ANSWERING YOUR QUESTIONS ON ANTICOAGULATION IN ATRIAL FIBRILLATION: TREATMENT SELECTION AND COMPLEX CASES

Transcript

This transcript is a supplemental resource to an educational video activity released on Medscape in October 2014. Please access the activity at www.medscape.org/viewarticle/833299 for complete information and content.

[00:00:20] THAD F. WAITES, MD, FACC: Welcome to our town hall. I'm here today with some outstanding colleagues and we're going to be talking about the subject of atrial fibrillation. We'll specifically be talking about the decisions around anticoagulation with atrial fibrillation, and to talk about anticoagulation, we are, of course, talking about stroke and death and disability that comes from stroke.

I'm Thad Waites. I'm an interventional cardiologist from Hattiesburg, Mississippi. I am a board member of the Board of Trustees, American College of Cardiology and a past member of the Board of Governors.

[00:00:56] CHRISTOPHER V. FLORES, MD: I'm Chris Flores. I'm board certified in family medicine and I'm in private practice in Palm Desert, California, but I'm also active in teaching and I'm Assistant Clinical Professor at Loma Linda University in the Department of Family Medicine.

[00:01:12] ANTHONY DEFRANCO, MD, FACC: I'm Dr. Anthony DeFranco. I'm an interventional and preventive cardiologist at Aurora St. Luke’s Medical Center in Milwaukee, Wisconsin, where I also direct the coronary intensive care unit, and I'm Clinical Adjunct Associate Professor of Medicine at the University of Wisconsin.

[00:01:25] DAVID GARCIA, MD: I'm David Garcia and I'm Professor in the Division of Hematology at the University of Washington in Seattle.

[00:01:33] THAD F. WAITES, MD, FACC: As to the prevalence of atrial fibrillation, in the United States alone, there are presently five to six million cases of atrial fibrillation. If the current trends continue, there will be as many as 16 million projected in the United States by 2050. If we can cut the increase, then we may have as few as 12 million, but it’s still a lot of patients with atrial fibrillation. In regards to stroke, we've had some recent good news that maybe the incidence of stroke and death from stroke is going down a bit.

The big problem we have in atrial fibrillation is undertreatment. If you look at studies from all around the world, and there have been as many as 29 studies looking at this, you’ll find that the best we do in any one study, in any one registry or even in one group, is about 60% of the patients are being treated with anticoagulation even if it is high-risk stroke. Even in our PINNACLE registry, which is a registry of outpatient clinics in the United States, we found the same type findings. About 25% of the patients were being treated with platelet inhibitors, quite a
number were not being treated at all, and then only about 60% were being treated with anticoagulants. So undertreatment is something we want to address today, and we will start that with questions of our panel.

We have some newly published guidelines. These are guidelines from the American College of Cardiology, American Heart Association, the Heart Rhythm Society, and endorsed by the Society of Thoracic Surgery, and I’d like to ask our panelists for their views on what are some of the take-home messages from our new guidelines. And, Tony, would you start this?

[00:03:15] ANTHONY DEFRANCO, MD, FACC: Well, there are many implications of these guidelines. I think we were all very impressed with how comprehensive they were and how many controversial issues in atrial fibrillation the guidelines addressed that we’ll be discussing during the next hour.

I would emphasize a few things. First is the classification of atrial fibrillation. There are four broad categories: the patient with paroxysmal atrial fibrillation, single sporadic episodes; the patient with persistent atrial fibrillation; longstanding persistent, where it proceeds for more than seven days; and permanent atrial fibrillation. These categories are not mutually exclusive. Patients can go from persistent to longstanding persistent or they can go directly to permanent atrial fibrillation if the patient and physician decide that rate control rather than a rhythm control strategy is going to be used. A second broad implication of the guidelines is broadening the numbers of patients who should be treated with anticoagulation for long-term stroke risk reduction. And a third broad aspect of the guidelines is the importance of shared decision making, engaging the patient in the decision on what therapy to pursue in order to reduce the long-term risk of stroke.

[00:04:28] THAD F. WAITES, MD, FACC: And, David, would you add to that?

[00:04:30] DAVID GARCIA, MD: Well, I’d love to. I totally agree with the points that Tony has highlighted. I think that the guidelines make some emphasis on using a CHA2DS2-VASc scoring system rather than the slightly simpler CHADS2 system to assess an individual patient’s risk of stroke. And, while I certainly don’t disagree with that recommendation from the guideline authors, I would hope that practicing clinicians realize that the most important thing is that they do some form of stroke risk assessment in any patient with atrial fibrillation, because whether they use CHADS2 or CHA2DS2-VASc, almost always, it’s gonna come out for most patients that there’ll be a net benefit of anticoagulant therapy.

[00:05:14] ANTHONY DEFRANCO, MD, FACC: You know, Thad, in the past we would sometimes give patients a break on one episode of atrial fibrillation, but one thing that the current guidelines emphasize is that a single episode of atrial fibrillation makes you an atrial fibrillation patient, and that should trigger the clinician into doing that stroke risk assessment in order to reduce the long-term risk of stroke. That doesn’t mean we don’t rule out or
explore potentially reversible causes of atrial fibrillation: alcohol consumption, caffeine, thyrotoxicosis, and so on, but once that patient has an episode of atrial fibrillation, the hunt for stroke risk reduction is on.

[00:05:53] THAD F. WAITES, MD, FACC: I would also like to point out that the word permanent isn’t necessarily permanent. It’s a decision at that point in time, as you mentioned, between the patient and that patient’s medical provider. They can decide later on that they want to pursue a course of trying to get it back into rhythm and be on anticoagulants continuously. Thank you. Excellent.

We all know that there is risk to the patient who has atrial fibrillation, but is there also risk of the treatment of atrial fibrillation and specifically the anticoagulation for reducing the risk of stroke? And do patients and doctors differ in—differ in their evaluation of these risks?

[00:06:36] CHRISTOPHER V. FLORES, MD: Yeah, that’s a great question and, you know, we talked about the undertreatment of atrial fibrillation in terms of the anticoagulation, but I would say that we are really doing a lot of undereducation of patients as well with respect to their disease state and the benefits of anticoagulation. There’s been some studies that have looked at knowledge assessments in patients with AFib, and what they find is that across the board, patients don’t really understand atrial fibrillation very well. In one study, about 50% of patients were able to even identify that it was a cardiology condition. They were not clear that it was their heart that was involved. And then, the most common response when patients were asked why are you taking a blood thinner medication, the most common response was because my doctor told me to take it, but they didn’t understand that they were preventing strokes.

There’s been some interesting studies looking at patient education and especially addressing what we call health literacy, where the instructors or the clinicians or the nurses in the office use multimedia materials, for example, flip charts with a lot of graphics and they talk about the risk of stroke and they talk about the role of anticoagulation. And when you offer that kind of education, then patients are really very, very willing, and sometimes more so than even the physicians, to accept the risks of anticoagulation. There was an interesting study that was done in Canada in Halifax through McMaster University, and they found that the patients were actually willing to tolerate more of a risk of bleeding if we could prevent strokes. So I think there’s a lot of opportunities to increase our education and effective communications with our patients.

[00:08:20] DAVID GARCIA, MD: Yeah, Chris, I totally agree, and I think that this study you referred to is a critical one because it reminds us about something that the guidelines have highlighted, which is how important it is to assess our own patients’ personal preferences and values as we apply guideline therapies. And we shouldn’t assume that we as physicians can predict what degree of risk or lifestyle burden they’re willing to accept in exchange for a particular benefit.
ANTHONY DEFRANCO, MD, FACC: Well, you both bring in the importance of engaging the patient in
the decision about anticoagulation. You know, patients are our best teachers, are they not? I’ve learned that
patients really fear stroke. Almost every patient over the age of 60 knows someone in their family or friends who
have had a stroke, and they’re very averse to that outcome.

Second, we clinicians are used to thinking about outcomes in terms of one- or two-year risk reductions.
Most of our patients want to live five years or 10 years or more if they’re healthy and 60, 70, or even 80, and I find
it useful to explain to patients risk reduction not only in terms of the one-year risk, if their CHADS2 score predicts a
5% one-year risk, but that that 5% risk turns into a 50/50 risk over 10 years. And if you explain to a patient that
anticoagulation will reduce that 50/50 risk to 1 in 10 or less, they grasp that immediately.

THAD F. WAITES, MD, FACC: Yeah, and we as physicians, I think, have tended to try to stay away
from the bleeding risk and it probably, at least, was partly because of the difficulty we’ve had in the past with
controlling INRs and the intense nature of using Coumadin [warfarin] in that regard. And so, if we saw any one
thing like even a slight risk of having some falls, we would say, well, they’re not candidates. But we’re finding
that’s just not the case.

ANTHONY DEFRANCO, MD, FACC: Well, we’re taught, first do no harm.

THAD F. WAITES, MD, FACC: Right.

ANTHONY DEFRANCO, MD, FACC: Because we fear sins of commission. We don’t see the patient
who comes to us and says, I would have had a stroke had you not prescribed that anticoagulation for me.

THAD F. WAITES, MD, FACC: Excellent. So definitely, we have risks and we have benefits, and we do
want to select our anticoagulation based on patient characteristics. Thank goodness we now have some choices
that we did not have before.

The NOACs are now available and that stands for novel oral anticoagulants or some say it stands for
new, but the novel part, I think, is appropriate because they’re not only new but they’re very different than what we
have had before. We also have potent antiplatelet medications and we have aspirin. So, David, I’d like to ask you,
what do you think about these choices and are there any that aren’t so good choices anymore?

DAVID GARCIA, MD: Well, specifically, Thad, when it comes to aspirin and antiplatelet drugs, I think
we’ve got a mountain of evidence now that as an antithrombotic strategy to prevent stroke in the setting of atrial
fibrillation, antiplatelet therapy is less effective than a variety of anticoagulant options that you just alluded to. So,
although, some sets of guidelines for stroke prevention still include aspirin as a secondary option or a “one might
consider this" sort of option for low-risk patients, my own view is that if a patient is at high enough risk for stroke to justify any antithrombotic therapy, it should really be an anticoagulant.

[00:11:48] THAD F. WAITES, MD, FACC: Thank you, David. That was excellent information. In our quest to break this barrier of undertreatment, we should follow guidelines, and we do have the new guidelines that I mentioned. In the new guidelines, it says that the NOACs are preferred treatment along with warfarin but, properly, because there’s not sufficient data to support this, they didn’t specifically say which NOAC to use or whether to use warfarin. So, let’s attack that subject as to how to choose which one. Tony, would you like to go first?

[00:12:22] ANTHONY DEFRANCO, MD, FACC: Well, one of the most elegant aspects of the new guidelines is that they do provide a very good structure within which the doctor and patient can jointly make decisions about the best choice of therapy, but they don’t dictate one particular drug in any one particular situation. There’s a lot of freedom. So, for example, in the patient who’s been on warfarin for stroke prevention, who’s been in the therapeutic range, who hasn’t had complications, and who doesn’t mind the monitoring monthly or thereabouts, there’s no reason to switch to one of the new agents.

On the other hand, the new agents do offer some advantages. For the patient who’s been on warfarin who’s had difficulty staying in the therapeutic range or who’s had a bleeding complication, that could be one potential reason to switch. Second, new patients with atrial fibrillation who are making their first choice about which anticoagulant to go on might choose one of the new agents due to convenience. Third, a patient who’s had a bleeding complication on warfarin might want to switch to one of the new agents. For example, all of the trials of the three agents currently approved by the FDA have consistently shown reductions in intracranial hemorrhage and that alone might choose—might lead some patients to choose going on one of the newer agents rather than warfarin.

[00:13:36] DAVID GARCIA, MD: I think that’s critical, Tony, because intracranial hemorrhage is the most feared risk of anticoagulant therapy as we apply it to stroke prevention and atrial fibrillation, and the consistency with which these newer, more targeted drugs have shown reductions in the risk of intracranial hemorrhage is really compelling. So, while that’s certainly not the only factor that one would want to consider, and I agree convenience is a huge driver on the pro side of the newer agents, intracranial hemorrhage risk reduction is not something that should be forgotten at the bedside in clinical decision making.

[00:14:16] CHRISTOPHER V. FLORES, MD: I have a question for Dave. I know you have a lot of experience with warfarin monitoring and warfarin clinics. If you have a patient who is not compliant with warfarin because they don’t keep their appointments, they’re missing their follow-up, what would you say about that patient as a candidate with the NOACs?
DAVID GARCIA, MD: Well, it’s a great question, Chris, because Tony is exactly right when he says that someone whose time in therapeutic range is low despite the best efforts of the patient and the doctor to do the right thing, being a—that person is a great candidate for the new oral agents because they have a wider therapeutic index, their difference between safety and toxicity is low, and the need for monitoring is eliminated. But in a person who has erratic INR values, not despite but because of suboptimal adherence to their doctor’s recommendations, the new drugs aren’t likely going to be any better than warfarin.

THAD F. WAITES, MD, FACC: This is the scenario: the patient has atrial fibrillation. You have now totally evaluated them as to risk and you have determined that they need to be on an anticoagulant, and you’re going to place them on one of the NOACs. Which one should we choose? David?

DAVID GARCIA, MD: Well, not a short answer to that question, and I don’t think there’s necessarily a right answer to the question. The good news is you’ve chosen to give some kind of anticoagulation, and that’s by far the most important decision. I think that, while there may be certain patient characteristics that would make you lean more toward one anticoagulant than the other in certain situations, a lot of the decision is going to be driven by what the patient’s insurance or third-party payer covers or is on their formulary, as well as by what the individual physician or health system is most familiar with. Some of these anticoagulants have unique features in how they’re absorbed, how they’re dosed, how their effect is measured, and the most important thing I think is that a physician or provider prescribe one with which here or she is particularly familiar and that the patient can get access to. I think outside of that, it’s a very complex question and may depend somewhat on individual patient characteristics, but again, the most important decision is that they get on an anticoagulant in the first place.

THAD F. WAITES, MD, FACC: There are a couple of discriminating factors on two of the drugs I was thinking about like dabigatran, you have to use it in the manufacturer’s packaging and you have to use it within a certain period of time. That’s a part of the drug information on it. And then, I believe with rivaroxaban, you have to or it’s recommended that you have that with a meal and it has really good absorption. David, per your absorption observation, would you comment on that?

DAVID GARCIA, MD: Sure. I think the general principle that one should follow is exactly what you highlighted, Thad, which is that the drugs are a little bit different in the way they are prepared, in the way they’re packaged, and in the way they’re absorbed, frankly. And, the practicing doctor, I think, really needs to familiarize him or herself with these individual traits of a particular drug, because they aren’t necessarily the same. You’re exactly right. Rivaroxaban is better absorbed if it’s taken with food.

THAD F. WAITES, MD, FACC: We’ll be having more trials on the new drugs and as we have those trials, there will start to be some discriminating differences and that’s where our shared decision making with the patients and deciding which ones are the right one for their particular situation will start playing a very major role.
We’ve talked a lot about INR. Now, what about monitoring the new drugs? David, are there any tests that monitor the NOACs?

[00:18:20] DAVID GARCIA, MD: Well, the answer is there are some tests that we can use to assess the anticoagulant effect of the new drugs. But I would say we should reserve such testing for very specific clinical situations and I like to use the word measure rather than monitor since monitor implies that we need to do some assessment on some routine basis even if a patient is asymptomatic, and that’s just not the case with these new drugs. They were developed without the need for routine monitoring. I would say that the best tests to measure the effect of dabigatran are—is really the dilute thrombin time or, if your institution doesn’t have that, a thrombin time, which is available in most places. For the anti-Xa inhibitors, an anti-Xa activity is the best test to order, although I realize that sometimes it’s not available in short order.

[00:19:17] THAD F. WAITES, MD, FACC: Thank you. Everyone has that question. So now, we—we have the patient on long-term therapy, either on warfarin or on the NOACs. Is there any way that we can mitigate the risks that these patients have during that time? Chris, would you answer that for us?

[00:19:33] CHRISTOPHER V. FLORES, MD: Sure, sure. From a primary care perspective, of course, I think it’s my job to make sure I'm on top of what other medications my patient’s on because obviously sometimes they themselves will start taking over-the-counter nonsteroidal anti-inflammatories or they’ll go to an orthopedist and get prescribed a nonsteroidal that I don’t necessarily know about. So I have to really stay on top of that. Blood pressure control, you know, making sure that we have adequate blood pressure control is imperative because we know that out of control blood pressure is a very significant risk with bleeding. And then we have to be aware of alcohol use in our patients and we have to have a good grip on that in patients who are on these long-term therapies because there’s obviously a lot of interaction there. And so we just have to be aware of all the other things that our patients are possibly taking and making sure that we’re doing the basics in terms of good blood pressure control.

[00:20:32] ANTHONY DEFRANCO, MD, FACC: Two other strategies to mitigate long-term bleeding risk including checking renal function at least yearly in patients who have CKD stage III. Another strategy is to make sure, as Chris just mentioned, that the patient mentions not only to pharmacists but to other providers, other physicians, that they’re taking these new agents because physicians outside of cardiology, hematology, and family practice, internal medicine may not be familiar with these agents and may not recognize that even though there are fewer drug interactions than there are with warfarin, there still are drug interactions.

[00:21:03] THAD F. WAITES, MD, FACC: In the field of atrial fibrillation, there are racial and ethnic disparities, and now we have some new drugs. I wonder if these new drugs will at all affect these disparities that we’ve seen. Chris, would you attack that question?
Sure. First of all, I’d have to say that there’s a lot we don’t know about racial and ethnic disparities with atrial fibrillation because, unfortunately, most of the findings come from subgroup analysis of the existing clinical trials that were obviously done for some other purpose, that was not the primary outcome. Or, there are several observational retrospective cohort studies that have been done, but again, they don’t necessarily show cause and effect.

But, one thing that’s interesting is that once the patients are diagnosed as atrial fibrillation—so if you have an ethnic minority patient who has a diagnosis of AFib—then they’re actually less likely to receive appropriate treatment, for example, anticoagulation—even less so than the white or Caucasian population—or interventional procedures. So, for example, cardioversion or ablation therapies don’t seem to be offered as much to black/African-American population or Hispanic/Latino population.

One thing that’s interesting, in addition, is that the rates of intracranial hemorrhage seem to be higher especially in the black/African-American population and some people say, well, that’s because of multiple risk factors, hypertension, it’s not just atrial fibrillation that we have to worry about. But there was a very well-designed study, again, it was observational, retrospective, but it was done with Kaiser Permanente in Southern California and that’s a big health maintenance organization that’s very well integrated, wonderful information technology, so they were able to look at the diagnoses, they were actually able to look at EKG tracings on a lot of these folks. And they looked at hospitalizations, and they still found that if you have an African-American patient with atrial fibrillation on warfarin, in this case, they were looking at patients with warfarin, they had higher rates of intracranial hemorrhage.

So, how do the new agents fit into this? Well, obviously, we don’t have a lot of data but, you know, one thing that seems to be promising is because the new agents do not require as much monitoring and they are somewhat more convenient to use, you know, they might be helpful in ethnic minority populations. There certainly is more attention on the topic now, partially just because of the preponderance of research on AFib in general, but also because we have these novel anticoagulants that we’re studying. So there’s more awareness, more education to physicians and patients alike, and then, possibly, there’s a role for these NOACs because they do seem to be associated with less risk of intracranial hemorrhage, so I kind of see that as a potentially promising thing.

David, did you have something to comment on?

Just the only addition I would make is that, while the data Chris is talking about is very interesting, I would emphasize that at least as of today, we don’t have any reason to think that anticoagulant therapy is going to be any less beneficial or more dangerous for a particular ethnic group than another. And,
similarly, we don’t have any reason to think that the treatment effects of the new agents, as Chris said, are any different better—for better or worse in a particular racial group.

[00:24:38] THAD F. WAITES, MD, FACC: The NOACs are very expensive, in fact, maybe prohibitively expensive at this point. Do we have anything in the near future where Medicare is going to help us find lower costs or are the insurance companies going to help us with this? Chris, would you address that?

[00:24:56] CHRISTOPHER V. FLORES, MD: Well, that’s a great question because I think for a lot of us clinicians, that’s kind of like the elephant in the room at times is the cost of these medications. And what I can say from a primary care perspective is that it’s just really important for us to know our patients and to be familiar with what their insurance is. Most of the patients, because of this diagnosis, tend to fall into the Medicare age group and so a lot of patients have Medicare Part D plans and sometimes it’s just a matter of filling out the appropriate paperwork or contacting the insurance to get that prior authorization through and then it brings down the cost of the medication to the patient.

Also, for patients that don’t have insurance or who have adequate—don’t have adequate resources to help with medications, there’s a lot of patient assistance programs that it behooves us to get familiar with because sometimes it’s fairly straightforward to be able to get ahold of these medications for patients that would not otherwise be able to afford them.

[00:26:02] DAVID GARCIA, MD: I think our health insurance system and the way we pay for it is so complicated in the United States. This can be a very difficult analysis to do both for an institution or pharmacy and therapeutics committee as well as for the clinician at the bedside, but there’s no question that cost is perhaps the most important barrier to the use of these newer direct oral agents. And, I guess I would just say that the analysis—the complexity of the cost-effectiveness analysis—is highlighted when one thinks about the fact that while warfarin is cheap to purchase as a drug, it has many associated costs including INR testing, healthcare provider time to follow up on and make phone calls about INR values, as well as others. So, no question, it’s probably the most important barrier to the uptake of these newer drugs, but it’s also very complicated when one tries to do the tradeoffs and do the math.

[00:27:06] ANTHONY DEFRANCO, MD, FACC: David, the point you just made about cost-effectiveness from a global sense is probably the reason why in our region, we’ve seen payers who have a drug benefit as well as the insurance part of the patient’s plan provide for these drugs because when you look at the total cost of care including the downstream cost of admissions for stroke, admissions for bleeding, the cost-effectiveness per QALY is actually well within the range of what we pay for other—for other therapies.

[00:27:34] DAVID GARCIA, MD: Yeah.
ANTHONY DEFRANCO, MD, FACC: The problem really is the patient who has no drug benefit coverage at all, and that’s the societal issue that we really have to address in a different way.

DAVID GARCIA, MD: No, absolutely, and talking about societal considerations, which we rarely have when we’re in the office or at the bedside with the patient, when you think about the lost work time or lost time of doing other things to travel to a lab, have an INR test performed, and go back home, that’s a whole ‘nother cost that we don’t even factor in when we’re trying to do these comparisons.

THAD F. WAITES, MD, FACC: I think about the analogy of clopidogrel with stents. We attack this before clopidogrel became generic by the fact that the patient absolutely had to be on Plavix [clopidogrel] for a year if they had a drug-eluting stent. So like we need to attack that they have to be on one of these anticoagulants, we attacked that and hospitals worked around it, and there was bulk order of the drugs and, you know, you just made it happen, and I think that we were fairly successful in that area of having patients on the proper drug even though the cost was really high on clopidogrel at that time.

DAVID GARCIA, MD: Frankly, Thad, I think you’re right, but I think one of the unique challenges here is that hospitals, health plans, and other institutions have built rather substantial infrastructure to do nothing but monitor warfarin. We’ve got full-time pharmacists, advanced practice providers, clinics, facilities, computers, that have all been set up solely for the purpose of monitoring anticoagulants and to now come in and say well, we don’t need those all anymore, but we’re gonna spend all this additional money from the pharmacy budget on these very expensive new drugs, it’s a challenge.

THAD F. WAITES, MD, FACC: And now we’re going to cycle into more complex situations—situations where there may need to be special changes and special considerations in how to manage the patient. And we’re gonna start with renal insufficiency and end-stage renal disease. And, David, that’s a fairly tough one, if you will start the conversation.

DAVID GARCIA, MD: Sure. I think there’s a lot to be said about this subject, Thad, but I’ll start by talking for a second about these new oral direct agents. All of them are to some extent eliminated by the kidneys, dabigatran more so than the factor X inhibitors. But, the fact is that there were virtually no patients whose creatinine clearance was below 30 milliliters per minute enrolled in any of the registration trials. So, although the FDA has included or approved some dose-reduction suggestions in the package inserts for patients whose GFR is between say 15 and 30 mL per minute, for some of the drugs, those recommendations are based on pharmacokinetic modeling, and my personal opinion is I’m rather reluctant to prescribe doses to patients in that category of the new drugs.
A related question though—and I want to see what Tony’s thoughts are on this is—are those patients with renal function that’s that severely impaired good candidates for anticoagulation at all?

[00:30:47] ANTHONY DEFRANCO, MD, FACC: Well, we really don’t know, David, because we do know, for example, that patients with end-stage kidney disease whether they’re on dialysis or whether they’re stage IV clearly have higher rates of bleeding even before they go on anticoagulation, so they’re predisposed from the start. Your point about risk-benefit in that population is very well taken. What we need are some new approaches. Now, you probably know the FDA recently approved an atrial appendage closure device. Why? Because the vast majority, if not all, atrial thrombi that are the cause of stroke, probably originate within the atrial appendage so perhaps for the end-stage renal disease patient, a closure device of one form or another or some other approach like surgical ligation might be better than anticoagulation. We just need more data.

[00:31:31] THAD F. WAITES, MD, FACC: In our country, we have an epidemic right now called obesity. What about these drugs and the obesity epidemic or even the malnourished epidemic, the small patient? Tell us what you think about that, Chris.

[00:31:44] CHRISTOPHER V. FLORES, MD: Yeah. That’s a—that’s a really challenging topic because we don’t have a lot of evidence, necessarily, to guide us on this. The clinical trials of the NOACs included some patients, for example, on the obese side that were over 120 kilograms, but those numbers are very limited and so, although, it appears that the medication seemed to work very well in patients who are heavier than 120 kilograms, we just have very small numbers to really guide us on that. So, I for one, if I have a patient that’s well above, you know, this about 240 pounds, 250-pound range, then I’m probably going to be more likely to give the tried and true warfarin because I can monitor that.

On the other hand, you know, you mention small patients. I’m in Southern California, and I actually have a fair amount of elderly women in their 80s who are about 100 pounds, and so in that population, again, the clinical trials don’t really help us too much because the numbers are so small. So if I have somebody who is under 50 kilograms, then again, I’ll probably be much more likely to give warfarin because I can monitor that.

[00:33:00] DAVID GARCIA, MD: Yeah. I think Chris is exactly right. You know, the great advantage of these newer direct inhibitors is that they don’t require monitoring for a variety of reasons, one of which is their predictable bioavailability. Another is that they likely have a wider therapeutic index than does warfarin, that is, the difference between safety and toxicity is not quite so—such a marginal thin line. But I do recognize that even in the clinical trials or healthy volunteers, one sees a huge variation between the 10th and 90th percentile for, say, the trough value—trough concentration of these drugs. And, when you start to get into somebody who’s either extremely heavy or extremely thin, then that difference is just going to be accentuated, and I’m not sure we know that the one-dose-fits-all strategy is really gonna work.
We know that, perhaps, one of the most important concomitant medications in a patient who’s anticoagulated is an antiplatelet drug. We know that when you start to give so-called triple therapy or even just simply add aspirin to background anticoagulant therapy, you’re going to substantially increase the risk of major hemorrhage in a particular patient. Tony, are there situations—I realize there are times when we have no choice but to do that—but are there situations where concomitant antiplatelet therapy can either be deescalated or eliminated altogether?

ANTHONY DEFRANCO, MD, FACC: Well, that’s a great question, David. First, let’s take the current status of aspirin in prevention of coronary atherothrombotic events to begin with. There are two ongoing studies right now looking at whether or not aspirin really provides any benefit in primary prevention. As you know, the current indications for aspirin are solely for secondary prevention in patients who have already had a myocardial infarction. So, the current ACC/AHA guidelines suggest that we shouldn’t be prescribing aspirin even in patients who aren’t on anticoagulation until the annual risk of MI reaches about 1.5% per year, about 15% over 10 years. Well, compare that to the risk of stroke. In patients with a high CHA2DS2-VASc score, the annual risk of stroke may be 4, 6, 8% or even higher.

So, in that patient, it makes much more sense to prevent stroke by prescribing only the anticoagulant and dropping the aspirin, especially if they’d never had an MI. So that’s why the current 2014 atrial fibrillation guidelines use as an—or specify as an option, dropping the aspirin in the patient in whom the risk of a thrombotic event from the AFib is much greater than the annual risk of myocardial infarction.

DAVID GARCIA, MD: A lot of practicing doctors, I think, don’t realize that warfarin and probably, although less certainly, the newer drugs do offer some protection against cardiac events and thrombosis within the coronary vascular bed. And while, of course, we’d love to have everyone at risk for coronary disease on aspirin or an antiplatelet drug, the marginal benefit of adding such therapy to somebody who’s already on an anticoagulant, as you said, has to be considered very carefully vis-à-vis the risk of doing so.

THAD F. WAITES, MD, FACC: And now we have a real problem. We’re presented with a patient that has a major bleed. Are there any reversal strategies for reversing the new drugs? David, that’s right in your wheelhouse.

DAVID GARCIA, MD: Well, there are some things that we can do, and I’ll talk about those in a moment, but for the moment, for now at least, we don’t have any great clinical outcome-based evidence to drive our decision making. One could use prothrombin complex concentrates, so-called PCCs, in case of truly life-threatening serious bleeding based on some animal and other preclinical evidence suggesting that these might, to some extent, reverse the effect of the novel drugs. But for the moment, we don’t have as much experience reversing these agents as we do with warfarin.
[00:37:05] THAD F. WAITES, MD, FACC: If we do the PCC, does it need to be the four-factor ion, I understand is the name of it, four-factor PCC?

[00:37:12] DAVID GARCIA, MD: Well, we did recently get a four-factor PCC approved in the United States and there are some theoretical reasons why one might use that. That's the particular type of PCC that's been evaluated in these preclinical studies that, again, did not involve bleeding patients or have clinical endpoints. So, if one is going to use a PCC, one's gonna to do it based on that very, very low-quality evidence and it—I guess it should be a four-factor one.

[00:37:45] THAD F. WAITES, MD, FACC: Now, before coming here, my PharmD got to me and she said, “Come back with some reversal strategy. Our emergency room doctors and our surgeons especially our neurosurgeons hate these new drugs.” Should this be a factor in us deciding not to use the NOACs?

[00:38:03] DAVID GARCIA, MD: Well, I don’t think it should, and I understand there’s a great deal of fear around the so-called lack of an antidote for these new agents, and we have a certain degree of comfort or confidence in our ability to reverse warfarin’s effects in a bleeding patient. But the reason I don’t think it should play a major role in deciding whether to use or not use one of these newer anticoagulants is several.

First, bleeding is very rare to begin with, especially with these novel agents if they’re used in properly selected individuals. Second, there is no evidence that fatal hemorrhage was more common on the new drugs in the large phase 3 trials than it was on warfarin. It’s worth remembering that, unfortunately, 10% of people who come in with a major warfarin-associated bleed will be dead 30 days later, despite the fact that we think we know how to reverse it extremely well.

So, again, luckily, bleeding is very rare irrespective of which anticoagulant we use, and there’s no evidence from the clinical trial data that fatal bleeding will be any more common on the novel drugs than it would be with warfarin, despite the lack of an evidence-based reversal strategy.

[00:39:27] THAD F. WAITES, MD, FACC: Those same specialties, I think, have been comforted by the four-factor PCC when they have patients that have high INRs and, correct me if I’m wrong, but I understand that even though you correct the INR very quickly with a four-factor PCC, you don’t necessarily stop the bleeding.

[00:39:45] DAVID GARCIA, MD: Well, I think you’re right there, Thad, in the following sense. The trial that lead to the approval of the four-factor PCC to reverse warfarin-associated bleeding in the United States was a positive trial only based on the surrogate endpoint of INR correction. That is, PCC was more effective than fresh frozen plasma at correcting the INR. However, the study was unable to show any reduction, any statistically significant reduction, in achievement of hemostasis or arrest of bleeding with the PCC versus fresh frozen plasma. That could be because it was underpowered or it could be because, in fact, lowering the INR, as you suggested, is not
as helpful as we’d like to think it is, but you’re exactly right. We need better data both for warfarin and the new anticoagulants about how best to manage patients who have major anticoagulant-related bleeding.

[00:40:49] THAD F. WAITES, MD, FACC: So now, we have a patient we’re going to cause them to bleed. They have an elective procedure coming up and they’re on the anticoagulants. How should we handle this patient, and I think it’s gonna be a good one for Tony to start with and then probably some dialogue among all of our panelists.

[00:41:03] ANTHONY DEFRANCO, MD, FACC: Well, thanks for calling on me for that one, Thad, because we face this all the time, don’t we? You know, fortunately, in the major trials that led to the approval of the new agents, some—anywhere between a quarter and a half of the patients in the study actually needed some sort of a procedure, necessitating temporary discontinuation of the medication during the one to two to three years of follow-up. So we’ve got data on this.

The general strategy is as follows. First, assess the bleeding risk of the procedure that the patient is going to have. There are many low-risk procedures, such as single tooth extractions or cutaneous procedures, carpal tunnel repair, that really don’t necessitate any cessation of anticoagulation at all. The challenge is that a lot of our colleagues in other specialties may not recognize that those procedures can be done safely without stopping these medications.

Second group of patients are those who are undergoing medium-risk or high-risk operations with respect to bleeding such as thoracic surgery or renal biopsy, liver biopsy, or abdominal procedures. If the patient has normal renal function, a good strategy is to stop the drug two days before the proposed surgery. The elimination half-life of all of these agents are in the range of seven to 12 hours, so four half-lives gets rid of most of the drug. So, if the patient has surgery on Wednesday, the last dose would be Sunday night, no drug on Monday, Tuesday, and then they have their procedure on Wednesday. One exception to that rule might be the person with impaired renal function whose clearance might be slower, and in that circumstance, we might want to stop the drug a little bit sooner especially if the patient is in sinus rhythm and is going to be monitored during the perioperative period.

Now, the nice thing about these agents is that after the surgery, it’s easy to resume them. Once the surgeon has hemostasis and the operation’s gone well, the drugs can be started either the evening of or the morning after surgery. The onset of action is rapid; the patient’s anticoagulated again within hours. The one exception to that is the patient who has GI surgery who may be NPO for several days who has a high thrombotic risk score and who’s in atrial fibrillation. That’s the situation where we might want to bridge that patient with another intravenous or subcutaneous anticoagulant in the days until they’re taking PO again.

[00:43:21] THAD F. WAITES, MD, FACC: Chris, anything?
[00:43:23] CHRISTOPHER V. FLORES, MD: No. I would just say that we in primary care end up doing a lot of preoperative clearances, and we are so sort of reflexively trained to look at heart and cardiac risk and we are used to sending people to cardiologists for that kind of risk factor evaluation and then we’re looking at liver function and kidney function. So this is just something else that we have to put into the equation and I just take it upon myself to try to communicate the best that I can with the specialist, with the surgeon who’s gonna be operating, and sometimes I’ll involve a hematologist or a cardiologist if I have a particularly complex case.

[00:44:00] THAD F. WAITES, MD, FACC: And, David, I would ask you specifically if this is an urgent situation, not necessarily emergent situation, can we wait less than two days on the NOACs?

[00:44:11] DAVID GARCIA, MD: Probably so. I think—I completely agree with what Tony said, and this idea of balancing risk and benefit is critical and that gets to your question, I guess it depends on the urgency. The surgeons have asked me as a general matter how long do I need to wait, and my answer to that is, what’s the risk of waiting, and that’s gonna depend on why they need to have the procedure that they need. We know that many surgeries, including thoracic surgery, can be performed on fully anticoagulated patients with a bleeding risk that, while it’s higher than it would be without the anticoagulation, is not necessarily prohibitive depending on why you’re needing to do that surgery in the first place. So, again, individual balancing of risk and benefit is critical, but the good news with the newer agents is that we’ve got to wait less of a—less number of hours than we do with warfarin for their anticoagulant effect to dissipate.

The one other thing I wanna mention is that, with respect to warfarin-treated patients who need a procedure, not only is this whole process more complicated because sometimes it is gonna involve the need for parenteral anticoagulation, I think we’ve learned in recent years from a number of different studies and published evidence that aggressive perioperative bridging, both pre- and postoperative with heparin or low-molecular-weight heparin, may sometimes be riskier than we once thought, and that the better part of valor for perhaps all but our highest thrombosis risk patients may be to simply interrupt warfarin for a few days preoperatively and then resume it postoperatively.

[00:46:04] THAD F. WAITES, MD, FACC: Well now we’re gonna go to a different type patient. This is a complex patient that has a stent—has a coronary stent—and they’re on DAPT, and that’s dual antiplatelet therapy. Now, they have atrial fibrillation and a high CHADS score. So, actually, they need anticoagulation but they’re already on two potent antiplatelet agents. So, Tony, what are we gonna do?

[00:46:26] ANTHONY DEFRANCO, MD, FACC: Well, Thad, that’s a very common scenario, as you know. You and I, as interventional cardiologists, I know we agree that once we implant a stent in a patient, we assume a lifetime risk of being involved in that patient’s decision about antiplatelet therapy, anticoagulation, and the risks of
procedures. But, even beyond that, the fact that those cases have to be decided on a case-by-case basis, there are some general guidelines that we can share with our colleagues outside of cardiology.

First is that the latest third-generation drug-eluting stents don’t require one year of dual antiplatelet therapy routinely. Later this year, we’ll have the results of the DAPT study, which, hopefully, will support that finding. Now, second, in the setting of an acute MI, the current ACC/AHA guidelines do recommend dual antiplatelet therapy for a year. So, if the patient has had an MI within the last year, that’s an individual decision about when it’s safe to stop dual antiplatelet therapy and whether or not triple therapy should be continued—should be started. The third consideration is that in those patients in whom you do need triple therapy, clopidogrel should probably be the antiplatelet agent until we have more data about prasugrel and ticagrelor. And then, finally, there is one study from Europe that suggests that in selected patients, at low risk of stent thrombosis—that is, straightforward stent, good result, no evidence of post-stent ischemia—it’s probably safe, especially after 30 days, to drop the aspirin and maintain the patient on just warfarin and clopidogrel, but then again, that has to be decided on a case-by-case basis as well.

Now, you gave me the easy one, Thad. I’m gonna give you the more difficult one. A patient with anticoagulation because of atrial fibrillation comes in with a STEMI and you’re on-call, Thad. What do you do?

THAD F. WAITES, MD, FACC: Well, thank you for the easy one. First of all, I would stop the anticoagulant at that point, whichever anticoagulant they happen to be on, and I would definitely advise against any fibrinolysis or thrombolysis. That would be a no-no in this particular situation. And then, after you do that, then decide on puncture site. I know the European Society says, pretty well across the board, use radial on that approach. I don’t think it rules out using the groin puncture, but the radial would be easier to control. Then, you use the anticoagulant, the parenteral anticoagulants like you always would, except in this case you might want to avoid low-molecular weight and use unfractionated heparin or bivalirudin, which has a much more rapid response. Then, as soon as you can and depending on—always—the patient characteristics, you do want to get them back on their oral anticoagulation fairly soon, and you want to continue them on that for the six weeks afterwards that is always recommended. And then, you get into what you had already just now said. At some point, you want to potentially cut back on the dual antiplatelet therapy, but that depends on so many things, it would be hard to say it right here.

And, I think I failed to say early on, and my cardiology colleagues out there are saying you can't forget this one, you probably want to choose the bare-metal stent and not the drug-eluting stent. The bare-metal stent would give you the option of stopping everything anti-antiplatelet in six weeks. With the drug-eluting stents, as you implied, you have to do it longer but maybe shorter than we used to think now that we have third-generation stents there.
[00:50:03] ANTHONY DEFRANCO, MD, FACC: Well, these patients are so complicated, sometimes, there’s no better option than just picking up the phone and having that discussion between primary care, hematology, and the cardiologist who put the stent in in the first place.


[00:50:15] DAVID GARCIA, MD: You know, just to chime in on my perspective on this, a person who comes in therapeutic or let’s say supra-therapeutic on warfarin with an INR of maybe 3 or 4 and in whom the cardiologist feels a strong need to start heparin or some other paran—parenteral anticoagulation like bivalirudin, I would even consider, depending on the individual patient, perhaps reversing the effect of the warfarin either with plasma or vitamin K simultaneous with the initiation of the direct thrombin inhibitor or whatever other anticoagulant is going to be used because the risk of stacking those on top of each other is really not well known.

[00:50:55] THAD F. WAITES, MD, FACC: David, I'm glad you said that. It’s not in the guidelines to do that approach, but it’s also not in the guidelines to not do that approach. It’s not a harm situation, but it certainly makes empirical sense, rational sense, to do it that way, so thank you very much.

We’re gonna move to a question about patients on anticoagulants that have malignancy, and that would seem to be a very special category or complex question. And, we’re gonna turn to both Chris and David to answer this question.

[00:51:23] CHRISTOPHER V. FLORES, MD: That—That’s a great question and with the aging of our population, we’re seeing this quite often now where a patient either with preexisting atrial fibrillation develops a malignancy and needs treatment for that or, you know, someone who is in the midst of getting treated for their cancer then develops atrial fibrillation. For simplicity, I just divide them up into patients that are getting active treatment at the current moment, active treatment of their cancer and, specifically, what I’m talking about is chemotherapy. And, in that situation, I have to have a very, very thorough discussion with the hematologist and the oncologist who’s on that case because there’s a lot of potential interactions, especially with a lot of the newer chemotherapeutic agents; they can interfere with the hepatic metabolism and the cytochrome P3A4 mechanism or they can also interfere with the GI absorption and the P-glycoprotein pathway. And so we have to take these into account because they can be very complicated.

When we’re looking at patients who are in remission and who have already completed their treatment and, perhaps, a patient with breast cancer who now is just on her aromatase inhibitor, then, you know, I think that kind of goes back into my court as a primary care physician to look out for the risk of stroke. And so, in that situation, I’m very comfortable initiating or maintaining anticoagulation. Obviously, if someone has completed their
treatment and they’re not on any other agent, then I think that is even more simplified, but Dave, I’d be interested to see what your perspective is on this as a hematologist.

[00:53:05] DAVID GARCIA, MD: Well, I think you’re exactly right that the presence of malignancy, particularly if a person needs active treatment for their cancer, only complicates the risk-benefit calculations. On the one hand, we know cancer in—generally speaking is a very prothrombotic condition. For example, deep vein thrombosis and pulmonary embolism is much more common in people with active malignancy receiving chemotherapy. On the other hand, as you’ve alluded to, Chris, a person receiving treatment for cancer may well have suppression of hematopoiesis and may have long periods of thrombocytopenia as a result of their therapy and that, of course, tips the risk scale for bleeding related to anticoagulation in a different direction.

So all these things have to be factored in. I think, if anything, the presence of active cancer requiring chemotherapy can only add to the likelihood that a person would have a clot form in their left atrium, although we don’t know for sure. And one’s just gonna have to balance that against the complex potential for drug interactions, both with warfarin and the newer oral agents, as well as possible additional bleeding risks that could come as a result of procedures related to the cancer or thrombocytopenia related to the therapy.

[00:54:28] THAD F. WAITES, MD, FACC: And now, for another category of the complex patient, and this category is one that’s complex no matter what your medical field might be, and that’s the geriatric patient. Let’s have special consideration of how to treat this patient with both the new oral anticoagulants as well as with warfarin, and I’ll open it up to the group.

[00:54:49] CHRISTOPHER V. FLORES, MD: Well, I’ll start off with that. You know, we’re all, because of the aging of the population, all of us who are doing primary care are definitely seeing more geriatric patients. And, in my area, I’m in Southern California in a retirement community, so I’m kind of a de facto geriatrician because so much of my practice is weighted toward patients over 65, over 70, even over 75. I have to say that from a primary care perspective, even just a few years ago, I was somewhat fearful about anticoagulants in the elderly because you worry about falls, you know, and you worry about head injuries, and it seems to me that I was kind of trained with a notion that there’s a certain age where, you know, perhaps we shouldn’t anticoagulate. But, the more data that we have coming across, and especially with these recent guidelines, it definitely gives me a little more backup and guidance as to the appropriate use of anticoagulation in AFib.

I would say that the main concern that I would have in an elderly patient is their renal clearance, you know, creatinine clearance, because that obviously plays into the decision making. And then, just also, their overall comorbidities and polypharmacy, you know, because a lot of times, the elderly patients are being treated for a myriad of different comorbidities and that complicates our decision making. So, I guess that’s where I would start off with in terms of this discussion.
ANTHONY DEFRANCO, MD, FACC: From the cardiology perspective, the geriatric patient with atrial fibrillation is very complex. First, with respect to the discussion of rate control or rhythm control, there are many patients who are older, who are not very active, in whom a rate control strategy is adequate. But, on the other hand, there are many elderly patients who have concomitant diseases such as LV dysfunction or moderate aortic stenosis in which sinus rhythm is desirable in order to maintain cardiac output. In other words, those patients are more likely to have symptoms if they’re not in sinus rhythm. But, that raises a whole host of challenges because anti-arrhythmics may be more pro-arrhythmic in the elderly population. There’s a greater potential for drug interactions since those people are on many more medications than is a younger population. So, rate versus rhythm control is a very complex decision in the elderly.

Second, with respect to anticoagulation, the decision is equally complex. Age is a very potent driver of thrombotic risk and stroke risk, but age is also the most important driver, in addition to degree of anticoagulation, to bleeding risk. So, as David has taught us this past hour, that ratio of risk-benefit in the elderly can be very difficult to calculate and has to be done on an individual basis.

And, the third aspect is if we fail to anticoagulate the geriatric patient, we may actually be cursing them with a higher risk of stroke than patients who are younger or at lower risk because, as a general principle in cardiology, it’s the patients at greatest risk who benefit the most from aggressive, proven, guideline-based therapies.

THAD F. WAITES, MD, FACC: In regard to the rate, I believe the guidelines are pretty lenient on the rate we need to get them below—I believe it was 120, if I’m not mistaken, and that’s for the asymptomatic patient. You wanna shoot for below 120.

ANTHONY DEFRANCO, MD, FACC: Yes. Due to a—one very well-conducted study that showed that a lenient versus a strict rate control strategy were rela—were similar or identical to patient outcomes.

THAD F. WAITES, MD, FACC: David?

DAVID GARCIA, MD: Again, very complex topic, as my colleagues have alluded to, and I don’t have a lot to add to their comments. I do think that while it was controversial for some years as to whether age is an independent predictor of bleeding risk, I agree with Tony that it is, even when one adjusts or controls for things like hypertension, concomitant medications, and other comorbidities that are more prevalent in this population. I think even after adjusting for all that, those differences, advanced age in and of itself predicts a higher risk of anticoagulant-related bleeding.

How best to mitigate that? I think we’ve alluded to in some of our other comments that would apply to this discussion as well. And, I would say that, by and large—because stroke risk also comes with age—that, by and
large, benefit of anticoagulation is gonna outweigh the risk, even in this group of patients, but advanced age may have some impact on which of the various anticoagulants we choose.

[59:25] THAD F. WAITES, MD, FACC: With these complex patients, do we have any tools out there that the practicing provider can utilize to help them through the CHADS₂, CHA₂DS₂-VASc, HAS-BLED, the other risk evaluators, and the answer is that is that we do. In fact, if you go to TEAManticoag.com, you’ll find numerous tools on that site as well as patient brochures and pamphlets. It’s an excellent site to get information about all of this. And then, the ACC also has an anti-coag evaluator, which is an app for your smartphone. Chris, do you have a favorite tool out there?

[01:00:01] CHRISTOPHER V. FLORES, MD: Yeah. I use Medscape a lot. I find it very, very useful to link to calculators but also to look at continuing medical education articles in the area of atrial fibrillation and then also news updates. They usually post any breaking news from conferences and the new studies that are released.

[01:00:21] ANTHONY DEFRANCO, MD, FACC: My favorite site, Thad, is CardioSmart.org by the American College of Cardiology. It has great tools that physicians and patients can use together in the office setting such as a video of what atrial fibrillation is and some diagrammatic tools to help educate the patients on a wide variety of topics, not just atrial fibrillation.

A second favorite tool of mine is that many electronic medical records have embedded within them now calculators for the CHA₂DS₂-VASc scores and drug interaction protocols built in. I find these very helpful in taking care of patients.

[1:00:52] DAVID GARCIA, MD: And rather than emphasize a particular tool, I just want to make sure we talk about how important it is that our colleagues who are in practice use some sort of risk stratification for every patient with atrial fibrillation, where, in most cases, the benefit of anticoagulants are gonna outweigh the risk.

[01:01:12] THAD F. WAITES, MD, FACC: There are now technologies available that will aid us in the diagnosis of atrial fibrillation. Dr. Eric Topol wrote the book a few years ago about The Creative Destruction of Medicine, where he discussed insertable technologies that were gonna be part of medicine and those are now here. And, I'm going to ask Chris to tell about a few of these and then I'm gonna follow up.

[01:01:31] CHRISTOPHER V. FLORES, MD: Yeah. I think this is kind of a fascinating area of medicine, especially as we move forward. You know, with atrial fibrillation, I think we all recognize that it’s probably more common than we thought, you know, even 10 years ago or five years ago. It seems like if we look for it, especially in our elderly patients, I’ve seen statistics that say that above the age of 80, there’s probably 10% prevalence or maybe more of atrial fibrillation in our patients, so if we look for it, we’re probably gonna find it.
On the one hand, we’re seeing much more in the realm of consumer electronics. Like, I have patients who come in who are wearing heart rate monitors or who have an app on their phone and they’ve been checking their pulse. It doesn’t check an EKG—there are devices that do that, that Dr. Topol has actually talked about. But they’ll come in and say, well, you know, why is my heart rate so erratic at times or sometimes in exercise, and that prompts me at times to go further and get a 12-lead Holter monitor, for example. And, occasionally, that consumer electronic device or that app on their phone is actually showing something that’s going on. So, this is kind of exciting and new.

And then, on the other hand, the devices that we’re putting into people, like pacemakers and implantable cardiac defibrillators, we’re starting to see data and studies that are looking at that to diagnose subclinical atrial fibrillation. And we have found, again, that if we look for it in an elderly patient who has other risk factors, hypertension and diabetes most notably, we’re probably going to find it. So, I think that as time goes on, we’re gonna have much more data coming at us from multiple sources, which will help us zone in on the diagnosis of atrial fibrillation, and we’re just starting to see the tip of the iceberg right now.

[01:03:24] THAD F. WAITES, MD, FACC: And, Chris, I’m glad you mentioned pacemakers because there have been studies that have shown that pacemakers not only detect atrial fibrillation that we might not have known about, but actually, the atrial fibrillation therapies that are available on some of the pacemakers now have been shown in trials like—I think it’s the MINERVA trial—to actually be doing a good job of controlling the incidence of atrial fibrillation. They help control persist—persistent and even paroxysmal atrial fibrillation.

But what I wanted mainly to talk about with the group was the implantable or the insertable continuous monitors. There is one now that you can basically do in your office that’s inserted just underneath the skin and a Band-Aid goes over the device at that point. There was a study on this one called the CRYSTAL trial that has just been recently published in The New England Journal of Medicine. And they took cryptogenic strokes and they followed them out for three years, I believe, in the trial, and what they found was that at the end of the first year, they had seen seven times as much atrial fibrillation with this device as they did by standard way of approaching finding atrial fibrillation. And when you went all the way to the end of the trial, 30% of the patients in that trial that had the insertable device did develop atrial fibrillation, and this again was a population that had cryptogenic stroke, so pretty impressive.

[01:04:46] ANTHONY DEFRANCO, MD, FACC: Well, Thad, the patient with cryptogenic stroke is something that all three of us, all four of us see commonly. In that same issue of The New England Journal was the EMBRACE study, and as you know, we often look for atrial fibrillation in the two, three, or four days that someone is hospitalized with a stroke and, oftentimes, we don’t see it. What that study showed is that if you monitor those patients for three or four weeks, the incidence of the detection of atrial fibrillation goes from about 3% at 24 hours to almost 15% at four weeks. I think that in the next iteration of the guidelines that will probably elevate at least to
three weeks of monitoring after cryptogenic stroke in order to detect those people who happen to go back into sinus rhythm shortly before or shortly after they have their neurologic presentation.

[01:05:28] DAVID GARCIA, MD: The only thing I’d like to add is that for the patient who has incidentally detected subclinical atrial fibrillation, say from an implantable cardioverter defibrillator, but who’s not had a stroke or a thrombotic event, we know that means they’re probably at higher risk than a person without such subclinical AF to develop a stroke or systemic embolism, but is the risk high enough to justify anticoagulation at that point? And, I would say that’s still an unanswered question in my opinion, but I’d be curious to know how you guys see the literature.

[01:06:07] ANTHONY DEFRANCO, MD, FACC: One topic we haven’t discussed yet today is, is atrial fibrillation a reversible disease? You know, we know that it’s becoming more common by the aging of the population but also from the obesity epidemic, from uncontrolled hypertension, from hypertensive heart disease, and all of those factors are potentially reversible. Sleep apnea is a very important component or risk factor for atrial fibrillation. So, we can’t neglect the opportunity to try to reverse those factors that increase the incidence of atrial fibrillation because, perhaps, by reducing those risk factors, we’ll see less atrial fibrillation in the future.

[01:06:43] THAD F. WAITES, MD, FACC: Tony, I'm so glad you brought that up because the guidelines speak to that, don’t they? And these are the first guidelines that say look for those reversible causes and sleep apnea is in that and had not been in the prior guidelines, as I understand.

We’re going to now have some closing remarks from each of our panelists.

[01:07:01] DAVID GARCIA, MD: If there’s one message or take-home point that providers should remember when it comes to preventing stroke in patients with atrial fibrillation, in my view, it should be that anticoagulant therapy should be the default position from which we all start. While it’s true there’ll be the occasional patient for whom the risks of anticoagulant therapy outweigh the benefit, those patients will be exceptional and, in this day and age, we have a variety of options to choose from that will offer our patients substantial protection from the devastating complication of ischemic stroke.

[01:07:37] ANTHONY DEFRANCO, MD, FACC: The Institute of Medicine has identified patient centeredness as one of the key goals of the American healthcare system. The 2014 Atrial Fibrillation Guidelines try to fulfill that mission by placing the patient at the center of all decisions regarding anticoagulation and other aspects of the management of atrial fibrillation. Harlan Krumholz, a cardiologist at Yale, famously said that the best or highest quality patient care comes when the patient, along with the physician, makes the best decision in concert with his preferences, values, and goals. That’s really the spirit of the new atrial fibrillation guidelines, but it places a tremendous responsibility on we physicians to educate our patients because most of them if given in layman’s
terms, a clear understanding of the risk-benefit ratio of anticoagulation for the prevention of stroke, most will choose anticoagulation.

[01:08:37] CHRISTOPHER V. FLORES, MD: We cannot stress enough the importance of patient education in atrial fibrillation and anticoagulation. We need to address health literacy in patients, and we need to look at the cultural differences, language preferences. We need to look at our healthcare systems and make sure that we are communicating adequately with patients so that they can be a part of shared decision making. And luckily, there are a lot of validated tools that have been looked at and researched that we can use in our clinical settings to enhance patient education and to make them more able to obtain and process and understand all this medical information that we’re throwing at them.

[01:09:25] THAD F. WAITES, MD, FACC: This will conclude our town hall. I hope today that you have gained some knowledge about the management of the patient with the atrial—with atrial fibrillation and about their risk of stroke. I hope that you have gathered some knowledge about how to assess them for anticoagulation, and from this knowledge, I hope that you will be more confident in the future in the management of these patients. And, I want to thank my expert panel, my colleagues, for their participation today, and, again, to the audience, thank you for joining us.