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What Anticoagulation Options Are Available To Optimize Care in the Management of Elderly Patients With Atrial Fibrillation?

Announcer:

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Dr. Patel:

Hi, my name is Manesh Patel. I'm at Duke Cardiology, and welcome to this episode of: What anticoagulation options do we have for elderly patients with atrial fibrillation? I'm joined by a friend and a colleague, a star electrophysiologist in this space, that's Sean Pokorney. Sean, thanks for joining me.

Dr. Pokorney:

Yeah, thanks so much for having me, Manesh. Really looking forward to this conversation.

Dr. Patel:

Yeah, so first, maybe we should just start by defining the elderly. In the clinical trials arena in atrial fibrillation, it tends to be that these are considered people over 75 years of age. And I think that's likely from our CHADS2 score that we had initially and now the CHADS-VASc score. So over 75 tends to be how we think about elderly, but we know with an aging population, we've had people go on and on and age, which is great. And in these trials, some pretty elderly patients have been involved.

I guess the first option is warfarin. And I'll tackle that one. And then I'll give you the hard ones of all the new ones. But we've had warfarin for quite some time. And interestingly, even though we know there's a hazard with warfarin, both in the meta-analysis and other data, we've seen that warfarin is quite effective in people. Uh, there is an increased hazard as you age for bleeding, and that's probably where the newer agents have started to show maybe their best benefit is some of our older patients that are at the highest risk. But certainly, it is still potentially one of the options.

But what about the other options? You know, in the last 12 to 15 years, we've had four new therapeutics come about. And I used to say, you know warfarin was the Muhammad Ali, it was undefeated, it never lost in these clinical trials. But now there are four agents for the last 12 to 15 years that haven't. Maybe you can walk us through sort of the data with the elderly for both dabigatran, rivaroxaban, apixaban, and edoxaban; those are sort of the order of the trials, maybe walk us through those, Sean.

Dr. Pokorney:

Sure. Yeah, I guess first, I would maybe just say that one of the things I think is really important is just highlighting the undertreatment that happens throughout our society. And this is even more applicable in the elderly population, you know, which obviously we're focusing on today. I think that, as you mentioned, again, we had warfarin for decades, and everybody sort of assumed that once these newer agents came out, that all of a sudden, everybody who wasn't anticoagulated would now become anticoagulated. And that really hasn't been what we've seen. We've only seen about a 2 to 3% increase in the number of patients that are treated year over year with the introduction of the DOACs. And – and I think that's been a little bit disappointing as we know that really about 40% to maybe as much as 50% of patients who have a guideline indication for anticoagulation are not currently treated. Again, that's particularly true in

the elderly, where there are some of these concerns around falls.

I think that, you know, as we think through the different DOACs that are now available, I would say that, to me, one of the things that really comes in my mind is the renal clearance of the medications. And so dabigatran in particular, you know, I'm often cautious of in my elderly patients where you can get larger swings in their creatinine clearance and – and more of the medication is cleared renally. Obviously, that's less of a concern for the other three agents, with apixaban, rivaroxaban, and edoxaban.

And I would say, really across all the studies, what we've consistently seen is that if anything, the elderly patients benefit just as much, if not more, relative to warfarin. And we've seen that within the clinical trials, and we've also seen that in the real-world data where with ARISTOPHANES, there were over a third of the patients were over 80 years of age. NAXOS, a study in Europe, looking at the DOACs versus warfarin as well, also had a very well-represented population of patients that were over age 80. And really, consistently across the real-world evidence that we've seen with ARISTOPHANES and NAXOS, as well as the clinical trials, we consistently see the DOACs outperforming warfarin, especially in the older patient population.

Dr. Patel:

Yeah, I think all three of the DOAC or Xa trials, the elderly population did far better, if not equal, if not better and consistent with the DOAC versus warfarin. In fact, we know one of the ways these agents are better is that they had less intracranial bleeding and less fatal hemorrhage compared to warfarin. So, our elderly patients are potentially the best benefit-risk profile for these. And a lot of these trials, certainly ARISTOTLE, but certainly even ROCKET had 43% of people over 75. So, well-represented patients over 75 with renal function, so you should feel some confidence in using those agents, I think, in that space.

And then I think it's really important to also think about recent data where people have talked about a trial called FRAIL-AF. You had people that were on warfarin, and they got switched to a DOAC and didn't seem to significantly get a benefit from that. Maybe you describe your response to FRAIL-AF and then I'll come back to a few thoughts I have.

Dr. Pokorney:

Yeah, I think, you know, FRAIL-AF was, as you know, stopped early for futility. And so, there were no definitive findings as a result of that study. I think that one of the things that FRAIL-AF highlights to me is just the complexities that we face in our healthcare system as you make any changes in a patient's healthcare, their medications, it can be a higher risk time period. And I think that particularly in FRAIL-AF when patients initially make that transition from warfarin over to a DOAC, one, that needs to be monitored closely and it needs a lot of input by their providers. But two, you're going to need to follow those patients for a longer period of time to truly see that benefit.

And so, again, these in particular, intracranial hemorrhages are relatively infrequent events, which is great and important. But again, these are events that we certainly see more commonly in our elderly patients. And so, I think we really need to follow these patients for longer than we were able to in FRAIL-AF to potentially see some of those benefits.

I would say that you know, one of the reasons that we commonly get for not treating patients with anticoagulation is concerns about fall risk. And there have been secondary analyses, both from ARISTOTLE and from ROCKET that have looked at patients who had a history of falls and demonstrated that, if anything, those patients actually had more benefit with DOAC relative to warfarin, in the patients that had, you know, fall history. And so, I think that – that it really comes down to patient selection and making sure that you make that transition over safely for these patients. But interested in your thoughts as well.

Dr. Patel:

I think you hit the nail on the head. I mean, I think the unique things about anything is first and this started with your first conversation, which is some anticoagulation of any sort is better than none. And that we have way too many patients that are elderly who are not anticoagulated, or I'll call under-anticoagulated, the wrong dose of a medication or a suboptimal dose. So, making sure you treat them and treat them at the right dose is important. That's number one.

Number two, people that have been treated for some period of time, or I'll call responders; they haven't bled, they haven't had an episode. So, when you enroll those patients in a trial, compared to any other agent, it's going to take a while for the other agent to show a benefit. And that I think is what we see in FRAIL-AF because it's not as big as the bigger trials that we saw. And of course, if people have been doing okay for a while, it takes a while to see a different benefit.

So, I think those are the findings. And when we look at individual patient meta-analyses from the three or four large randomized DOAC trials, we still see a large benefit with I – the newer agents. So, I think it's likely that if I have a new patient, a patient I'm taking care of and their AFib is new, and they're older, I'm going to be reaching for one of the – the newer agents likely not dabigatran for the renal function issues you described. Apixaban or rivaroxaban, often figuring out the dose. Renal dysfunction, it's easier to dose rivaroxaban for me, but however you do it, you're going to treat these patients. Some of those patients with really high bleeding risk, edoxaban has

some really interesting data that's valuable too. So, I just think that, you know, that's what we see.

Either way, appreciate you joining me. And I guess our big take-home message is, understand the patient's risk, do shared decision-making, and recognize more times than not the elderly patient with AFib benefits from treatment versus no treatment. And we can talk about how to treat them, but really the key is to get them treated. And then we do think that newer agents are substantially better than warfarin. And the story with FRAIL-AF may be that we saw a sort of a responder evaluation in patients with atrial fibrillation.

Dr. Pokorney:

Yep, no, I completely agree. And we looked at this in the ORBIT-AF study as well. And we showed that there's sort of a myth of the stable INR patient, a lot of these patients have periods of instability even when they've had prior periods of strong stability. So again, couldn't agree more. I think it's a really important topic and making sure that we're getting these patients treated is really the key.

Dr. Patel:

Yeah. Well, it's been great talking to you about this. And again, thank you all for joining us. We look forward to working up and making sure we treat our elderly patients with atrial fibrillation.

Dr. Pokorney:

Great. Thanks for having me.

Announcer:

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