

*AHRQ's Effective Health Care Program: Applying Existing Evidence to Cardiac Care*

Monday, December 6, 2010

Transcript

OPERATOR: Good day, ladies and gentlemen, and welcome to *AHRQ's Effective Health Care Program: Applying Existing Evidence to Cardiac Care*. If you get disconnected at any time from the Web conference, you may dial back in with 888-632-5065 or 201-604-0318 and, when prompted, enter 77787674 pound. Again, the code is 77787674 followed by the pound sign. At this time, it is my pleasure to turn the floor over to Katherine Griffith. Ma'am, the floor is yours.

KATHERINE GRIFFITH: Thank you. Good afternoon, ladies and gentlemen; thank you for standing by. On behalf of the Agency for Healthcare Research and Quality, also known as AHRQ, welcome to today's Web conference, *Applying Existing Evidence to Cardiac Care*, held by AHRQ's Effective Health Care Program.

My name is Katherine Griffith. I'm a contractor for AHRQ's Office of Communications and Knowledge Transfer, and I will be moderating today's event. This event is part of a series of Web conferences we are holding over the next few weeks on Effective Health Care Program research on different findings on different clinical topics. So, we're happy you're able to join and hope you will be able to join us for future events.

Before I get started, I want to review some information about the Web conference technology. If you have questions during the presentation, you may submit them electronically by entering them into the—via the Ask Question button. The Ask Question button is located at the bottom of your screen.

When you click on that button, a box will appear, requesting that you enter your question. Once completed, press the Submit button. A selection of audience-submitted questions will be addressed during the moderated Q&A session at the end of the Web conference.

Also, if you are experiencing technical difficulties, there are a few options. You can click on the "Click Here for the Web Conference Help" link and be directed to a troubleshooting Web site to do a system check, or you can open the Web conference FAQs documents under the downloadable file button on the bottom of your screen, or you can also contact technical support by submitting your issue in the Ask Question box.

Under the downloadable files button, you'll also find the slides for today's event, which may be helpful for reviewing slide details and documents with speaker biosketches. Today's Web conference includes closed captioning. The captioning appears in a box below the slides through the Windows Media Player or Real Player buttons on the main page.

Finally, this presentation is being recorded and will be made available on the AHRQ Web site shortly. So, let's start with presentations. During this Web conference, Effective Health Care Program Investigator Dr. Ann Garlitski and I will highlight the benefits of using patient-centered outcomes research in clinical decisionmaking.

I'll kick off the conference by giving you a brief review of AHRQ's Effective Health Care Program before I turn it over to Dr. Garlitski to share her research findings related to cardiac arrhythmia, including the comparison of catheter-based radiofrequency ablation and anti-arrhythmic drugs.

As a reminder, you can submit questions electronically by entering them via the Ask Question button on the bottom of your screen. You can ask either of us questions about patient-centered outcomes research, the Effective Health Care Program, and the findings shared today. We will hold most of your questions at the end of the—take most of the questions at the end of the event. I encourage you to ask them throughout this event as you think of them. We'll do our best to address as many questions as we can during the Q&A session.

To begin, I'll be discussing the AHRQ Effective Health Care Program and how you can utilize patient-centered outcomes research in practice. Patient-centered outcomes research, also known as comparative effectiveness research, delivers unbiased, practical, evidence-based information to help you and your patients weigh different options to make the most informed health care decisions. It compares drugs, devices, procedures, tests, and methods of health care delivery.

Patient-centered outcomes research shows which treatments have been shown to work best in different clinical situations and how they compare when it comes to benefits, harm, and side effects. It also tells us what is known and what is not.

Most importantly, patient-centered outcomes research is descriptive, not prescriptive. It does not tell you how to practice medicine. It does not mandate a particular test or treatment for anyone. Nor does it prohibit any test or treatment. It gives you the tools, not rules, which you and your patients can use to make the best possible decision.

Here at AHRQ, the investment for patient-centered outcomes research has been built around the framework displayed here. The colored boxes and ovals show the different types of work involved with patient-centered outcomes research. Underneath is the research platform that supports the work, including research infrastructure, methods, development, and training of researchers.

The research process starts with scanning the horizon to identify new and emerging clinical interventions that may impact health care in the U.S. That leads to systematic review and synthesis of current medical research to compare effectiveness. Evidence synthesis often tells us where the gaps lie between existing medical research and the needs of clinical practice. We also promote and generate new scientific evidence and analytical tools to fill those critical gaps.

All of the information gained needs to be communicated in ways that make sense to the health care decisionmakers. This includes translating the research into plain language and making it accessible and useful to diverse audiences in order to improve health care. We've also made a commitment to

reach out to stakeholders in communities for input to make sure we get the research right. If it isn't relevant and applicable, then we can't expect it to make an impact.

The Effective Health Care Program has a cradle-to-grave research agenda that focuses on 14 priority conditions listed here. As you can see, one of the priority conditions is cardiovascular disease.

Since the inception of the Effective Health Care Program, AHRQ has funded and completed dozens of patient-centered outcomes—patient-centered comparative effectiveness research projects. These projects include comprehensive reviews of diagnostic or treatment options for breast and prostate cancers, diabetes, osteoarthritis, depression, and many other conditions.

The Effective Health Care Program creates a variety of products that are based on these research reviews and reports. These include executive summaries, summary guides written for clinicians, consumers, and policymakers. We've recently added to our portfolio a number of materials to support clinician education, including continuing education modules, interactive case studies, and faculty slide sets. We'll soon be adding patient decision aids as well.

I would like to highlight our consumer guides that summarize the evidence in plain language in an easy-to-read format. These guides are paired with our clinician guides to promote shared decisionmaking. Most of our consumer guides have also been translated into Spanish. The consumer guides can be found online or are available in print. We also have podcasts of the guides online as well.

Currently, the Effective Health Care Program offers various decisionmaking resources about heart and blood vessels, including cholesterol, hypertension, and the use—and using ACEIs [angiotensin-converting enzyme inhibitors] and ARBs [Angiotensin II receptor blockers]. Today, Dr. Garlitski will be discussing the research that she conducted leading to the Effective Health Care Program findings presented in the clinician and consumer guides related to atrial fibrillation. The other highlights can be found on the Effective Health Care Program Web site.

Finally, we want to encourage you to get involved in the Effective Health Care Program. Your participation is mutually beneficial. There are multiple points of which—have involvement in our program during and after the research is completed. Before, you can nominate topics for research on our Web site. If there is a heart- or blood vessel-related or other topic that you feel should be addressed, we will give you the instructions on how to nominate just that topic at the end of this conference.

During, you can give input on draft key questions and reports. This kind of involvement helps you get the type of research that will really help answer those controversial questions, and it helps us by getting the research right.

After the research is completed, you can disseminate the information to your colleagues and patients. You can implement the findings in your clinical decisions. This helps both you and us create an opportunity for better, more informed decisionmaking and making an impact on the quality of health care.

So, let's get started with the main presentation. We now have the pleasure of hearing from Dr. Ann Garlitski. Dr. Garlitski is an assistant professor of medicine and codirector of the Cardiac Electrophysiology Laboratory, a tertiary medical center. She's board-certified in internal medicine, cardiovascular disease, and cardiac electrophysiology, and she is a fellow of both the Heart Rhythm Society and the American College of Cardiology. Today, she will present her research on the comparative effectiveness of radiofrequency catheter ablation for atrial fibrillation.

Dr. Garlitski, please begin.

DR. ANN GARLITSKI: Thank you very much. I appreciate the invitation to speak. I'd like to state that I do indeed perform catheter ablation of atrial fibrillation. I have no other conflicts of interest.

Briefly, I'd like to mention a few background points for emphasis. Atrial fibrillation increases with age from 0.1 percent in people less than 55 years of age to greater than 9 percent by 80 years of age, making it the most common sustained arrhythmia that we see in clinical practice.

The risk factors for atrial fibrillation are also common. The disease processes include hypertension, diabetes, structural heart disease, myocardial infarction, and the history of cardiothoracic surgery. The consequences of atrial fibrillation include the possibility of congestive heart failure, ischemia, tachycardia-mediated cardiomyopathy; it does impose an increased risk in stroke as well as an increased risk in mortality. It may also have an impact on the quality of life. Therefore, you can see how it has a significant burden to the health care system.

The management of atrial fibrillation is multifactorial and patient-specific. The good news is that we have many tools in our armamentarium. We can treat patients via rate control, i.e., AV [Atrioventricular] nodal blocking agents, such as beta blockers, calcium channel blockers, or Digoxin.

In particular circumstances, we may perform an AV node ablation and pacemaker implant. Of course, that does make the patient pacemaker-dependent. We have rhythm control options. Those are anti-arrhythmic agents with the specific goal of keeping patients in sinus rhythm.

There's the possibility of surgery, which is a Maze procedure, and that is open heart surgery, and there is radiofrequency catheter ablation.

Radiofrequency energy used to treat cardiac arrhythmias has been around since 1987, but its specific use to treat atrial fibrillation was presented in a *New England Journal* paper of Dr. Haissaguerre in 1998. Since that time, the procedure has evolved because of new understanding of physiology as well as because of technical developments in catheter use and imaging.

So, to our review, the key questions that we posed are as follows: What is the effect of radiofrequency ablation compared to surgical or medical treatment on both short- and long-term outcomes, particularly the outcome of rhythm control?

Also, what are the patient and intervention-level characteristics associated with the effect of RFA [Radiofrequency Ablation] on rhythm control? How does the effect of RFA on rhythm control differ among techniques, and what are the harms and complications associated with it?

Our study proceeded as follows. We queried the Medline and Cochrane Central Trials Registry, 2,169 citations were noted; of that, we reviewed 120 articles in full. These articles were from the years 2000 to 2008. The study selection was that we included all randomized control trials of any sample size, prospective cohort studies greater than 50 subjects and retrospective cohort studies greater than 100 subjects.

We then proceeded to rate the strength of the evidence of each key question. We did that based on the number and quality of primary studies, the duration of the followup, and the consistency across these studies. After that, we were able to state high, moderate, or low confidence that the evidence reflects the true effect. In the circumstance that the evidence was either unavailable or not sufficient enough to make a statement, we stated that indeed it was insufficient.

So, to begin with the results, RFA versus surgery, there is no study that directly compares the two. This next slide, this is the take-home slide. This is the answer to question number one: RFA versus medical therapy. And, again, we specifically are referring to anti-arrhythmic agents with the goal of rhythm control.

I'd also like to define first what we mean by first-line and second-line therapy. First-line therapy means that RFA or medications were used with the initial diagnosis of atrial fibrillation plus or minus AV nodal blocking agents, but it was a first-line, first attempt to use either ablation or an anti-arrhythmic agent for rhythm control. Second-line therapy means that an anti-arrhythmic drug was already used.

With that being said, a moderate level of evidence exists. That second line of therapy of RFA is effective at 12 months. Again, meaning an anti-arrhythmic drug was used first, and then the patients proceeded to have an ablation.

That statement that there's a moderate level of evidence is based on three randomized control studies. There's insufficient evidence to state that that first-line therapy is effective at 12 months. You'll notice that there's one randomized control trial that did indeed show a very positive benefit.

So, it's a very positive outcome for radiofrequency ablation, but we stated that that was an insufficient level of evidence because of the fact it was one randomized control trial with only 67 patients. In regard to the outcome of congestive heart failure and volume changes, the strength of evidence was insufficient.

In regard to stroke and avoiding anti-coagulation, we stated that the strength of evidence was low. This is an important question because I'll put it in the clinical context. You may have patients who come to you and say, "Should we have an A-fib ablation? Then can I get off of Coumadin?" That's a very common question that we receive.

So, this question about whether stroke or avoiding anticoagulation is affected by ablation or anti-arrhythmics is important. As it stands now, the strength of the evidence is low. I would like to also point out that, at this time, there is an NIH-sponsored trial called CABANA, which is specifically addressing this issue in a randomized fashion.

Patient and intervention-level characteristics. There's a high level of evidence that there is no association with sex, being male or female, in A-fib recurrence. There's a high level of evidence that there is also no association between age and A-fib recurrence, the caveat being that the majority of patients who were in these trials were between roughly the ages of 40 and 70.

There is not a significant amount of data that has been collected specifically to deal with elderly or octogenarian patients. In regard to operator experience and setting, no study directly addressed this question. Paroxysmal versus nonparoxysmal AF. By the term paroxysmal, we refer to persistent, longstanding, persistent patients or those who were termed chronic in older studies.

The results, 11 studies found no statistically significant association between A-fib and recurrence. Excuse me, A-fib type and recurrence. Six, however, did find that nonparoxysmal AF predicted higher recurrence. Because of the types of analysis that were done, they were mostly univariable; we stated that there was a low level of evidence.

In regard to left atrial diameter and injection fraction, 4 out of 20 studies found an association between larger left atrial diameter and an increase in A-fib recurrence. Eight out of 17 studies found an association between low AF and increased A-fib recurrence.

There's a moderate level of evidence for these findings. And, of course, those are consistent with what we would think, from a physiologic perspective, with a larger left atrial diameter; with a decrease in injection fraction, there has been structural remodeling. So, intuitively that does make sense that there is an increase in A-fib recurrence.

Regarding different techniques and different catheters, 8-millimeter tips versus irrigated tips. Those irrigated tips are generally 3.5 to 4 millimeters. There's a moderate level of evidence to state that there is no significant difference in rhythm control.

Harms and complications of radiofrequency ablation, there is a low level of evidence to state that these complications are uncommon and that is primarily because the nonuniform definitions and assessments in the reporting of the complications.

Of note, there was not a significant, in fact, very little data which defined complications and the time at which they occurred, with the exception of pulmonary vein stenosis, which was looked at in a more rigorous fashion at time 0 and at time 3 months. Eighty-three studies reported one or greater complicating events.

Major adverse events included pulmonary vein stenosis, cardiac tamponade, stroke or TIA, atrio-esophageal fistula, and five deaths. The way in which it was reported that there is a possibility that those may have been duplicates, so it is not clear that it was five deaths, in fact, total.

This is again a summary slide to try to hone the major points. Atrial fibrillation catheter-based ablation is effective as a second-line therapy with a followup of 12 months or less. There are insufficient data for greater than 12 months. There are insufficient data on first-line therapy, albeit there was a very positive randomized control study, there was only one that specifically addressed this question in a randomized fashion.

Major complications are less than 5 percent, but the quality of data again, by statistical standards, is considered poor because of the nonrigorous way in which the data were reported. There are a lot of data that we now know, but clearly we need more data specifically on elderly patients, patients with multiple comorbidities. The patients who were studied generally had injection fractions that were 40 percent or greater.

We need more information on long-term rates of recurrence in the order of years, not just 6 to 12 months, further comments on effects from radiation exposure, quality of life, and mortality. And, again, I would like to mention that there is an effort to address many of these issues in an NIH-sponsored randomized control trial, which is ongoing.

This slide is actually taken from ACC [American College of Cardiology] guidelines on the management of atrial fibrillation. And the good news is that the way we practice reflects the evidence that we have assessed to this point. You'll note that catheter ablation is in aqua, and it is depicted as an appropriate second-line therapy. First, there are recommendations to use anti-arrhythmic agents and then the possibility of catheter ablation as a tool to maintain sinus rhythm.

Of course, there is a caveat that there are some patients who have side effects who cannot tolerate certain medications and, with appropriate clinical judgment, they can be considered for first-line therapy.

Thank you very much and certainly, if you have any questions, I'd be happy to answer them.

GRIFFITH: Thank you so much, Dr. Garlitski, great presentation. I'm sure we all appreciate making this information salient to the clinician audience. I will now open it up for questions. As I've noted before, if you'd like to ask a question, you can click on the Ask Question box below the slide and type it in, and we will get to them as we receive them.

We already have a few. The first one for you Dr. Garlitski is: How many concurring randomized controlled trials are required to know we have found the true effect?

DR. GARLITSKI: So, that is an excellent question, and certainly I'm a clinician and do not pretend to be formally trained in statistical analysis on that scale. But I can tell you from my experience with the rest of my team, who have that level of experience, that it's not how many, you know, is it one, is it five? You know, you noticed that, for example, we made a statement that there was a moderate level of evidence for rhythm maintenance with atrial fibrillation ablation based on three randomized control studies.

You know, one study clearly that I can say is not enough. But is two, three, four, or five? What is the right number? Probably can't say that. It's really, How was the study designed? How many

patients? Certainly what is the N? And what was the followup? That's also very important. So I'd say there is no magic number. Certainly more than one, but the rest is how the study was designed.

GRIFFITH: Great, thank you. There's another one here. Is there evidence to support discontinuing anticoagulation following AF ablation as a result of decreased risk in stroke?

DR. GARLITSKI: So, it's a beautiful question. It's really the most clinical question. Again, as I mentioned, we have many patients—you know, I can say I have many myself—who come in and say, "Okay, that's great. I have an A-fib ablation. Can I come off of Coumadin?" There is only a low level of evidence to support that.

Again, in CABANA, that question will be addressed in a randomized prospective trial. At this time, the recommendations are, if someone comes in with a certain CHADS2 score and that's how we assess their risk factors for stroke, that's what they come out of the A-fib ablation with.

We do not discontinue Coumadin just because someone has had an AF ablation at this time. We may come to that, but if their risk score was such that the patient has been on Coumadin prior to the ablation, then generally it is indeed continued afterward indefinitely.

GRIFFITH: Great, thank you. This is a question—it's about guidelines, and I don't know, it sounds like there's some coming out soon around this area, and so the question is based on your review of the data. Do you think catheter ablation will be moved to a first-line therapy? And I don't know what guidelines the question's referring to, but hopefully you do.

DR. GARLITSKI: Right. So, as of right now, the guidelines reflect the diagram that I placed up. I can go back to that here so that we can look at it. And, as of 2006, it is still second-line therapy. I don't know for certain because obviously there is not just one person, there will be a team of experts that will once again review the updated literature. Our literature goes to 2008.

Certainly, over the last few years, there has been even more data and more trials on atrial fibrillation ablation. One of them was in particular a thermal ablation trial, and not all of those have been incorporated into our study because, again, time flies and there are more data that have come out. So, I think it's very possible that catheter ablation will move forward. Here, again, it is an option for first-line therapy. It's not clearly stated as such, but I think that there's certainly the possibility that it will move forward.

We're all very aware that, you know, there are risks to the anti-arrhythmic agents as well. It's not just that there are potential complications from a procedure. There's also the flip side, there are potential long-term side effects from these anti-arrhythmic agents. So, given that information, I do think it's possible it may move up as first-line.

GRIFFITH: Great, thank you. Another audience question, they just keep coming. What will Dabigatran do to the "can I get off oral anti-coagulants" question?

DR. GARLITSKI: Well it's—again, phenomenal questions that everyone's been asking. Dabigatran at this time, or as the trade name is Pradaxa, is in place of Coumadin, not in place of nothing. So, I think this new medication is really going to be extremely helpful for patients because it will eliminate the need for INRs. The metabolism of it appears to be much more steady; doesn't have all the ups and downs in the INR that Coumadin does, so I think it'll make patient management of anticoagulation much easier.

But I think it still holds that we do not have good prospective data yet that say, if I have an A-fib ablation, I can come off Coumadin or I can come off Dabagatrin. I hope that answers the question.

GRIFFITH: Yes, thank you. Another question, is there evidence to support efficacy of AF ablation in elderly?

DR. GARLITSKI: Yes. So, again, you know, there in the guidelines there is no limit, there is no absolute cutoff. We all know that patients are getting older right now. There's a larger population of older patients, so and certainly it is not contraindicated. When you ask me specifically are there data, there is not a significant amount for patients greater than 70 years of age.

We certainly need more well-designed trials specifically looking at that age group. What we do at this time is again a clinical judgment to extrapolate the safety and efficacy for the younger populations to the older population. So, much of it is based again on clinical judgment and extrapolation.

GRIFFITH: Great, thank you. I think that's actually all of the questions we've received. So, I'm just going to move on unless we get any last-minute questions. But I'll just review some of the materials we have on the Web site. And, if we do get any, we can come back to them.

So, as I mentioned, you can access all of the materials that we've discussed today on the Effective Health Care Program Web site, and the link is here. All of the materials are free, and you can order them through the AHRQ Publications Clearinghouse at the phone number listed here.

The various resources and reports we discussed plus many more are on the Web site. All the features, in addition to signing up for an e-mail update, can be easily navigated in the panel on the left hand side of the Effective Health Care Program Web site.

Also, as I noted earlier, we're—this is an—this event is in a series of Web conferences we're holding. We've had a few already that will be posted on the Web site, and the two upcoming events are listed here. Both are next week, Monday and Tuesday. And the one for pharmacists and patients that are in medical homes, it does offer CPE [continuing pharmacy education] credit, so we're looking forward to those.

And, finally, I'd like to thank our Ann Garlitski for sharing her research findings with us today. It was very helpful. I'd also like to thank our many participants for joining today. We hope the information presented here informed you about how you can implement patient-centered outcomes research into everyday practice and how the Effective Health Care Program resources are available to assist you and your patients with decisionmaking.

As we conclude this Web conference, let me remind you that this event will be archived and available on the Effective Health Care Program Web site shortly. Finally, as you leave the event, a feedback question will pop up. We ask that you please answer that question. Your feedback is very important to us as we develop more resources and plan similar events.

Thank you so much. Have a nice day.

OPERATOR: Thank you. And, again, this does conclude today's Web conference. We thank you for your participation. You may disconnect at this time, and have a great day.

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