patients with STEMI

Two RCTs evaluated the impact of mechanical thrombectomy devices on coronary perforation versus control.[11,39] The use of mechanical thrombectomy devices nonsignificantly increased the risk of coronary perforation [RR 1.04 (0.15, 7.04)] (Figure 57). Publication bias could not be evaluated since only two studies were available. Both trials were determined to be of good methodological quality. [11,39]

One controlled observational study evaluated the association between the use of a mechanical thrombectomy device and coronary perforation versus control.[134] Patients undergoing PCI with a mechanical thrombectomy device, either the AngioJet XMI or XVG catheter, were compared to patients undergoing PCI without mechanical thrombectomy. The use of a mechanical thrombectomy device was associated with a nonsignificantly lower rate of coronary perforation compared to PCI without a mechanical thrombectomy device (0.0 percent versus 0.2 percent, $p > 0.99$).

Mechanical thrombectomy devices in other ACS populations

No trials or studies evaluated the impact of mechanical thrombectomy devices on this outcome.

Distal filter embolic protection devices in patients with STEMI

One RCT evaluated the impact of a distal filter embolic protection device on coronary perforation versus control.[94] The risk of coronary perforation could not be calculated because no events occurred in either control or treatment group.

No controlled observational studies evaluated this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

No trials or studies evaluated the impact of distal filter embolic protection devices on this outcome.

Distal balloon embolic protection devices in patients with STEMI

Two RCTs evaluated the impact of distal balloon embolic protection devices on coronary perforation versus control.[110,111] In one trial no events occurred in either the control or treatment group.[110] In the other trial the use of a distal balloon embolic protection device nonsignificantly increased the risk of coronary perforation [RR 5.11 (0.53, infinity)]. Publication bias could not be calculated. Both trials were determined to be of good methodological quality.[110,111]

No controlled observational studies evaluated this endpoint in this population.

Distal balloon embolic protection devices in other ACS populations

No trials or studies evaluated the impact of distal balloon embolic protection devices on this outcome.

Proximal balloon embolic protection devices in patients with STEMI

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this outcome.

Proximal balloon embolic protection devices in other ACS populations

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this outcome.

Embolic protection devices combined in patients with STEMI

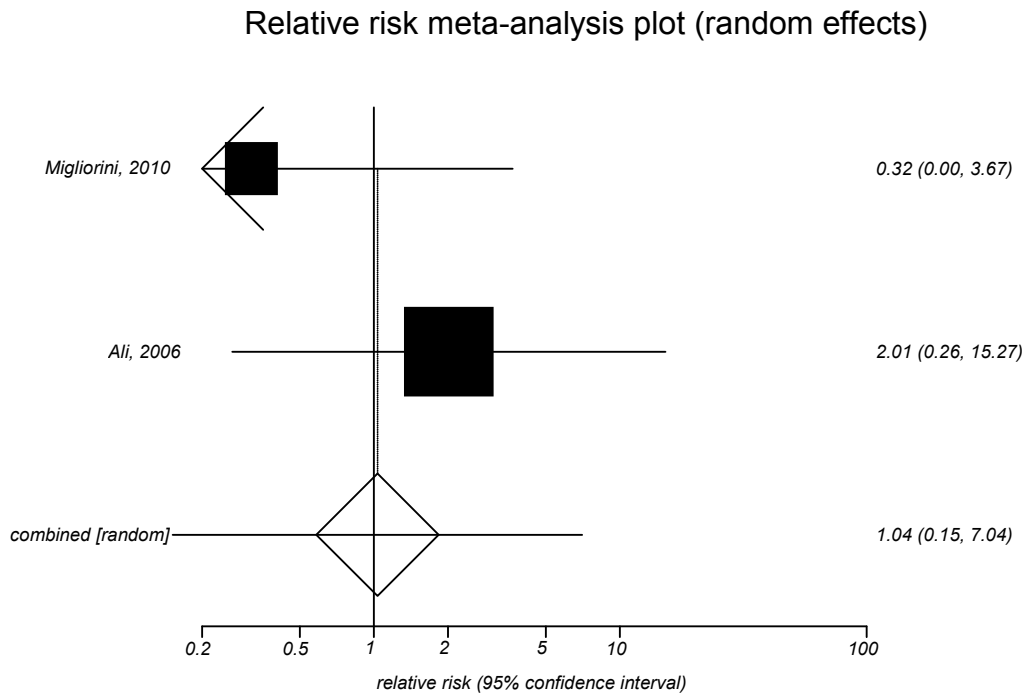
Three RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on coronary perforation versus control.[94,110,111] In two trials no events occurred in either control or treatment group.[94,110] In another trial,[111] the use of an embolic protection device nonsignificantly increased the risk of coronary perforation [RR 5.11 (0.53, infinity)]. All of the trials were determined to be of good methodological quality.[94,110,111]

No controlled observational studies evaluated this endpoint in this population.

Embolic protection devices combined in other ACS populations

No trials or studies evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on this outcome.

Figure 57. Impact of mechanical thrombectomy devices on coronary perforation versus control.



Cochran Q: P = 0.366
I²: Too few strata
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Prolonged Procedure Time

Direct Comparative Trials

Catheter aspiration device versus catheter aspiration device in patients with STEMI

One direct comparative randomized trial evaluated the impact of the Diver CE catheter aspiration device versus the Guardwire Plus distal balloon embolic protection device on procedure time.[149] In this trial, there was no significant difference in procedure time between the Diver CE and Guardwire Plus groups (60 min ± 24 versus 65 min ± 28, p = 0.36). This trial was determined to be of good methodological quality.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Nine RCTs evaluated the impact of catheter aspiration devices on procedure time versus control but were not amenable to pooling.[12,15,16,61,67,70,73,82,151] In the first trial, the mean procedure time was not significantly different between the catheter aspiration device group and control (75.7 ± 33.0 min versus 75.9 ± 38.7 min, p = 0.90).[12] In the second trial, patients were

only included in the trial if they achieved a TIMI-3 blood flow post-procedure.[151] The mean procedure time was not significantly different between the catheter aspiration device group and control (39.5 ± 10.1 min versus 32.3 ± 18.6 min, p = 0.14). [151] In the third trial, the mean procedure time was not significantly different between the catheter aspiration device group and control (36.7 ± 18.0 min versus 34.5 ± 21.5 min, p = 0.08).[15] In the fourth trial, the mean procedure time was not significantly different between the catheter aspiration device group and control (87.0 ± 32.4 min versus 93.6 ± 78.6 min, p = 0.16).[16] In the fifth trial, the median procedural time was not significantly different between the catheter aspiration device group and control [28 min (14-42) versus 26 min (12-40), p = 0.92].[61] In the sixth trial, procedure time (defined as lab to TIMI-3 blood flow time) was not significantly different between the catheter aspiration device group and control (49 ± 18 min versus 53 ± 23 min, p = 0.54).[67] In the seventh trial, the median procedural time was significantly prolonged in the catheter aspiration device group compared to control [39 minutes (29-48) versus 29 minutes (23-38), p < 0.0001]. [70] In the eighth trial, the mean procedure time was not significantly different between the catheter aspiration device group and control (57 ± 19 minutes versus 54 ± 21 minutes, p = 0.36).[73] In the final trial, the mean procedure time was not significantly different between the catheter aspiration device group and control (81 ± 43 minutes versus 72 ± 34 minutes, p = 0.41).[82] All included trials were determined ot be of good methodlogical quality.

No controlled observational studies evaluated this endpoint in this population.

Catheter aspiration devices in other ACS populations

No trials or studies evaluated the impact of mechanical thrombectomy devices on this outcome.

Mechanical thrombectomy devices in patients with STEMI

Three RCTs evaluated the impact of mechanical thrombectomy devices on procedure time versus control although were not amenable to pooling.[11,26,28,39] In the first trial, the median procedure time was significantly prolonged in the mechanical thrombectomy device group compared to control [59.5 minutes (45-70) versus 46 minutes (35-60), p < 0.001].[11] In the second trial, the mean procedure time was significantly prolonged in the mechanical thrombectomy device group compared to control (75.4 ± 30.9 minutes versus 59.2 ± 26.8 minutes), p < 0.001).[39] In the third trial, the mean procedure time was significantly prolonged in the mechanical thrombectomy device group compared to control (54 ± 28 minutes versus 45 ± 25 minutes, p = 0.009).[28] All three trials were determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Mechanical thrombectomy devices in other ACS populations

No trials or studies evaluated the impact of mechanical thrombectomy devices on this outcome.

Distal filter embolic protection devices in patients with STEMI

One RCT evaluated the impact of distal filter embolic protection devices on procedure time versus control.[94] In this trial, the SpideRX device was used. The median procedure time was significantly prolonged in the distal filter embolic protection device group compared to control [52 minutes (43-70) versus 43.5 minutes (30-54), p <0.001]. This trial was determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Distal filter embolic protection devices in other ACS populations

One RCT evaluated the impact of distal filter embolic protection devices on procedure time.[145] The mean procedure time was only reported for the device group (63 minutes ± 17).

No controlled observational studies evaluated this endpoint in this population.

Distal balloon embolic protection devices in patients with STEMI

Three RCT evaluated the impact of distal balloon embolic protection devices on procedure time versus control although were not amenable to pooling.[106,111,132] In the first trial, mean procedure time was significantly prolonged in the distal balloon embolic protection device group compared to control (75.8 ± 30 minutes versus 53 ± 25 minutes, p <0.01).[106] In the second trial, the mean procedure time was not significantly different between the distal balloon embolic protection device group and control (29.7 ± 18.3 minutes versus 29.5 ± 18.2 minutes, p = 0.91).[132] In the third trial the median procedure time was significantly prolonged in the distal balloon embolic protection device group compared to control [53 minutes (42-69) versus 39 minutes (29-51), p < 0.001].[111] This trial was determined to be of good methodological quality.

One RCT evaluated the impact of distal balloon embolic protection devices on procedure time versus abciximab therapy.[153] In this trial, the PercuSurge device was used. The median procedure time was not significantly different between the distal balloon embolic protection device group and the abciximab group [58 minutes (35-88) versus 43 minutes (25-87), p = NS].[153] This trial was determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Distal balloon embolic protection devices in other ACS populations

One RCT evaluated the impact of distal balloon embolic protection devices on procedure time in patients with acute myocardial infarction.[124] In this trial, the GuardWire device was used. The mean procedure time was significantly prolonged in the distal balloon embolic protection device group compared to control (25.01 minutes ± 11.89 versus 31.98 minutes ± 15.33, p = 0.03). This trial was determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Proximal balloon embolic protection devices in patients with STEMI

One RCT evaluated the impact of proximal balloon embolic protection devices on procedure time versus control.[18] In this trial, the Proxis device was used. The median procedure time was significantly prolonged in the proximal balloon embolic protection device group compared to control [45 minutes (36-58) versus 31 minutes (25-40), p <0.01].[18] This trial was determined to be of good methodological quality.

No controlled observational studies evaluated this endpoint in this population.

Proximal balloon embolic protection devices in other ACS populations

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this outcome.

Embolic protection devices combined in patients with STEMI

Five RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on prolonged procedure time versus control although were not amenable to pooling.[18,94,106,111,132] The procedure time results have been reported in each of the respective embolic protection device categories above. No additional data was available. In four of the five trials, the procedure time was significantly prolonged in the embolic protection device group versus control.[18,94,106,111]

Embolic protection devices combined in other ACS populations

One RCT evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on prolonged procedure time versus control[124] whose results are reported under distal balloon embolic protection devices in other ACS populations. No additional data was available.

Side Branch Occlusion

Direct Comparative Trials

No direct comparative trials evaluated the impact of thrombectomy or embolic protection devices on this outcome.

Trials versus Control

Catheter aspiration devices in patients with STEMI

Two RCTs evaluated the impact of catheter aspiration devices on side branch occlusion versus control.[15,61] The use of catheter aspiration devices nonsignificantly increased the risk of side branch occlusion [RR 1.19 (0.40, 3.54)] (Figure 58). Publication bias could not be calculated since only two studies were available. Both of the trials were determined to be of good methodological quality.[15,61]

No controlled observational studies evaluated this endpoint in this population.

Catheter aspiration devices in other ACS populations

No trials or studies evaluated the impact of catheter aspiration devices on this outcome.

Mechanical thrombectomy devices in patients with STEMI

One RCT evaluated the impact of a mechanical thrombectomy device on side branch occlusion versus control.[43] In this trial, the use of a mechanical thrombectomy device did not impact the risk of side branch occlusion versus control [RR 1.00 (0.11, 9.41)]. This trial was determined to be of good methodological quality.[43]

No controlled observational studies evaluated this endpoint in this population.

Mechanical thrombectomy devices in other ACS populations

No studies evaluated the impact of mechanical thrombectomy devices on this outcome.

Distal filter embolic protection devices in patients with STEMI

One RCT evaluated the impact of a distal filter embolic protection device on side branch occlusion versus control.[94] In this trial, the use of a distal filter embolic protection device nonsignificantly decreased the risk of side branch occlusion versus control [RR 0.33 (0.00, 3.80)]. This trial was determined to be of good methodological quality. [94]

Distal filter embolic protection devices in other ACS populations

No trials or studies evaluated the impact of distal filter embolic protection devices on this outcome.

Distal balloon embolic protection devices in patients with STEMI

Two RCTs evaluated the impact of distal balloon embolic protection devices on side branch occlusion.[106,111] The use of distal balloon embolic protection devices nonsignificantly decreased the risk of side branch occlusion versus control [RR 0.93 (0.61, 1.42)] (Figure 59). Publication bias could not be calculated since only two studies were available. Both trials were determined to be of good methodological quality. [106,111]

Distal balloon embolic protection devices in other ACS populations

No trials or studies evaluated the impact of distal balloon embolic protection devices on this outcome.

Proximal balloon embolic protection devices in patients with STEMI

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this outcome.

Proximal balloon embolic protection devices in other ACS populations

No trials or studies evaluated the impact of proximal balloon embolic protection devices on this outcome.

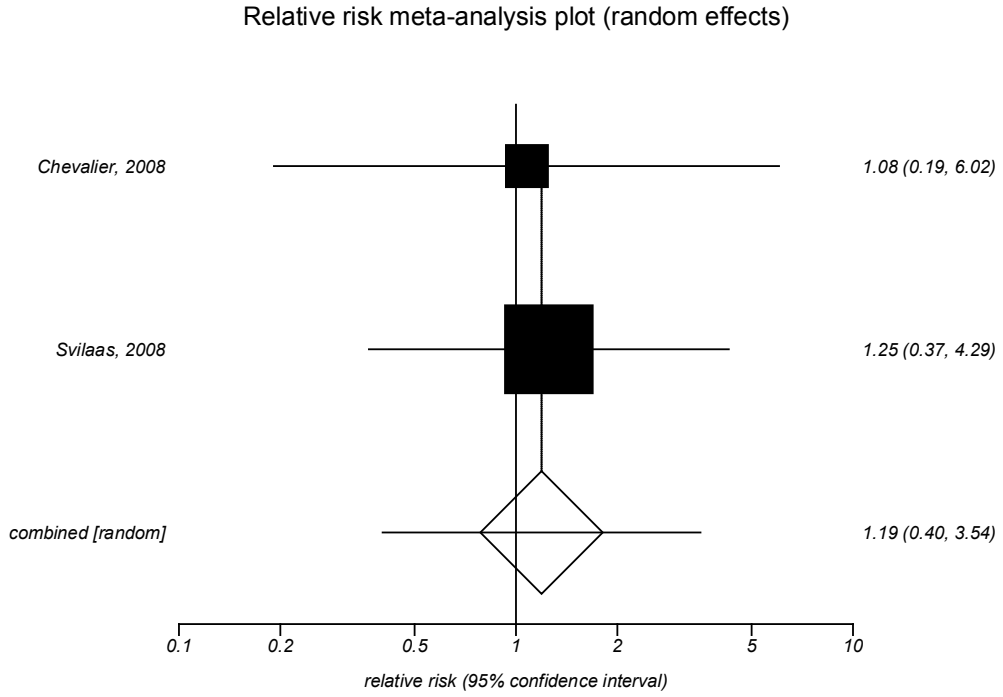
Embolic protection devices combined in patients with STEMI

Three RCTs evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on side branch occlusion.[94,106,111] In these trials, the use of embolic protection devices nonsignificantly decreased the risk of side branch occlusion [RR 0.91 (0.60, 1.39)] (Figure 60). Statistical heterogeneity was not detected (I^2 = 0 percent) and publication bias could not be determined due to the number of studies available. All of the trials were determined to be of good methodological quality. [94,106,111]

Embolic protection devices combined in other ACS populations

No trials or studies evaluated the impact of embolic protection devices combined (distal or proximal; filter or balloon) on this outcome.

Figure 58. Impact of catheter aspiration devices on side branch occlusion versus control.



Cochran Q: P = 0.898

I²: Too few strata
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

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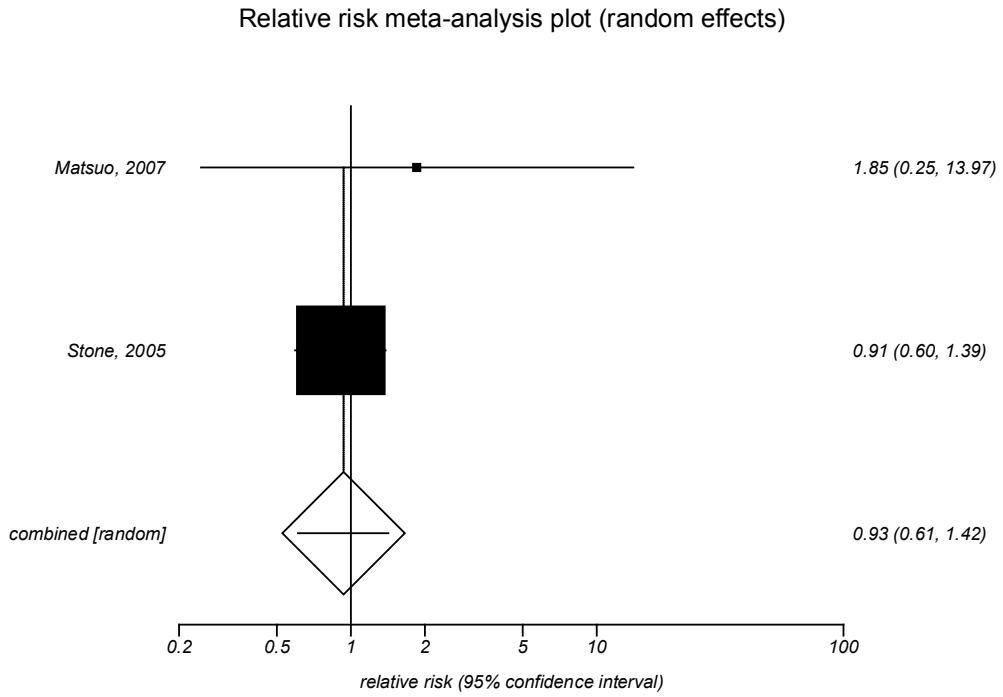
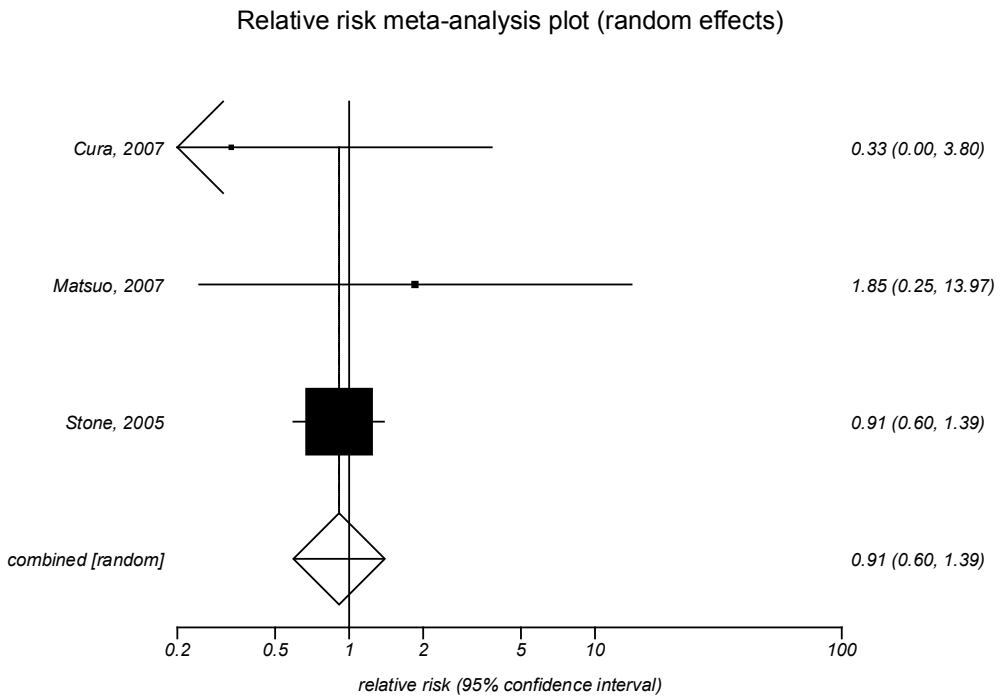
Figure 59. Impact of distal balloon embolic protection devices on side branch occlusion versus control.



Cochran Q: P = 0.565
I²: Too few strata
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 60. Impact of embolic protection devices combined on side branch occlusion versus control.



Cochran Q: P = 0.697
I^2: 0%
Egger: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Table 27. Adverse events in randomized controlled trials evaluating catheter aspiration devices in patients with ST-segment elevation myocardial infarction

Adverse event	Relative Risk (95% CI)	I^2 for Relative Risk
Coronary dissection	0.30 (0.12 to 0.75)	0%
Coronary perforation	---*	---*
Side-branch occlusion	1.19 (0.40 to 3.54)	NA

*Risk could not be calculated because one trial evaluated the outcome and no events occurred

Abbreviations: CI=confidence interval; NA=not applicable

Table 28. Adverse events in randomized controlled trials evaluating mechanical thrombectomy devices in patients with ST-segment elevation myocardial infarction

Adverse event	Relative Risk (95% CI)	I^2 for Relative Risk
Coronary dissection	1.51 (0.57 to 4.01)*	NA
Coronary perforation	1.04 (0.15 to 7.04)	NA
Side-branch occlusion	1.00 (0.11 to 9.41)*	NA

*Result is based on a single trial

Abbreviations: CI=confidence interval; NA=not applicable

Table 29. Adverse events in randomized controlled trials evaluating distal filter embolic protection devices in patients with ST-segment elevation myocardial infarction

Adverse event	Relative Risk (95% CI)	I^2 for Relative Risk
Coronary dissection	---*	---*
Coronary perforation	---*	---*
Side-branch occlusion	0.33 (0.00 to 3.80)†	NA

*Risk could not be calculated because one trial evaluated this outcome and no events occurred; †Result is based on a single trial

Abbreviations: CI=confidence interval; NA=not applicable

Table 30. Adverse events in randomized controlled trials evaluating distal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction

Adverse event	Relative Risk (95% CI)	I^2 for Relative Risk
Coronary dissection	---*	---*
Coronary perforation	5.11 (0.53 to infinity)†	NA
Side-branch occlusion	0.93 (0.61 to 1.42)	NA

*Risk could not be calculated because one trial evaluated this outcome and no events occurred; †Result is based on a single trial

Abbreviations: CI=confidence interval; NA=not applicable

Table 31. Adverse events in randomized controlled trials evaluating proximal balloon embolic protection devices in patients with ST-segment elevation myocardial infarction

Adverse event	Relative Risk (95% CI)	I^2 for Relative Risk
Coronary dissection	---*	---*
Coronary perforation	---*	---*
Side-branch occlusion	---*	---*

*Risk could not be calculated because no trials evaluated this outcome

Abbreviations: CI=confidence interval

Table 32. Adverse events in randomized controlled trials evaluating embolic protection devices combined in patients with ST-segment elevation myocardial infarction

Adverse event	Relative Risk (95% CI)	I^2 for Relative Risk
Coronary dissection	---*	---*
Coronary perforation	5.11 (0.53 to infinity)†	NA
Side-branch occlusion	0.91 (0.60 to 1.39)	0%

*Risk could not be calculated because in the two trials that evaluated this outcome no events occurred; †Result is based on a single trial

Abbreviations: CI=confidence interval; NA=not applicable

Summary

In patients with STEMI undergoing PCI and comparing a catheter aspiration, mechanical thrombectomy, or embolic protection device versus control, only a minority of trials reported on the occurrence of the four most important adverse events (coronary dissection, coronary perforation, prolonged procedure time, and side branch occlusion). This makes it difficult to determine the balance of benefits to harms for these devices.

The use of catheter aspiration devices versus control significant reduced the risk of coronary dissection and did not significantly impact the risk of side branch occlusion. One trial reported the outcome of coronary perforation although risk could not be calculated since no events occurred in either group. Overall, the use of catheter aspiration devices versus control did not significantly prolong procedure time in eight of nine trials. When evaluated qualitatively, the procedure time were shortened in one trial, prolonged by 5 or less minutes in four trials, and were more than 5 minutes prolonged in another four trials.

The use of mechanical thrombectomy devices versus control appears to be safe overall. In RCTs, the use of mechanical thrombectomy devices versus control did not significantly impact the risk of coronary dissection, coronary perforation, or side branch occlusion. However, mechanical thrombectomy devices appear to prolong the procedure time versus control. Three trials evaluated the impact of mechanical thrombectomy devices versus control on procedure time although were ineligible for pooling. In all three trials the procedure time was significantly prolonged in the mechanical thrombectomy device group versus control. The mean procedure time was prolonged by 9 - 16.2 minutes and one trial reported a median in which the procedure time was prolonged by 13.5 minutes.

Limited data was available to analyze the adverse events associated with the use of distal filter embolic protection devices versus control. In RCTs, the use of distal filter embolic protection devices versus control did not significantly impact the risk of side branch occlusion. The risk of coronary dissection and coronary perforation could not be calculated in the one trial in which it was reported. One trial evaluated procedure time which was significantly prolonged in the distal filter embolic protection device group versus control by a median of 8.5 minutes.

In RCTs, the use of distal balloon embolic protection devices versus control did not significantly impact the risk of coronary perforation or side branch occlusion. The risk of coronary dissection could not be calculated in the one trial which reported this outcome because no events occurred. Three trials evaluated the impact of distal balloon embolic protection devices

versus control on procedure time although were not amenable to pooling. In two of the three trials, procedure time was significantly prolonged with the use of a distal balloon embolic protection device versus control. In these two trials, the procedure time was prolonged by a mean of 22.8 minutes and a median of 14 minutes.

The only adverse event which was reported in trials evaluating proximal balloon embolic protection devices versus control was procedure time. In one controlled trial, the procedure time was significantly prolonged in the proximal balloon embolic protection device group versus control by a median of 14 minutes.

When evaluating embolic protection devices combined (distal or proximal; filter or balloon), similar trends were observed as those evaluating the individual embolic protection device categories. The risk of coronary dissection could not be calculated because no events occurred in the trials which reported this outcome. Only one trial reported coronary perforation (distal balloon embolic protection device) therefore results did not change. The majority of trials evaluating embolic protection devices demonstrated a prolonged procedure time (four of five trials). The use of embolic protection devices combined did not significantly impact the risk of side branch occlusion, although a trend towards decreased risk was seen.

No trials or studies evaluating patients with NSTEMI or UA undergoing PCI and comparing thrombectomy or embolic protection devices versus control on adverse events were identified.

One trial evaluated patients with mixed ACS (ST-segment elevation or non-elevation myocardial infarction, or UA) undergoing PCI and comparing thrombectomy or embolic protection devices versus control on adverse events. In this trial, the use of a distal balloon embolic protection device versus control significantly prolonged the procedure time by a a mean of 6.97 minutes.

Key Question 3

In ACS patients undergoing PCI of native vessels, which patient characteristics (e.g., gender, age, ethnicity, diabetes, smoker, ejection fraction, primary or rescue PCI, use of glycoprotein IIb/IIIa inhibitors, ischemia time, presence of thrombus-containing lesion, infarct-related artery and pre-PCI TIMI flow, use of direct stenting) affect outcomes?

Key Points

A total of nine RCTs, an individual patient data meta-analysis and four observational studies provided useful data for Key Question 3.

- RCTs evaluating treatment effect stratified by subgroups found the following:
    - No statistically significant difference in outcomes with catheter aspiration, mechanical thrombectomy or embolic protection devices efficacy based on differences in gender, age, diabetes, smoking status, primary or rescue PCI, presence of thrombus-containing lesion, pre-PCI TIMI flow, or the use of direct stenting.

- A trend (P-value for heterogeneity<0.10 between subgroups) towards greater improvements in attaining complete ST-segment resolution with proximal balloon embolic protection in those receiving a glycoprotein IIb/IIIa inhibitor versus those without such therapy.
- A trend (P-value for heterogeneity<0.10 between subgroups) towards greater improvements in attaining complete ST-segment resolution with proximal balloon embolic protection in those with an anterior infarct-related artery lesions versus lesions in other arteries.
- Conflicting data was identified regarding the effect of ischemic time on outcomes following the use of catheter aspiration devices.
  - There was a trend (P-value for heterogeneity<0.10 between subgroups) towards greater achievement of a higher MBG with catheter aspiration in those with ischemic times < 180 minutes versus longer ischemic times.
  - There was significantly greater improvement (P-value for heterogeneity between subgroups = 0.02) in the achievement of TIMI 3 flow with catheter aspiration and a trend (P-value for heterogeneity <0.10 between subgroups) towards greater reductions in slow flow or no reflow in those with prolonged ischemic times (6 to 24 hours from symptom onset) versus those with shorter ischemic times.

- It should be noted that results of subgroup analyses from RCTs may be prone to type 2 error and false findings resulting from multiple hypothesis testing.
- No RCTs evaluated the effect of ethnicity or ejection fraction on thrombectomy or embolic protection device efficacy.
- The individual patient data meta-analysis by Burzotta and colleagues[160,161] found that the use of aspiration or mechanical thrombectomy was associated with a survival benefit in the subgroup of patients treated with glycoprotein IIb/IIIa inhibitors but not in those not receiving them.
  - No qualitative differences in mortality were seen when splitting the study population according to the presence or absence of diabetes, earlier or later time to reperfusion, type of vessel (left anterior descending, circumflex, right coronary artery) containing the culprit lesion,,and lower or higher pre-PCI TIMI flow.
- The controlled observational study by Nakatani and colleagues[138] found Killip class (a correlate to heart failure and ejection fraction) not to be a modifier of 30-day mortality with catheter aspiration device use.
  - This constitutes the only data available to evaluate the potential confounding effect of heart function on outcomes.
- Observational single arm studies found catheter aspiration and/or embolic protection device effectiveness to be negatively affected by increased age, prolonged ischemic time, female gender, presence of diabetes and absence of baseline thrombus.

Detailed Anlaysis

Study Design and Population Characteristics

A total of nine RCTs, an individual patient data meta-analysis and four observational studies were included in Key Question 3. All RCT data were in patients experiencing STEMI. STEMI was also an inclusion criterion for all trials in the individual patient data meta-analysis. Some of the observational studies included a mixed ST-segment and non-ST-segment elevation myocardial infraction population. Of the RCTs, 5, 2, 1, and 1 evaluated catheter aspiration, distal filter embolic protection, distal balloon embolic protection and proximal balloon embolic protection, respectively. None evaluated mechanical thrombectomy devices, although RCTs of these devices were included in the individual patient data meta-analysis. Outcomes evaluated in these trials included MBG, complete (>70 percent) ST-segment resolution, slow- and/or no-reflow, target vessel revascularization, MACE, TIMI blood flow and distal embolization.

Outcomes Results

Two trials provided subgroup results based on gender (Table 33).[61,88] In the trial by Svilaas and colleagues, males were significantly less likely to experience a MBG of 0 or 1 if they received catheter aspiration than if they did not [RR 0.60 (0.44, 0.82)]. While females did not experience a significant reduction in achieving a MBG of 0 or 1 when the device was employed [RR 0.74 (0.49, 1.11)], the reductions noted between the genders was not found to be statistically differ (P-value for heterogeneity = 0.43 between subgroups) (Svilaas 2008). In the trial by Kelbaeck and colleagues, males and females both had non-significant improvements in ST-segment resolution (≥70 percent at 90 minutes post-PCI) when a filter distal embolic protection device was employed and the reductions were not found to differ statistically between genders (P-value for heterogeneity = 0.79 between subgroups).[88]

Table 33. Results of subgroup analysis from randomized controlled trials evaluating the effect of gender on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Svilaas, 2008[61] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Male	RR 0.60 (0.44 to 0.82)	0.43
				Female	RR 0.74 (0.49 to 1.11)	
Kelbaek, 2008[88] (N=626)	Distal Filter Embolic Protection	FilterWire-EZ or SpiderX	STSR ≥ 70% 90 min post-PCI	Male	RR 1.04 (0.93 to 1.16)	0.79
				Female	RR 1.08 (0.84 to 1.40)	

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; min-minutes; N=total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

Three trials provided subgroup results stratified by age;[61,82,88] however, numerical data was obtainable for only one (Table 34).[61] The trial by Svilaas and colleagues demonstrated that both

those over 65 years [RR 0.74 (0.55, 0.99)] and 65 years or younger [RR 0.58 (0.39, 0.88)] were less likely to experience a MBG of 0 or 1 if they used a catheter aspiration device, with no differences noted between groups (P-value for heterogeneity = 0.34 between subgroups). These findings are supported by results of the trial by Burzotta and colleagues, which also found that a catheter aspiration device was beneficial (obtained both a MBG≥2 and complete ST-segment resolution) in both those greater than 60 and 60 years or younger (no numerical data reported). (Burzotta 2005) The trial by Kelbaeck and colleagues suggested that age (<70 or ≥70) did not affect the efficacy of filter distal embolic protection (P-value for heterogeneity of effect between subgroups >0.10).[88]

Table 34. Results of subgroup analysis from randomized controlled trials evaluating the effect of age on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)	P-Values for Heterogeneity Between Subgroups
Svilaas, 2008[64] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Age > 65 y/o Age ≤ 65 y/o	RR 0.74 (0.55 to 0.99) RR 0.58 (0.39 to 0.88)	0.34

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; N=total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; y/o=years old

The impact of ethnicity was not evaluated as part of subgroup analyses and was only sporadically reported in the demographic tables of included trials. Thus we were unable to assess its affect on any outcome.

Two trials evaluated the impact of using filter distal embolic protection devices in patients with diabetes mellitus (Table 35).[88,94] One trial provided subgroup results based on the presence or absence of diabetes mellitus while a second trial only provided the results in the diabetic subgroup. In the trial by Kelbaeck and colleagues, there was a non-significant reduction in the risk of achieving ST-segment resolution (≥70 percent at 90 minutes post-PCI) in diabetic patients [RR 0.81 (0.55 to 1.19)] but a nonsignificant increase in nondiabetic patients [RR 1.07 (0.97 to 1.17)], with a weak trend towards differences between the groups (P-value for heterogeneity = 0.17 between subgroups).[88] In the trial by Cura and colleagues, those with diabetes had a nonsignificant reduction on the risk of achieving ST segment resolution (≥70 percent at 60 minutes post-PCI) [RR 0.91 (0.65 to 1.29)].[94] In the total population of the trial by Cura and colleagues, the use of the device did not increase the proportion of patients achieving complete ST-segment resolution at 60 minutes (61 percent versus 60 percent; p=0.91) or any other time point.[94] The device and endpoint were similar between trials so a pooled analysis of the diabetic subgroups of these two trials yielded a nonsignificant reduction in the risk of achieving ST-segment resolution [RR 0.86 (0.67 to 1.12)]. Due to the limited number of data points in this analysis statistical heterogeneity could not be assessed. Our literature search also identified a single individual patient data meta-analysis by Burzotta and colleagues.[160,161] This meta-analysis pooled data from eleven RCTs of adjunctive thrombectomy devices (catheter aspiration or mechanical thrombectomy) (N = 2686 patients) in patients with STEMI. Embolic protection device trials were not included in this meta-analysis. Kaplan–Meier analysis conducted in this meta-analysis showed that randomization to a thrombectomy device was associated with significantly lower risk of all-cause mortality (p = 0.049), MACE (p=0.01) and the composite endpoint of death or myocardial infarction (p=0.01). Upon subgroup analysis undertaken in this

meta-analysis, no qualitative difference in mortality was seen when splitting the study population according to the presence or absence of diabetes. [160,161]

Table 35. Results of subgroup analysis from randomized controlled trials evaluating the effect of diabetes mellitus on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Kelbaek, 2008[88] (N=626)	Distal Filter Embolic Protection	FilterWire-EZ or SpiderX	STSR ≥ 70% 90 min post-PCI	Diabetes No Diabetes	RR 0.81 (0.55 to 1.19) RR 1.07 (0.97 to 1.17)	0.17
Cura, 2007[94] (N=140)	Distal Filter Embolic Protection	SpiderRX	STSR ≥ 70% 60 min post-PCI	Diabetes	RR 0.91 (0.65 to 1.29)	N/A

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; min=minutes; N=total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

Three trials evaluated the impact of using embolic protection devices in patients with a history of smoking (Table 36).[18,94,111] Two trials provided subgroup results based on the presence or absence of a history of current smoking while a third trial only provided the results in the current smoker subgroup. While the use of a proximal balloon embolic protection device in the trial by Haeck and colleagues significantly increased the risk of achieving ST-segment resolution (>70 percent post-PCI) in smokers [RR 1.41 (1.11, 1.80)] but not nonsmokers [RR 1.32 (0.90, 1.95)], the results were similar between subgroups (P-value for heterogeneity = 0.78 between subgroups) (Haeck 2009). In the trial by Stone and colleagues, the use of a balloon distal embolic protection device did not significantly impact the risk of achieving an ST-segment resolution (>70 percent at 30 minutes post-PCI) in current smokers [RR 0.99 (0.81, 1.22)] or nonsmokers [RR 1.05 (0.87, 1.27)] with no difference seen between subgroups (P-value for heterogeneity = 0.68 between subgroups) (Stone 2005). In the trial by Cura and colleagues, smoking did not significantly impact the risk of achieving an ST-segment resolution (>70 percent 60 minutes post-PCI) [RR 1.12, 0.93, 1.34)].[94] As noted above, in the total population of the the trial by Cura and colleagues, the use of the device did not increase the proportion of patients achieving complete the ST-segment resolution at 60 minutes (61 percent versus 60 percent; p=0.91) or any other time point. When the current smoker subgroups of the trials were pooled, the risk of achieving an ST-segment resolution from embolic protection devices was nonsignificantly increased [RR 1.16 (0.95, 1.41)], but due to differences in the devices employed and the definitions of ST segment resolution, statistical heterogeneity was high (I^2 = 63.3 percent).

Table 36. Results of subgroup analysis from randomized controlled trials evaluating the effect of smoking on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Cura, 2007[94] (N=140)	Distal Filter Embolic Protection	SpiderRX	STSR ≥ 70% 60 min post-PCI	Current smoking	RR 1.12 (0.93 to 1.34)	NA
Stone, 2005[111] (N=501)	Distal Balloon Embolic Protection	GuardWire Plus	STSR ≥ 70% 30 min post-PCI	Current smoking No current smoking	RR 0.99 (0.81 to 1.22) RR 1.05 (0.87 to 1.27)	0.68
Haeck, 2009[18]	Proximal Balloon	Proxis	Post-PCI STSR ≥ 70%	Current smoking	RR 1.41 (1.11 to 1.80)	0.78

(N=284)	Embolic Protection	No current smoking	RR 1.32 (0.90 to 1.95)

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; min=minutes; N=total number of participants enrolled; NA=not applicable; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

The impact of ejection fraction on outcomes was not evaluated in subgroup analysis, thus precluding evaluation.

Only the trials by Burzotta and colleagues[82] and Stone and colleagues[111] provided subgroup results based on whether the device was used for primary angioplasty or for rescue angioplasty; however, the trial by Burzotta and colleagues did not provide any numerical data and thus was not included in (Table 37). In this trial, a catheter aspiration device was not statistically significantly beneficial (obtained both a MBG≥2 and complete ST-segment resolution) in either the subgroup of patients undergoing primary or rescue angioplasty (no numerical data reported).[82] In subgroup analysis within the trial by Stone and colleagues, neither those receiving a balloon distal embolic protection device for primary [RR 1.05 (0.90, 1.22)] nor rescue angioplasty [0.91 (0.64, 1.29)] had significant impact on ST-segment resolution (>70 percent at 30 minutes post-PCI) and no statistically significant difference was noted between subgroups (P-value for heterogeneity = 0.46 between subgroups).[111]

Table 37. Results of subgroup analysis from randomized controlled trials evaluating the effect of failed thrombolysis on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Stone, 2005[111] (N=501)	Distal Balloon Embolic Protection	GuardWire Plus	STSR ≥ 70% 30 min post-PCI	Primary angioplasty Rescue angioplasty (after failed thrombolysis)	RR 1.05 (0.90 to 1.22) RR 0.91 (0.64 to 1.29)	0.46

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; min-minutes; N=total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

Only one trial evaluated the effect of concurrent GP IIb/IIIA inhibitor use on a catheter aspiration device's efficacy.[82] In this trial by Burzotta and colleagues, the use of a catheter aspiration device was not statistically significantly beneficial (obtained both a MBG≥2 and complete ST-segment resolution) in either the subgroup who did or did not receive a GP IIb/IIIa inhibitor (no numerical data reported). In the aforementioned individual patient data meta-analysis,[160,161] subgroup analysis according to administration of GP IIb/IIIa inhibitors showed that randomization to an adjunctive thrombectomy device was associated with a mortality benefit in the subgroup of patients treated with GP IIb/IIIa inhibitors [n=1787 patients; hazard ratio 0.61 (0.38 to 0.90); p=0.045], but not in those without GP IIb/IIIa inhibitors [n=899 patients; hazard ratio 0.93 (0.48 to 1.80); p=0.84]. In addition, two trials evaluated the affect of concurrent GP IIb/IIIa inhibitor use on an embolic protection device's (distal filter and proximal balloon) ability to obtain complete ST-segment resolution (Table 38).[18,94] In both the trial by Cura and colleagues and Haeck and colleagues, the subgroup of patients administered GP IIb/IIIa

inhibitors achieved statistically significant increased rates of complete (>70 percent) ST-segment resolution [RR 1.36 (1.09 to 1.69) and RR 1.97 (1.17 to 3.32), respectively]. However in the trial by Haeck and colleagues, the subgroup not receiving a GP IIb/IIIa inhibitor did not realize a statistically significant improvement in complete ST-segment resolution [RR 1.20 (0.97 to 1.49)] The P-value for heterogeneity comparing the GP IIb/IIIa inhibitor use and nonuse groups in this trial (proximal embolic balloon protection) was nearing statistical significance (p=0.08), suggesting concomitant GP IIb/IIIa inhibitor use may enhance the ability of embolic protection to achieve complete ST-segment resolution.[18]

Table 38. Results of subgroup analysis from randomized controlled trials evaluating the effect of glycoprotein 2B 3A inhibitor use on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Cura, 2007[94] (N=140)	Distal Filter Embolic Protection	SpiderRX	STSR ≥ 70% 60 min post-PCI	GP2B3Ai use	RR 1.36 (1.09 to 1.69)	NA
Haeck, 2009[18] (N=284)	Proximal Balloon Embolic Protection	Proxis	Post-PCI STSR ≥ 70%	GP2B3Ai use No GP2B3Ai use	RR 1.97 (1.17 to 3.32) RR 1.20 (0.97 to 1.49)	0.08

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; GP2B 3Ai=glycoprotein 2B 3A inhibitor; min=minutes; N=total number of participants enrolled; NA=not applicable; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

A total of eight trials evaluated the affect of ischemia time on the efficacy of adjunctive devices to improve post-ST-segment myocardial infarction outcomes; however, only six provided numerical results (Table 39).[16,18,61,67,82,88,94,111] In the trial by Svilaas and colleagues, regardless of total ischemia time (≥180 minutes or <180 minutes) patients were less likely to have a MBG of 0 or 1 post-PCI when catheter aspiration was used [RR 0.73 (0.55 to 0.99) and RR 0.45 (0.28 to 0.74), respectively].[61] However, the P-value for heterogeneity between subgroups trended towards statistical significance (p=0.09) suggesting catheter aspiration may be more effective in patients undergoing PCI within 180 minutes. The trial by Ikari and colleagues also supported the conclusion that catheter aspiration devices had beneficial effects on MBG in patients undergoing early- (≤6 hours from symptom onset) and late- (6-24 hours) reperfusion [RRs of achieving a MBG-3 were 2.32 (1.50 to 3.58) and 2.34 (1.21 to 4.54)], respectively; with no difference between subgroups (p-value for heterogeneity 0.98 between subgroups) (ikari 2008). However, when looking at the slow/no-reflow or achievement of TIMI-3 blood flow endpoints in this trial, only patients undergoing late perfusion realized statistically significant benefits between longer and shorter ischemic times [RR 0.23 (0.07 to 0.72) and RR 1.45 (1.12 to 1.86)] (Ikari 2008). The P-value for heterogeneity between subgroups of effect trended towards statistical significance for slow/no-reflow (p=0.07) and was statistically significant for the TIMI-3 blood flow endpoint (p=0.02). Neither results from the trial by Ikari and colleagues nor from an additional trial by Chao and colleagues demonstrated any ischemia time subgroup to statistically significantly benefit from catheter aspiration in respect to final health outcomes

including target lesion or vessel revascularization, mortality, or combined major adverse cardiac events (all crossing the line of unity). Data from Chao did qualitatively appear to suggest decreasing efficacy of catheter aspiration on terminal endpoints as ischemic times increased; however, the effects between subgroups in each of these trials and endpoints were not found to be statistically significantly different (P-values for heterogeneity all >0.25). On their own, the three trials evaluating embolic protection devices (one each of distal balloon, distal filter and proximal balloon) did not suggest embolic protection devices allowed patients to achieve complete ST-segment resolution to a greater or lesser extent in different ischemia time subgroups (P-value for heterogeneity >0.22 for all between subgroups). Only those within the shorter ischemia time subgroup receiving proximal balloon embolic protection were found to have a statistically significantly increased chance of complete ST-segment resolution [RR 1.38 (1.06 to 1.80)]. When results from these three trials were pooled separately by shorter and longer ischemia subgroups, similar results were seen [pooled RR for shorter ischemia time 1.08 (0.85 to 1.38), $I^2 = 63.8$ percent and pooled RR for longer ischemia time 1.09 (0.95 to 1.24), $I^2 = 0$ percent). The trial by Burzotta and colleagues found that a catheter aspiration device was beneficial (obtained both a MBG≥2 and complete ST-segment resolution) in both those with ischemia times greater than 250 minutes and 250 minutes or less (no numerical data reported).[82] The trial by Kelbaeck and colleagues suggested that ischemic time (stratified at 6 hours) did not affect the efficacy of distal filter embolic protection (P-value for heterogeneity of effect between subgroups >0.10). Upon subgroup analysis undertaken in the individual patient data meta-analysis, no qualitative difference in mortality was seen when splitting the study population according to shorter, intermediate or longer ischemia times.[160,161]

Table 39. Results of subgroup analysis from randomized controlled trials evaluating the effect of ischemic time on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Svilaas, 2008[61] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Total ischemic time ≥ 180 min Total ischemic time < 180 min	RR 0.73 (0.55 to 0.99) RR 0.45 (0.28 to 0.74)	0.09
Chao, 2008[67] (N=74)	Catheter Aspiration	Export Aspiration Catheter	ΔTIMI	Onset-to-lab interval of 0-240 min Onset-to-lab interval of 241-480 min Onset-to-lab interval of 481-720 min	MD 0.30 (-0.60 to 1.20) MD 1.30 (0.46 to 2.14) MD 0.10 (-1.05 to 1.25)	0.15
Chao, 2008[67] (N=74)	Catheter Aspiration	Export Aspiration Catheter	ΔMBG	Onset-to-lab interval of 0-240 min Onset-to-lab interval of 241-480 min Onset-to-lab interval of 481-720 min	MD 1.30 (0.20 to 2.40) MD 1.60 (0.84 to 2.36) MD 0.60 (-0.71 to 1.91)	0.44
Chao, 2008[67] (N=74)	Catheter Aspiration	Export Aspiration Catheter	6 m MACE	Onset-to-lab interval of 0-240 min Onset-to-lab interval of 241-480 min Onset-to-lab interval of 481-720 min	RR 0.35 (0.08 to 1.56) RR 0.27 (0.03 to 2.11) RR 2.29 (0.26 to 20.13)	0.30
Chao, 2008[67] (N=74)	Catheter Aspiration	Export Aspiration Catheter	6 m mortality	Onset-to-lab interval of 0-240 min Onset-to-lab interval of 241-480 min Onset-to-lab interval of 481-720 min	RR 0.83 (0.02 to 39.24) RR 1.07 (0.02 to 50.43) RR 2.60 (0.13 to 53.46)	0.88
Chao, 2008[67] (N=74)	Catheter Aspiration	Export Aspiration Catheter	6 m TVR	Onset-to-lab interval of 0-240 min Onset-to-lab interval of 241-480 min Onset-to-lab interval of 481-720 min	RR 0.29 (0.03 to 2.54) RR 1.08 (0.07 to 15.50) RR 3.40 (0.16 to 71.52)	0.42
Ikari, 2008[16] (N=355)	Catheter Aspiration	TransVascular Aspiration Catheter	Slow flow/No reflow	Early reperfusion (hospital arrival ≤ 6 h from symptom onset) Late reperfusion (hospital arrival 6 h to 24 h from symptom onset)	RR 0.80 (0.42 to 1.52) RR 0.23 (0.07 to 0.72)	0.07
Ikari, 2008[16] (N=355)	Catheter Aspiration	TransVascular Aspiration Catheter	Final MBG=3	Early reperfusion (hospital arrival ≤ 6 h from symptom onset) Late reperfusion (hospital arrival 6 h to 24 h from symptom onset)	RR 2.32 (1.50 to 3.58) RR 2.34 (1.21 to 4.54)	0.98
Ikari, 2008[16] (N=355)	Catheter Aspiration	TransVascular Aspiration Catheter	Final TIMI flow grade=3	Early reperfusion (hospital arrival ≤ 6 h from symptom onset) Late reperfusion (hospital arrival 6 h to 24 h from symptom onset)	RR 1.04 (0.94 to 1.15) RR 1.45 (1.12 to 1.86)	0.02
Ikari, 2008[16] (N=355)	Catheter Aspiration	TransVascular Aspiration Catheter	TLR (PCI or CABG)	Early reperfusion (hospital arrival ≤ 6 h from symptom onset) Late reperfusion (hospital arrival 6 h to 24 h from symptom onset)	RR 0.69 (0.36 to 1.31) RR 0.31 (0.09 to 1.002)	0.25
Ikari, 2008[16] (N=355)	Catheter Aspiration	TransVascular Aspiration Catheter	MACE	Early reperfusion (hospital arrival ≤ 6 h from symptom onset) Late reperfusion (hospital arrival 6 h to 24 h from symptom onset)	RR 0.74 (0.40 to 1.37) RR 0.37 (0.13 to 1.05)	0.26
Svilaas, 2008[61] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Total ischemic time ≥ 180 min Total ischemic time < 180 min	RR 0.73 (0.55 to 0.99) RR 0.45 (0.28 to 0.74)	0.09
Cura, 2007[94] (N=140)	Distal Filter Embolic Protection	SpiderRX	STSR ≥ 70% 60 min post-PCI	Median time to admission < 150 min Median time to admission ≥ 150 min	RR 0.89 (0.69 to 1.16) RR 1.12 (0.87 to1.45)	0.22
Stone, 2005[111] (N=501)	Distal Balloon Embolic Protection	GuardWire Plus	STSR ≥ 70% 30 min post-PCI	Symptom onset to hospital arrival < 1 h Symptom onset to hospital arrival ≥ 1 h	RR 1.04 (0.82 to 1.32) RR 1.03 (0.87 to 1.24)	0.95
Haeck, 2009[18] (N=284)	Proximal Balloon Embolic Protection	Proxis	Post-PCI STSR ≥ 70%	Symptom onset to balloon time < 3 h Symptom onset to balloon time ≥ 3 h	RR 1.38 (1.06 to 1.80) RR 1.27 (0.90 to 1.78)	0.70

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CABG=coronary artery bypass graft; CI=confidence interval; h=hours; m=months; MACE=major adverse cardiac events; MBG=myocardial blush grade; MD=mean difference; min=minutes; N= total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution; TIMI=thrombolysis in myocardial infarction; TLR=target lesion revascularization; TVR=target vessel revascularization

Six trials evaluated the effect of visible thrombus at baseline on the efficacy of adjunctive devices (Table 40).[18,61,88,94,111] The trial by Svilaas and colleagues evaluated the effect of catheter aspiration use on MBG in patients with and without visible thrombus. Regardless of the presence of visible thrombus at baseline, catheter aspiration use resulted in fewer patients having a MBG of 0 or 1 post-procedure [RR with visible thrombus 0.61 (0.43 to 0.87) and RR without visible thrombus 0.70 (0.50 to 0.98)]. A test for heterogeneity between these subgroups showed no statistically significant difference in effect (p=0.58).[61] The trial by Burzotta and colleagues found that a catheter aspiration device was beneficial (obtained both a MBG≥2 and complete ST-segment resolution) in the subgroup of patients with a high thrombus burden (thrombus score of 4 to 4), but not those with a lower burden (thrombus score of 1 or 2) (no numerical data reported).[82] The remaining four trials evaluated embolic protection devices use on obtainment of complete ST-segment resolution in patients with and without visible thrombus. In the trial by Kelbaeck and colleagues, those patients without visible thrombus at baseline were more likely to achieve complete ST-segment resolution when using a filter distal embolic protection device versus control [RR 1.17 (1.01 to 1.37); however, the same device did not appear to benefit patients with visible thrombus [RR 1.00 (0.89 to 1.12). The difference between these subgroups what not found to be statistically significant (P-value for heterogeneity = 0.11 between subgroups).[88] The trial by Haeck and colleagues demonstrated contradictory results [RR with 1.31 (1.02 to 1.68) and RR without 1.39 (0.94 to 2.05) baseline thrombus, P-value for heterogeneity = 0.80 between subgroups).[18] In both the trial by Cura and colleagues and Stone and colleagues, the use of distal embolic protection (filter or balloon) was not found to be statistically significantly beneficial in either the visible thrombus or no thrombus subgroups.[94,111] When embolic protection studies were pooled separately by baseline thrombus subgroup, neither the visible thrombus nor no visible thrombus subgroups demonstrated statistical significant effects on complete ST-segment resolution [RR with baseline visible thrombus 1.10 (0.95 to 1.27), I^2 = 24.5 percent and RR without thrombus 1.12 (0.76 to 1.64), I^2 = not estimable).

Table 40. Results of subgroup analysis from randomized controlled trials evaluating the effect of visible thrombus on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Svilaas, 2008[61] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Visible thrombus on angiography No visible thrombus on angiography	RR 0.61 (0.43 to 0.87) RR 0.70 (0.50 to 0.98)	0.58
Kelbaek, 2008[88] (N=626)	Distal Filter Embolic Protection	FilterWire-EZ or SpiderX	STSR ≥ 70% 90 min post-PCI	Visible thrombus No visible thrombus	RR 1.00 (0.89 to 1.12) RR 1.17 (1.01 to 1.37)	0.11
Cura, 2007[94] (N=140)	Distal Filter Embolic Protection	SpiderRX	STSR ≥ 70% 60 min post-PCI	Baseline thrombosis	RR 1.02 (0.78 to 1.35)	NA
Stone, 2005[111] (N=501)	Distal Balloon Embolic Protection	GuardWire Plus	STSR ≥ 70% 30 min post-PCI	Baseline thrombus No baseline thrombus	RR 1.04 (0.89 to 1.22) RR 0.94 (0.70 to 1.27)	0.56
Haeck, 2009[18] (N=284)	Proximal Balloon Embolic Protection	Proxis	Post-PCI STSR ≥ 70%	Baseline thrombus No baseline thrombus	RR 1.31 (1.02 to 1.68) RR 1.39 (0.94 to 2.05)	0.80

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; min=minutes; N= total number of participants enrolled; NA=not applicable; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

A total of six trials evaluated the effect of the infarct-related artery on the efficacy of adjunctive devices to improve post-ST-segment myocardial infarction outcomes (Table 41).[18,61,82,88,94,111] In the trial by Svilaas and colleagues, catheter aspiration was found to reduce the risk of post-procedure MBG of 0 or 1 in patients with the RCA as the infarct-related artery [RR 0.48 (0.29 to 0.81)] or other arteries [RR 0.71 (0.53 to 0.93)]. A test for heterogeneity between these infarct-related artery subgroups showed no statistically significant difference in effect (p=0.19). The trial by Burzotta and colleagues found that a catheter aspiration device was not statistically significantly beneficial in obtaining both a MBG≥2 and complete ST-segment resolution in either those with a LAD or a RCA/CX as the infarct-related artery (no numerical data reported). Upon subgroup analysis undertaken in the individual patient data meta-analysis,[160,161] no qualitative difference in mortality was seen when splitting the study population according to the type of infarct-related artery (left anterior descending or circumflex artery or RCA). The remaining four trials evaluated embolic protection devices. In three of these four trials,[88,94,111] distal embolic protection devices (balloon or filter) failed to improve patients chance of attaining complete ST-segment resolution when evaluating patients by specific infarct-related artery subgroups. In addition, tests for heterogeneity between infract-related artery subgroups showed no statistically significant difference in effect in these three trials (p>0.20 for all). However, in the trial by Haeck and colleagues, proximal balloon embolic protection was found to increase patients chances of achieving complete ST-segment resolution when the lesion was in an anterior artery [RR 2.41 (1.11 to 5.19)], but not in other arteries [RR 1.20 (0.99 to 1.46)].[18] A test for heterogeneity between these infarct-related artery subgroups showed a trend towards a statistically significant difference in effect (p=0.09). Due to the heterogeneous nature by which trials divided subgroups, pooling was deemed inappropriate.

Table 41. Results of subgroup analysis from randomized controlled trials evaluating the effect of infarct-related artery on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Svilaas, 2008[61] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Infarct-related vessel: RCA Infarct-related vessel: other	RR 0.48 (0.29 to 0.81) RR 0.71 (0.53 to 0.93)	0.19
Kelbaek, 2008[88] (N=626)	Distal Filter Embolic Protection	FilterWire-EZ or SpiderX	STSR ≥ 70% 90 min post-PCI	LAD treated CX/RCA treated	RR 1.16 (0.96 to 1.40) RR 1.03 (0.94 to 1.14)	0.27
Cura, 2007[94] (N=140)	Distal Filter Embolic Protection	SpiderRX	STSR ≥ 70% 60 min post-PCI	Infarct-related vessel: LAD Infarct-related vessel: Non-LAD	RR 1.14 (0.78 to1.68) RR 0.93 (0.81 to 1.08)	0.33
Stone, 2005[111] (N=501)	Distal Balloon Embolic Protection	GuardWire Plus	STSR ≥ 70% 30 min post-PCI	LAD RCA or LCX	RR 0.83 (0.55 to 1.24) RR 1.09 (0.98 to 1.22)	0.20
Stone, 2005[111] (N=501)	Distal Balloon Embolic Protection	GuardWire Plus	STSR ≥ 70% 30 min post-PCI	Proximal vessel (LAD, RCA, or LCX) Non-proximal vessel	RR 1.00 (0.80 to 1.25) RR 1.04 (0.86 to 1.24)	0.78
Haeck, 2009[18] (N=284)	Proximal Balloon Embolic Protection	Proxis	Post-PCI STSR ≥ 70%	Anterior artery No anterior artery	RR 2.41 (1.11 to 5.19) RR 1.20 (0.99 to 1.46)	0.09

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; CX=circumflex coronary artery; LAD=left anterior descending coronary artery; LCX=left circumflex; MBG=myocardial blush grade; min=minutes; N=total number of participants enrolled; PCI=percutaneous coronary intervention; RCA=right coronary artery; RR=relative risk; STSR=ST-segment resolution

In addition to the effect of infarct-related artery, trials have also evaluated whether proximal or nonproximal location of the lesion within an artery affects the efficacy of adjunctive devices to improve post-ST-segment myocardial infarction outcomes (Table 42). The trial by Svilaas and colleagues demonstrated that catheter aspiration devices work equally well in preventing a post-procedure MBG of 0 or 1 in proximal and nonproximal lesion subgroups [RR 0.60 (0.43 to 0.85) and RR 0.69 (0.49 to 0.97), respectively] (P-value for heterogeneity between subgroups = 0.57).[61] While, in trial by Haeck and colleagues, only patients with proximally located lesions were shown to achieve a higher rate of complete ST-segment resolution with the use of proximal balloon embolic protection [RR 1.71 (1.14 to 2.55)].[18] Those in the nonproximal lesion subgroup did not realize statistically significant benefit [RR 1.18 (0.92 to 1.51)]. A test for heterogeneity between these infract-related artery subgroups showed no statistically significant difference in effect (p=0.12). The trial by Kelbaeck and colleagues suggested that proximal or nonproximal lesion location did not affect the efficacy of filter distal embolic protection (P-value for heterogeneity of effect between subgroups >0.10) (numerical data not reported).

Table 42. Results of subgroup analysis from randomized controlled trials evaluating the effect of lesion location on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Svilaas, 2008[61] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Proximal lesion No proximal lesion	RR 0.60 (0.43 to 0.85) RR 0.69 (0.49 to 0.97)	0.57
Haeck, 2009[18] (N=284)	Proximal Balloon Embolic Protection	Proxis	Post-PCI STSR ≥ 70%	Proximal lesion Non-proximal lesion	RR 1.71 (1.14 to 2.55) RR 1.18 (0.92 to 1.51)	0.12

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; N= total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

Five trials evaluated the effect of baseline TIMI flow on the efficacy of adjunctive devices to improve post-ST-segment myocardial infarction outcomes; however, the trial by Burzotta and colleagues did not provide numerical data and is therefore not included in (Table 43).[61,82,88,94,111] In the trial by Svilaas and colleagues, catheter aspiration was found to reduce the risk of post-procedural MBG of 0 or 1 in patients with a pre-procedural TIMI blood flow of 0 or 1 [RR 0.72 (0.55 to 0.95)], but fell just shy of significance in those with a TIMI flow graded at 2 or 3 [RR 0.60 (0.36 to 1.10)] (P-value for heterogeneity between subgroups = 0.54). Similar results were found in the trial by Burzotta and colleagues, which found that a catheter aspiration device was beneficial (obtained both a MBG≥2 and complete ST-segment resolution) in those with a baseline TIMI flow of 0 or 1, but not those with a TIMI flow of 2 or 3 (no numerical data reported). Upon subgroup analysis undertaken in the individual patient data meta-analysis,[160,161] no qualitative difference in mortality was seen when splitting the study population according to

pre-procedural TIMI flow (0–1 or 2–3). Three trials evaluated distal embolic protection (two filter, one balloon). In each of these trials, no pre-procedure TIMI subgroup was found to provide a statistically significant effect on complete ST-segment resolution.

Table 43. Results of subgroup analysis from randomized controlled trials evaluating the effect of baseline thrombolysis in myocardial infarction flow on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Svilaas, 2008[61] (N=1,071)	Catheter Aspiration	6-French Export Aspiration Catheter	Post-PCI MBG 0 or 1	Pre-PCI TIMI flow 0 or 1 Pre-PCI TIMI flow 2 or 3	RR 0.72 (0.55 to 0.95) RR 0.60 (0.36 to 1.01)	0.54
Kelbaek, 2008[88] (N=626)	Distal Filter Embolic Protection	FilterWire-EZ or SpiderX	STSR ≥ 70% 90 min post-PCI	Baseline TIMI 0 to 1 Baseline TIMI 2 to 3	RR 1.05 (0.93 to 1.18) RR 1.09 (0.94 to 1.26)	0.70
Cura, 2007[94] (N=140)	Distal Filter Embolic Protection	SpiderRX	STSR ≥ 70% 60 min post-PCI	Baseline TIMI 0/1 Baseline TIMI 2	RR 1.02 (0.79 to 1.33) RR 0.90 (0.66 to 1.23)	0.55
Stone, 2005[111] (N=501)	Distal Balloon Embolic Protection	GuardWire Plus	STSR ≥ 70% 30 min post-PCI	Baseline TIMI 0 or 1 Baseline TIMI 2 or 3	RR 1.03 (0.86 to 1.23) RR 0.99 (0.79 to 1.25)	0.79

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; MBG=myocardial blush grade; min=minutes; N=total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution; TIMI=thrombolysis in myocardial infarction

Only one trial evaluated the effect of direct stenting on the efficacy of adjunctive devices to improve post-ST-segment myocardial infarction outcomes (Table 44).[74] In both the direct stenting and no direct stenting patient subgroups, use of catheter aspiration in this trial had no effect on patients' chances of attaining a post-procedure TIMI flow of 3, experiencing distal embolization or no reflow. The P-values for heterogeneity of effect between subgroups was not statistically significant for any of these endpoints ($p>0.68$). When evaluating the MBG-3 and the complete ST-segment resolution endpoints in this trial, patients not undergoing direct stenting received statistically significant benefit from catheter aspiration use [RR 2.07 (1.33 to 3.22) and RR 1.56 (1.00 to 2.45)], but patients undergoing direct stenting did not [RR 1.41 (0.96 to 2.07) and RR 1.41 (0.81 to 2.47), respectively]. However, the P-value for heterogeneity of effect between subgroups was not statistically significant for either endpoint ($p\geq0.20$ for both).

Table 44. Results of subgroup analysis from randomized controlled trials evaluating the effect of direct stenting on clinical outcome

Study, Year (Total N)	Device Type	Device	Outcome	Characteristic	Effect Size ("X"R 95%CI)*	P-Values for Heterogeneity Between Subgroups*
Silva-Orrego, 2008[74] (N=148)	Catheter Aspiration	Pronto Extraction Catheter	Post-PCI TIMI 3	Direct stenting No direct stenting	RR 1.18 (0.91 to 1.54) RR 1.23 (0.93 to 1.61)	0.83
Silva-Orrego, 2008[74] (N=148)	Catheter Aspiration	Pronto Extraction Catheter	MBG 3	Direct stenting No direct stenting	RR 1.41 (0.96 to 2.07) RR 2.07 (1.33 to 3.22)	0.20
Silva-Orrego, 2008[74] (N=148)	Catheter Aspiration	Pronto Extraction Catheter	Maximal STSR > 70%	Direct stenting No direct stenting	RR 1.41 (0.81 to 2.47) RR 1.56 (0.995 to 2.45)	0.78
Silva-Orrego, 2008[74] (N=148)	Catheter Aspiration	Pronto Extraction Catheter	DE	Direct stenting No direct stenting	RR 0.35 (0.02 to 5.35) RR 0.38 (0.09 to 1.54)	0.96
Silva-Orrego, 2008[74] (N=148)	Catheter Aspiration	Pronto Extraction Catheter	No Reflow	Direct stenting No direct stenting	RR 0.12 (0.01 to 2.81) RR 0.25 (0.03 to 1.80)	0.68

*Some values were calculated based upon available trial data or estimated from figures

Abbreviations: CI=confidence interval; DE=distal embolization; MBG=myocardial blush grade; N=total number of participants enrolled; PCI=percutaneous coronary intervention; RR=relative risk; STSR=ST-segment resolution

In addition to the results from the above-mentioned RCTs and individual patient data meta-analysis, four observational studies were identified that provide data addressing key question 3.

The largest of these observational studies was the prospective, multicenter Osaka Acute Coronary Insufficiency Study (OACIS).[138] Researchers evaluated 3,913 patients who underwent PCI within 24 hours after symptom onset, of which, 990 patients (25.3 percent) were treated with catheter aspiration before PCI. Overall, OACIS found a trend towards 30-day mortality benefit with intracoronary thrombectomy (hazard ratio 0.658, p = 0.17). Intracoronary thrombectomy was an independent predictor of a lower 30-day mortality risk in patients aged ≥70 years (hazard ratio 0.239, p=0.007) and patients with diabetes mellitus (hazard ratio 0.275, p=0.039), but not in patients < 70 years of age or nondiabetics. P-value for heterogeneity between subgroups was statistically significant for age (p=0.008), but not diabetes status (p=0.17). Furthermore, baseline TIMI flow, gender, smoking and Killip class (a correlate to heart failure and ejection fraction) were not found to be modifiers of 30-day mortality (P-value for heterogeneity of effect between subgroups >0.24).

The remaining three single-arm observational studies conducted multivariate analysis. Cohen and colleagues evaluated catheter aspiration with the Export catheter in patients experiencing STEMI and undergoing primary PCI to identify co-variates associated with successful thrombectomy (increase in TIMI flow grade of at least 1). Upon multivariate logistic regression analysis, researchers identified ischemic time <6 hours as the only independent predictor of successful thrombectomy (p=0.04).[135] Kramer and colleagues evaluated the use of catheter aspiration (Rescue or Export) or proximal balloon embolic protection (Proxis) in 914 patients experiencing STEMI and undergoing primary PCI. They found that age >60 years [hazard ratio 1.83 (1.14 to 2.93)], female gender [hazard ratio 4.22 (2.29 to 7.76)] and the presence of diabetes mellitus [hazard ratio 1.73 (1.09 to 2.76)] were all independent predictors of increased mortality by four years, where as, current smoking, total ischemic time and having the LAD as the infarct-related artery were not.[143] Ochala and colleagues conducted a multivariate analysis to determine independent predictors of achieving a post-procedure TIMI flow of 2 or 3 in the distal balloon embolic protection (PercuSurge) arm of a RCT of 120 ST-segment elevation patients undergoing primary PCI. In this analysis, the presence of baseline thrombus was found to independently predict increased odds of TIMI 2 or 3 flow in embolic protection device treated patients. LAD as the infarct-related artery, ischemic time greater than or equal to 6 hours and presence of diabetes mellitus were not found to be predictors of TIMI 2 or 3 flow attainment.[153]

Summary

While a clinical trial or observational study may demonstrate an overall benefit for an intervention, this benefit may or may not occur to a similar extent across different types of constituents. As such, it is important to determine what, if any, data exists evaluating the impact of an intervention in these important subgroups. For Key Question 3, nine RCTs, an individual patient data meta-analysis[160,161] and four observational studies provided some insight. However, most of the evidence is in the form of subgroup analysis stratified by covariate within RCTs.

These subgroup analyses were typically underpowered to demonstrate statistically significant differences within and between subgroups and we cannot be sure that the results attained were due to a lack of impact or lack of power. Clinical trials with larger sample sizes would be needed to draw more definitive conclusions from such analyses. Secondly, many of the included trials and studies conducted subgroup analyses on large numbers of co-variates making conclusions susceptible to bias resulting from multiple hypothesis testing.

Finally, the clinical trials provide univariate evaluations and we do not know if the results are due the factor being investigated or due to a confounder that one subgroup has in a differing amount from another subgroup.

Randomized trials and an individual patient data meta-analysis of RCTs have not demonstrated statistically significant effect modification of aspiration, mechanical thrombectomy or embolic protection device efficacy by gender, diabetes, smoking status, primary or rescue PCI, presence of thrombus-containing lesion, pre-PCI TIMI flow, or the use of direct stenting. Furthermore, no RCTs evaluated the effect of ethnicity or ejection fraction on thrombectomy or embolic protection device efficacy. While randomized trials and the individual patient meta-analysis did not show an affect of age, diabetes, baseline thrombus and gender on aspiration or thrombectomy device efficacy, a limited number of observational studies did.

Individual randomized trials did not demonstrate a modifying effect of glycoprotein IIb/IIIa use on aspiration or mechanical thrombectomy device efficacy. However, the individual patient data meta-analysis found that randomization to aspiration or mechanical thrombectomy was associated with a survival benefit in the subgroup of patients treated with glycoprotein IIb/IIIa inhibitors, but not in those not receiving them. This may suggest a modifying effect of glycoprotein IIb/IIIa inhibitors with these devices. While embolic protection devices were not studied in the individual patient meta-analysis, a single randomized trial of proximal balloon protection demonstrated a similar modifying affect of glycoprotein IIb/IIIa inhibitor use; with greater efficacy in those receiving a glycoprotein IIb/IIIa inhibitor. Limited data exists evaluating the effect of glycoprotein IIb/IIIa inhibitor use on the efficacy of distal embolic protection devices.

It appears doubtful that ischemic time affects the efficacy of aspiration or mechanical thrombectomy devices or embolic protection devices. Data regarding the affect of ischemic time on efficacy of aspiration catheter efficacy (MBG and TIMI 3 flow) was conflicting in randomized trials; while, the OASIS observational study suggested prolonged ischemic time negatively affected the ability of thrombectomy or embolic protection devices to reduce mortality. Neither beneficial nor harmful associations between ischemic time and aspiration or mechanical thrombectomy devices were observed in the individual patient data meta-analysis.

Individual randomized trials and the individual patient meta-analysis suggested no modification of aspiration or mechanical thrombectomy device efficacy based upon infarct-related artery. However, a single trial, found a trend towards statistically significant greater efficacy (complete ST-segment resolution) of proximal balloon embolic protection in those with an anterior infarct-related artery. No studies have evaluated whether distal embolic protection device efficacy is impacted by infarct-related artery location.

Strength of Evidence and Applicability

Strength of Evidence

A summary of the strength of evidence for Key questions 1 and 2 are in Table 45 and Table 46 while the full evaluation of the strength of evidence for each outcome is found in Appendix G.

A majority of the available evidence was in the STEMI population. In patients with STEMI, there was a high strength of evidence that catheter aspiration devices versus control decreased the risk of MACE, distal embolization and no reflow. The strength of evidence was moderate that catheter aspiration devices increased the attainment of ST-segment resolution, MBG-3, or TIMI-3 blood flow and had no effect on ejection fraction and the risk of stroke versus control. The strength of evidence was low that catheter aspiration devices had no effect on the risk of mortality, myocardial infarction, or target revascularization versus control. There was a strong trend towards the reduction in mortality risk [RR 0.69 (0.47, 1.02)] and when limited to trials of higher methodological quality, catheter aspiration devices significantly reduced the risk of mortality versus control [RR 0.67 (0.45, 0.997)]. Regarding adverse events, the strength of evidence for catheter aspiration devices versus control was high that the risk of coronary dissection was decreased and that there was no effect on prolongation of procedure time. For side branch occlusion, the strength of evidence was moderate that catheter aspiration devices had no effect versus control, and insufficient for coronary perforation.

The strength of evidence associated with outcomes in the STEMI population undergoing PCI with a mechanical thrombectomy device was predominately moderate to low. There was moderate strength of evidence that mechanical thrombectomy devices had no effect on the risk of mortality, myocardial infarction, stroke, target revascularization, distal embolization, no reflow, impact on ejection fraction or attainment of TIMI-3 blood blow versus control. The strength of evidence was low that mechanical thrombectomy devices had no effect on MACE, ST-segment resolution, or attainment of a MBG-3. When analyzing different time points for the outcome of MACE, there was a signficant reduction in the risk of MACE at 365 days [RR 0.66 (0.44, 0.97) not seen in evaluations at earlier time periods, although this was based on a single randomized controlled trial. The strength of evidence for prolongation of procedure time was high for mechanical thrombectomy devices versus control, while the strength of evidence was low that there was no effect in coronary dissection or perforation with the use of mechanical thrombectomy devices versus control. Strength of evidence was insufficient for side branch occlusion.

For comparisons between distal filter embolic protection devices and control, only one evaluation had a high strength of evidence. The strength of evidence was high that distal filter embolic protection devices have no effect on the risk of MACE versus control. The strength of evidence was moderate that there was no effect on the risk of mortality, myocardial infarction, ST-segment resolution, or attainment of a MBG-3. The strength of evidence was low that there was no effect on the risk of target revascularization, no reflow, attainment of TIMI-3 blood flow, or impact on ejection fraction. The strength of evidence was insufficient for the risk of stroke and distal embolization. For adverse outcomes, the strength of evidence was insufficient for all outcomes with one exception. There was a low strength of evidence that distal filter embolic protection devices have no effect on the risk of side branch occlusion.

The strength of evidence was high that there was an increased risk of attaining a MBG-3 with the use of a distal balloon embolic protection device versus control. The strength of evidence was moderate that there was no effect on the risk of mortality, myocardial infarction, target revascularization, MACE, ST-segment resolution, distal embolization, no reflow, or impact on ejection fraction and low that there was no effect on attainment of TIMI-3 blood flow with the use of distal balloon embolic protection devices versus control. The strength of evidence was insufficient that distal balloon embolic protection devices had no effect on stroke versus control. Regarding adverse outcomes, strength of evidence was moderate that there was no effect on the risk of side branch occlusion, low that there was no effect on the risk of coronary perforation and that there was prolonged procedure time, and insufficient for coronary dissection when comparing distal balloon embolic protection devices versus control.

For all final health, intermediate and adverse outcomes the strength of evidence was insufficient for the comparison of proximal balloon embolic protection devices versus control with one exception. The strength of evidence was moderate that proximal balloon embolic protection devices prolong procedure time versus control.

For comparisons between embolic protection devices combined versus control, the strength of evidence was high that there was no effect on the risk of mortality or target revascularization. The strength of evidence was moderate that the attainment of a MBG-3 was increased with the use of an embolic protection device versus control, and that there was no effect on the risk of myocardial infarction, stroke, MACE, distal embolization, no reflow, or impact on ejection fraction. The strength of evidence was low that there was no effect on the risk of ST-segment resolution or attaining a TIMI-3 blood flow with the use of embolic protection devices combined versus control. In terms of adverse outcomes, the strength of evidence was moderate that the use of embolic protection devices combined prolong procedure time versus control and have no effect on the risk of side branch occlusion. The strength of evidence was low that embolic protection devices combined have no effect on the risk of coronary perforation and was insufficient for coronary dissection.

In the mixed ACS population strength of evidence was predominately insufficient or low for all device categories versus control. There was a high strength of evidence that distal balloon embolic protection devices decreased the risk of no reflow versus control, which was propagated into the embolic protection devices combined analysis. There was a moderate strength of evidence that distal balloon embolic protection devices increased the attainment of ST-segment resolution and a MBG-3 versus control, both of which were propagated into the embolic protection devices combined analyses. The strength of evidence was insufficient for all adverse health outcomes in all device categories with one exception. For distal balloon embolic protection devices the strength of evidence was moderate for prolonging procedural time versus control, which propagated into the embolic protection devices combined analysis.

In the UA / NSTEMI population the strength of evidence was insufficient for all final health and intermediate outcomes for all device categories with one exception. For distal filter embolic protection devices versus control, there was moderate strength of evidence for no effect on TIMI-3 blood flow, which was propagated into the embolic protection devices combined analysis. Evidence was also insufficient for all adverse health outcomes for all device categories within this patient population.

Applicability

The applicability of evidence was high for the evaluation of distal balloon embolic protection devices impact on stroke versus control. Applicability of the trials was in the moderate to low range (63% and 34% of comparisons, respectively) for all other outcomes because the trials were mostly conducted outside of the United States. The applicability of individual trials, studies, and the body of evidence per outcome assessed can be found in Appendix H along with the description of factors that impacted the applicability of the body of evidence.

Table 45. Summary of the strength of evidence for Key Question 1

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
STEMI-Catheter Aspiration Devices					
	Mortality	RCTs and observational	11 (10,1)	No effect	Low
	Myocardial infarction	RCTs and observational	11 (10,1)	No effect	Low
	Stroke	RCTs and observational	4 (3,1)	No effect	Moderate
	Target revascularization	RCTs and observational	10 (9,1)	No effect	Low
	MACE	RCTs and observational	12 (11,1)	Decreases risk	High
	ST-segment resolution	RCTs and observational	16 (15,1)	Increases risk	Moderate
	Ejection fraction	RCTs	10 (10,0)	No effect	Moderate
	Myocardial Blush Grade 3	RCTs	13 (13,0)	Increases risk	Moderate
	TIMI-3	RCTs	13 (13,0)	Increases risk	Moderate
	Distal embolization	RCTs and observational	11 (10,1)	Decreases risk	High
	No reflow	RCT	7 (7,0)	Decreases risk	High
STEMI-Mechanical Thrombectomy Devices					
	Mortality	RCTs and observational	5 (4,1)	No effect	Moderate
	Myocardial infarction	RCTs and observational	4 (3,1)	No effect	Moderate
	Stroke	RCTs and observational	5 (4,1)	No effect	Moderate

Table45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Target revascularization	RCTs and observational	4 (3,1)	No effect	Moderate
	MACE	RCTs and observational	4 (3,1)	No effect	Low
	ST-segment resolution	RCTs	5 (5,0)	No effect	Low
	Ejection fraction	RCTs	2 (2,0)	No effect	Moderate
	Myocardial Blush Grade 3	RCTs	4 (4,0)	No effect	Low
	TIMI-3	RCTs and observational	5 (4,1)	No effect	Moderate
	Distal embolization	RCT	3 (3,0)	No effect	Moderate
	No reflow	RCTs	3 (3,0)	No effect	Moderate
STEMI- Distal Filter Embolic Protection Devices					
	Mortality	RCTs	4 (4,0)	No effect	Moderate
	Myocardial infarction	RCTs	4 (4,0)	No effect	Moderate
	Stroke	RCT	1 (1,0)	No/limited data	Insufficient
	Target revascularization	RCTs	2 (2,0)	No effect	Low
	MACE	RCTs	4 (4,0)	No effect	High
	ST-segment resolution	RCTs	4 (4,0)	No effect	Moderate
	Ejection fraction	RCTs	2 (2,0)	No effect	Low

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Myocardial Blush Grade 3	RCTs	2 (2,0)	No effect	Moderate
	TIMI-3	RCTs	4 (4,0)	No effect	Low
	Distal embolization	RCT	1 (1,0)	No/limited data	Insufficient
	No reflow	RCTs	2 (2,0)	No effect	Low
STEMI- Distal Balloon Embolic Protection Devices					
	Mortality	RCTs	4 (4,0)	No effect	Moderate
	Myocardial infarction	RCTs	5 (5,0)	No effect	Moderate
	Stroke	RCT	1 (1,0)	No/limited data	Insufficient
	Target revascularization	RCTs	5 (5,0)	No effect	Moderate
	MACE	RCTs	5 (5,0)	No effect	Moderate
	ST-segment resolution	RCTs	4 (4,0)	No effect	Moderate
	Ejection fraction	RCTs	5 (5,0)	No effect	Moderate
	Myocardial blush grade 3	RCTs	6 (6,0)	Increases risk	High
	TIMI-3	RCTs	6 (6,0)	No effect	Low
	Distal embolization	RCTs	4 (4,0)	No effect	Moderate
	No reflow	RCTs	4 (4,0)	No effect	Moderate

Tabl 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
STEMI-Proximal balloon embolic protection devices					
	Mortality	RCT	1 (1,0)	No/limited data	Insufficient
	Myocardial infarction	RCT	1 (1,0)	No/limited data	Insufficient
	Stroke	RCT	1 (1,0)	No/limited data	Insufficient
	Target revascularization	RCT	1 (1,0)	No/limited data	Insufficient
	MACE	RCT	1 (1,0)	No/limited data	Insufficient
	ST-segment resolution	RCT	1 (1,0)	No/limited data	Insufficient
	Ejection fraction	-	0	No /limited data	Insufficient
	Myocardial blush grade 3	RCT	1 (1,0)	No/limited data	Insufficient
	TIMI-3	RCT	1 (1,0)	No/limited data	Insufficient
	Distal embolization	RCT	1 (1,0)	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
STEMI- Embolic Protection Devices Combined					
	Mortality	RCTs and observational	10 (9,1)	No effect	High
	Myocardial infarction	RCTs	10 (10,0)	No effect	Moderate
	Stroke	RCTs	3 (3,0)	No effect	Moderate

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Target revascularization	RCTs	8 (8,0)	No effect	High
	MACE	RCTs and observational	11(10,1)	No effect	Moderate
	ST-segment resolution	RCTs	9 (9,0)	No effect	Low
	Ejection fraction	RCTs	7 (7,0)	No effect	Moderate
	Myocardial blush grade 3	RCTs	9 (9,0)	Increases risk	Moderate
	TIMI-3	RCTs	11 (11,0)	No effect	Low
	Distal embolization	RCTs	6 (6,0)	No effect	Moderate
	No reflow	RCTs	6 (6,0)	No effect	Moderate
UA/NSTEMI-Catheter Aspiration Devices					
	Mortality	-	0	No/limited data	Insufficient
	Myocardial infarction	-	0	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	-	0	No/limited data	Insufficient
	MACE	-	0	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	-	0	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Myocardial blush grade 3	-	0	No/limited data	Insufficient
	TIMI-3	-	0	No/limited data	Insufficient
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
UA/NSTEMI-Mechanical Thrombectomy Devices					
	Mortality	-	0	No/limited data	Insufficient
	Myocardial infarction	-	0	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	-	0	No/limited data	Insufficient
	MACE	-	0	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial blush grade 3	-	0	No/limited data	Insufficient
	TIMI-3	-	0	No/limited data	Insufficient
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
UA/NSTEMI-Distal Filter Embolic Protection Devices					
	Mortality	RCT	1 (1,0)	No/limited data	Insufficient
	Myocardial infarction	RCT	1 (1,0)	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	RCT	1 (1,0)	No/limited data	Insufficient
	MACE	RCT	1 (1,0)	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial blush grade 3	-	0	No/limited data	Insufficient
	TIMI-3	RCT	1 (1,0)	No effect	Moderate
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	RCT	1 (1,0)	No/limited data	Insufficient
UA/NSTEMI-Distal Balloon Embolic Protection Devices					
	Mortality	-	0	No/limited data	Insufficient
	Myocardial Infarction	-	0	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Target revascularization	-	0	No/limited data	Insufficient
	MACE	-	0	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial blush grade 3	-	0	No/limited data	Insufficient
	TIMI-3	-	0	No/limited data	Insufficient
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
UA/NSTEMI-Proximal Balloon Embolic Protection Devices					
	Mortality	-	0	No/limited data	Insufficient
	Myocardial infarction	-	0	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	-	0	No/limited data	Insufficient
	MACE	-	0	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial blush grade 3	-	0	No/limited data	Insufficient
	TIMI-3	-	0	No/limited data	Insufficient
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
UA/NSTEMI-Embolic Protection Devices Combined					
	Mortality	RCT	1 (1,0)	No/limited data	Insufficient
	Myocardial infarction	RCT	1 (1,0)	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	RCT	1 (1,0)	No/limited data	Insufficient
	MACE	RCT	1 (1,0)	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial Blush Grade 3	-	0	No/limited data	Insufficient
	TIMI-3	RCT	1 (1,0)	No effect	Moderate
	Distal embolization	-	0	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	No reflow	RCT	1 (1,0)	No/limited data	Insufficient
Mixed ACS-Catheter Aspiration Devices					
	Mortality	RCT and Observational	2 (1, 1)	No effect	Low
	Myocardial infarction	-	0	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	-	0	No/limited data	Insufficient
	MACE	-	0	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial Blush Grade 3	RCT	1 (1,0)	Increases risk	Low
	TIMI-3	RCTs	2 (1,1)	No effect	Low
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
Mixed ACS-Mechanical Thrombectomy Devices					
	Mortality	RCT and observational	2 (1,1)	No effect	Low
	Myocardial infarction	Observational	1 (1,0)	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Target revascularization	RCT and observational	2(1,1)	No effect	Low
	MACE	RCT and observational	2 (1,1)	No effect	Low
	ST-segment resolution	RCT	1 (1,0)	Increases risk	Moderate
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial Blush Grade 3	-	0	No/limited data	Insufficient
	TIMI-3	RCT and observational	2 (1,1)	No effect	Low
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
Mixed ACS-Distal Filter Embolic Protection Devices					
	Mortality	RCT	1 (1,0)	No/limited data	Insufficient
	Myocardial infarction	RCT	1 (1,0)	No/limited data	Insufficient
	Stroke	RCT	1 (1,0)	No/limited data	Insufficient
	Target revascularization	RCT	1 (1,0)	No/limited data	Insufficient
	MACE	RCT	1 (1,0)	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	RCT	1 (1,0)	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Myocardial Blush Grade 3	-	0	No/limited data	Insufficient
	TIMI-3	RCT	1 (1,0)	No/limited data	Insufficient
	Distal embolization	RCT	1 (1,0)	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
Mixed ACS-Distal Balloon Embolic Protection Devices					
	Mortality	RCT	2 (2,0)	No effect	Low
	Myocardial infarction	-	0	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	-	0	No/limited data	Insufficient
	MACE	RCT	1 (1,0)	No/limited data	Insufficient
	ST-segment resolution	RCT	1 (1,0)	Increases risk	Moderate
	Ejection fraction	RCT	1 (1,0)	No/limited data	Insufficient
	Myocardial Blush Grade 3	RCT	2 (2,0)	Increases risk	Moderate
	TIMI-3	RCT	2 (2,0)	No effect	Low
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	RCT	1 (1,0)	Decreases risk	High

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
Mixed ACS-Proximal Balloon Embolic Protection Devices					
	Mortality	-	0	No/limited data	Insufficient
	Myocardial infarction	-	0	No/limited data	Insufficient
	Stroke	-	0	No/limited data	Insufficient
	Target revascularization	-	0	No/limited data	Insufficient
	MACE	-	0	No/limited data	Insufficient
	ST-segment resolution	-	0	No/limited data	Insufficient
	Ejection fraction	-	0	No/limited data	Insufficient
	Myocardial Blush Grade 3	-	0	No/limited data	Insufficient
	TIMI-3	-	0	No/limited data	Insufficient
	Distal embolization	-	0	No/limited data	Insufficient
	No reflow	-	0	No/limited data	Insufficient
Mixed ACS-Embolic Protection Devices Combined					
	Mortality	RCTs	3 (3,0)	No effect	Low
	Myocardial infarction	RCT	1 (1,0)	No/limited data	Insufficient

Table 45. Summary of the strength of evidence for Key Question 1 (continued)

In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect final or intermediate health outcomes compared to usual care?

Population-Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Stroke	RCT	1 (1,0)	No/limited data	Insufficient
	Target revascularization	RCT	1 (1,0)	No/limited data	Insufficient
	MACE	RCTs	2 (2,0)	No effect	Low
	ST-segment resolution	RCT	1 (1,0)	Increases risk	Moderate
	Ejection fraction	RCTs	2 (2,0)	No effect	Low
	Myocardial Blush Grade 3	RCTs	2 (2,0)	Increases risk	Moderate
	TIMI-3	RCTs	3 (3,0)	No effect	Low
	Distal embolization	RCT	1 (1,0)	No/limited data	Insufficient
	No reflow	RCT	1 (1,0)	Decreases risk	High

* Outcomes reported are those with the longest duration of follow –up

Abbreviation: ACS=acute coronary syndrome; MACE=major adverse cardiovascular event; MBG=myocardial blush grade; NSTEMI=non-ST-segment elevation myocardial infarction; RCT=randomized controlled trial; STEMI=ST-segment elevation myocardial infarction; TIMI=thrombolysis in myocardial infarction; UA=unstable angina

Table 46. Summary of the strength of evidence for Key Question 2

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
STEMI- Catheter Aspiration Devices					
	Coronary dissection	RCTs and Observational	5 (4,1)	Decreases risk	High
	Coronary perforation	RCT	1 (1,0)	No/limited data	Insufficient
	Prolonged procedure time	RCTs	8 (8,0)	No effect	High
	Side branch occlusion	RCTs	2 (2,0)	No effect	Moderate
STEMI- Mechanical Thrombectomy Devices					
	Coronary dissection	RCT	1 (1,0)	No effect	Low
	Coronary perforation	RCTs and Observational	3 (2,1)	No effect	Low
	Prolonged procedure time	RCTs	3 (3,0)	Prolongs time	High
	Side branch occlusion	RCT	1 (1,0)	No/limited data	Insufficient
STEMI- Distal Filter Embolic Protection Devices					
	Coronary dissection	RCT	1 (1,0)	No/limited data	Insufficient

Table46. Summary of the strength of evidence for Key Question 2 (continued)

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Coronary perforation	RCT	1 (1,0)	No/limited data	Insufficient
	Prolonged procedure time	RCT	1 (1,0)	No/limited data	Insufficient
	Side branch occlusion	RCT	1 (1,0)	No effect	Low
STEMI- Distal Balloon Embolic Protection Devices					
	Coronary dissection	RCT	1 (1,0)	No/limited data	Insufficient
	Coronary perforation	RCT	1 (1,0)	No effect	Low
	Prolonged procedure time	RCTs	3 (3,0)	Prolongs time	Low
	Side branch occlusion	RCTs	2 (2,0)	No effect	Moderate
STEMI- Proximal Balloon Embolic Protection Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	RCT	1 (1,0)	Prolongs time	Moderate

Table46. Summary of the strength of evidence for Key Question 2 (continued)

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Side branch occlusion	-	0	No/limited data	Insufficient
STEMI- Embolic Protection Devices Combined					
	Coronary dissection	RCTs	2 (2,0)	No/limited data	Insufficient
	Coronary perforation	RCT	1 (1,0)	No effect	Low
	Prolonged procedure time	RCTs	5 (5,0)	Prolongs time	Moderate
	Side branch occlusion	RCTs	3 (3,0)	No effect	Moderate
UA/NSTEMI- Catheter Aspiration Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
UA/NSTEMI- Mechanical Thrombectomy Devices					

Table46. Summary of the strength of evidence for Key Question 2 (continued)

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
UA/NSTEMI-Distal Filter Embolic Protection Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
UA/STEMI-Distal Balloon Embolic Protection Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient

Table46. Summary of the strength of evidence for Key Question 2 (continued)

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
UA/STEMI-Proximal Balloon Embolic Protection Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
UA/STEMI-Embolic Protection Devices Combined					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient

Table46. Summary of the strength of evidence for Key Question 2 (continued)

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
Mixed ACS-Catheter Aspiration Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
Mixed ACS-Mechanical Thrombectomy Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
Mixed ACS-Distal Filter Embolic Protection Devices					
	Coronary dissection	-	0	No/limited data	Insufficient

Table46. Summary of the strength of evidence for Key Question 2 (continued)

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient
	Side branch occlusion	-	0	No/limited data	Insufficient
Mixed ACS-Distal Balloon Embolic Protection Devices					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	RCT	1 (1,0)	Prolongs time	Moderate
	Side branch occlusion	-	0	No/limited data	Insufficient
Mixed ACS-Proximal Balloon Embolic Protection					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	-	0	No/limited data	Insufficient

Table46. Summary of the strength of evidence for Key Question 2 (continued)

KQ2 In patients with acute coronary syndrome who are undergoing percutaneous coronary intervention of native vessels, does the use of an adjunctive device affect adverse outcomes compared to usual care.

Population- Device Category	Outcome*	Type of Study	Total Number of Studies N (RCT, Observational)	Conclusion	Strength of Evidence
	Side branch occlusion	-	0	No/limited data	Insufficient
Mixed ACS-Embolic Protection Devices Combined					
	Coronary dissection	-	0	No/limited data	Insufficient
	Coronary perforation	-	0	No/limited data	Insufficient
	Prolonged procedure time	RCT	1 (1,0)	Prolongs time	Moderate
	Side branch occlusion	-	0	No/limited data	Insufficient

*Outcomes reported are those with the longest duration of follow –up

Abbreviation: ACS=acute coronary syndrome; MACE=major adverse cardiovascular event; MBG=myocardial blush grade; NSTEMI=non-ST-segment elevation myocardial infarction; RCT=randomized controlled trial; STEMI=ST-segment elevation myocardial infarction; TIMI=thrombolysis in myocardial infarction; UA=unstable angina

Chapter 4. Discussion

The determination of the balance of benefits to harms is difficult because many of the final health outcome and adverse event evaluations are underpowered. We cannot know for certain whether the nonsignificant increases or decreases are due to a real effect or to chance. The applicability of the body of evidence is highest for male patients with STEMI undergoing primary PCI of the native vessels. Data is moderately applicable to female patients. The majority of data is derived from trials and studies conducted outside of the United States evaluating devices that are not currently available in the United States, therefore the applicability is limited. Overall, applicability is low in patients with other ACSs or in patients undergoing rescue PCI.

The use of catheter aspiration devices significantly lowered the risk of MACE and coronary dissection in the overall analysis and the good quality trial analyses while mortality was significantly lower in good quality trials and nonsignificantly lower in the overall analysis versus control. The risk of myocardial infarction and target revascularization were nonsignificantly reduced versus control. However, the risk of stroke and side branch occlusion was nonsignificantly increased and eight of nine trials found a nonsignificant prolongation of the time needed to conduct the PCI procedure versus control. Intermediate health outcomes show significant reductions in distal embolization and no reflow and significantly more patients experience ST-segment resolution, higher MBG, and near normal (TIMI 3) blood flow though the target vessel versus control which supports the nonsignificant beneficial findings noted above. As such, more research is needed to truly determine the balance of benefits to harms.

Mechanical thrombectomy devices did not significantly affect the risk of outcomes as the use of catheter aspiration devices did. The use of mechanical thrombectomy devices nonsignificantly increase the risk of mortality, stroke, MACE, coronary dissection, and coronary perforation in the overall analyses and analyses limited to good quality trials while significantly increasing the time needed to conduct the PCI procedure in three trials. While the risk of myocardial infarctions and target revascularization were nonsignificantly reduced, this did not translate into nonsignificant reductions in mortality or MACE. However, these nonsignificant findings may be misleading since many of the trials evaluating this procedure versus control had a shorter duration of followup. When we evaluate mortality and MACE in studies of 365 days or longer, there is a nonsignificant reduction in mortality and significant reduction in MACE, althought the significant reduction in MACE is based on the results of a single trial. Unlike with catheter aspiration devices, there are no significant beneficial effects on intermediate health outcomes and while most are in the right direction of effect, the chance of achieving near normal (TIMI 3) blood flow was nonsignificantly reduced. As such, more research is needed to truly determine the balance of benefits to harms with mechanical thrombectomy devices.

The use of embolic protection devices are based on a limited number of studies and no significant effects on any final health outcomes were seen in overall analyses or those limited to good quality trials. It is difficult to assess the impact on final health outcomes and intermediate outcomes for these devices. In ST-elevation myocardial infarction, distal balloon devices significantly increase the chance of achieving a MBG-3 and provide nonsignificant benefits on ST-segment resolution, near normal (TIMI 3) blood flow, and preventing no reflow, but nonsignificatly increase the risk of distal embolization. Distal filter devices showed more of a

mixed picture with nonsignificant beneficial effects on ST-segment resolution, distal embolization, and no reflow but nonsignificant detrimental effects on MBG and the attainment of near normal (TIMI 3) blood flow. There was a paucity of trials available to evaluate adverse events with any of the embolic protection devices. The only significant findings being an increased time to perform a PCI procedure for all three types of embolic protection devices individually and when evaluated all together versus control. Distal filter and distal balloon devices nonsignificantly reduce the risk of side branch occlusion but distal balloon devices nonsignificantly increase the risk of coronary perforation. As such, the balance of benefits to harms cannot be determined for these device classes.

Given the inadequate power in overall analyses or lack of data, we cannot definitively determine the impact of therapy in subpopulations. No data was available to determine if the results differed based on ethnicity or ejection fraction. Given the available data, the concomitant use of a glycoprotein IIb/IIIa receptor antagonist and a device may be associated with a survival benefit.

Future Research

Limitations of Current Research

The use of thrombus removal and embolic protection devices hold promise in the adjunctive treatment of patients with ACS undergoing primary percutaneous coronary intervention. However, to truly discern the role of these devices in contemporary practice, a number of important research questions need to be answered.

While two direct comparative randomized trials had been conducted and evaluated for multiple endpoints, one comparing one catheter aspiration device to another and one comparing a catheter aspiration device to an embolic protection device, no significant differences were found and the trials were vastly underpowered to evaluate for final health outcomes and underpowered to evaluate for intermediate health outcomes as well.

In our analysis, we found that for many endpoints, nonsignificant increases or decreases were found versus control, even when we evaluated compound endpoints, used the maximum duration of followup, and combined three different types of embolic protection devices together. All of these were strategies to enhance power to detect differences between groups but by and large, did not provide adequate power. Ultimately, the impact of using these devices on long term (180 to 365 day) final health outcomes versus control needs to be determined.

Applicability of the trials was in the low to moderate range for almost all outcomes because the trials were mostly conducted outside of the United States. It will be important to determine if the devices are equally effective in the hands of average interventional cardiologists in the United States. In addition, it is unclear how much experience the interventional cardiologists had in performing the procedures before enrolling in the clinical trials. It is unclear whether the use of the devices by average interventional cardiologists will result in a different balance of benefits to harms versus the more experienced, high volume interventional cardiologists.

Given the inadequate power in overall analyses or lack of data, we cannot determine the impact of therapy in subpopulations (e.g., gender, age, ethnicity, diabetes, smoker, ejection fraction, primary or rescue PCI, use of glycoprotein IIb/IIIa inhibitors, ischemia time, presence of thrombus-containing lesion, infarct-related artery and pre-PCI TIMI flow, use of direct stenting).

Based on these research gaps we propose the following avenues for future research.

Future Avenues for Research

Clinical Trials

- We believe that additional multicenter, randomized, placebo-controlled trials should be conducted to determine the impact of adjunctive clot removal or embolic protection devices on final health outcomes using a long term followup of 180 to 365 days.
    - Such trials should have adequate representation of interventional cardiologists from the United States and include both tertiary academic medical centers and large community based hospitals as well.
    - Even if the trials are not large enough to determine efficacy in subgroups (e.g., gender, age, ethnicity, diabetes, smoker, ejection fraction, primary or rescue PCI, use of glycoprotein IIb/IIIa inhibitors, ischemia time, presence of thrombus-containing lesion, infarct-related artery and pre-PCI TIMI flow, use of direct stenting); such data should be recorded and included in the results so future comparative effectiveness reviews could pool these results and determine if the benefits or harms are uniformly distributed across the population or are centered within a certain subgroup.
    - Conducting these additional clinical trials would facilitate the conduction of mixed treatment meta-analyses or individual patient data meta-analyses to estimate the comparative effectiveness of different device classes.
- To truly determine the comparative effectiveness, the devices found to have the best balance of benefits to harms in placebo controlled trial should be directly compared in a multicenter, randomized, active controlled trial to determine the impact of adjunctive clot removal or embolic protection devices on final health outcomes using a long term followup of 180 to 365 days.
    - Such a trial should have adequate representation of interventional cardiologists from the United States and include both tertiary academic medical centers and large community based hospitals as well.
    - Even if the trial is not large enough to determine efficacy in subgroups; such data should be included in the results.
    - Along with additional placebo controlled trials, conducting direct comparative clinical trials would facilitate the conduction of mixed treatment meta-analyses or individual patient data meta-analyses to estimate the comparative effectiveness of device classes that are and are not being directly compared.

Observational Studies

Future observational studies should determine if certain subpopulations may have accentuated or attenuated benefits or harms and whether benefits or harms differ between high volume academic medical centers and lower volume community hospitals

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List of Acronyms/Abbreviations

Acronym/Abbreviation	Definition
ACC	American College of Cardiology
ACS	Acute coronary syndrome
ACT	Activated clotting time
AHRQ	Agency for Healthcare Research and Quality
AMI	Acute myocardial infarction
CAD	Coronary artery disease
CABG	Coronary artery bypass graft
CER	Comparative effectiveness review
CHF	Congestive heart failure
CI	Confidence interval
cm	centimeters
Cr	Creatinine
cTFC	Corrected TIMI frame count
Cx	Circumflex coronary artery
D	Days
DE	Distal embolization
ECG	Electrocardiogram
ECHO	Echocardiogram
EF	Ejection fraction
EPC	Evidence-based Practice Center
FHx	Family history
GI	Gastrointestinal
GP2B3Ai	Glycoprotein 2b3a inhibitor
GRADE	Grading of Recommendations Assessment, Development and Evaluation
H	Hours
HCL	Hypercholesterolemia
HD	Hemodialysis
HTN	Hypertension
IABP	Intra-aortic balloon pump
IRA	Infarct related artery
IU	International units
IV	Intravenous
IVUS	Intravascular ultrasound
Kg	Kilograms
LAD	Left anterior descending artery
LBBB	Left bundle branch block
LCX	Left circumflex
LV	Left ventricle
LVEF	Left ventricular ejection fraction
M	Month

MACE	Major adverse cardiovascular event
MACCE	Major adverse cerebrovascular and cardiovascular event
MBG	Myocardial blush grade
Mg/dL	Milligrams per deciliter
MI	Myocardial infarction
Min	Minutes
mm	Millimeters
MRI	Magnetic resonance imaging
MtPA	Mutant TPA
mV	milivolts
NR	Not reported
NSTEMI	Non-ST-segment elevation myocardial infarction
PCI	Percutaneous coronary intervention
PO	By mouth
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCA	Right coronary artery
RCT	Randomized controlled trials
RD	Risk difference
RR	Relative risk
S	Seconds
SCr	Serum creatinine
SPECT	Single-photon emission computerized tomography
STEMI	ST-segment elevation myocardial infarction
STSR	ST-segment resolution
SVG	Saphenous vein graft
TEP	Technical Expert Panel
TBG	TIMI blush grade
TIMI	Thrombolysis in myocardial infarction
TMPG	TIMI myocardial perfusion grade
TL	Thrombolysis
TLR	Target lesion revascularization
TS	Thrombus score
TVAC	Transvascular aspiration catheter
TVR	Target vessel revascularization
U	Units
UA	Unstable angina
Y	Years