

Announcer: Hello everyone and welcome again to another in our series of interview with the experts. I'm your host for this session, Malcolm Bell, and it gives me great pleasure today to introduce a, a very special, a guest, a a colleague of mine, Dr. Mohamad Alkhouli. He's a professor of medicine and as an interventional cardiologist with expertise that covers many different procedures, but included in those is, is vast experience of left atrial appendage closure. And so the today's topic is left atrial appendage occlusion, or anticoagulation for drug prevention in atrial fibrillation. So Mohamad, welcome to to our interview here.

Dr. Mohamad Alkhouli: Thank you very much, Malcolm. It's a pleasure to be here.

Dr. Malcolm Bell: So let's just start off with, you know, very simple question, patients with atrial fibrillation, why, why do they need to take anticoagulants?

Dr. Mohamad Alkhouli: Right. So, you know, atrial fibrillation by definition is irregular rhythm that primarily impacts the top chamber of the heart. Left atrium is ineffectively contracting. So there is less emptying or less effective emptying of blood in the atrium, which leads to blood stagnation and eventually can lead to clot formation. The clot can then eventually exit the heart and travel and cause most likely stroke, but can also lead to, you know, occlusion of arteries in other parts of the, of the body. So that's why atrial fibrillation is by, you know, by definition associated with higher risk of having a stroke.

Dr. Malcolm Bell: And, and, and we know that this tends to occur maybe at at any age, but particularly as people would be get older, can you give us an idea of what the prevalence of atrial fibrillation and the patients at risk of this, let's say from middle aged to onwards?

Dr. Mohamad Alkhouli: Yeah, so, you know, with the aging of the population, we see more and more of this. So there is an estimated 12 million people in the United States now with atrial fibrillation, which, you know, this estimate has surpassed all of the prior old secular estimates that were made 20, 30 years ago. It does increase by age, as you alluded to. So if you are over eight years of age, then the likelihood of you having atrial fibrillation is north of 10% and it's much less if you are like less than 50 years of age. And then it goes in between, between the two ranges.

Dr. Malcolm Bell: And of course, you know, we we're here to talk about prevention of stroke, you know, in, in these patients it obviously can be a, you know, a devastating complication. But let's just move on because the, one of the things we wanna discuss today is left atrial appendage occlusion and as a potential alternative to anticoagulation. So for those of our audience who, who don't work in, in this area, and particularly you working in the cath lab, could, can you just explain what left atrial appendage occlusion is?

Dr. Mohamad Alkhouli: Yeah, I'd be happy to. So maybe we just give the historical context. You know, blood thinners have been the cornerstone of preventing a stroke. You have blood stagnation. If you use a blood thinner you're less likely to form a clot for many, many years. However, people realize that a good proportion of patients cannot take a blood thinner. And even among those who start to take a blood thin, they drop it off over the next couple of years. And it's estimated that maybe only 30 to 40% of PE people who are indicated to be on a blood thinner actually do take it for the long term. So that unmet need prompted people to search for an alternative. And, you know, plot thinner is a systematic approach where you thinning the blood throughout the body. So the, the search has led to this concept that most of the clots do form in the side pouch of the left atrium that's known as the left atrial appendage. And maybe if we, if we close that pouch without impacting other things in the body, then we will prevent stroke effectively. So left atrial appendage occlusion is the closure of the appendage, which is a side pouch of the left atrium that can be undertaken either by percutaneous means or surgically.

Dr. Malcolm Bell: No surgically. I, I think maybe we can just maybe pass on that briefly, but nevertheless, I mean this is usually for someone who's having some other cardiac surgery that we would then offer, you know, closure at the time. It would be uncommon for us to do an appendage closure as the only reason for cardiac surgery is that,

Dr. Mohamad Alkhouli: Is that fair? Very uncommon. Yeah, it can be done minimally invasively, but it's very uncommon. I only mentioned this is because there was a larger randomized trial published in the last year that really demonstrated or documented for the first time an advantage of doing lift lip and dig occlusion surgically on top of blood thinner. But we could, we could leave that on the side and focus on the transcatheter approach.

Dr. Malcolm Bell: Yeah, so these percutaneous approaches, and I think the device that you many people would be familiar with is the Watchman device probably the most commonly used, but there are some other devices. Can you tell us how many and whether these have, you know, similar efficacy and safety to the Watchman device?

Dr. Mohamad Alkhouli: Absolutely, yeah. So the Watchman device was approved in 2015, so about eight years ago. It has now, you know, we have a second generation of third generation of it. So it has evolved over time. It's the most commonly used in the us. There is a second device called amulet. It's slightly different mechanism, but sort of does the same job that is also approved. So only two currently approved in the US a few more are used in Europe and a lot more in the pre pre-human testing.

Dr. Malcolm Bell: And we've talked about you, you used the term transcatheter or percutaneous. How long does this procedure take is done under local anesthetic, moderate sedation, or do you need to have a general anesthetic? Maybe you just describe that to our listeners, how this is typically done.

Dr. Mohamad Alkhouli: Yeah, so first of all, this is a venous procedure, right? So we typically don't get arterial axis, which lower the risk of bleeding. The vast majority of cases in the country are still undertaken under general anesthesia. We at Mayo have switched to moderate sedation about four years ago, and I would say 99% of our cases are done with moderate sedation. Skin to skin is about an hour or less and most of our patients are discharged home same day.

Dr. Malcolm Bell: And so then the, the question comes up, you know, who should have anticoagulation and who should have a left atrial appendage closure. And, and I can think of perhaps of your two groups of patients, you, you have a, a group of patients that may have a very high risk of bleeding or maybe they've had active your bleeding and this, you know, is obviously a, a good alternative, you know, to, to at least consider. On the other hand, you know, we have many patients who may not have had a bleed but may be fearful of the bleed and they may say, well, if I, if I don't need to take anticoagulants and as a device, I could have instead I, I'd rather have the device. So maybe you could just briefly tell us, you know, who are the patients that typically we would offer left atrial appendage occlusion, and particularly I guess your, what situations is it actually approved for and, and, and reimbursed.

Dr. Mohamad Alkhouli: And I love your classification. I think that simplifies it a lot. So you have the patients who've had a problem with the blood thinners and those who are afraid of a problem, right? So as of today, 10, 10, 20 23, we can only offer this therapy to the first category of patients, patients who've had a problem with a blood thinner. If you read the FDA label of CMS label, let's say that people who are indicated to be on a blood thinner to prevent a stroke but have an appropriate rationale to seek an alternative therapy. It's kind of broad, but what we see in clinic is somebody had a GI bleed or a brain bleed or had a fall or uses a cane at a high risk of fall. These are the vast majority of our patients. It is not approved yet for somebody who just doesn't like a blood thinner, doesn't wanna be on a blood thinner. However, there are two large randomized trials, one from each company, from each device. There are that, that should be coming up in the next year or two with the results. Each is about in the 3000 range of patient enrollment that are trying to address the second population. So patients who don't have a reason to seek an alternative to blood thinner, but just don't wanna be on a blood thinner for a long time. So I would say that that is in the future will remains to be seen. But as of today, somebody who's had a problem with a blood thinner is an appropriate person to be referred to the clinic.

Dr. Malcolm Bell: Well I'm, I'm sure there are, you know, probably patients listening to this or physicians who were referring or taking care of patients with atrial fibrillation be very excited to, you know, to hear the results of, of those trials that you just mentioned. But there's always a risk, isn't there, you know, with any invasive procedure. So maybe it seems simple enough to close off this appendage with, with a special device, you know, moderate sedation in 30 or 40 minutes. But what are the risks?

Dr. Mohamad Alkhouli: Yeah, that you're right, exactly right. There is nothing, there's no free lunch. The procedural risks fortunately have really come down significantly over time. So now we quote about one to 2% risk of any complication, less than 1% risk of major complication in our practice. But that's just the procedural complication, you know, around the procedure. There are a couple of things that haven't been completely resolved yet with the long-term se quality of the device. One of them is the propensity or the likelihood of forming a clot on the device itself. That's called device related thrombus. That still occurs in about two to 4% of the patient. Not a high number, but considering this is a preventative procedure, right, we wanna be careful of that.

Dr. Malcolm Bell: Is that something that occurs early or within the first few weeks or months or beyond that?

Dr. Mohamad Alkhouli: Unfortunately it happens throughout, but the fir the, the highest number of observed cases are in the first six months. But we've had seen cases later on, so, so that risks and until today it hasn't been resolved. The, the newer generation of the Watchman device has a coating drug coating on the device to try to prevent that. But that's one risk we usually discuss with the patient. This is all odds of different things happening, right? Are you gonna have a stroke? We're gonna have a DRT or nothing or bleeding. So, so we're playing with a lot of odds. That is really the major one there. There is a smaller risk of, you know, the device not sealing completely because the append anatomy is extremely variable that has been associated with a slight increase of adverse event over the long time, long term, but not, not a substantial increase. So device related thrombus, in my opinion, remains the, the one sticky sticking point for, for long term.

Dr. Malcolm Bell: Now just going back to the reason why you're gonna put these in, in the first place is to prevent stroke. So how effective is it as preventing stroke? I mean, what, what would be the risk of stroke after having one of these devices placed maybe compared to someone who's taking anticoagulation and maybe compare to someone who cannot take anticoagulation or refuses to take it?

Dr. Mohamad Alkhouli: Yeah, so if you look at all kind of strokes in the randomized trials, there was no difference between taking plot thinners versus they doing a device. If you wanna dig a little bit deeper, I don't know if it's appropriate for, for this, you know, kind of audience, but I think it is, it's important for people to know that the mechanism is mostly by preventing bleeding strokes. When you take away the, you know, the risk of, of stroke by eliminating blood thinners, the watchman does great or the device left occlusion does great, but there is a slight increase in ischemic strokes if you stop the warfarin two. But if you combine all together, any kind of stroke, you get numerically similar numbers. And we tell the patient, you know, with blood thinners, we know in the literature blood thinners reduce the stroke risk by 50%. So if your stroke risk was 6%, it'll be 3%, it's never zero. But that we, we quote similar, you know, performance between the two based on the trials.

Dr. Malcolm Bell: So Mohamad, you know what one of your other major interests and and contributions has really focused on innovation and as we think about this device, maybe you could just as we finish here or wrap this up, can you give us perhaps a little glimpse into the future of how these devices may be improved? And secondly, do we have tools that we can predict who's gonna be better off having a left atrial appendage occlusion versus either no therapy or anticoagulation?

Dr. Mohamad Alkhouli: Yeah, thank you. Very good question. So on the first one, what does the future hold? I think the future 10 years from now will be devices with very, very low footprint and they're already around the corner now there are devices that you can go and twist the appendage and close it and leave a really, a tiny knob there. I think people will be excited if it's effective in the closure mechanism to have that versus having a large device with, you know, chances of problems on it in the future. As far as prediction, that has been our, an interest of ours and I, I don't think we have anything effective now we even, even predicting stroke in general, we use a very old historic crude score as you all know, the chads vasc score, but predicting who should do this versus that. We we're doing some work with flow dynamics to see, you know, if you have this pattern of flow, would you do better with this? And that that's something to, to, you know, watch out for the future. But as of today, we don't really have a good predictor, unfortunately.

Dr. Malcolm Bell: Well unfortunately that's all the time we have today. But I mean, I think this has been a very good discussion. I think some important information presented here and also I think it just gives us a real glimpse into the future about what may we, we may expect you to see for our patients in the future. So thank you so much for spending the time with us today and look forward to further updates in this area.

Dr. Mohamad Alkhouli: It's my pleasure. Thank you very much for having me.