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TRANSCRIPT - GR 10 13 23 "It's Not Just tPA and Aspirin Anymore: Updates in Stroke Care For the Internist" guest speaker Sherita Chapman, MD from the University of Virginia

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- Hello, everyone! Welcome to Medicine, grand rounds.
- I have the distinct pleasure of introducing our speaker, Dr. Shrita Chapman.
- Dr. Chapman attended Howard University Medical School. She stayed to complete her neurology residency, where she served as chief resident. She then traveled here to Uva for her vascular neurology, fellowship, and subsequent research fellowship in vascular neurology.
- She currently has an academic appointment at both Uva and Vcu and the Richmond Va. Where she is the Stroke Division Director.
- Dr. Shaman has received many awards, including your awards for research, for teaching skills and her leadership abilities.
- Her scholarly work is focused predominantly in 4 areas, acute prehospital stroke care, telo stroke implementation, Science and Health Service of underserved populations. She is a highly productive researcher and is an investigator on many projects in these realms, trying to improve the care of both our patients and our understanding of this disease process. Please join me in welcoming Doctor Chapman.
- Well, good afternoon, everyone, and I will first like to say, thank you for providing me. The opportunity to present to you guys.
- So the title of my presentation is is not just Dpa and aspirin anymore updates the stroke, care for the internus.
- I'll start off by saying, I have no disclosures. And you know, as as far as objectives, we're going to talk about updates in medical management and acute scheme and stroke and secondary stroke prevention.
- In addition, you're running over some case scenarios and identifying appropriate management solutions. And in that process kind of looking at the benefits and risks of different treatment options.
- Yeah, as mentioned, and with the title is not just Cpa and aspirin anymore, and I would say it was never that easy. You know, with when it comes to stroke and stroke care, you're really looking at the 5 h. The 5 h framework where you know, and many you may know or think about when y'all call us for a stroke, alert or for a console. We kinda maybe start asking a bunch of kept questions already on the phone. And you know, it's really that all of that information is really needed, even if it is a decision about secondary still care, or whether to start aspirin clavics both anticoraculate. What have you? Because, you know, you're really looking at that patient? You know. What age is that patient, the past medical history? Do they have a fib? Have they had a recent surgery, especially when you're thinking about acute stroke treatment. And then, you know, do they have a history of cancers so maybe they could be hyperaguable? When did the symptoms start, you know, when the family member said that they noticed that at 2 0 PM. Was at 2 0 PM. When they walked in the door from coming from the grocery store, and the last time they really saw their loved one normal was 8 Am. That morning. You know, and as far as like if they did have a heart attack or stroke before. When was that when was their previous surgery?

Also, when do you start anticoragulation after they didn't have a stroke as far as like that. What? What was the workup that was done so far? What was the results?

- And then, even when you're thinking about medication, what can that patient afford? But you know even all of that, and you doing all that to really determine. Where was the where you localize? Does the presentation actually match with the imaging show? If you're thinking about doing it to plate lit? Is that stenosis and a clinically relevant areas. So they can explain those symptoms. So you know, it's a lot of questions that help you get to that. Why?
- So when you really look at the data, it may seem as if we don't have that many advances in stroke treatment. But a lot of changes has really went around how we approach the patient? Not necessarily the treatment involved.
- So yeah, I figured the best way to go about this was to kind of go through cases and scenarios and really look at some of these updates and the treatment. So we'll say, kind of will be a little bit of a bumpy ride. There will be some twists and turns here and there, and after we finish everything is gonna be clear as mud.
- So let's go back to that case that might be helpful. So let's say, we have a 65 year old right handed man that has all of the cardiovascular risk factors, hypertension, diabetes, diabetes, dyslipidemia CAD. He's a smoker. Last known well was a hour and a half ago. He come in by Ms. With a. Q. Onset of right sided weakness and ability to get his words out. The only blood dinner he's on is aspirin and really based off your exam. The most prominent things, you know, is the fact that, you know he's non fluent, impaired comprehension. He has a gaze reference to the left, right-sided weakness.
- So you know, we're thinking about that presentation in mind, you know, typically for us, we're already trying to localize that because we're really trying to figure out. Can we really put this in a vascular territory cause if we can, then we can say, Okay, now, this is probably definitely a a stroke of me. Looking at this, I'm thinking, left Mca. So even approaching this patient from the start.
- So again, this is a hypothetical, hypothetical situation. So just say you have. This image is normal. There's no bleed. You're not seeing any acute changes. I'll just say that as far as anything related to any of these treatment options that we, talking about the criteria. The patient meets the criteria. There's no exclusion, you know. What would you think would be your next step? You don't have to answer. You don't have to raise your hands right. I just want you to think about it and just take a moment again. Based off an exam acute onset last moment. Well, hour and a half ago. And the fact that you're thinking left Mca, you know.
- I will hope that you're thinking. Let's give him iv thrombotic. However, this is where that new update comes. Which one are you going to think about? Are we going to give ultimately? So, Tpa, are we going to the T. And K. Well tk, is the new kid on the block. I will say not. Everybody is using tk, so it would depend on where you go, and as you guys know, not everybody have a neurologist in place. So you know, you might be forced with them, being the one that has to make that decision.
- So it'd be good if you have a little knowledge about Tk or connect to place. So the reason why connect to place is new kid on a block is that it is a modified version of form of Altar Place and because of these modifications to it had a grayer selectivity for fiber about 15 full hire which you know, makes it, you know. Good, you know. It seems like the thought idea. Would that it would even work better than Tpa. Only for other data. We kind of approve that. But in addition to that, it has a longer half life. So the fact that I have a longer have half life with a half life, with 22 min compared to the 4 min a tpa. That means that it could be a single bolus which would be great in the situations of you. Don't have to worry

about giving that initial bolus, and then having a continuous infusion for a hour. That makes it a lot easier for your instead of you thinking about the drip and ship.

- I don't know what we gonna call this bolus and drop. I don't know whatever you could think of, but you know I'm just keeping that in mind. So then, when you're transporting that patient to another hospital. You also don't have to have a advance, Ems providers transporting that our patient, which makes it a little bit better. And then one of the other big ones is the cost. So you know, with the original Va, we have this ability. When we are in medications, it likes to let us know how much that medication costs. So when you look at all, to place is about 5,000 $5,500 when you look at to neck to place this 2,500. So you can kinda see that that is definitely price difference. So again, as I mentioned, you know some people thought with some of these modifications it probably would be even better than Cpa.
- Well, there's been a lot of studies that's done. What I'm kinda giving you the results of is a group that conducted a systematic review and Meta analysis on this year that really look at the present evidence of comparing Tk and all to place they included all original studies based off of predetermined criteria. So they was looking at patients with accounting is schema stroke where the intervention was to neck to place and a control was all to place, and looking at the outcomes of a modified breaking scale 0 to one 0 to do mortality and systematic intracranial hemorrhage.
- Now, just to kind of give you a little reminder. You may already know this, you may not, but a modified break and scale. So that's from your 0 to 6, where you know 0 good. No symptoms. We're we're we're fine one, some slight disabilities still having some symptoms, but they can still do their day-to-day activities 2 little bit more disability. They can't afford all their day to day activities, but they can handle anything. That they truly need to handle there. A dl well, 6 is deaf. So that leaves you with the 3, 4, and 5, where, 5 being severe and your 3 and 4, you're moderate and moderate, severe.
- So we kind of consider a functional outcome or a good functional outcome. Some people use the 0 to one most days. You see, they use 0 to 2.
- So we're really looking at these studies. There was 9 studies. They were identified. They were all Rcts, there was a total of 3,700 patients. And when they looked at the data, when it was really looking at that modify rake in they were comparable to all, and the rates, as far as hemorrhage and mortality was the same, and they also was looking at the dosing cause. Some of these studies did use different dosing, and then notice no difference with the dosing. I will say one of the reasons why they really looked at that dosing. Is that your test? 2 trial, that last trial that you see that was the only trial that was included in the analysis that reported worse outcomes with T. And K.

  Compared to all to place not only that they also noted higher bleeding risk, but what they? What they thought was that this was really due to the fact that they used higher dose of t and K. So again, that's another reason why this group was looking at the dosing again really saw no difference. However, the data was stronger for your 0 point 25 milligrams per kg.

- So more than 4. You might think, with all of these advances, such as the fact that I mean, it's just cheaper, is easier to give. Why haven't we made this change a long time ago, because again, we've had Tpa since 1995. Here we are in 2,024. Well.

- I will say that Uva was a little bit of a headed game. You might know that that young gentleman right there in the photo. That is Dr. Hailey. He was pretty much. He's retired now.
- But he is, was the head of the Stroke Division. He was actually one of the the investigators on original study for Tpa. He has started working on in 2010, however, due to funding issues. It. It just didn't go through. And almost 12 years later or more. Here we are.
- For those that do like to see the data. That is a graph just really showing that related to that functional outcome. You know we were going that midline. We won't better and we won't worse as far as Tk.
- Alright. So we talked about T. And K. But the thing is in the most important thing. What is different, what? What? What changes needs to be made? So a good percentage same, the treatment indication. Who you know, the exclusion. Same thing as it was with Tpa. Your post treatment or monitoring same consent process same. The only thing that really changed is your dosing, and it's very important to note that because you know, the current dosing that is on the package is, for am I?
- So you would not be following that. You have to know and kind of keep in mind. That is the 0 point 25 milligrams per kg. With a Max of 25. You give it as a single Iv bolas over to 5 min. And again, that's different from your Tpa with the point 9, and you give a 10 bolus iv over 1 min, and you do the remaining 90 over a hour.
- So not a significant change there.
- So let's say that instead of your patient that we talked about presenting with a last known well of an hour and a half, your patient come in, and they woke up with the symptoms, you know, one might say, should I still consider thrombolity?
- Well from all the the information that we've known before, you might say, no, they are not. They then present within the 3, and you know we can go up to 4 and a half hours in particular patients, so that patient would not qualify.
- Well, we're gonna change the game again a little bit on you. So in 2,018 there was a study that was conducted within 8 European countries to determine whether acute stroke patients of unknown time of onset, I will say mainly your wake up. Strokes
- could benefit from thermoltics at the time they did use Tpa based on imaging results.
- Now this is where the complication comes in, because this imaging result is an MRI.
- So you have to have a mi what they call a mismatch that mismatch has to be where there's this hyper intensity on the dwi. Did you see up top and no corresponding hyper intensity in that area on your flair? This has been shown to be predictive of symptom onset within 4 and a half hours before imaging.
- So you know again, that's why I was called a wake up trial. And that's because the thought is most of the time. Those patients that you know go to sleep overnight, and they wake up with symptoms that, you know, is a big possibility, and probably happen a lot earlier sooner than we think you did so in this study. What they did was they randomize patients that did demonstrate this mismatch and therefore they and was not being considered from thrombectomy. There's another key thing that you have to keep in mind so just have to be a patient. That imaging was done and did not show a clot. Do you think that you can go after that you would consider, maybe Thrombolt? And if your place can quickly get a dwi and you can get this image and at these institutions they were able to do so. They was randomized.
- It was stopped early due to funding. So only 503 patients was enroll enrolled instead of the anticipated 800 patients. But you would see from the figure that again, we talked about that modified scale. You know where the the favorable outcome typically is usually 0. Say, I would say, in this they were looking at 0 to one as a favor outcome. But when you look at

the figure, let's see if I can. Right here in the middle you see that there was a shift favoring Tpa for each of their scores with a p-value of 0 point 0 0 3. Now, again, if you, looking at the primary outcome. Which for them they was looking at monitor raking a 0 to one that occurred. And with a p-value of 0 point 0 2.

- So looks good there. So again, you know, one of the biggest thing that has always been from thermolytics is, do we increase the risk of death and bleeds. And that was not the case here on devi was about the same. Had a p-value 0 7, and I will say the symptomatic bleeding was higher in a Tpa group, which has always been the case even in our original Tpa studies. But it did not affect mortality.
- So you might want to consider thrombolated in this patient. But again, you got to determine one thing here, right, regardless of the last known well, or the patient present it after waking up with symptoms? Or if this patient was one and a half, is there something else you want to check again before you consider Thrombolt or anything else, any additional imaging or any additional treatment.
- I would say yes, and let's look at what that probably would be. You probably want to cta right? You want to. Cta cause you want to see if there's potential clot there, because, again, if there's a clot then you might want, and it can be obtainable. You might want to call our colleagues with. Sometimes I like to call plumbers. Don't tell them that I said that, but you know you might want them go in and rotate out. So you know. That's where you see with this image here, this is a Cta, and let's see what I can do with this else.
- Alright. So this is your right, Mca. Here, this is your left, Mca again, because we always from the beginning based on, as am we already trying to localize? We already mentioned that we think this patient have a left, Mca, and cut off. There you go. Your is occluded right there Now a lot of places or some places. In the beginning they felt like all they needed was a Cta and a CT. And based on what we call the aspect score, which I would say is very difficult to calculate, because multiple people want to do it differently all the time. They kinda see if there's any early changes there, and that's what they use a kind of base, whether they are safe
- to give whether from back to me, or with that expanded time for Thrombolytic. If that is safe however, now we have more advanced profusion imaging. And all these apps rapid. Vizi, there's different app apps that supposed to kind of help us map out that area. So the thing is here. What you're trying to do is in the green oops. Wrong thing.
- Alright. There we go, and the green over here. You're looking at that Mca territory, and that's showing you what's the area that is at risk. Right? So it's showing you the whole area that is not receiving that blood flow, that oxygen, and is probably in the process of dying right? And here in that pink, what you're seeing is you're actually seeing that area that is dead.
- That's gone right? So the idea is, could we save the penumbra. Could we could save that area that you subtract from there. That, you know, is is on the verge. But just maybe just maybe we can remove that clot and get that blood flow there. You know we can save it.
- So based off of this I think that is worth us going in and let's trying to see if we can remove that clock. But you only rely on just what I'm telling you. Let's see if the data shows us the same thing. So end of vascular. So I will say that prior to 2,014 you know, there had been a lot of studies with the thought of hey? If we just go in, take the clot out, regain the blood flow there. This gonna be better than Tpa, you know. Let's just do that right. And they had a series of some studies. They try to look into that.
- And you know, people was changing their career at idea, thinking that you know they won't go in and do endovascular. Then, in 2,013, the 3 major studies came out Ims 3 Synthesis and Mr. Rescue they showed no benefit.

- So then, of course, cause again. At that time we just had Tpa. We were all excited. We thought we was going to something, and then it was like, Oh, what do we do now? We just go back to our Tpa. But you know they tried again.
- They thought maybe it was related to the devices that they use. Maybe it was the protocol. They was a little bit more stringent with things they had this second generation thrombolytic devices together, and they did some more studies and 5 came out and that is our Mister clean escape with prime. You know. I don't know where they come up with these names, but you get it. So they all came out and they were all successful. But what I'm gonna show you now is pretty much a Meta 9 analysis that was looking at it. And there's some key things I want to point out. We're looking at these studies is that they
- only included patients that had occlusion in the anterior circulation so proximal anterior circulation. They had to be within 12 h of the last known well, and let me see if I can get my thing straight.
- So you know, when they took all these studies it represented about 12,000 patients, I would say, here we go.
- So, looking at the breakdown, and that about 50% was randomized under the control arm, which was medical management that included Tpa and of that 53 or 50, 87% did receive Tpa.
- And then you had your endos. That was randomizing it in the vascular group that was about 49%. And of that group, 83% received Tpa in addition to the endovascular and within again, that group about 83 did have the second generation stint retriever, a device.
- So and all of the 5 studies did look at a primary outcome. With the modify reagan and base off of the studies. It did show that endovascular therapy experience, those there was randomized therapy experience like 2.2 2 times greater odds of a better functional outcome compared to medical management alone.
- In addition, again, as always, we look at mortality and systematic hemorrhage, and there was no association with either of those.

  So you know, felt like we were. We were doing. It's good. We we going somewhere. We're kind of going in a different direction. Thank goodness!

- There was another study that looked at the individual. It was another Meta analysis of those same studies looking at the individual patient data, because even after those results came out, there was still question about certain particular groups, such as those over the age of 80 those they did not receive. Iv Tpa, you know that time period.
- Yeah, I will say that within these studies most of the patients were randomized and thrown back to me to start it with at least within the 4 to 6 h range more so closer to the 4. So you know? How about those that were a little bit later? Did they really get benefit?
- So when this study was done with one thing, they did know that that the number needed to treat for one with endovascular therapy, to reduce disability by at least one level on that that modified rak and scale, for one patient was 2.6.
- So 2 people in a dog. Alright, so you know. And then the other thing again, they was looking at those in the visual group. So you see that you know a favor in the vast group for those over the Asia 80. So let's not discriminate between our older folks greater than 300 min from symptom, also onset, and even those that receive Tpa.
- All right. So we always trying to move that needle again. We just have the thermal, and now we have fromectomy. But we still struggle with that time. Right? We all know that most of our patients did not come within definitely, not within that 3 h not within that 4 and

a half. We may not even get on within 24. So can we move that that window on on thrombectomy? Can we see if maybe we can just push it a little bit more? And the first study we're looking at is diffuse 3 which look again using, imaging. So using that profusion, you know, making sure that we have salvageable tissue up a number that that we can potentially save and select patients that way can we offer thrombectomy between 6 to 16 h and selected patients? And so they conduct their study 38 Us. Centers. It was terminated early. But this time based off of group results. So a good thing after 182 patients, which have been randomized with 92 going through the thrombectomy arm and 90 going to the medical arm. And, as you can see, looking at that modified rakein again, functional good functional outcome 0 to 2. You see that about 45% of patients in the end of accent versus 17. And now, medical group, I don't think I had to tell you the P. Value for that, but you see it right up there. Again, we wanna look at mortality and systematically, and it's about the same so can we extend it a little bit further? Can we go up to 24 h? So Don decided that that group decided to look at that, and they enrolled a total of 206 patients with a hundred 7 and throw back to me group and 99 in a control, and it was terminated in 31 months. But this is due to interim analysis. That again kinda showed the same thing something similar, you know, with those with that good functional outcome, we had 48% in that Inovac group and 13 in a medical group. And again, no difference between mortality and symptomatic lead. So for those that decided back in 2,012 that they wanted to move over and endovascular, and maybe felt a little down in the press, and 2,013, they have something to be happy about.

- So unfortunately, as I mentioned a good percentage, our patients still don't come in that 24 h time period. But I think that we have talked enough about our queue treatment, and it's time that we can go on to a another case. So let's go into these group that maybe make it outside of that window, and we don't have anything to offer, or they don't meet the criteria so kind of similar situation.
- You know. We still got a 65 year old right handed man, but this time with the same risk. Factors on the same medication exam is a little different, though. You know, it's just a little slur speech. There's a mouth facial droop on the right. You know. You notice that the pronation drift. It can address a little bit, maybe even turn some, and you know he's a little weak on that that right side, particularly with rip stress.
- Pretty good. But you do notice a little weakness there in the grip, and he tells you that, you know he came in today this morning, he said. It's something started yesterday morning. So well. and we get the image.
- And of course this is probably a couple of days later, because the likelihood that we probably gonna get an MRI is probably not gonna happen. But again, this is my hypothetical world where everything works in a great time period. So let's say, we did get this. MRI with a patient is in the video, at least on that same day, and we see this little small cortical infar.
- I in your left Mca territory, you know. What do you guys think would be the best choice for early secondary. Again, we'd have moved over to the secondary slide stroke prevention in this case. Do you think it's aspirin? Do you think it's copila grill, aspirin, and co-pilot, grill or pixaband.
- All right now, I will say this might be a little unfair, I say this, but fault you pick any one of those. But I will say that we do have some data that support the idea of using aspirin and plavids. So the thought come along with the whole idea that we know that stroke is common. A recurrent stroke is common. During the first few weeks after a tia or a minor stroke one report or a study reported that about 10 to 20% of stroke patients have another

stroke within 3 months after the initial stroke, with most of those occurring within the first 2 days.

- So you know, it was proposed. I thought that maybe just maybe the combination of 2 antiplatelets during that time period may be able to reduce the risk or recurrent stroke within that that first 3 months after a minor stroke or a ta.
- So, of course, you know, we had to go and check that out. And there is a group in China. That did the chance study that randomized about 5,000 patients. This was conducting 114 centers in China. They randomized the patient within 24 h of onset of a minor esteemed stroke or a tia, and that is pretty much defined minor, as if their Nia Stro scale is equal, or less than 3, or as far as high risk. Tia is their Abcd. 2 score is greater or equal to 4. So that's how that was defined as far as minor stroke or tia and what they did was they randomized those patients, and one group, the patient received a loading those 300 of plavits followed by 75 for 21 days with aspirin, and then it was, continue on classics for 90 days. And I will say that they did notice a reduction in stroke in the group that was on dual anti platelet, with no change in moderate or severe hemorrhage.
- Therefore it was thought that aspirin plavics was superior than aspirin alone, and reducing stroke in the first 90 days, with no increased risk of hemorrhage.
- However, since the trial was only done in the Chinese population, and their more common risk of stroke is different than what we have here and other places, and we wasn't really sure we can just rely on that information. So that prompted the point study which was an international study of about 4,800 patients that were enrolled in 269 international sites. And it was slightly different. So the way this study was done was that it was a loading dose of 600 of clavics, followed by 75, with aspirin for a total of 90 days.
- Now this study was stopped, and that was mainly due to the high risk of bleeding that they noted now, when they did some secondary analysis. What they noticed was it was beneficial within the first 7 days and then maybe not as much, but it was also beneficial up to 30 days.
- But then, when you started looking at bleeding, the risk for bleeding increased after 7 days. So that's where we came up with the 21. So we did a combination of chance endpoint, and we definitely feel like it is beneficial in that initial time period. But there is this increased risk of bleeding from what we can tell, based off of studies later down the line. So we said, Let's do aspirin plates for minor stroke or tis for 21 days, and then after that you can pick wherever and to plate that you want aspirin plavics agronauts if you want, whichever one
- However, I do want to point out, and I didn't include a slide about it. But you know, I think it is important to note this is different than doing the draw, antiplating for the 90 days which was based off Sam for study. And that's for your intracranial synosis clinically relevant. So patient. Come in stroke symptoms. You get your Mr. Your imaging your vessel imaging. You see, let's say in this, in that patient they're reporting Case one instead of them having a inclusion, and they're left Mca. They end up having a severe synthesis. There that would be the patient that you know. Let's say they didn't meet criteria for a queue you might have did. Aspirin, flat and flat, is based off 21 days initially, when you saw him in Ed. Well their exam was a lot, you know, higher. But let's say they had a minor exam, and it looked like a minor stroke, and IH. Was on 3. Then you might would do asthma flags with the thyla. Okay, we doing this for 21 days. But then, let's say you get the image. You see, the vessel you see us in those. Then you probably gonna increase that to 90 days.
- That's the difference between those 2. So that's when it comes to what I want to do I enter it for 21 days, 90 days or not at all. They can just get mono therapy.

- So we going back to that case right? So you know the patient presented. We was able to get that somehow. We don't see the MRI to later again. Work with me is my hypothetical patient. You know we got the MRI. We saw that little occlusion there. We put them on the aspirin plavics with the thought that we have them on it for the 21 days, because we, you know we feel that they have a a you know, minor stroke. But then we get the MRI.
- The MRI shows no significant stenosis. Now again, we still working this patient up. So now we gotta think about okay, is this a patient that I'm going to do the 21 days. Do I need to do some further investigation again? Looking at this, MRI, it looks like it's a cortical stroke, you know, I'm kind of thinking it's not in the area, that is.
- I'm probably gonna walk through these answers with you. It's not an area that I'm thinking of a la Cooner or a small vessel. Is not that sub cortical region? You know their blood vessel again there was no stenosis, so I'm not thinking large artery after sclerosis. You know the patient didn't come in with symptoms that I think might have been a dissection or something else. Again, it's cortical he? Probably it probably came from somewhere. Where did it come from? I'm thinking. That is a embodied stroke of unknown source. So again, we had to further complicate things. So in 2,000, 22,014, someone decided to think of adding another mechanism to the mix which is our eases.
- So you know, I like to think of stroke as the whole idea of you know.
- Stroke is like your final product, you know. You might, or someone might, come to your house. And this is why I think, when the toast criteria I don't know why they call it the crow, the toast criteria. But this is pretty much a breakdown of the different mechanisms for stroke. But in my mind I look at it, as you know, when you someone say, you want a piece of toast, you say? Sure. But the next thing you're thinking in your head this is what they gonna bring you. But they bring you this, you know. Maybe they then toasted some hot dog buns, or they might bring you some toasted hamburger buns, hey? It might be Texas toast, or I'll be even happy if they brought me that.
- So you know, it's kind of the same thing, right? You know. I think of a stroke, you know, is your toes. There's different types, you know, ways that that it could come, or it can happen. And you know we have that last one that is cryptogenic and you know, cryptogenic is that we just don't know.
- Again, we wanted to further complicate it. So under cryptogenic we throw in esis correct uses is a subset of cryptogenic, and what it is you think is a cardiac source.
- But you haven't felt the cardiac source yet.
- And you've been able to rule out anything else so based off of that, if you think it's a cardiac source, and you know that in patients that have embolic strokes with a fifth that anticoagulants have worked. The thought was, Well, hey, let's just give these patients a anticoagulant, and we feel like their outcomes would be better.
- So that's how navigate Esis came up. So they did. An international study of 459 centers and 31 countries. They decided to do River Oxford, and don't know whether that was the one of choice and they compared with aspirin, and it didn't work it was stopped early because lack of benefit. But when they did some se secondary analysis, what they did see, or they had the question of okay. If there was a patient that it was at a greater risk of having a fit would they benefit? And they stratified, you know, by clinical predictors of a fifth, such as the left atrial diameter and the frequency of premature atrial contractions, and they didn't notice that maybe they saw a slight reduction or reduction, and patients that had a left atrial diameter of more than 4.6.
- So based off of that they came another study, Arcadia that decided to randomize patients. They did have it in large left atrial diameter and unfortunately, that was terminated earlier this year because they saw no benefit. They did use a pixel band. But again no benefit.

- So now we're gonna talk about, we're going back to our case number 2, you know you're thinking again. This is eases. The patient, you know, may have personal a fifth, and I sure you haven't captured anything yet, or you know you want to further look, what do you think would be the best test to rule that out?
- And I will say it would be your 30 day cardiac monitor. Now someone say, though maybe we should monitor for even longer. So your motto, your 30 day, or implanting a device, a loop recorder, and I will say, and also based off of time, you know, looking at the crystal Af trial, it did show that prolong monitoring with implantal loop will capture more a fit, which, if you monitor someone for 3 years, you will capture more. A fit.
- And again they, you know, made sure. They followed out to 3 years, and they showed the same thing. So yes, we will say that prolonged cardiac monitoring is superior. I don't think anyone really know about that cost benefit yet. But you know I would say definitely, in patience that you strongly feel, feel that they have a feel. Let's say you've done the 38 cardiac monitor, and you haven't captured. You may want to consider implantable in those.
- So let's say you do have a patient. He did have a fit which anticoragnant would you like to use, or you think, you should use? And I'm going to tell you all of them.
- So you know it all depends on the situation. You know you, you can use your or friend. We have all the new anticoagulants. You can use those. You can even use a combination, especially if the patient has CAD has a step place, it is safe to be able to do so. Of course, you know benefits versus risk, but you can do it. And those patients, they cannot take a anticoagulant. You can use aspirin. You know, there is data show that join the dual is actually better. The one thing I will like to point out is because, you know, some people like to take patients, especially out older ones that had a couple of falls, all for anti coagulant because of the risk for fall. There was a study that was done that a modeling study that suggested that a patient with a fib on a r anticoagulant would have to fall about 295 times a year before the risk of a fall related. Subdural hemorrhage would outweigh the benefit of stroke prevention. So, you know, if they fall one or 2 times, you still might not want to take them off their anticoragon.
- Now I wanna make sure I give a little time for some questions. I think I got one or 2 related to this case, and then I had a spot that I figured I was going over so that we can stop. We'll see we can get through this real quick. So let's say we change the patient up a little bit. Still have all those risk factors. I even threw in a fifth in the mix. Still, that clinical presentation. We still have this image again. Y'all see how just a little bit of the history or anything, could can make a big difference when it comes to this patient. Would you get a tte with bubble study?
- I would say, please don't give the tte with bubble study on this patient only because one he's 65. He has all the risk factors.
- and you can think of, and they're uncontrolled, mind you, and maybe have a fit.
- So is it going to change anything? You gonna still have him on anti-correation. You know him closing his Pfo is not gonna make a difference. But the great thing is, we have the rope score.
- We have something that there's apps you can pull. I think. The Mv. Whatever that thing is. Has it. You can simply put it in, you put all this information in their risk factors. And, for example, this patient would have had a score of 2 meaning. It was 0% chance that his stroke was due to his Pfo.
- But again I change it up. Let's say you didn't have all those risk factors. He just had high blood pressure, which I said was even controlled. And you decided to go ahead and get that bubble study, and it shows he has a normal wall motion again. This is my hypothetical, imaginary patient that in the real world, in my world

- they would report how many bubbles went through the Pfo. And they mentioned that he has aneurysm which you
- close it.
- Yes, you would. So you know there was a study, the reduced study where they looked at patients about closure with anti-platelet or just antiplatelet alone, and I will say one of the the biggest criteria was making sure these patients they did not include patients that had the risk factors, especially they was for other potential causes for their stroke, especially if they was not well controlled. So it had to be cryptogenic, so you couldn't say that the stroke was due to anything else.
- And one thing they did also, monitor, is that you know, they tried to make sure that it was a moderate to large. Pfo. And again, that's where those bubbles come in. How many bubbles go through. Kind of lets you know how big that Pfo is. And you know a lot of the earlier studies did not show benefit of closure. But another thing to be to note is the fact that they did not keep the patient on antiplatelet after the closure. This study did so even if you close the Pfo. Keep the patient on an antiplatelet.
- So you know. I was, gonna talk about hyper coageable, you know, this is just that same patient just throwing in at the patient had multiple miscarriages. And one thing I wanted to point out is that, you know, is really only antibody syndrome or the hyper homocymemia that really had a definite association with stroke and the other part is is only anti-fosolithic antibody syndrome that we're really changed medical management, that you will use warfret. So sometimes I kind of lean to the thought of you. Maybe don't have to test for these things, because it really not going to change medical management, but just a fyi. If you are defer testing for protein CS. Or antiothermic levels until Oha, or repeat so either for repeat at least 4 to 6 weeks after the acute stroke, because those proteins levels will be altered during the acute stroke phase. Anyway. if you think anti phospholip lipid, anti phospholipid, syndrome is characterized by persistent. So you have to have repeat testing at 12 week of the presence of lupus, anticoagulant, anti carbolypen, or anti beta, 2 glycoprotein plus evidence of clinical syndrome. So if you have a isolated anti-five flow of it antibody, and you don't, you know you repeat testing it does not come up, that person should just get aspirin.
- So again, it has to be proven. You have the data, you have the evidence, and that's when you would want to use warfare. So cause I figured it's amazing. When I don't prepare. I'm usually shorter than the time when I add extra stuff I go over. So this time I was smart enough to give myself a spot that it felt like we was running over. We were in here. So you know just a thing I was gonna talk about dissection, you know, if you have any questions, feel free to ask me about anything related to that section, and therefore I was just in there.

  Are there any questions?

- Thank you, Dr. Chapman, particularly helpful for those of us who haven't rotated with neurology in a while, and my question is pertaining to tia treatment per the point and chance trial. If we're in the primary care setting, and we see a patient who is complaining of neurodeficits day prior, and by time you see them the exam is normal and they've got no deficits anymore.
- Your concern for a Tia. Should we be sending all those patients over to the Ed? You're trying to get a neurologist to weigh in or do you see a point where Pcps can be prescribing adapt, or situations where that might be appropriate. Gotcha, I would say, you know, the thing with Tia is, you know, Tia. to really, truly define. Ta, it has to be. The imaging is

negative, because, you know, patients can have symptoms less than 24 h, and we get the image. And they did have a small impact. Right? So you know, I would say that you know it would depend on how strongly that history is kind of pointing you to. Yeah, this definitely. Now, they were just a little dizzy, you know, or something that you like. Hmm, yeah, I really don't feel like this was even a tia stroke. Then, you know, I would say, just give them a follow up and neurology. Now, if it was a situation where you know that gut is telling you. Hey? This might have been a ta.

- They do need that image and you trying to get it in that that in the real world setting outside is, gonna take some time unless you have a place that you can just send them, and you can get the image with rarely happens right? So I would say, it's probably best go ahead and just send them to them are using room because that's gonna be what really kind of determine what that workup is gonna be.
- I hope that answered thanks so much for a great talk. When you mentioned the study of people getting treatment when they have an MRI with an unknown duration of stroke. And you said that if you're at an institution that you can get a dwi within a reasonable amount of time. And Uva is a excellent tertiary care institution. But I don't know. That's always true here, and I've been given multiple reasons for that. People have said, you know, the government will only let you have some MRI machines been told that it's the cost of the MRI machines. But in my 3 years of Residency we had more than one eminem and we don't do M. And M's that often on a patient, that this stroke was found very later on, MRI, and it weren't able to treatment. That's just on the medicine side of things, and perhaps it's cause we're worse or at picking up strokes. I think that's probably true. And perhaps it's also that we don't order priority. One Mr's as often as we should. But is that something? You feel very strongly on the neurology side? And if so, as a leader in the field, are you kind of pushing for both institutional support at the 3 institutions you work at, but also are you advocating that at the government side to have better access to MRI machine.
- Well, I will say, doctor, Rohini and I feel like I'm saying her first name is her last, and I'm completely yes, that's able she is, has worked hard on developing a protocol here for quick, Mris. Now, being that, you know you have stroke here. And you have someone that can push for that, and it doesn't always work. I will say I think she's really trying to get in place, that we are getting that fast. Mri.
- It will depend on the institution, too. You know I've seen some private institutions that they get an MRI with the patient, Ed, with no problem. And you know Vcu is pretty good on trying to get or successfully, sometimes getting an MRI if they feel strongly that they need one. So in a situation like this it would be in place. But you have to have a good protocol in place, and you have to have people that's going to really push.

  Let's talk about the real world. That's not the way it is in the real world, unfortunately, and you know. And that kind of leads to that implementation side, you know. For me, you know, we do all of these research studies, but when you really look at it. Most of them do not really work in the real world, setting so ideally, I would say, yes, I think we should be doing it, you know, I think that we need it. But you know if we're having such a difficult time here, can you imagine what a role plays that don't even have neurology or don't even have MRI on site and only have it on the weekends or on a day in a trailer in the back. It's not. It's not feasible. So of course, in my imaginary world, where everything works the way I want it to work now and say, yes, we should have the protocol, and we should be able to get those Mris quickly. But in the real world is, gonna be that exam and you know we a neurologist, don't get it right all the time. But you know it all leads to that slide where I

show, you know is that that 5 of you and one H, which stroke is read? That exam is is the biggest thing for us, the exam in the history, you know, and and it is our in a science to it. If you have that exam in the history, and you can kinda almost try to localize that area and kind of almost confirming your head. That is a stroke, you know you have a better chance of like solidifying and training people in that way to be able to function. And, you know, maybe identify stroke earlier than you probably gonna ever have with imaging, because systems and protocols is never gonna work that way where you have every place that's gonna be able to get an MRI that quickly. That makes a lot of sense. Thanks. Yeah.

- Yes. And Dr. Chairman. Good talk.
- I see given like thinking about the community and being able to reach people. I know that I think they have like, be fast signs for stroke everywhere. But doing neurology here. And then thinking about that last? No? Well, and how you really define it. And thinking about, you know, family members or people that you know that are older, like, is there any advice or guys that you give to? People are like man like you need to talk to your older loved ones often, or like checking on them because they even give examples of like, yeah, my grandma lives with me, or something like that. I saw her, but I didn't really talk to her, and then it turns out, yes, she was having a stroke but she seemed fine, but I didn't, you know, engage with us? I really didn't know. Is there any advice that you give to people in terms of I don't know better checking in, for you know this type of thing. It's hard, you know. They've done a lot of work. They've done public service. There's been commercials. They did research on that. They show that additional benefit for time period. But then overall, it's just, you know, people forget all over again. So it's something that has to constantly be in place.
- So such as you know, we really have to rely on our organization. America, hard American stroke, working with them to try to develop ways again. That information out cause we also think about it for a stroke, doctor. For a stroke, doctor. We don't see the patient till after has happened. So you know we do a lot of you know education, and trying to, you know. Make sure there were strokes, symptoms. Then we do. We do community research to try to, you know. Make sure public is aware, given out pamphlets, and stuff like that. But you know it, it's hard to change behavior.

  And that's really what you have to change. You can usually change it from that short time period. But if it's not a continuous thing, you, it's hard to change. And I will say that there are some people that do aware. Well, like cancer organizations. But I will say we don't do it as well as we. We should on trying to find ways to make sure that the public you know, is aware, and those symptoms are constantly being reminded and come to the hospital. If you have those symptoms. I have people that have recurring strokes, and they come back after noon and happen, and they still didn't come in the time frame. And they tell me oh, they still give me the same excuse. But I thought it was gonna go away or you know, II just I just decided not to come because I was gonna see you tomorrow, anyway. Or what have you? So you know, II don't know how to change that human behavior, you know but we need. We need to work on that part. I just don't have an answer for it.

- Alright. Thank you.