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Oral Anticoagulation Management in Patients with Atrial Fibrillation

Announcer Open:
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Dr. Alexander:
Hi, I'm John Alexander, a Professor of Medicine and Cardiology at Duke Health. And I'm here today to talk about oral anticoagulation management in patients with atrial fibrillation.

We're fortunate to have new guidelines out from the American Heart Association, American College of Cardiology, and Heart Rhythm Society related to atrial fibrillation. There's a new classification scheme for atrial fibrillation: it can be clinical or subclinical, first detected, paroxysmal, persistent AF if it lasts more than 7 days, longstanding persistent AF if it lasts more than 12 months, and permanent AF once attempts to return to sinus rhythm have been abandoned. The terms chronic AF, valvular and nonvalvular AF, and lone AF are considered obsolete.

The pillars of AF management include stroke risk and prevention, optimizing all modifiable risk factors, and symptom management related to AF burden and rhythm control. Today, I'm going to focus on stroke risk and its prevention.

First, let's talk about calculating stroke risk. The CHADS-VASc score is the most useful and widely used score. It ranges from 1 to 9 and includes single variables of heart failure or LV dysfunction, hypertension, age more than 75 years, diabetes, stroke or TIA, vascular disease, age 65 to 74 years, and female sex. And based on these, you get a score of 0 to 9. And you can see over on the right side of this slide how your risk of stroke, your annual risk of stroke, goes from 0.78 with a CHADS-VASc score of 0, up to almost 25% a year with a CHADS-VASc of 9 with a nice gradation in between.

Now, to reduce stroke risk, there are currently six options. There's aspirin, which has been around for a long time, but is not particularly effective and has substantial bleeding risk. And then there's warfarin, targeting an INR of between 2 to 3. But in the last decade, we have four new options: apixaban, dabigatran, edoxaban, and rivaroxaban; all together called the direct oral anticoagulants, or DOACs. Three of these are factor X inhibitors, and dabigatran is a thrombin inhibitor. They have half-lives of between 6 and 17 hours. They have renal clearance between 25% for apixaban and a high of 80% for dabigatran. And in the United States, they each have one primary dose that's approved, with a dose reduction for selected populations. There are other doses that were studied, but they're not approved or available in the United States.

Now, these drugs offer substantial advantages over warfarin, against which they were all tested. Apixaban results in less stroke, less bleeding, and less intracranial hemorrhage than warfarin. You can see the other patterns with these other agents, dabigatran also reduces stroke compared to warfarin, but causes similar amounts of bleeding. Edoxaban and rivaroxaban cause similar amounts of stroke, and edoxaban less bleeding. All these drugs cause less intracranial hemorrhage than warfarin does.

Now, very importantly is the dosing of these drugs. For the majority of patients, patients should be getting the standard higher dose of

these drugs that's approved. But each of these drugs has criteria for dose reduction. For apixaban, patients should get 2.5 mg twice a day instead of 5 mg twice a day if they have two out of three of age over 80 years, weight less than 60 kilograms, or creatinine greater than 1.5 mg/dL. For dabigatran, the dose should be reduced from 150 to 75 mg BID only in those patients with end-stage renal disease. For edoxaban, the dose should be reduced from 60 to 30 mg daily for people with a creatine clearance of less than 50 but still over 30, who are on a strong PGP inhibitor, or of low body weight. And for rivaroxaban, the dose should be reduced from 20 to 15 mg a day for those who have a creatinine clearance of less than 50.

Now, there's a lot of underdosing of NOACs in clinical practice. And this is important because low doses of NOACs, where they've been tested are less effective at preventing stroke than standard doses of NOACs. There was a 41% increase in stroke with low-dose edoxaban compared to warfarin in ENGAGE.

And then importantly, in the ARISTOTLE trial, apixaban 5 mg twice a day, even in people with one dose reduction criteria, resulted in similar lower rates of bleeding compared to warfarin, as apixaban did in people with no dose reduction criteria.

So, the real opportunity is to treat more patients with atrial fibrillation with oral anticoagulation. There are 3 to 4 million people in the United States who have atrial fibrillation, fewer than half of these are anticoagulated. And of these, the stroke rate is about 5% a year. This translates to 100,000 strokes a year, and we think 70% of these, or 70,000 strokes a year, are preventable with oral anticoagulation. Worldwide, with 10 million people with atrial fibrillation, this translates to 200,000 preventable strokes per year.

So, in our patients with atrial fibrillation, the real imperative is to assess for stroke risk, and treat patients who are at increased risk of stroke with appropriate oral anticoagulants at the appropriate dose to reduce stroke.

Thank you very much for joining us today.

Announcer Close:
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