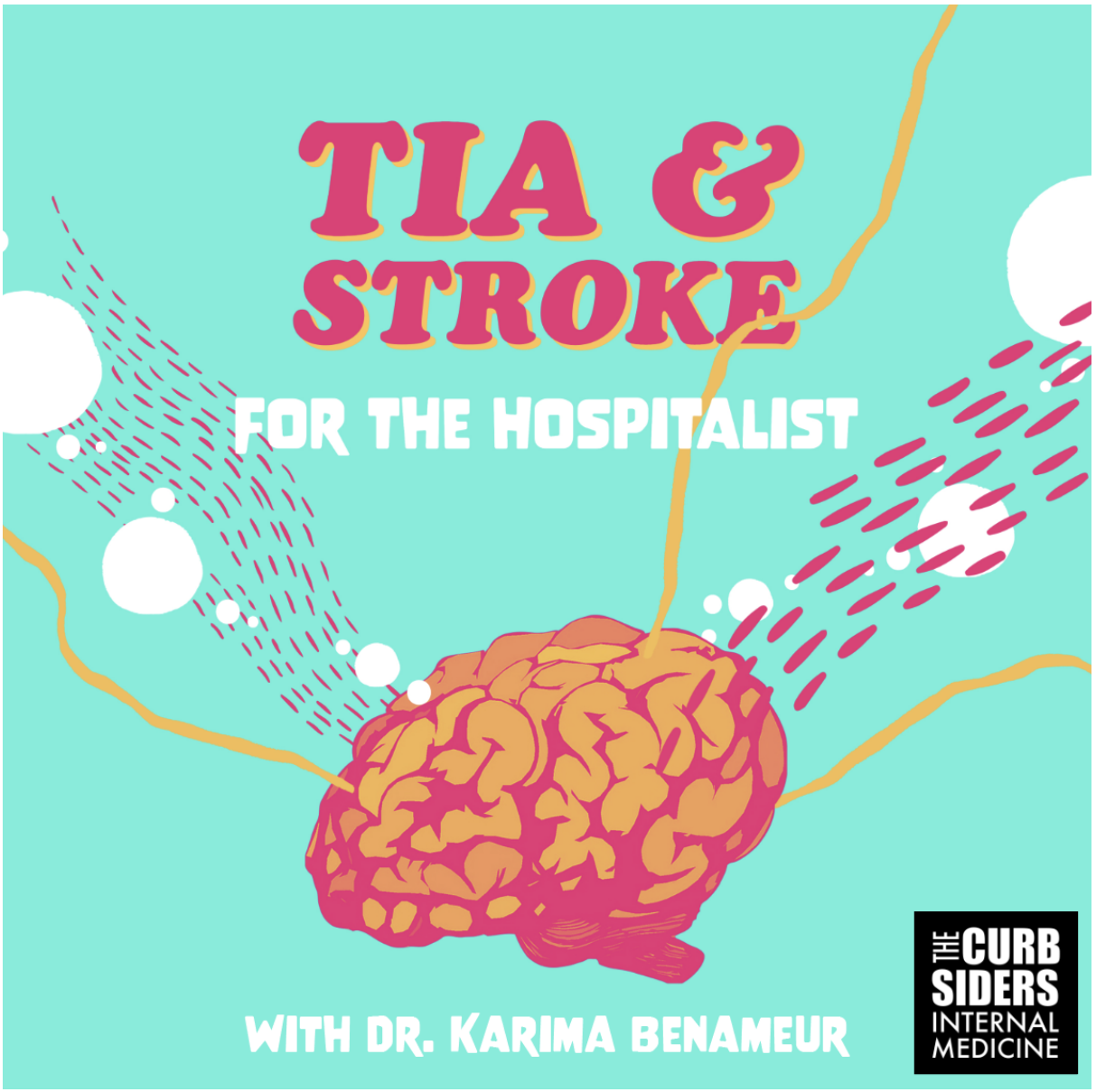
#385 TIA/Stroke for the Hospitalist featuring Dr. Karima Benameur



Meredith: So, tonight, we're talking a little bit about strokes. And Monee, since we both love sports, I'm curious if you know which sport works the hardest to reduce strokes.

Monee: Oh, God, I don't want to know. I feel like this is going to be bad.

Meredith: It is. Golf. You don't want those penalty strokes. [laughs]

Monee: You are the worst.

[Disclaimer]

[The Curbsiders theme]

Monee: All right, welcome back to Curbsiders. I'm Dr. Monee Amin, which means we're in for another inpatient episode with my cohost, Dr. Meredith Trubitt. How are you this evening?

Meredith: Doing well. How are you?

Monee: Fantastic. On tonight's show, we discuss inpatient management of strokes and TIAs with our guest, Dr. Karima Benameur. In just a moment, our first-time producer, Caroline Coleman will tell you a little bit more about our guest and the topic. But first, Meredith, will you please remind the people and and the audience, what it is we do on this show?

Meredith: Sure, Monee. I'd love to. We are *The* Internal Medicine Podcast. We use expert interviews to bring you clinical pearls and practice changing knowledge. Before we jump to our bio for our guests, we do want to just plug some prior episodes that the Curbsiders team has put out before on TIAs and strokes. So, check out Episodes 164 and 290, if you want a little bit more in depth information. But tonight, we aim at hitting the high yield pearls for the hospital specifically. And tonight, we're super excited to have one of our graphic extraordinaires turned producer on her first episode. So, Caroline, do you want to tell us a little bit about yourself and then about our guest tonight?

Caroline: Sure. I am finishing up my third year of residency at Emory [unintelligible [00:02:07] Atlanta in Internal Medicine and I will be joining you all at the Atlanta VA next year doing hospital medicine. And tonight, we are talking with Dr. Karima Benameur. We had a great conversation about TIAs and strokes. Dr. Benameur is a neurologist at Emory and she is completely obsessed with the role of nutrition and brain health and with bringing attention to this important topic to the neurology and overall physician community. She is an educator at art and works tirelessly to educate residents and students about the importance of this forgotten facet of neurologic care.

Monee: A reminder that this and most episodes are available for free CME credit for all healthcare professionals through VCU health at *curbsiders.vcuhealth.org*. Caroline, will you please take us to the first case from Kashlak?

Caroline: Mrs. Toast is a 61-year-old with a past medical history of hyperlipidemia, coronary artery disease, who had a PCI two months ago and an unprovoked DVT on lifelong anticoagulation, who presents with one day of right leg weakness. She was sitting at home and got up off the couch, and her right leg gave way, and she fell to the floor. Her weakness has persisted and she now presents for evaluation. Her current medications include aspirin 81 mg milligrams, clopidogrel 75 milligrams, apixaban 5 milligrams BID, and atorvastatin 20 milligrams daily.

On arrival in the emergency department, the stroke team sees her as a stroke alert and her NIH stroke scale is 6. So, given this elevated NIH stroke scale, Dr. Benameur, how do you balance going straight to imaging versus needing to consider thrombolytics, and essentially which one of those do you prioritize?

Karima: Imaging is one of the very first steps that happens in a stroke alert. When a patient presents with acute, what we call BEFAST positive symptoms. BEFAST stands for balance, eyesight, face droop, arm weakness, speech change, and time to call 911 or time to call a stroke alert if you're in the hospital. So, if they're BEFAST positive, the sequence of events is that a stroke alert is called, they get examined very quick, triage exam, vitals and blood sugar, and then straight to imaging, because you always have to rule out a hemorrhage before being able to give thrombolytics. So, the first order is always a non-con head CT.

Then, since the recent trials in 2015 for large vessel occlusions, a lot of times patients will get CTA head and neck at the same time and CT perfusion, although, that's not always the case. But a non-con head CT is a nonnegotiable part of the stroke alert to rule out a hemorrhage. Once a hemorrhage is ruled out, then you can consider thrombolytics.

Monee: Along those lines about thrombolytics, I think the best place to start is, especially in this case, like, what are some contraindications or things that would make you not a candidate for TPA?

Karima: Being on anticoagulation is probably one of the biggest, so either taking the DOAC in the 24 hours before or being on Coumadin and had an INR that's more than 1.5. That would be a contraindication. And then other contraindications are recent stroke within the last three months, head trauma within the last three months, surgery within the last three months, or any kind of active bleeding, like GI bleed, hematuria that kind of thing.

Monee: And then on the flipside, I think the next appropriate question is, what are the sorts of things that put somebody into the tPA window, like, timeframe and stuff like that?

Karima: Yeah.

Monee: Then I think I also heard something about the thrombectomy timeframes have also maybe changed recently. So, could you maybe go through those two things?

Karima: Yeah. So, for tPA the current guidelines are that if a patient has no contraindications and is a candidate, they can get it up to four and a half hours after the last seen normal. The last known normal is a very important concept, because a patient will go to bed at 10:00 PM and wake up the next day at 08:00 AM and they already have symptoms. The symptoms started at 10:00 PM. It's when they were less than normal, not at 08:00 AM when they discovered their deficits. So, four and a half hours from last known normal for IV tPA and then for thrombectomy, it's actually now up to 24 hours. But there are many things that go into that decision. We basically use imaging algorithm to see how much salvageable tissue there is and decide whether they're good candidates or not for thrombectomy.

Meredith: Meredith: When you say salvageable tissue, you mean like how much functionality they would be able to get back?

Karima: So, on imaging, as part of a stroke alert, when they come, they get the CT head, CTA head and neck and CT perfusion. The CT perfusion will actually show you various maps. And within those maps, it will show you a core which is dead tissue, and then what's called the penumbra, which is tissue at risk, but actually not infarcted. So, if there is a large mismatch between the core and the penumbra, those are good candidates, because there is a large tissue at risk that can be salvaged. But then if there is no mismatch and the core and

the penumbra are the same, then that means that the tissue is already dead and there is nothing to salvage there.

Meredith: I see. So, it's pretty much entirely like an imaging decision.

Karima: Correct.

Meredith: Okay. So, for Mrs. Toast, who's had symptoms for the last 24 hours, let's say that wasn't the case for her. Let's say she came in 6 to 8 hours or something like that. You mentioned this in the first answer when you said, sometimes you would consider getting CTA head and neck with it with them when they first come in. How do you make those decisions for that first CTA head and neck and what's your thought process for that versus MRI and MRAs, head and neck?

Karima: So, if they come within the window of an acute intervention, we will typically get a CTA head and neck. If they come after 24 hours, which unfortunately still happens, a lot of patients will wait home and see if things get better and then come two days later, then there is no value in getting a CTA head and neck emergently because it's not going to change management. So, that's the first thing.

The second thing is as far as CTA versus MRA, both have their pros and their cons. So, CTA is readily available, you can get it in a couple of minutes, you can get it easily, emergently, pretty much everywhere in the US and it's very useful and it has been actually the only modality used in the large randomized controlled trials for large vessel occlusions. So, we use CTAs in those cases.

Actually, for MRA with contrast, it has a very high sensitivity and specificity almost equal to CTA. CTA is just slightly better. We typically use the MRA if we don't need emergent vessel imaging, so if it's not an acute stroke patient, an interventional candidate. The MRA also has advantages in that sometimes you can actually get an MRA without needing to do contrast. It's called time-of-flight MRA, and that's useful in patients who are either renal and should not be getting contrast or patients who have allergy to contrast. So, that's a good use for MRAs.

Then there are actually certain MRA modalities, like what's called an MRA vessel wall modality that we use when we're suspecting vasculitis, that can give us really good information, almost equal to angio. So, pros and cons to each.

Meredith: When is then like an MRI brain by itself useful? Only when the CT head doesn't show hemorrhage, but also, they haven't shown the acute stroke yet or something else?

Karima: I think about getting an MRI in very practical terms. So, if the patient's symptoms match what their CT is showing, let's say, and me getting an MRI is not going to change their management, I will typically not get an MRI. Let's say, a patient is anticoagulated and they come in and they have right face, arm, and leg weakness, and I see a lacune that fits with that on the CT. They have AFib, if they're already anti-coagulated, the MRI is not going to change anything.

The MRI is really useful in other times. We actually use MRI a lot in that it's a multimodality imaging. So, when you get an MRI, you get multiple sequences including diffusion imaging, which is the most sensitive imaging modality for ischemia. You get flare, you get what's called susceptibility imaging looking at micro bleeds and angiopathies and things like that. So, the MRI gives a lot more information than what the CT does.

The other thing that the MRI does is that the CT sometimes will not always show all the strokes and then you'll get an MRI and you see strokes everywhere. Well, that right there

has changed your assumptions that the mechanism of the stroke is embolic rather than thrombotic, and that takes you down a particular pathway of treatment or workup.

Monee: Yeah, I think that's really helpful in the sense that I frequently am not sure how useful having both of them is and I appreciate a framework to think about the practicality of it more than anything. So, let's say, Mrs. Toast, we have established that she's had a stroke. So, let's just start with the basic management stuff. Obviously, we're going to maintain her SATs greater than 94%, make sure that she's not hypoglycemic. So, beyond that, I think the next best place to start is the missing vital sign from that, which is the blood pressure. So, permissive hypertension, obviously, we've all heard of that. Are there any contraindications to that? Yeah, and for how long should she be kept permissively hypertensive?

Karima: So, a hemorrhage is obviously a contraindication to that. Permissive hypertension is, I actually find that it's a fascinating concept, the guidelines say that you have to allow 24 up to 48 hours of permissive hypertension when patients come in with an acute stroke and that's 48 hours after the onset of symptoms. So, if a patient comes in and they've been sitting at home like many of my patients with three days of symptoms, and then they come in, they're past that permissive hypertension window. But if they come in immediately, permissive hypertension is actually very useful. It's basically allowing the body to heal itself. So, you have cerebral autoregulation, which is, when you're having a stroke, your body will essentially autoregulate to allow for perfusion of the brain, and so will increase your blood pressure.

I always explain to my patients or their families when they come in that we want the blood pressure to be high initially, because imagine you have a hose with a kink in it and you need to push pressure, water pressure through it to push water through that hose, so that when they're seeing on the monitors high blood pressure, they don't get alarmed. And so, it's useful in basically salvaging what we were talking about earlier the penumbra. If there is any tissue at risk that has not infarcted yet, that's what the permissive hypertension is doing is allowing that to not become infarcted irreversibly. So, the guidelines are 48 hours and then you can normalize it.

Monee: Okay. And presumably, if they're showing other signs of end-organ damage, that would also be probably an indication to not, because that would put them in the emergency category.

Karima: Correct.

Meredith: I really appreciate you saying that it counts from when onset of symptoms started, because that's usually my number one question. Because I agree, I feel like we see a lot in the hospital who had two or three days of symptoms and then I'm often like, "Well, do I allow them to be hypertensive?" I don't know what's been happening the last two days. So, I appreciate you saying that.

Karima: The other thing I would say, there is a tiny little caveat there is that if patient is having what we call stuttering symptoms, meaning, their symptoms are fluctuating, they come and go, they come and go with basically like a tiny blood vessel that's opening and closing, and opening and closing. In that case, we will let the blood pressure ride for up to five days.

Meredith: Okay. Keeping within the vital sign realm, let's talk a little bit also about temperatures and fevers that happen after the stroke, and the role for antipyretics, and what we should be thinking about as the hospitalist taking care of those patients, because I think that is definitely something that's within our realm to be managing.

Karima: Yeah. So, we know that a fever or increased temperature from animal models is deleterious to the injured brain. If you have a brain that is injured, either traumatic brain injury or stroke and you add high temperature to that, it will make it worse. We know that from the animal data. And so, we like to favor normothermia in patients who have any kind of brain injury. There is this concept of having, what we call, central fever, any type of brain injury can give you fever and that is true. Having said that, if a patient with a stroke develops a fever, it's always important to look into infectious causes for that fever because up to 60% of patients will have some kind of complication during their initial hospital stay, their acute hospital stay, and the most common causes are either a UTI or pneumonia, a lot of times aspiration pneumonia because patients with stroke will have dysphasia and aspirate. So, it's important to look into that kind of scenario of complications in the setting of stroke and definitely favor normothermia.

Monee: Okay. That's helpful as well. I don't know if I've ever spent enough time thinking about fever, actually, when it comes to strokes. And then I think about a patient that I've recently taken care of a few times, and realize that this patient tends to fever. And then I realize they do have some central nervous system issues. And so, I have to slap myself and be like, "No, no, that's what it is, because we've already ruled it out."

Karima: Ruled out everything else.

Monee: Yeah, yeah, yeah and it's kind of a cycle. Well, this is a little bit off base, but really just in that initial orders that you're putting in for the patient. Is it safe to use prophylactic heparin or should we just be using SCDs in these patients? I feel like I am terrified of giving them a hemorrhagic conversion because I gave them a little bit baby dose of heparin or Lovenox.

Karima: Yeah. So, actually, that's a really good question, because DVT prophylaxis is actually a part of the metrics, the quality metrics, that every single hospital has to go through. So, it's not only safe, it is recommended that you use DVT prophylaxis in stroke patients, and that is for both ischemic and hemorrhagic. You can use Lovenox or heparin. In ischemic stroke immediately on day one you can start it, and then in hemorrhagic strokes, we typically start it after 24 hours, and they are both safe in the prophylaxis dose.

Monee: I think you just blew my mind about being able to do this for hemorrhagic strokes. So, thank you for that.

Karima: Yeah. [laughs]

Monee: Mind blown.

Meredith: I might ask a follow up to that. So, on the hemorrhagic stroke, do you just wait the 24 hours or do you have to repeat any imaging to make sure that that bleed is stable?

Karima: No, just wait 24 hours and then you can-- [crosstalk]

Meredith: Oh, my gosh, my mind is blown too.

Monee: [laughs]

Meredith: [laughs] Okay. So, I think that's a good kind of high points of some of the supportive care we should be providing probably to our stroke patients when they come in. So, we'll go into, I think, at least for me, what I have a ton of questions on. So, Mrs. Toast was already on aspirin, but we're going to put her to the side for a second. Let's say she's not on any aspirin. Should it just be started as soon as she came in with signs of stroke or do you wait for any imaging confirmation?

Karima: No need to wait for any imaging confirmation. If you suspect a stroke, you start aspirin within the first 24 to 48 hours. You can always stop it afterwards. But it's another actually quality metric to start aspirin within the first 24 to 48 hours if you have a clinical suspicion for stroke.

Meredith: In which dose?

Karima: I actually really like that question, because every time my residents rotate with me, they go, "Which dose of aspirin?" So, very simple practical tips. Aspirin 81 for everybody, except if they have AFib and they are not candidates for anticoagulation, then you can use aspirin 325 mg, which has been shown to have an effect for stroke prevention in AFib, but not as good as anticoagulation, but better than 81.

Meredith: So, the loading dose that I sometimes see given is actually not necessary or that could be an 81 that would still be sufficient?

Karima: Yeah, no need for loading dose. Just start at 81 milligrams.

Meredith: So, then for our lady, Ms. Toast, who had the previous issues, like the CAD, is already on an aspirin, now coming in with a new stroke, do you go to a higher dose? Sometimes, I see people do 162, like, doubling the 81. I feel like I was taught to just keep it at the 81, and I feel like that's what you're going to say based on what you just said.

Karima: Yeah. There is actually no data to support that if a patient had a stroke on aspirin 81 mg that you would increase their aspirin to 325. I think it treats us more than it treats the patient to feel like we're doing something.

Meredith: Yeah, it seems like it.

Monee: Okay. Also in Ms. Toast's case, she was on a home DOAC and she's also on clopidogrel. So, what do we do with those exactly before we get too much into some of the other questions I have?

Karima: Aspirin and Plavix can be continued. We don't typically stop aspirin or Plavix. For anticoagulation, it really depends on the size of the stroke. The rule of thumb is, if the stroke size is more than a third of the MCA territory, then we hold anticoagulation for 10 to 14 days and then we resume it if it's a large stroke, that's more than a third of the territory of the MCA. Other than that, you can continue it as well, assuming it's ischemic, of course.

Monee: Yeah. With the DOAC also, is there an indication that you would keep it regardless of the size or that's like a hard stop?

Karima: Yeah. If it's a large stroke, we stop it.

Monee: Okay.

Karima: We recommend to stop the anticoagulation whether it's a DOAC or Coumadin, because the risk of hemorrhagic transformation is large.

Meredith: Is there any indication when you would restart them?

Karima: So, typically, like I said, 10 to 14 days. Sometimes, we will repeat imaging and then make a decision based on that. But a lot of times within 10 to 14 days, you should be able to restart anticoagulation if it's a large stroke.

Meredith: Then I think for her, she's already on the Plavix, so she would continue on the Plavix or the clopidogrel. Let's say she wasn't on it. We may get to this in a little bit, but I'm

just curious, would you just jump to adding it or are you going to work up the ideologies first before you would add the dual antiplatelet?

Karima: Yeah. So, the mainstay of doing the stroke workup actually is to figure out what the mechanism of the stroke was, to know what the best treatment is. So, the whole point of doing the MRI, the MRA, the TTE, or TEE, or whatever it is that you're doing is to figure out the mechanism of the stroke, ischemic stroke, that is. There was a trial that was called a toast trial, T-O-A-S-T that categorized strokes into five categories. So, cardioembolic, large artery atherosclerotic, small vessel disease, other determined etiology, and then unknown etiology. So, these are the five classifications. The most common ones being the cardioembolic, the large artery, and the small vessel disease.

Really, when you think about it, the reason we do all this work up is because for cardioembolic strokes, you would have to anti-coagulate them versus for other strokes, they would usually benefit from anti-platelet therapy. So, that's the rationale behind doing the workup.

Monee: Okay. So, bringing us back in, you just briefly touched on what all the subcategories from the TOAST trial are. I think the first three are pretty intuitive. So, the large artery atherosclerotic events, cardioembolic, and small vessel occlusion. The part that made a little bit less that I'm having a harder time keeping straight when I read the guidelines, the stroke of other undetermined etiology versus the stroke of undetermined etiology. What's the difference between other and then not?

Karima: So, the stroke of other determined etiology, so that's where you have vasculitis and dissection and the sickle cell stroke that kind of thing. And then the unknown etiology is, you have a 30-year-old with no vascular risk factors who comes in with a stroke that's the kind of scenario.

Monee: Yeah. Along those lines, so keeping all those in mind, where do we start with our workup? Do we just do everything for everyone and then what do we do? Or, are there things that help you decide one thing versus the other?

Karima: So, typically, all stroke patients assuming doing a workup is going to change their management would benefit from a brain imaging modality, MRI much more than CT. And then as far as vessel imaging, you would need some kind of vessel imaging of the head and neck and you can use CTA head and neck or MRA head and neck depending on your patient population and what your resources are.

The next thing you need is evaluation of the pump to those vessels. So, you want a TTE if you have a suspicion that the mechanism of the stroke is embolic, then you would do a TEE. Or, if you have a suspicion that the stroke is related to, for example, an endocarditis, then you would also do a TEE. Those would be the two indications for doing a TEE.

Monee: How do you base that decision on? What makes you suspicious?

Karima: When you actually get a brain MRI, the way the strokes are distributed in the brain will give you an inkling as to what the mechanism is. If you look at a diffusion-weighted image on MRI and you see strokes in multiple vascular territories, that makes you think that it's cardioembolic, because it's basically one clot that traveled up and then showered everywhere. That would actually make me get a TEE. If a patient is young and has no vascular risk factors, I will get a TEE because I am hunting for the cause of the stroke. Basically, that's what it is. I am hunting for a cause of the stroke that would make me change management.

Monee: Okay. And then along all that, frequently patients get a monitor of some kind on discharge?

Karima: Correct. So, they need to be on telemetry while in the hospital. The patients that do get a monitor on discharge are the patients where we suspect an embolic etiology, but we were not able to capture AFib in the hospital. So, then there's data that shows that prolonged monitoring actually increases your chances of capturing AFib.

Meredith: And then, just to clarify, so let's say you have the patient who comes in and very clearly, it's like a large vessel occlusion, and there's nothing else on the imaging that would suggest a cardioembolic pathway. Do you still go down that work up? I would imagine you keep them tele like or whatnot in the hospital, but are you still going down like the TTE, TEE?

Karima: Yes, pathway.

Meredith: Yep. Okay. That's because potentially, they could have multiple etiologies that could have caused the stroke?

Karima: So, for the scenario of a large vessel occlusion, you're basically looking for where that clock came from. And so, that's the purpose of doing-- Because having a large vessel occlusion by itself is actually not an indication for anticoagulating a patient with a stroke. But if you find an LV thrombus that caused that large vessel occlusion, then that's an indication or if you find that they have AFib and then that caused their large vessel occlusion, then that's an indication for anticoagulation. But just seeing an occlusion in a cranial vessel is actually not an indication.

Meredith: Okay. If you can't tell, Monee and I sometimes struggle to get [Monee laughs] specific echocardiograms done. And so, we're just trying to see if there's any reason we could skip it. But it sounds like pretty much in any scenario, you would have to get it.

Karima: Not a TEE. The TTE, yes, you get in every scenario. So, transthoracic echo in every scenario and then transesophageal echo, TEE, you would get in certain scenarios where you have a really high suspicion for an embolic etiology.

Monee: Yeah. Presumably with a bubble study, correct?

Karima: Yeah.

Monee: Okay.

Karima: Yeah. All TTEs are done with bubble study because the recommendations actually changed. The old recommendation used to be that there was no indication for PFO closure. Then there were a couple of recent trials that were done that showed that there was actually a benefit for PFO closure in a subset of patients. And so, that's why TTEs and stroke are always done with a bubble study.

Meredith: So, keeping within, I think, the etiologies that we just talked about, could we now walk through how those different etiologies are going to change management while they are acutely in the hospital?

Karima: Yeah. So, let's say a patient comes in with a stroke and they're on telemetry and their telemetry picks up paroxysmal AFib, that would be an indication for them to be started on anticoagulation rather than antiplatelet. Let's say a patient comes in with a stroke and we get an MRI, and then we see strokes in multiple vascular territories. We do a TTE and we do not find anything, the tele is not showing any AFib, we go hunting and get a TEE and that

shows an LV thrombus or a source of embolus that would be an indication for using anticoagulation rather than antiplatelets. So, it does actually change management in the acute setting.

Meredith: It's really helpful to go through each of those etiologies and talk a little bit about the treatment. I think we've talked about a lot of information so far. So, Caroline, do you want to maybe just recap the high points that we've talked about thus far?

Caroline: Yeah, absolutely. So, it sounds like for all comers, everyone's going to get a CT head when they come into the emergency room or when the stroke alert is called. If it's within 24 hours, you can get the vessel imaging with a CTA right off the bat to evaluate for immediate therapies if they're a thrombectomy candidate. For the supportive management initially, the permissive hypertension will be for the first 24 to 48 hours support that penumbra tissue if it's there. We'll try to avoid fevers if we can and also trying just to support the damaged tissue. And then absolutely we can use our DVT pharmacologic prophylaxis. It's actually going to be meeting standard of care for us to do that even if it's a hemorrhagic stroke after 24 hours, which is pretty mind blowing.

Then talking into some of this immediate med rec and medication decisions that we have to make, it's pretty safe for all comers just to be started on that aspirin 81. They don't need the loading dose and they don't need to get a double dose if they were already on aspirin when they had the stroke, 81 for all. Then if they are on the DOAC and it's a large stroke something over a third of the size of the MCA, we will hold the DOAC for 10 to 14 days, and otherwise they can stay on it and they can stay on their Plavix as well, no need to save or to hold that. We reviewed some of these immediately identifiable ideologies where we would start the DOAC again if there's no contraindications and can consider the Plavix as well as if that's or the clopidogrel if that's indicated.

Meredith: Thanks, Caroline. So, I think the one thing that may be going over all of that would be worthwhile is to talk a little bit too about the indications for dual antiplatelet therapy while the patient is in the hospital. So, Karima, could you walk us through that?

Karima: Yeah. So, for the longest time in the stroke world, we shied away from dual antiplatelet therapy. The reason for that is because there were many trials in the past that showed that dual antiplatelet therapy actually caused an increase in bleeding risk without too much benefit in stroke prevention.

The first indication for neurologists to start using dual antiplatelet therapy came from the SAMMPRIS trial. SAMMPRIS is spelled S-A-M-M-P-R-I-S. So, the SAMMPRIS trial randomized patients to patients with moderate to severe intracranial atherosclerotic disease to aggressive medical management versus intracranial stenting. The aggressive medical management arm was using dual antiplatelet therapy. So, aspirin and clopidogrel for 90 days. They also had a health coach who was basically coaching them for behavior change, medication, being on top of their meds, nutrition, exercise, lifestyle factors.

The study had to be stopped early because the medical management arm was doing much better than the stenting arm. Everybody took as a conclusion from the SAMMPRIS trial that patients with moderate to severe intracranial atherosclerotic disease needed to be on dual antiplatelet therapy for 90 days.

In my mind, the patients actually needed a health coach. [giggles] I feel like that's what made the biggest difference. But the indication for dual antiplatelet therapy is for symptomatic moderate to severe intracranial atherosclerotic disease for 90 days. The second indication is, there were a couple of trials that came out in the last few years, the CHANCE trial and the

POINT trial. So, CHANCE looked at patients with mild stroke. They got dual antiplatelet therapy for 21 days. So, they got a loading dose of clopidogrel of 300 milligrams followed by aspirin plus clopidogrel 75 for 21 days. Those patients did better than the patients who were only on monotherapy. So, that was the CHANCE trial. CHANCE stands for Clopidogrel in High-risk patients with Acute Non-disabling Cerebrovascular Events.

Then in around 2018, the POINT trial came out. So, POINT stands for Platelet-Oriented Inhibition in New TIA and minor ischemic stroke. It had a similar design to the chance trial. What they did was they gave a loading dose of 600 milligrams of clopidogrel with aspirin versus aspirin alone for 90 days. In that study, the patients who were on dual antiplatelet therapy did better than the patients who were on aspirin alone.

So, high-risk TIA or stroke with minor non-disabling deficits, dual antiplatelet therapy for 21 days. Moderate to severe intracranial atherosclerotic disease that is symptomatic, dual antiplatelet therapy for 90 days. There is no indication for indefinite dual antiplatelet therapy in stroke at all, never. The longest we go is 90 days. So, these are really the only indications.

Monee: I think I always have to remind myself, I think as a hospitalist, it's not infrequent that I have to look at a med rec and try to figure out why someone is on dual antiplatelet therapy and how long they've been on it. And to know that 90 days is like a hard stop is very helpful.

Karima: So, it's a hard stop for stroke. Sometimes, they'll be on it for cardiac reasons and then we will tell the hospitalist that from our standpoint, they don't need it. But if the cardiologist needed, this is a different story.

Monee: Yeah. No, exactly. Okay. So, Ms. Toast, she was on DAPT with clopidogrel. Is there any situation in which we would maybe switch to something different like ticagrelor? Is there any benefit to that?

Karima: Yeah. So, the only scenario where we would switch somebody from clopidogrel to ticagrelor is in what we call Plavix resistance scenarios. There is a subset of patients who are Plavix non-responders. That is a concept that we know exist for certain patient demographics with certain risk factors. Those patients have a higher proportion of having no response to Plavix versus others. So, you can actually get a Plavix inhibition assay. It's called a P2Y12. I guess, it's called different things in different hospitals. But that would give you an idea of how much inhibition the Plavix is causing in platelet aggregation. If a patient is not having enough inhibition, then they would be candidates to switch from clopidogrel to ticagrelor.

Monee: Okay. Resistance, not limited to antibiotics, it's good to know.

Karima: That's right.

Caroline: [laughs]

Monee: The last piece about clopidogrel before we begin some other stuff, EMRs just bombard you with interactions. A lot of patients are on the clopidogrel and those same patients are also on omeprazol PPI. One of the pop ups that I'm sure I've ignored like a thousand times is the interaction between the two. Could you maybe talk about how important or how much I should not be clicking past that interaction?

Karima: I click past that. [laughs]

Monee: Awesome.

Karima: I click past that. No problem.

Monee: I appreciate the permission.

Meredith: [laughs] I feel like we've asked other guests similar questions and they also all say they click past it. So, maybe we should stop asking about these.

Karima: Acknowledge, next.

Monee: It's would be great joy to know that I have someone's permission.

Karima: [laughs]

Meredith: So, now we feel good about Ms. Toast leaving the hospital. I think that usually there's a fair amount of counseling and other kind of last-minute things you want to think about. Two are medically related, one is specifically, probably your passion, I think, based on prior conversations. But the two that come up, I think, in reading a lot is the depression and the SSRI need, and then treating their sleep apnea with getting them a CPAP. But I think the other thing we talked about prior to the recording was the impact on brain health and nutrition. And so, if you want to talk about all of that for a few, so that we can have a better understanding what we should be counseling our patients on as they leave the hospital.

Karima: It's definitely a big passion of mine. [laughs] I could talk about this all day. So, it's very easy to see certain deficits in stroke patients. If somebody cannot move their arm or their leg or they're aphasic, it's right there in front of you and you can see it. You will get PT and OT to see them and you'll send them to rehab. But there are these, what we call, the invisible deficits, which are cognitive decline and depression post stroke.

Cognitive decline post stroke is actually the most common cause of cognitive decline. A lot of times people will hear cognitive-decline Alzheimer's. Post stroke is actually much more common. So, in the US, the literature says that up to about 69% of stroke patients will have post-stroke cognitive decline, and about a third will have post-stroke depression. These two are things that really go under the radar and they are huge burdens because they will prevent a stroke survivor from being able to get back to work, for example, or from being able to do what is required of them as far as taking their medications and lifestyle changes that they need to do to prevent another stroke from happening.

There are certain centers in the US that are looking at screening patients for these. At Kashlak, we did a study where we have a neuropsychologist who actually sees all stroke patients acutely and then to basically screen for these deficits. If they're present to make sure that these patients get the treatment that they need as outpatient as far as cognitive therapy, and treatment of depression, and that kind of stuff. So, that's as far as the invisible deficits.

Then one of the things that I think really does not get the exposure that it should get is nutrition and its role in cardiovascular prevention. In my case, it's stroke prevention and in brain health in general. So, there is a lot of data that actually shows that, for example, the Mediterranean diet is very effective in preventing recurrent stroke. So, there was the PREDIMED trial, PREDIMED is spelled P-R-E-D-I-M-E-D. It was a trial where they randomized patients to low-fat diet versus Mediterranean diet supplemented with extra virgin olive oil or supplemented with nuts. They looked at the cardiovascular benefits and secondary prevention of MI, stroke. It showed that there was a 30% decrease in risk of stroke for the Mediterranean group versus the low-fat group. The effect size of aspirin in stroke prevention is about 15%, Mediterranean diet is 30%. The number needed to treat for aspirin and stroke prevention, for stroke and aspirin, it's 154, for Mediterranean Diet it's 60.

So, it is actually superior to the medications that we prescribe and yet, we do a very poor job in getting the patients the resources they need to be able to stick with this kind of lifestyle change. So, I'm on a mission and I preach to whoever will listen to me that we really need to do better by our patients in teaching them about the Mediterranean diet and other lifestyle changes. I keep saying the Mediterranean diet because that's where the most data is.

I think the other thing to keep in mind is that when we're counseling our patients, we really have to be culturally cognizant. So, I always say Mediterranean diet-- For me, here in Atlanta, what does Mediterranean diet mean to my patients in inner-city Atlanta? So, you have to tailor it to their culture and explain to them what the Mediterranean diet is about and how to go about changing their behavior, so very important.

Actually, we did a study where we counseled acute stroke patients in the hospital. We educated them about the Mediterranean diet, and then they were discharged and we followed-- It was a feasibility study and we followed their weight, blood pressure, and A1c. The patients actually stuck with the diet for up to 90 days, we followed them for 90 days, they lost weight, they decreased their A1c. So, they will do it and I really believe that it's important to actually do it in the acute phase. So, for the hospitalists to do it. A lot of times we think, "Oh, this is a clinic thing," and they'll take care of it in the clinic. And for us, neurohospitalists too, right, send to the stroke clinic. Patient when they're in the hospital, they're really scared and that would be the perfect time to educate them about what they can do to not have this happen to them again. So, I feel like it's a missed opportunity that we need to take advantage of.

Monee: Okay. Ms. Toast, she's gone home after my bad joke about her diet. So, we're going to call it a day for Ms. Toast. Caroline, will you please tell us about our next patient?

Caroline: This time we have Ms. Tia. She is 62 years old. She has a past medical history of hypertension, type 2 diabetes. She comes into the hospital with the complaint that this morning she had 90 minutes of left arm and left leg weakness that both spontaneously resolved on their own. Her head CT and MRI brain are both unremarkable. So, briefly, is this episode, you know, does it qualify for a TIA and then how do we characterize the severity in a way that's maybe comparable to the NIH we have for strokes?

Karima: So, that's a really good question. The old definition of TIA was transient symptoms lasting less than 24 hours. With the advent of the MRI and diffusion imaging, we started seeing a lot of patients who were having transient symptoms and had a positive diffusion imaging MRI. And so, the definition of TIA has actually shifted from time based to tissue based. That is actually one of the reasons we get MRIs with diffusion imaging. It's because we do not know whether this was a TIA or not until we actually get an MRI. If she had transient symptoms and the MRI shows positive DWI, then that's a stroke. If the DWI is negative, then that's a TIA.

Meredith: So, I think then for her, we'll call her a TIA because the MRI didn't show anything. So, how do you walk through what would be her recommended treatment for her TIA?

Karima: The workup for TIA is the exact same workup as for stroke, because it's essentially a warning sign. It's telling the things that cause a TIA are the same things that cause a stroke, you were just lucky this time that you did not have irreversible brain damage. And so, actually, just this past week, the AHA and ASA guidelines came up with their latest guidelines for TIA workup. It's the exact same as for stroke. So, brain imaging with MRI and MRA head and neck or CTA, echo, we call stroke labs, which is a fasting lipid profile, a hemoglobin A1c, and a TSH, and in certain populations, RPR and a B12 and a homocysteine. But they get the exact same workout.

Meredith: Coming back to Ms. Tia in her case specifically, are there any scoring systems that you might use that might help classify severity and who should get the workup that you just described, inpatient or outpatient?

Karima: So, severity, you can use the ABCD² score. It's actually a very good tool to know whether patient needs to be, for example, on dual antiplatelet therapy or not for 21 days per the POINT trial. Because the POINT trial showed that if they were a high-risk TIA, then they were good candidates for being started on dual antiplatelet therapy, and that is 4 and above. So, calculating that score is always useful.

Meredith: I was just curious, because some TIAs I feel like leave the ER and get a rapid sequential workup. So, is that also based on the ABCD²ed score or is that off of some other decision making pathway?

Karima: Where I am, all TIAs go to the CDU and get the entire workup in the CDU within 24 hours. I would think the only time that you could do it as outpatient is if this patient has amazing resources and they can get an MRI and all of this stuff the next day and their reliable follow ups, which almost never happens. So, typically, they go to the CDU and stay there for 24 hours.

Meredith: Yeah, that was my sense when I was reading about these rapid outpatients. I was like, "Who does this happen for and where do I find that?"

Monee: Definitely not our Kashlak.

Meredith: Yeah, not mine, either.

Monee: So, obviously, after we've established that someone has had a TIA and we've gotten their work up, the next question is what we do with their treatment. So, I know some people get aspirin only, and then some people get DAPT. So, how do you make that decision and then the three weeks thing too?

Karima: Right. That's your ABCD score, right? If their ABCD score is 4 and higher, then they get DAPT. If it's a low score between 0 and 3, then they get aspirin alone. They all get statins and then they all get vascular risk factor modification. One of the things that we forget very often is that patients don't know to measure their blood pressures on a regular basis. And so, I wish we had a hemoglobin A1c for the blood pressure to know where their blood pressure runs, but we don't. The only way for us to know where the blood pressure is running is to have a log of it. It's actually the most common risk factor for recurrent stroke or stroke after a TIA. So, very important to control the blood pressure.

I always educate my patients to get a blood pressure cuff and measure their blood pressure every single day, so that they can get a log and take it to their primary care physician and work on that if it needs to be worked on. And then I also, of course, tell them about the Mediterranean diet, [laughs] about the falafel. [laughs]

Monee: Sorry, it's like one of my favorite foods. Okay. Well, I think we've covered a lot of ground and I think all the ground we wanted to cover. So, I guess, for this last section, would you just give us some of your main take home points, maybe like three or four take home points that you would want the audience to go home with today?

Karima: I would say, consider TIA and stroke as similar, just because their symptoms resolve does not mean that they are not at risk. They are at high risk and they need to get the exact same workup as a stroke patient. The second take home point is, the entire reason we're doing the stroke workup is to figure out the mechanism of the stroke, so that we can

decide on whether we are anticoagulating or using antiplatelet therapy. And that decision gets made as inpatient. So, if we do the indications for anticoagulation are AFib or hypercoagulability, antiphospholipid syndrome, and that kind of stuff, or finding an LV thrombus. Otherwise, patients will get antiplatelet therapy.

The decision for mono antiplatelet therapy versus dual antiplatelet therapy is pretty easy. If they have symptomatic moderate to severe intracranial atherosclerotic disease, they get dual antiplatelet therapy for 90 days. If they have a TIA, that's a high risk with a high ABCD score of 4 or more, they get dual antiplatelet therapy for 21 days. And don't forget to screen for depression. I think cognitive screening, a lot of times, you probably would need the help of your friendly neurologists to help with that. But with a PHQ-9, it's very easy to screen for depression.

Monee: Is there anything you'd like to plug, other than the Mediterranean diet?

Karima: [laughs] There are many things that promote brain health other than nutrition. Nutrition is one of my passions, but exercise, sleep, many things that are important in educating not only patients, but also ourselves and how to take care of our own brain. So, I blabber about brain health on my social media accounts. If you're interested in that for your patients or for yourself, you can look me up Karima Benameur, MD, the ones that are not locked. [laughs] The ones that are locked have all my kids pictures on them. The accounts that are Karima Benameur, MD on Twitter or on Instagram are where I will post evidence-based data because there is a lot of misinformation out there. So, evidence-based data about how to promote brain health for the healthy adult as well for patients with neurological diseases.

Monee: Awesome. Thank you so much, Karima. It's been so much fun talking to you.

Karima: It was such a pleasure. Thank you so much for inviting me.

Meredith: So, Karima is here with us. We just recorded this great episode and we're going to jump into our lightning round. So, we're going to ask you a few questions to get to know you a little bit better. So, Monee and I are mixing this up a little bit and we're going to ask similar questions, but in a little bit different way. We like to ask our residents when we're on service about something that's bringing them joy in the last week, so that they can reflect on the things that are making them happy. So, for you, what's making you happy this week?

Karima: [laughs] What is making me happy is I just finished 15 days in a row of service and it is my second day off. [laughs] That's what's making me happy right now. [laughs]

Monee: What do you have planned for this glorious day or two that you have to yourself?

Karima: Vegging, not moving, Netflix.

[laughter]

Monee: I respect that. I feel that started in residency and it never stopped. Like, your single day off in that seven days and you would just lay back.

Karima: In neurology, we call it the refractory phase, [laughs] we're nerds.

[laughter]

Monee: I think we call it [unintelligible [00:58:33.]

Meredith: Karima, do you have anything planned out on Netflix to watch?

Karima: So, I actually just discovered *Mo* today. Apparently, it came out last year in August and I did not see it. I watched the first episode today and I've really liked it. So, I think that's what's going to happen. [laughs]

Meredith: Awesome. Monee, do you want to jump to picks of the week or do you want to ask anything else?

Monee: No, I think we'll do some picks of the week. So, I am bringing back a tradition that I had before COVID and I had not done since COVID, which is, I have an end of January party because we can all agree January is like the worst month. It's cold, it's gross outside, and it happens to be championship weekends. So, there'll be football, and food, and people that I like, and Meredith. [laughs] So, Meredith, what's your pick of the week?

Meredith: So, mine is, I was just in LA last week for my brother-in-law and now sister-in-law's wedding. It was fabulous. I spent a day sitting on the beach just reading a book and watching the sunset, and it was the most magical thing I've done in a while. So, not everyone can do that in Atlanta, but it was great. Yeah, I highly recommend if anyone can get out there and do that. So, Caroline, do you have a pick of the week before we move on?

Caroline: I have something that is bringing me joy on my social media feed. It is someone called Pattie Gonia. They are a drag queen, but they focus on doing activism around, like, outdoors, climate change, and then just queer activism as well. But they do amazing stuff, like, they'll make drag out of completely out of trash from the ocean or they'll go repelling down the side of the mountain and complete drag. So, it just bringing those two areas of activism together. But give them a follow, *@pattiegonia* and they'll make you smile.

Meredith: That's awesome. Are they on all the social media sites or--?

Caroline: I'm a kind of Gen Z millennial sandwiching those too, so the TikTok and Instagram is what I know they're on, but I think they're on other stuff too. Yeah.

Monee: That dig at our age was unnecessary, Caroline.

Caroline: [laughs] Well, [unintelligible [01:00:59] is my older job, but yeah, it's okay.

Meredith: Good time. So, this has been another episode of The Curbsiders bringing you a little knowledge food for your brain whole.

Monee: Yummy.

Meredith: Awesome. Get your show notes at *thecurbsiders.com* and sign up for our mailing list to get our weekly show notes in your inbox, plus twice each month you'll get our Curbsiders Digest recapping the latest practice changing articles, guidelines, and news in Internal Medicine.

Monee: And we are committed to high value practice changing knowledge. And to do that, we need your feedback. So, please subscribe, rate, and review the show on YouTube, Spotify or Apple Podcasts, or email us at *askcurbsiders@gmail.com*. A special thanks to our writer and producer for this episode, Caroline Coleman and to our whole team. The Curbsiders is produced and edited by the team at Pod Paste. Elizabeth Proto runs our social media, and Stuart Brigham composed our theme music. Until next time, I've been Dr Monee Amin.

Caroline: I've been Caroline Coleman.

Meredith: And as always, I've been Meredith Trubitt. Thank you and good night.

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