Robert Canby:

Welcome to the American Heart Association's third podcast in a series on Getting to the Heart of Stroke. HCA Healthcare is proud to be the national supporter of this program. Today's episode will focus on the relationship between atrial fibrillation and ischemic stroke and the appropriate and optimal monitoring for uncovering atrial fibrillation and initiating oral anticoagulation, incorporating patient and families in shared decision-making strategies. Discussion regarding atrial fibrillation burden and subclinical atrial fibrillation with respect to future strokes is included. The views and the opinions are those are those of the speakers and they reflect our interpretation and synthesis of the current science. So content should not be considered the official policy of the American Heart Association. My name is Dr. Robert Canby. I am a cardiac electrophysiologist with Texas Cardiac Arrhythmia Institute at St. David's Medical Center in Austin, Texas. I am honored to be the moderator of this exciting scientific session. We are joined by our co-host, Dr. DJ Lakkireddy and Dr. Rawan Albadareen. Thank you for being here. Let's get everyone to introduce themselves please, starting with Dr. Albadareen.

Rawan Albadareen:

Hello everyone. My name is Rawan Albadareen. I am a vascular neurologist at Overland Park Regional Medical Center where I serve as the medical director for the stroke program. It's my pleasure to be here with you all discussing very important topics in the world of stroke.

Dhanunjaya Lakkireddy:

Hi, my name is DJ Lakkireddy. I'm the executive medical director for the Kansas City Heart Rhythm Institute. I'll be working along with Dr. Canby and Dr. Albadareen today in really dissecting further the nuance of stroke and atrial fibrillation. Bob, thank you for the opportunity to be here today.

Robert Canby:

Absolutely. And thank you both for joining us today and let's get started. First, let's review today's learning objectives before we dive into our conversation. After listening to this podcast, we hope that you'll be able to first explain the definition of cryptogenic stroke from a clinical perspective as well as a research standpoint along with the controversies that surround that definition. Second, identify the role of proper ECG monitoring to detect atrial fibrillation following an ischemic stroke. Third, describe the relationship between atrial fibrillation and future stroke, and finally outline some of the racial and social disparities surrounding these topics, their effect on stroke care and outcomes and what we can do about them.

Let's start with a quick background on the scope of the issues regarding ischemic stroke and atrial fibrillation, and then we can move on to an informative discussion. Ischemic stroke is among the leading causes of death and disability. Annually with data from 2020, nearly 800,000 cases of stroke occur in the United States, and nearly a quarter of them are recurrent strokes.

Atrial fibrillation is the most common sustained arrhythmia. Atrial fibrillation increases with age. The overall prevalence is rising with an aging population. Atrial fibrillation is associated with a five times increased risk of stroke. These strokes tend to be more severe with higher morbidity and mortality. It's estimated that 125,000 strokes in the United States may be due to atrial fibrillation. Strokes in the aged population are even higher. Cardio embolic strokes are expected to triple by 2050. Atrial fibrillation and stroke clearly is a public health problem. Dr. A, to set the grounds for our talk today, can we go over the definition of cryptogenic stroke?

Rawan Albadareen:

This is an excellent starting point. So cryptogenic strokes as a category was first devised for research purposes by the NINDS Stroke Data Bank, then later modified as part of the TOAST Trial. It defines strokes of undetermined etiology, which means strokes cannot be explained by one of three major causative mechanisms, whether cardio embolism, large vessel atherosclerosis, or small vessel disease. The problem with this classification, that it did include patients with strokes of more than one plausible etiology from the above mentioned three categories as well as including patients who did not undergo any diagnostic evaluation. So this triggered multiple follow-up classification system updates devising a subtype of stroke called embolic strokes of undetermined source or ESUS, which by definition implies that the stroke should not be lacunar, which means subcortical infarct in the distribution of small penetrating cerebral arteries of certain dimensions. As well, this stroke should not be associated with proximal arteries stenosis of larger than 50%, whether in intracranial or extracranial vessels, and should not have a clear cardio embolic source or other known cause of stroke.

As well, by definition, ESUS assures us that full standard evaluation was completed as opposed to the problems we faced with the TOAST criteria. The major concern for causative mechanisms in such cases is either subclinical, paroxysmal atrial fibrillation or other arrhythmias or aortic atheromatous disease [inaudible 00:06:05] atherosclerotic disease.

Robert Canby:

So that means that detecting atrial arrhythmias would be of paramount importance in stroke patients, particularly when the etiology is not clear. Guidelines in general recommend a confirmed diagnosis of atrial fibrillation prior to the initiation of oral anticoagulation and cryptogenic stroke. However, this very intermittent nature that atrial fibrillation has makes the detection somewhat challenging. DR lack among the different available clinical tools that we have, what carries the highest likelihood of detecting atrial fibrillation? And in general, what percentage of patients with cryptogenic stroke do you believe are seen at 12 months of monitoring?

Dhanunjaya Lakkireddy:

Well, I think that's an excellent question because I think as the technology evolved, our ability to really do a continuous dynamic monitoring, whether externally or internally has really gone up tremendously. But then the adaptation of these tools and juxtaposing it and leveraging these tools and detecting arrhythmia has really not kept up. If we really look at the guidelines that we followed as residents many years ago, I would say 30 years ago or as fellows or practicing electrophysiologist and compared to today, there has been a paradigm evolution in technology, memory capacity and everything else, but we still see physicians ordering halter monitors as part of evaluation of cryptogenic strokes or ESUS. And we very well know that these monitors really provide a very short point in time arrhythmia detection. So the longer the arrhythmia detection is and the more continuous and dynamic it is, the better it is.

I would say if you look at the external monitors that are currently limited only to up to four weeks, that's the long term [inaudible 00:07:56] monitors you could see, versus implantable cardiac monitors or loop recorders. Obviously the ICMs and ILRs provide you a much longer term monitoring with greater detail around the clock, and I think your ability to detect these arrhythmias is significantly higher. So depending on how long you monitor, if it's there 12 months, you probably pick up anywhere from 18 to 20%. If you monitor them for much longer to two years, then that percentage of people that you pick up is going to be significantly higher. And this really calls for an immediate attention from all the professional medical societies to really re-look at the guidance that we are providing for practicing

neurologists as well as the practicing internal medicine docs who deal with some of this and cardiology as well. I think EP has definitely moved on very quickly and adapted the concepts a lot faster.

Robert Canby:

So when patients present with their stroke and it's not clear what that etiology is, do you think it's reasonable to place an implantable loop recorder during that admission?

Dhanunjaya Lakkireddy:

Absolutely, yes, because a recurrent stroke in these patients, especially those patients who have silent atrial fibrillation, which happens to be a vast majority of patients who actually present with strokes are with neonatal fibrillation oftentimes don't have any symptoms. That's the unfortunate reality of it. And then to be able to really help these patients, a dynamic long-term monitoring, I think is the best way to go. And I think every patient deserves an implantable loop recorder for this particular purpose. And I also say that this is probably a lot cheaper to actually manage patients, detect early atrial fibrillation and intervene in a timely fashion. The long-term cost savings to the healthcare systems is going to be dramatically better with an ILR.

Robert Canby:

Now, it's not unusual, DJ, in our clinical practices, depending on the insurance carriers, particularly some of the commercial carriers, some require an ambulatory monitor, a patch or a wearable or some type of external monitor prior to implanting a device. Not so much of an issue necessarily with CMS, but some commercial carriers. Your thoughts? Do you find that that's an impediment to providing care?

Dhanunjaya Lakkireddy:

Absolutely, yes. Let's run a practical scenario. So Dr. Albadareen works in the same hospital as I and say, imagine she calls me, "Dr. Lakkireddy or an EP doc, come and evaluate these patients for stroke. I'm worried about AFib." If I chose an external monitor, say even the best external monitor that lasts for four weeks, I put it on, the patient may not have a single episode of Afib. The monitor comes off. And by the time the results come through and then I see the patient and then I make a case, "Oh gee, I didn't find anything," it's most likely that the patient is going to be unmotivated to do any further because they have this false sense of confidence in that four week monitor that was absolutely the wrong choice from my end.

And by the time we go through the hoops and get an approval for an ILR, it may be another four to six to 12 months. And in the meantime, patient may have had another episode and another event and we would've missed the opportunity. So to really make this foolproof, I would say putting an implantable loop recorder at the time when the patient is in the hospital really makes the most compliance sense, economical sense and data sense.

Rawan Albadareen:

Completely agree. And just to support what Dr. Lakkireddy just mentioned, we all know that it's a level one recommendation based on the updated 2021 AHA's guidelines for stroke care that all patients would get at least a baseline monitoring during their hospital stay or an ECG, right? But now with the new updated guidelines, there is a level 2A recommendation reflecting the importance of the prolonged monitoring and suggesting the importance of obtaining whether like loop recorder or other approaches. They kept it open as the chances of detecting AFib as shown in multiple trials improved significantly.

Robert Canby:

So that leads us to the question of subclinical atrial fibrillation, atrial fibrillation that that is detected, but with no clinical signs and symptoms. How do we monitor for that? How do we take care of those patients? What guidelines should we follow there?

Dhanunjaya Lakkireddy:

It's a terrible question, Bob, because how much AFib is too much and how much AFib is really relevant in terms of stroke? I think there's a lot of heterogeneity in how the duration of atrial fibrillation impacts the potential contribution towards an embolic event is I think grossly unknown. I think that several of the attempts that have been made, is it three minutes? Is it five minutes? Is it 30 minutes? So there are a lot of these variable definitions. And when you really look at the spectrum of patients that we see in clinical practice, oftentimes you see that there are certain individuals, even with five minutes of atrial fibrillation, they would've had a stroke. And then there are patients that are living in permanent atrial fibrillation for 10 years, absolutely not in any anticoagulation and antiplatelet ages, and they never get a stroke, right?

So when you really juxtapose these two sort of contradicting clinical scenarios, the interplay of a individual patient's morbidity profile and their individual risk factors, their thrombogenicity, inflammatory status and their appendage status, atrial contractility, ejection fraction really play a very important role in determining that. So when we talk about population based therapy strategies, we can be hung up on the duration of atrial fibrillation anymore because what is really critical, it may not be critical for that other patient, and medicine has not evolved to that level of personalized care at this juncture. So I would say every all AFib is important at this point in time. Maybe Dr. Rawan has a different take on it.

Rawan Albadareen:

No, no, actually I definitely second what Dr. Lakkireddy said, and my rational actually to add on what Dr. Lakkireddy mentioned is supported by the ASSERT study. Okay? The ASSERT study did show increased hazard ratio of about 2.5 for the combined endpoint of ischemic strokes and systemic emboli. What is really fascinating about that study, the fact that the occurrence of this subclinical AFib that was detected did not necessarily happen within 30 days of the clinical embolic event. What can we conclude from that? It actually tells us what Dr. Lakkireddy mentioned. It does not need to be the specific episode of atrial fibrillation that will increase the risk of future stroke. A rather is the detection of atrial fibrillation itself with everything that comes with it, the subtle changes in the atrial chambers, the atrial fibrosis, the atrial dilatation, the associated biochemical changes, right?

All that might be underlying the cause or the etiology of the increased embolic event. That being said, I think researchers can safely drop the fight about, how long should the episode of atrial fibrillation detected be? Rather, we should concentrate on the fact that AFib was detected in the first place and that on its own indicates increased future risk of stroke.

Robert Canby:

So I think it's fair to say then that it's more complex than a simple matter that you need a certain amount of atrial fibrillation to cause stasis, that leads to clot formation and then subsequent embolization. Is that a fair statement?

Dhanunjaya Lakkireddy:

Yeah. I think there is a genetically mediated or a comorbidity profile mediated difference in thrombogenicity and stasis I think which has to be taken into account. And maybe 10, 15 years from now where our imaging modalities become significantly better and our genetic profiling capabilities dramatically get better, maybe we'll be in a position to detect APRI. Maybe Bob, when we get old, our future doctors are going to be able to tell us, "Lakkireddy, your risk of stroke from atrial fibrillation is going to be significantly higher even with five minute episodes so you better get on anticoagulation." And then the same doctor can turn around and tell you, Bob, that, "Oh, don't worry about it. Your risk profile is much different."

Robert Canby:

So with all this complexity then, we also concentrate on the non-cardiac risk factors for stroke including diabetes, hypertension, obesity, and other factors. How do we take all those factors in the account then in accounting for identifying patients at high risk for not only stroke, but for having atrial fibrillation?

Dhanunjaya Lakkireddy:

This is an age old question, right? So how do we stratify somebody's APRI arrived before you detected the fibrillation in them. And then starting from the Framingham study atrial fibrillation risk scoring system from 25 years ago, Amelia Benjamin did great work on that, and then it didn't quite pan out the way we wanted it to pan out, and then the CHADS-VASc score came about. So I think when we are dealing with somebody with a very high CHADS-VASc score that overall risk really becomes important in creating predictive models for atrial fibrillation. But that again, has not panned out the way we wanted it, and that's the reason why this confusion about having to establish the diagnosis of atrial fibrillation before we can place them on oral anticoagulation really comes about. I think the ESUS trial that we did earlier on in the control groups where if we had a higher pass CHADS-VASc without detectable atrial fibrillation, do you have benefit of anticoagulating these people? I think that that question is yet to be answered in a proper way, and I don't think we have been updated to say that.

Robert Canby:

Do you think there's room for a randomized trial related to that?

Dhanunjaya Lakkireddy:

Absolutely. Yes. Much larger randomized controlled trials,

Rawan Albadareen:

And I want to support what Dr. Lakkireddy mentioned as well that when we had the trial detecting the atrial fibrillation, and they did not find that there is a difference between initiating anticoagulation in the control groups compared to the subgroup that had the atrial fibrillation detected in regards to recurrent strokes or subsequent strokes, where even when they pulled the data in the meta-analysis, they blanked on the idea that these studies were not powered enough or they were underpowered for the secondary outcomes of recurrent subsequent strokes. So that being said, I mean, we cannot say that those patients despite anticoagulation did not reach different outcome because these studies that they were reporting is not powered to answer that scientific research question. So I hope that also supports what Dr .Lakkireddy mentioned.

Robert Canby:

So from a clinical perspective now, once you detect atrial fibrillation in a stroke patient or other high risk patients, do you place them all on oral anticoagulation from the very start?

Rawan Albadareen:

I would send them to Dr. Lakkireddy, but the answer is yes. That's from my standpoint.

Robert Canby:

Absolutely. And is there any room for any platelet therapy in this scenario?

Rawan Albadareen:

Yeah. That's an excellent question. So let me tell you, we treat all the stroke patients as comprehensive as we can. So a patient with atherosclerotic risk will be on some sort of antiplatelet therapy. If they have diabetes, we maximize their diabetic control. If they have lipid problems, they will get on a statin. So they will get all the risk stratification they deserve. They will be taught about the importance of diet and exercise. They will get all the stroke education about smoking cessation, all the risk factors. Now, if we have those patients during their hospital stay and then we detect atrial dilatation on the regular echocardiogram we do, then I have increased concern about them being at higher risk of atrial fibrillation in the future.

So in these circumstances, I will contact Dr. Lakkireddy and his team telling them that I have concerns for this patient about having future atrial fibrillation would request further monitoring, and Dr. Lakkireddy's team will come on board and they will help us. Now, we need to keep in mind that as you mentioned in the introduction, that the aging population as they grow older, their risk of atrial fibrillation increases anyways. So if we're detecting some of the structural changes that can indicate future risk of AFib, we go ahead and actually start the monitoring hoping that we can detect AFib before the clinical event with the detrimental effects that can happen with it

Robert Canby:

In regards to that aging population. One of the common clinical scenarios that we hear from referring physicians, at least I do as an electrophysiologist is I'm too aggressive about any coagulation in patients over age 80 or 85, their fall risk, their gait instability. Their other medical problems increase their bleeding risk so much that they feel uncomfortable with us maintaining any coagulation status. How do you approach those patients at this point?

Rawan Albadareen:

That's actually a very reasonable concern. Let's put it this way. And actually it's a common issue that we encounter. First of all, like the beauty of the DOACs with aging population or impaired kidney function, as we know, we can have lower dosages to be associated with hopefully less risk of bleeding. As well when we face these circumstances or this subtype of population, I usually tell and consult with Dr. Lakkireddy and his team telling them that this is a patient that I have high concerns about AFib or maybe AFib is detected, but about anticoagulation, can we consider alternatives? And that's where Dr. Lakkireddy and his team and their expertise help us significantly, whether it's like with the blockage devices. So I will give the mic now to Dr. Lakkireddy to weigh in on the alternatives that are not anticoagulation, but I agree with you Dr. Lakkireddy. This is a concern that a lot of practitioners have.

Dhanunjaya Lakkireddy:

So Bob, you bring up two very important critical points here. But how do we really change the paradigm. Your question's with respect to bleeding risk and elderly population, how do you mitigate that? I think the work that has been done in this entire space for the last say three decades, left atrial appendage exclusion I think could be a very important strategy in these unfortunate patients who are not great candidates for oral anticoagulation, which unfortunately quite a few of them actually, or they have Parkinson's, they frail, they bleed a lot and all of that. In those scenarios, I think left atrial appendage occluder is a very reasonable strategy to consider so that we can mitigate the morbidity and mortality related to bleeding from oral anticoagulants. On the other hand, in younger patients who actually have strokes, these unfortunate patients, and who have a much longer life ahead of them, I say aggressive rhythm control along with strategies to mitigate recurrent strokes would be very important in these cases.

We have a small series that we have done, Dr. Albadareen's team and ours. We have looked at a series of young patients, reasonably young patients, not too frail, where we offered aggressive rhythm control using antic drugs and catheter ablation along with an appendage closure to see how it impacts the risk of future stroke as well as their neurological recovery. I mean, I kid you not the very first time I took care of this relatively young ER physician who suffered a stroke while working in the emergency room who has been in AFib for two years, and we put him back in normal rhythm, we took his appendage out.

All of a sudden he is now recovered neurologically significantly better. Now he can walk without the help of a cane. He thinks he can actually think better. He's enjoying his retirement with his family really well. So just because somebody had a stroke from atrial fibrillation and they have a significant neurological deficit, not thinking about putting them back into normal rhythm and giving their brain to perfuse better at the same time embracing strategies like anticoagulation and or left atrial appendage occlusion therapies, that is something that we got to really pay attention to and to really bring in this multidisciplinary team approach in tackling this very important problem.

Robert Canby:

It sounds like specifically in this case, and I think you're very clear on how you're stating this, catheter ablation doesn't preclude the use of anticoagulation necessarily in this population. Is that what you're saying?

Dhanunjaya Lakkireddy:

Absolutely. Absolutely. Just because you fixed the rhythm, it doesn't mean that the risk is going to go away completely. So it helps to perfuse their brain better, their neurological recovery would be better, and I don't think we will completely eliminate the future risk of a recurrent stroke in this patient. So having alternative strategies in the form of oral anticoagulation and or an appendage exclusion is something that we got to take into consideration.

Robert Canby:

Are there special considerations in those patients who've had a recent stroke in terms of timing when you have to use a left atrial appendage occlusion device or consider ablation? Do you generally give them a certain amount of time to recover before moving forward all individually based or what are your-

Dhanunjaya Lakkireddy:

It's amazing this question comes from you. I asked this exacting question to Dr. Albadreen about five years ago when we were trying to really take care of these immediate post acute patients. Usually I

guess from their standpoint, I'll let her answer it, but at least this is the information I got, we wait for at least a month. But it depends on the size of the infarct. And so we in an indirect way, we have a dictum among the EP docs in our group where we say, "Let's wait for a month, and then at that point in time, we can think about an intervention, either reintroduction of oral anticoagulation or a catheter ablation or an appendage occlusion," hoping that the patient has come out of the acute phase of stroke, they're going through the rehab and they're kind of emotionally and physically a little better before we put them through general anesthesia and then all these other things that come along with that.

Rawan Albadareen:

Absolutely. I agree with Dr. Lakkireddy on this. So there is no clear cut and there is a lot of studies tackling this question. So from a pathological standpoint, we like to at least if possible, allow two weeks to allow the stroke to mature so that the risk of hemorrhagic transformation with the changes in perfusion or the need of anticoagulation used with the procedure be limited. Now, if they can wait for a month, that is even better because that will allow the brain to further heal. There are case scenarios where we need the anticoagulation sooner, like mechanical valves or acute clot, whether it's the ventricle or the atria, in which cases we go by the stroke size. If the stroke is really small and tiny, then we can start anticoagulation within 48 hours. If it's medium size, not huge, we can go by seven days, okay? Seven to 10 days.

It all depends on the size of the stroke and the risk of hemorrhagic conversion. That two weeks is more from pathological studies hoping for the stroke to mature. Now, what goes further, it depends also on the patient because we have to personalize the care as Dr. Lakkireddy mentioned because we have to allow the patients to recover and remember that in the stroke world, the first 90 days are the ultimate chance for recovery for the patient. So we want to make sure we don't add more stressors to them when their brain is trying to heal. So again, there is no clear cut answer, but I give you just the general term of the timeframes that we consider in the world of stroke.

Robert Canby:

I think that's been a great discussion and I appreciate that. I thought maybe at this point we can change direction a little bit and perhaps discuss barriers of stroke prevention in atrial fibrillation because clearly they do exist. I know in a recent global anticoagulation round table, there was a crisis cited regarding the limited public awareness of atrial fibrillation and its relationship to stroke, under diagnosis of atrial fibrillation and under utilization of anti-thrombotic and anticoagulation drugs in general. What are your thoughts about such barriers and even social and gender and racial discrepancies that interfere with care?

Rawan Albadareen:

Absolutely. Actually sort of fully disparities in stroke care has been well studied, and there is an a statement about that. Different registries showed that there is increased incidence of cryptogenic strokes in African Americans and Hispanic populations when compared to white Americans. It's about double the annual incidents. Not only that, but what is more sad that less than 50% of African Americans will seek medical attention within 24 hours after the stroke onset as opposed to a much higher percentage of white Caucasian Americans. So I absolutely agree with you. This is definitely a problem.

Dhanunjaya Lakkireddy:

Well, what do we need to do about that?

Rawan Albadareen:

That's an excellent question. So this should be an effort from everyone. We have to reach out to our communities. We have to spread knowledge, awareness, education to those underserved communities and minorities. We should not wait until the patients suffer from stroke. We should start at a much earlier level. So in our experience, for example, which is something I'm very proud of, we try to address middle and high school students to educate them about the importance of recognizing stroke symptoms and the importance of seeking medical attention in a timely manner so that the patients can benefit from the clot-busting medications.

We tell them that each and every one of them can be the stroke hero so that they can protect their loved ones from the detrimental effects from stroke, significantly decreasing morbidity and mortality. Another thing I try to teach my girls in the community about time management, I always tell them that in the business world, they teach us that time is money, and in the stroke world, they teach us that time is brain. It's really interesting the effort that has been put to spread education and awareness. One of my colleagues during residency, she actually carried her research project about stroke education in a beauty salon. That was a phenomenal idea at that time and that was long ago. So if we continue to do that, we can gradually melt these barriers, right? There is lack of trust. We want to melt and destroy these barriers so that we can get more equality for everyone in the stroke care.

Dhanunjaya Lakkireddy:

I agree with everything Dr. Albadareen said. I think if you really look at the social determinants of health, I think it's a multi-layered problem that requires a multi-pronged approach addressing the risk factors at an individual level, we as physicians being more purposeful about our ability to communicate with our patients. Every patient needs a different level of education and a different approach, cultural sensitivities being part of that. And then what do we do at a community level? And then what do we do at a governmental policy level and medical professional society level? There is one idea that I absolutely loved about what Dr. Albadreen said about leveraging beauty salons. So if you really look at it in the African American population or in South Asian population, hypertension is an important risk factor for stroke, whether it is A-fibrillated or non A-fibrillated. So the barber shop hypertension study is a fantastic example of how removing a hurdle for education and awareness could result in some impressive results in overall reduction of cardiovascular and cardio cerebral morbidity reduction.

So a study done in the African American population here in the United States, and then the study done in India by one of my buddies, [inaudible 00:32:51] using the Anganwadi approach where the village level health nurse or health educator actually manages hypertension on just blood pressure medications for these people, the village congregation area. And this study that was done on over 50,000 patients actually clearly showed a dramatic reduction in cardiovascular events in this patient. So I think these approaches and then active deliberate effort that is currently being put forward by organizations like AHA, HCA and others, other professional medical societies and organizations I think is very critical. We've got to keep pushing the envelope, and we got to bring this up for discussion at every chart and every opportunity we have as we're doing today. I think this will really bring us close to closing these gaps at some point.

Robert Canby:

Clearly also, there's more research that needs to be done. From your perspective, what would you suggest next steps and where do you think we should concentrate our efforts?

Dhanunjaya Lakkireddy:

I think as there is a global effort to really improve the engagement of minorities and underserved population, because most of the clinical research studies oftentimes end up being studied involving patients of one particular race or gender. We ignore the rest of the population because whatever is the easiest way to enroll patients in a given study, pharmaceutical companies or medical device companies are trying to get an indication for their respective products and move on. And then as a result of which we missed out an amazing opportunity to study the much needed work on the subgroups of populations who oftentimes are ignored and they have no access to these things. So I think we got to focus on that, and there needs to be a deliberate legislative effort to really curb the gaps of underserved population who live in the most underrepresented areas of the world. So that has to be changed as well.

Robert Canby:

Dr. A?

Rawan Albadareen:

Yes, so I'm passionate about this as well. So I want to give a small piece of advice for stroke researchers. The field of stroke is a dynamic field. It's rapidly evolving. So I would advise everyone to just stay open-minded, don't be rigid as things that we have taken for granted for decades is starting to change. So let's take an example like of TPA. So TPA is still the gold standard therapy for strokes. It has been the scientific blessing that changed the future of our stroke patients, right? Yet there is new data that is showing that aspirin and Plavix in mild strokes is not inferior to TPA and it's associated with less hemorrhagic crisp. So this actually can rock the boat. By the same token, I want to bring the concept that Dr. Lakkireddy mentioned, like we were long told that rhythm control is not superior to rate control in atrial fibrillation when we were younger in medical school, and it has more adverse events.

Now the newer data is showing no, rhythm control is superior with advancing catheter ablation and the improvement in safety for rhythm medications. Now, if we take this, we can apply the same concept of changing knowledge for the combination of antiplatelet anticoagulation therapy. So this is a tough topic, but I want us to stay open-minded because we don't know what the future will carry because the old studies, it's decades old studies whether it's the [inaudible 00:36:22], it failed to show that there is benefit of the combination studies for of anticoagulation and anti-platelet therapy together for stroke prevention with increased risk of bleeding.

But now as there is advancement in science with the development of DOACs and the larger role they're playing in anticoagulation compared to traditional warfarin with the less associated bleeding risk and the consideration of lower dosages, the future research can carry real pleasant surprises for the combination used similar to the signal that we noted in the COMPASS trial. Finally, it's all about study design. So as researchers become more keen, study designs improved. I'll give you an example. The NAVIGATE ESUS trial for example, it gave us like negative results, but one of the problems in that trial, that it had a sum lump of [inaudible 00:37:18] atherosclerotic disease as well as embolic looking strokes. So that might have caused the negative results. Finally, never say never. We should stay tuned for what the future will hold for and be looking eagerly for future research. And that's it.

Robert Canby:

Well, I think this has been a terrific discussion and I very much appreciate the conversation that we've had here today. Both of you have provided very valuable comments for today's program. As a reminder, the views and opinions in the podcast are those of our speakers and reflect their training and experience. We've talked about a number of issues today. At the same time, none of them are official policy for the American Heart Association, but we appreciate that it represents our synthesis of the

science out there for the betterment of our patients and the physicians that refer patients to us for their care.

I'd like to remind everybody to please review the ASA 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attacks that can be found on the American Heart Association website. I want to thank everybody for joining us on our conversation today with this podcast, and I hope they look forward to the future podcasts that we have in getting to the heart of stroke. Thank you very much.

Rawan Albadareen:

Dr. Canby. Thank you so much for moderating and the great effort you put. Thank you for AHA and ASA, HCA for all the effort in putting this podcast together, helping our community learning more about stroke. Thank you, Dr. Canby, and thank you Dr. Lakkireddy.

Robert Canby:

Thank you both.