GAYATRI ACHARYA: Greetings. I'm Dr. Gayatri Acharya, cardiology fellow at Mayo Clinic. During today's recording, we'll be discussing stroke rates in atrial fibrillation with and without anti-coagulation. I'm joined by my colleagues, electrophysiologist, Dr. Paul Friedman, and neurologist, Dr. James Klaas, who specialize in this area. Welcome.

JAMES KLAAS: Thank you.

PAUL FRIEDMAN: Thank you.

GAYATRI ACHARYA: Glad to have you. Dr. Friedman, I'd like to start by asking you what's the risk for stroke in atrial fibrillation.

PAUL FRIEDMAN: The most common risk for atrial fibrillation has to do with the clinical risk factors actually more so than the arrhythmia. The most commonly used risk score system is the CHADSVASC risk. Each letter, of course, stands for something most people recognize. The first is C for congestive heart failure, which can include clinical congestive heart failure irrespective of ejection fraction the way it was initially defined.

H is hypertension. And similarly, a history of hypertension confers a risk. Each of these risk factors, by the way, is worth one point, with an exception of stroke.

A is age. Over 65 confers a point. D-- diabetes. S is stroke or TIA, which is worth two points. V is vascular disease, which can be coronary artery disease, aortic atherosclerosis, peripheral vascular disease. SC is sex category, or one point for being a woman.

The key point of any scoring system is that we want to identify who's at high enough risk to warrant treatment. And not all of the points are truly-- truly confer the same amount of risk. So for example, a woman under 65 with no other risk factors, well, she may have one point. The risk is low enough such that most people wouldn't anti-coagulate.

The general consensus among experts is that if the annual risk is 2% or more of thromboembolism, then anti-coagulation, which has its own risks, warrants that risk, because the benefit of anti-coagulation is then warranted.

GAYATRI ACHARYA: Now Dr. Friedman, a question I feel like I pose to myself all the time is, what do I do with my patients who have a CHADSVASC score of one. How do I approach them for anti-coagulating or not?

PAUL FRIEDMAN: Now that's a great question, because patients with a CHADSVASC score of zero have such a low risk that the risk of anti-coagulation is warranted. And we do nothing. Patients with a CHADSVASC score of two or more have such a high risk of thromboembolism that on the balance, the vast majority of these patients-- and guidelines and experts agree-- should be anti-coagulated. When CHADSVASC has been studied, it depends on what you got the one point for, because not all the risk factors are the same. And in population studies that have been done in Sweden and in Taiwan, there have been different outcomes likely reflective of the difference of that population.

So I think in that situation there are a couple of approaches. One is if the HASBLED score is higher, then you wouldn't anti-coagulate. It does involve more shared decision making. One of the things I find particularly useful in that case, because the nice thing about CHADSVASC is it's easy enough to remember that we can just calculate it on the fly. But when I have someone where I get a 1, sometimes you could actually look up, either with an app or on the web page, the exact risk for that specific risk factor. Because it can range from 0.6 to over 2-- 2 and a 1/2 or so.

And if it's 2 or more, then I really lean towards anti-coagulation. And if it's less than 1%, I never anti-coagulate. And generally when it's under 2, I tend to avoid anti-coagulation.

GAYATRI ACHARYA: And does it matter if the atrial fibrillation is persistent versus just paroxysmal?

PAUL FRIEDMAN: Yeah, so the short answer is the guidelines, of which there are roughly five now, indicate that either one should be anti-coagulated. We are getting a lot of additional information about how much atrial fibrillation confers a risk of stroke. And an ongoing debate amongst experts is is it the amount of atrial fibrillation. Or is atrial fibrillation itself simply a marker to suggest that there is a vasculopathy or an atriopathy conferred by all the risk factors, and potentially an inflammatory condition associated with those, that confers a risk of stroke.

But to answer your question, large studies and some analyzes, for example, of the edoxaban versus warfarin studies, suggest that paroxysmal atrial fibrillation may have a lower risk than persistent atrial fibrillation. The magnitude of that difference, however, is such that in clinical practice today, we treat both the same in anti-coagulated.

Additional information is emerging from implantable devices. And studies such as the ASSERT trial have looked at patients who may have subclinical atrial fibrillation picked up by a pacemaker, suggesting that if you have six minutes or more of an atrial rate above 180 beats per minute, or so an atrial tachyarrhythmia more broadly, there is an increased risk. That risk is further modulated by the CHADSVASC score.

But without belaboring the point, there have been a number of studies with different cutoffs ranging from six minutes-- subsequent analysis of the same trial showing 24 hours is what really confers a risk-- and other trials showing six hours or more. So bottom line is, it seems that more atrial fibrillation is associated with a higher risk. We don't really have a good way of differentiating it. It's too complex to really tease apart in a given patient. And a good rule of thumb is if there is a clinical atrial fibrillation, use the CHADSVASC score to then make the treatment decision.

GAYATRI ACHARYA: Great. And when you think about making a treatment decision, anticoagulating a patient, how much is the risk lowered for stroke when you anticoagulate.

PAUL FRIEDMAN: So significantly, and typically 60% to 80%. So it's a substantial reduction in the risk of stroke. Now of course when you give an anti-coagulant, there is a risk of bleeding. The most concerning form of bleeding would be intracranial bleeding, which for warfarin is going to be about 0.5% to 0.6% per year across the studies. With some of the newer DOACs, or Direct Oral Anticoagulants, it may be reduced substantially, I mean from a very tiny amount to a tiny, tiny amount of about 0.3%, 0.4% per year.

GAYATRI ACHARYA: And Dr. Klaas, what are the other risk factors for stroke that we should be thinking about in all our patients?

JAMES KLAAS: Well, of course, cardioembolic stroke is a major category for strokes. About 20%, 25% of strokes come from the heart. But there are-- the remaining percentage are from other etiologies. And just because we have a patient with atrial fibrillation, doesn't mean that we should stop there. We have to evaluate and make sure that we aren't missing some other cause of stroke.

I tend to approach the patient by thinking proximately, meaning the heart first, and then working my way up to the brain in a sequential pattern. And so right after the heart, the next thing I worry about is the aorta or large vessel causes of stroke. Off the aorta, then there can be the other large vessels that feed the brain, the carotid arteries and the vertebral arteries. Of all these large vessels, atherosclerotic disease is probably the most common cause of stroke that we encounter. But there are others; arterial dissections, vasculinities, et cetera.

Then we move into the brain itself. And that's where we really get into the small vessel disease category. And that can also have some of these other causes, most commonly atherosclerosis, usually due to typical vascular risk factors; high blood pressure, high cholesterol, smoking, diabetes, et cetera.

And then the final category I think about is not anatomic limited, but more of a systemic. Is there a coagulation disorder? Are these people that are hypercoagulable due to protein C and S deficiency, due to anti-phospholipid antibody syndrome, or due to hypercoagulability from a malignancy. And if you go through all of that kind of sequential process, then you're not going to miss a potential stroke cause.

GAYATRI ACHARYA: That's a great organizational scheme. I know I'm going to be using that from here on out. Now we talked a little bit about anti-coagulation. But who do we not anti-coagulate? You've mentioned intracranial hemorrhage. How do we make these decisions?

PAUL FRIEDMAN: Sure, so one scoring scheme that has been proposed is still not that widely used in practice, but that we keep in our minds is the HASBLED mnemonic. Where H here stands for hypertension, which can be uncontrolled hypertension or a systolic pressure above 160. And each one here again gives one point. A would be abnormal renal function or abnormal liver function.

An abnormal renal function is either dialysis or creatinine above roughly 2 and 1/4. Abnormal liver function would be known cirrhosis or total bilirubin twice normal, or liver enzymes that are three times normal. The S is previous stroke. B would be bleeding history. L would be labile INR, so a therapeutic ratio of less than 60%, or simply lability in patients who are anti-coagulated.

E is elderly, which is almost all of our patients. The cut off for this is 65. And then D would be use of drugs, which can include anti-platelet agents, alcohol, or other such agents. And if you have a score of 3 or more, that's considered to be high risk. And those are patients where we would certainly consider alternatives to anti-coagulation if they were at high risk for thromboembolism. But of course, there are other potential bleeding risk factors that are more neurologic in nature.

GAYATRI ACHARYA: And Dr. Klaas, would you like to comment on that?

JAMES KLAAS: Sure, I mean, to piggyback off on that, I use the HASBLED frequently in clinic to kind of help me in not only making my own clinical decision but having those conversations with the patient. From a neurologic standpoint, really what I worry about mostly is, as Dr. Friedman led off, is intracranial bleeding. And of course, the most feared for that, for me, is intracerebral hemorrhage, especially a lobar intracerebral hemorrhage that may suggest an underlying condition known as cerebral amyloid angiopathy.

GAYATRI ACHARYA: And can you tell us more about that? I think that's something that I'm hearing more and more about but don't fully understand yet.

JAMES KLAAS: Yes, cerebral amyloid angiopathy, as imaging has advanced, we've been able to diagnose it more readily. And it's not as uncommon as we once thought. It's actually fairly common. It's something that occurs more so in the elderly. In fact the diagnostic criteria means that you have to be above the age of 55.

And what it is, it occurs when there's an abnormal deposition of amyloid beta in the blood vessels in the brain. Now even though it has the term amyloid in it, it's important to recognize this has no relationship to systemic amyloidosis. But some of you might recognize amyloid beta as the same protein that accrues in senile plaques in Alzheimer's disease.

So if you get this accrual of this abnormal protein, amyloid beta, in the brain cells, the neurons, you get Alzheimer's disease. If you accrue it in the blood vessels, you get cerebral amyloid angiopathy. Now what does that do to the blood vessels? The deposition is abnormal protein makes the blood vessels very fragile and prone to cracking and bleeding. So this is a very high risk for intracerebral hemorrhage.

GAYATRI ACHARYA: And how do we diagnose it?

JAMES KLAAS: So if you see somebody who's actually had an intracerebral hemorrhage, and it's a lobar bar location-- and by that I mean the amyloid beta has a predisposition for getting deposited in the cortical or the superficial blood vessels. So you're going to look for a hemorrhage near the surface. And that's what we mean by lobar. If they have a lobar hemorrhage, already you should be suspicious, especially if they're above the age of 55.

But then we can look on advanced imaging sequences. And this really relies on MRI. We can't diagnose it on CT scan. But there are certain sequences that are very sensitive for hemosiderin or previous blood products. And those would be your T2 star, your GRE, SWI, SWAN sequences.

And what we look for in them is what's called microbleeds. And these are little tiny black dots on these scans that suggest the patient has had subclinical little tiny bleeds that didn't manifest or didn't cause a frank hemorrhage. But we can see the sequelae of them on these scans. Just like the lobar location, we look for these in the lobar location, because if they're in the deep parts of the brain, it could be indicative of some other process, not cerebral amyloid angiopathy.

GAYATRI ACHARYA: Is there any way to prevent this?

JAMES KLAAS: Unfortunately right now, we haven't found a way to prevent it. There's no real prevention. And there's no real treatment. What we do is try to mitigate the risk of intracerebral hemorrhage. So we look at are there other things that increase the risk of a hemorrhage. And that's why it's important that we use judicious use of anti-platelet or anti-coagulant medications in these patients. And although there's not much evidence, we tend to make sure that we maintain a very normal tense of blood pressure in the patient.

GAYATRI ACHARYA: That's great. That's very helpful to better understand that topic. Are there non-medical options for stroke prevention for our patients?

PAUL FRIEDMAN: There are. In patients with atrial fibrillation specifically, 90% of the thrombi that have been seen in the absence of valvular heart disease have come from the left atrial appendage. The left atrium itself embryologically comes from sinus spinosa tissue. It's very smooth, whereas the left atrial appendage has multiple pectinates and trabeculations and anatomical and structural complexity.

There have been a number of studies now that have looked at left atrial appendage occlusion with occlusion plugs. There's one that's been approved in the United States, specifically the WATCHMAN device. And the concept there is by excluding this complex region of atrium from the central circulation, you can then eliminate the need for anti-coagulation.

Now the conundrum is that, of course, you're putting a foreign body in the central circulation. And a clot may form on that. In the clinical trials, warfarin and aspirin was used for a period of six weeks following plug placement, followed by Plavix and aspirin up to six months, and then aspirin alone. There has been evolution in the practice of that. And certainly in Europe, there's a good-sized experience of using Plavix and aspirin alone. There are ongoing studies specifically to address that question to see if the endocardio plugs can be placed without the need for anti-coagulation.

There are also epicardial approaches where percutaneous epicardial access is obtained, essentially putting a sheath into the pericardial space, but then permits placing a loop of suture over the appendage and closing it down. Now here there's no foreign body in the central circulation. And the majority of patients who've had closures of this form have not had periprocedural or postprocedural anti-coagulation. Although there's been some variability in how it's been adopted and tested.

GAYATRI ACHARYA: And are there any other selection criteria we should be considering for patients we may want to refer for non-medical appendage closure?

PAUL FRIEDMAN: So I think a good rule of thumb would be a risk of stroke from atrial fibrillation in the absence of significant value of the disease, so that the appendage is the most likely culprit. Second, it would be important that their risk is high. Any procedure is going to have some risk associated with it.

In studies over time comparing specifically the WATCHMAN device to warfarin was found to be non-inferior. And on late four-year follow up, the mortality was actually lower in the WATCHMAN group. There was not a reduction in thrombus-- or thromboembolism. But there was a significant reduction of bleeding, as you would expect. So the sweet spot would be a CHADSVASC score of 3 or more. And particularly if there is an increased bleeding risk, whether it be from amyloid angiopathy or HASBLED score of 3 or more, those would be the people who would get the most benefit from the procedure.

GAYATRI ACHARYA: Great. Well, Dr. Friedman, Dr. Klaas, thank you so much for these very important insights. And thank you for joining us on theheart.org on Medscape Cardiology.