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THOMAS M. MUNGER: Hello, and welcome back to the Mayo Clinic Medscape video series. I'm Tom Munger, electropysiologist and Heart Rhythm Chair at Mayo Clinic Rochester. Today we'll be discussing the pros and cons of WATCHMAN and other left atrial appendage occlusion devices for prevention of stroke in non-valvular atrial fibrillation.

I'm joined by my colleague Fred Kusumoto, Professor of Medicine and expert in this area. Welcome, Fred.

FRED KUSUMOTO: Hi, Tom. It's wonderful to be here.

THOMAS M. MUNGER: It's terrific to have you with us. And initially, I want you to answer the question, what's the rationale for left atrial appendage closure anyway? What's the big deal?

FRED KUSUMOTO: Yes, as you know our colleagues, Joe Blackshear and John O'Dell, years ago, found that most of the clots originated from something called the left atrial appendage. This is the blind pouch that's in the left atrium. And because of this, there is slow flow in that area.

And when patients have atrial fibrillation, the notion is that there is irregular activation of the atrium and slower velocities in this area. And so sludge builds up and this is where clots form.

THOMAS M. MUNGER: And I gather that these clots then could embolize the other parts of the body, and so eliminating that virtual space would actually reduce the risk of stroke. Do all of the clots actually come from the appendage, or are there some that come from other areas too?

FRED KUSUMOTO: So the left atrial appendage has all sorts of nooks and crannies. And because of that, and the slow flow, in fact, a great majority of the clots form from that area, but not all the clots. So it can be anywhere from 80% to 90% in those patients without mitral valve disease.

THOMAS M. MUNGER: Sure. Well, who should be considered a candidate for this procedure anyway, as an alternative to the anticoagulants we prescribe right now?

FRED KUSUMOTO: Well, it's important to remember that we should be guideline directed. The most recent 2019 guidelines for atrial fibrillation, really outlined the use for left atrial appendage occlusion. They gave it a 2b recommendation.

What 2b means is that remember our recommendations are divided into class 1 class 2 and class 3. Class 1 means you really ought to do it, class 3 means you ought not to do it. And class 2 is that huge area in between, where one can consider it or not consider it based on clinical characteristics.

We further divide two into 2a and 2b. 2a, where you'd be more inclined to do it, and 2b, where you wouldn't. So they gave a 2b recommendation for left atrial appendage occlusion in those patients who weren't candidates for long-term anticoagulation.

It's important to note though that in their discussion, with this recommendation, they said that oral anticoagulation remains the preferred method for reducing the risk of stroke.

THOMAS M. MUNGER: I know there's concerns that have been raised from recent studies, suggesting compliance with oral anticoagulation is poor. And in fact, I've seen data suggesting even with the newer novel agents that the compliance may be no better than 50% or 60%. So another thing for us, I guess, to consider when prescribing this as an alternative to those drugs, since many patients actually don't take the drugs either.

How about aspirin? I know there's a lot of our viewers who have looked at aspirin as an alternative to the anticoagulants, and the high-risk patients who can't take anticoagulants, or they're concerned about falls or whatever. What's your thoughts about aspirin here in 2019?

FRED KUSUMOTO: That's right. Remember, studies long ago looked at aspirin use. And there was one study called, the SPAF Trial, which suggested that aspirin had a significant benefit. The problem with that is that's the only study of the aspirin studies which showed a benefit.

For this reason, many people think that this is an outlier with regards to the other studies. And so actually, the most recent recommendations for atrial fibrillation and stroke risk reduction suggest that aspirin has really no use, and there is no recommendation specifically for aspirin in the most recent guidelines.

THOMAS M. MUNGER: So I gather, if you're going to prescribe nothing, or effectively nothing, not giving aspirin would be the recommendation currently, and you just follow patients on no therapy? Which makes appendage closure perhaps, again, a little more attractive at least thinking about it as an alternative.

FRED KUSUMOTO: Well, it's interesting thinking about aspirin totally. First of all, there was a couple of trials. Particularly a study called [INAUDIBLE], where they took patients who were thought to be not candidates for anticoagulation and randomized them either to aspirin, or one of the new oral anticoagulants called, apixaban.

In fact, there was no increased bleeding risk in those patients who received apixaban compared to aspirin, while there was a significant stroke risk and systemic embolism risk reduction in those patients on the apixaban. It is interesting to think about aspirin. Aspirin was used though in the trials, looking at left atrial appendage occlusion, and still can be used after the anticoagulant period has been stopped.

THOMAS M. MUNGER: I suppose aspirin we can't completely ignore either, since many of these patients do have multiple reasons for stroke. And some of them have vascular disease that still would benefit from having a anti-platelet approach for a period of time too. How about the general approaches to appendage closure? I know that WATCHMAN was released in 2015 by FDA. Are there other methods for closing the appendage that are approved now, or on the horizon that you see that might come into use in the future?

FRED KUSUMOTO: This is an area that is really exploding. In fact, there are multiple devices that are designed to close the left atrial appendage. They can really be divided into two parts.

One, an epicardial approach, where you do a suture or some borat or some method where you actually clamp the outside of the left atrial appendage. And the other would be an endovascular approach, like the WATCHMAN, where you then plug the left atrium up. So when you look then at the different technologies and these different approaches, in fact there are multiple technologies that are looking to try to identify the best ways, either to close it from the outside or the inside. Having said that, none of those other techniques are approved here in the United States.

THOMAS M. MUNGER: I suppose it's critical that with any technique that you use that is verifiable that the appendage is closed. Particularly with some of the older surgical series that involved hand-tying closure of the appendage, they found that there wasn't much effect on stroke risk, and in some patients increased it if they didn't actually close the appendage completely. So any of these techniques do involve verification and surveillance to make sure that the appendage really is closed also.

FRED KUSUMOTO: You're absolutely right, Tom. As you know, when you then make an area even smaller, where the hole or the opening is smaller, in fact you can have more spaces of flow and potentially then have clot formation in those areas. As you point out, older surgical literature suggested that a simple ligation, in fact, was ineffective in terms of providing a permanent closure to the left atrial appendage in most patients.

And in fact, as you point out just earlier, in fact, even with our endovascular approaches, leaks between the device and the wall of the left atrial appendage can still occur, and that surveillance is required.

THOMAS M. MUNGER: Well, talking about effectiveness of these devices, I guess the best data we have is the two randomized clinical trials of Warfarin versus WATCHMAN. Can you speak to that as far as effectiveness for our viewers? How effective is the device when you compare it to long-term Warfarin therapy?

FRED KUSUMOTO: Yes, Tom. The studies are fairly consistent. Not only the studies that you mentioned, but actually subsequent registries when they compare them to historical controls. The WATCHMAN appears to be as effective as Warfarin, in terms of reducing risk of stroke.

The big issue is, by not being anticoagulation, do you then reduce the risk of bleeding and thus reduce the risk of other side effects that can be associated with anticoagulation? As you know, there have been some recent registry studies, which in fact suggest that this is true, particularly in our high-risk patient groups. It'll be interesting to see when the NCDR provides their initial data.

So I'm on the steering committee for the NCDR left atrial appendage occlusion group. And I can tell you that while the initial abstract has been presented and there have been a significant number of patients who have been studied, I can't give you the specifics with regards to complications here at this point just because it is still not released. But nonetheless, it seems to be that this is a device that is now becoming more widespread here in the United States and seems to be associated, at least with reduced outcomes in terms of complications--reduced complications in experienced hands.

THOMAS M. MUNGER: I've been struck by following the registry data here in the United States, noting how the complication rates with implantation, including stroke in particular, as well as perforation, has really reduced over the last 15 years since the early trials were done. And so, I think that was one concern. FDA, and with release of the device, here in the United States with the first randomized trial was the higher incidence of stroke with acute implant. And that really has fallen from the data I've seen by tenfold, since that first randomized trial was done.

So I look forward to hearing about the NCDR data when it comes out because I think it'll be critically important to understand where and when the devices are best used in our practices. If you look at the stroke rates with current use, again, they're quoted as one per 1,000. I'm still intrigued also about the reduced incidence of overall mortality in the last randomized trial that was done compared to long-term Warfarin. So I think that's something else we'll be wanting to look at, particularly as you get further out in years. Because anticoagulants still have the risks as you continue out following these patients, whereas a device implanted really does not at least to any appreciable degree.

FRED KUSUMOTO: Although Tom, we do have to consider the fact that the left atrial appendage occlusion has been compared to Warfarin, and that there have been no head-to-head comparisons with the new oral anticoagulants, which I think all would argue are better therapies, in terms of reducing risk of stroke, or alternatively reducing a risk of complications. So I do think that the important long-term data, as we get more experience with this, is going to be critical. But it is also important for us to acknowledge that the trials and the studies that we have, at least the randomized ones, have not compared the left atrial appendage occlusion device to our most recent armamentarium of oral anticoagulants.

THOMAS M. MUNGER: Yeah, I think that's an excellent point. We do not have any randomized trials in that space, and in fact, leads to the next question. Where are the major current knowledge gaps in this space, and what do you see, on the horizon, that are important questions that need to be answered?

FRED KUSUMOTO: Well, I think there are a couple. So we've mentioned the first. Remember, we've not tried to evaluate or to compare left atrial appendage occlusion to those patients who are on one of the new oral anticoagulants, or what are actually called direct oral anticoagulants.

Again, I think fairly strongly, and without very little argument, these are better drugs than Warfarin anticoagulants just because there offer a more stable anticoagulation milieu, and are associated with reduced risk of complications. The second issue is, remember that we have a big experience in terms of the director oral anticoagulants. These studies were anywhere from 15,000 to 20,000 patients.

Our analysis, at least in the prospective randomized controlled trials for the left atrial appendage occlusion, are much smaller. Having said that though, the NCDR has data on at least 40,000 implants of the left atrial appendage occlusion. So I think that as we get more experience, particularly long-term experience, as we see ultimately how these patients do in terms of stroke risk reduction or stroke events or systemic emboli events and other complications down the line and more long term, I think we'll provide a lot of information and provide guidance with where best this therapy should be placed.

THOMAS M. MUNGER: Well, Fred, this was terrific. And thank you for these very important insights today. I look forward to talking with you again, in the near term, once we have that NCDR data out and readily available for the community to review. And thank you for joining us on theheart.org Medscape Cardiology.

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