**Title: TCT 22: The AMULET-IDE Study: 3-year Outcomes of the Amulet Left Atrial Appendage Occluder in Patients With Atrial Fibrillation**

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**Date: 20th September 2022**

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"- Hi, my name is DJ Lakkireddy. I'm a Professor of Medicine at the University of Missouri Columbia, and I'm also the executive director for the Kansas City Heart Rhythm Institute in Kansas city, Kansas.

What is the importance of the AMULET-IDE Study?

Well, last year at the European Society of Cardiology, we presented the one year data. And we have shown the differences between the dual closure, Amulet closure device for the left atrial appendage, versus the single closure mechanism, Watchman device. And so this is an extension of that in terms of all the primary and secondary endpoints following these patients up to three years now. As you very well know, the story doesn't end right at 12 months or 18 months, as most of the clinical trials are. The real effectiveness of these devices in mitigating stroke and protecting patients who have atrial fibrillation that are at very high risk for the strokes, it needs to be further followed along. And this is exactly what this three year follow up study does.

What was the study design and main findings of the trial?

So as you know, it's a prospective randomised controlled trial that randomised the Amulet device to the Watchman 2.5 version. And so this study was conducted over five years. The intent was to create as homogeneous of a group as possible, and they got randomised between the two. A total of about 934 patients were enrolled in the Amulet, and 944 patients in the Watchmen arm. And of whom about 721 patients completed the three year follow up, and 659 patients in the Watchmen arm completed follow up. I mean, you really look at it for any major clinical trial this large, an interventional trial, 92% being followed up and 86.7 being followed up, at the end of this actually a pretty amazing number. Most of the times there is a lot of attrition because these trials are usually the elderly patients. They have difficulty with transportation, they move around. And so it's actually a very powerful data set that provides us some amazing insights into the effectiveness of appendage closure devices in general, and also specify some specific differences between the Amulet and the Watchman devices. And in a lot of ways, the mechanism of action actually plays in really well in highlighting these differences. So for example, what are some of the discovered insights from the Amulet trial? Right? So what the major take home points here are the number of patients who withdrew from the trial were much higher in the Watchman group during the follow up. A lot of that happened because of increased patient mortality related to cardiovascular as well as non cardiovascular deaths. And then the cardiovascular and all cause trends were definitely higher in the Watchman arm than it was in the Amulet arm. And there were really no major pericardial effusions in a delayed fashion. There was an early concern for the dual-closure Amulet device. In the immediate postoperative period, there was a slightly higher incidence of pericardial effusions that was trending higher. But then this trend kind of stopped, and beyond six months, there were no pericardial effusions between the two devices, I mean as it should be, right? So as the device settles in and, and endothelializes the risk of subacute or chronic pericardial effusion is actually pretty rare with these type of endocardial closure devices. What they also learned was more patients were on oral anticoagulation in the Watchman arm, compared to that of the Amulet device. This partly could be because there was a relatively higher incidence of devices related to the thrombus in the Watchman group than it was with the Amulet arm, right? So anytime you have a higher incidence of DRT, the natural course of these patients is that you have to put these patients on oral anticoagulation to mitigate the risk of embolization and risk of stroke. So the, this once again, highlights that a dual-closure mechanism device like Amulet that has a nice, smoother, wider disc obviously has tremendous advantages in terms of helping a smooth, proper closure. As you see, the Amulet has a lobe on a disc and the smooth, rounded, outer disc really promotes a better closure of the ostium. So the opportunity to miss the crevices or the primary proximal lobes, are difficult anatomies that are oftentimes limited by the Watchman 2.5 version I think could be overcome by the, by the, by the mere design of the Amulet device. And then that's a reason why you found these differences in lower risk of DRT. Even though there were a lower number of DRTs at the five year follow up mark, there was no significant difference in strokes or systemic thromboembolic events between those. But I think the longer you follow these patients, I think some of those trends in differences I think could become more exaggerated and become more obvious, really helping us understand how these two different devices behave when we follow them in the long term. The overall ischemic strokes and major bleeding rates were pretty comparable between the two groups.

What are the clinical implications of these findings?

What's also interesting is, when you really look at and do analysis of the factors that kind of go into the mix of why do people develop strokes. We have patient-related factors and then you have device-related factors, and then you have implantation-related factors, and all of that, right? So when you zone in on some of the device-related factors, like, I mean, is it the DRT or is it the peri-device leak? All of that. What you would notice is that it's a significantly higher incidence of peri-device leaks in patients in the Watchman arm, right? When you look at the the numbers, they're actually pretty fascinating and relatively revealing because what you would notice is as we have presented this data in last year's TCT, the number of patients who had complete closure of the appendage, like zero leak, were significantly higher in the Amulet arm than it was in the Watchman, 63% versus 46%. When you follow these patients long enough, at 12 months you will notice that the number of patients in the Watchman arm actually that had a complete closure improved significantly, right? So it's 63% versus 53%. That means the Watchman 2.5 version device took a much longer time to settle in, to endothelialize, to really accomplish a zero leak. But when you really use the cutoffs of five millimetres or maybe more, like, three millimetres, or anything more than three millimetres nowadays, is considered as a reasonably large leak that we need to be paying attention to. So in those circumstances, I suggest that the number of patients who actually had a leak more than three millimetres was significantly higher in the Watchman arm, right? 22% versus 10%. That's a pretty, pretty big number. So as the standards for accepting what is considered to be an acceptable leak continues to trend down, Amulet really plays out really well because of its design. And the dual-mechanism closure device definitely offers a lot more options, in some of these very wide, and large, and relatively difficult anatomies that are oftentimes hard to close with the help from Watchman device.

Where are the gaps in knowledge, and how can further research improve this?

So, I say this trial continues to offer amazing insights into improving the design of these closure devices, and perhaps we should still continue to work on minimising the risk of leak. And we should also continue to work on minimising the risk of device-related thrombus. So there are a lot of amazing clinical trials that are coming up that I think are going to fill some of these gaps that the current technologies are able to offer. And be able to really push the envelope in making left atrial appendage closure much more efficient, much more safer. And in our efforts to really reduce the risk of systemic thromboembolism in patients who have atrial fibrillation. So that's kind of the, the meat and bones of this trial.