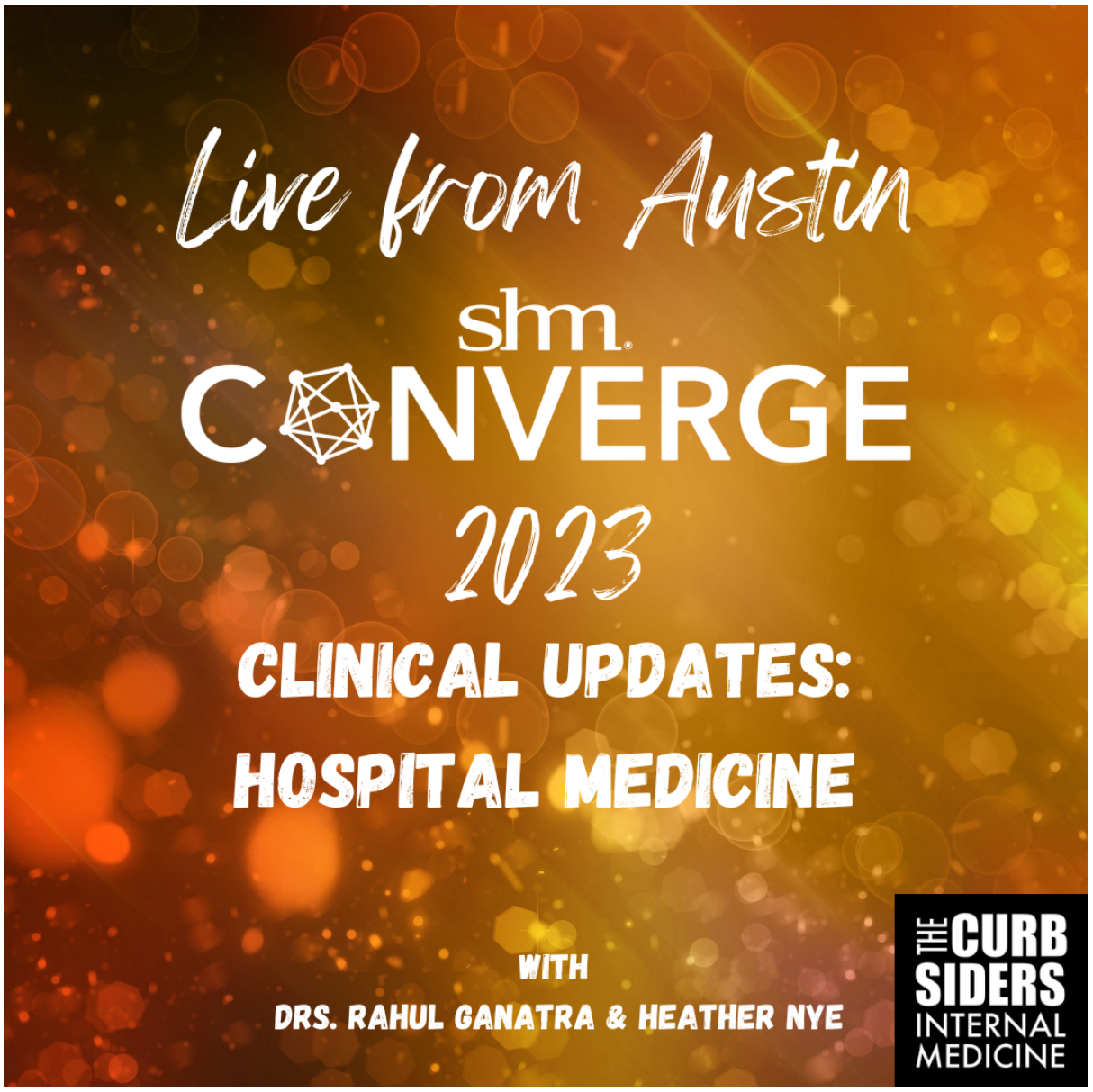
#393 Live from SHM: Clinical Updates in Hospital Medicine



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[The Curbsiders theme]

Meredith: The Curbsiders, Meredith and Monee here. Just wanted to let you guys know that we're going to have a little bit more regular show for hospital medicine which will come out on the first Mondays of every month. So, if you guys are looking for more hospital medicine content, tune in first Monday each month and you'll get to hear a great episode from Monee and myself. So, tune in.

Monee: Get excited, people. Hey, Curbsiders, Monee here. This next episode is a little different for us. It's recorded live at SHM in Austin this past March. We're really excited to have a couple of these live ones in the bank for you. This first one is the clinical updates with fan favorite, Dr. Rahul Ganatra as well as Dr. Heather Nye out of the VA out in California and San Francisco. We're really excited about this one. So, here we go.

[music]

All right, welcome back to Curbsiders. Still in Austin, SHM live, super pumped. This is the end of day 2 and we just got to see fantastic updates in hospital medicine articles, talk from esteemed Curbsider, Dr. Rahul Ganatra and first-time guest, Dr. Heather Nye out of the San Francisco VA. We're so excited to have you. How are you doing?

Heather: I'm doing good. I'm really happy to be here.

Monee: Yeah. Before we get started, would you mind telling the audience like a one-liner?

Heather: Oh, sure. I'm the Associate Chief of Medicine and I'm a hospitalist at the San Francisco VA and UCSF, obviously, is where I'm academically associated.

Monee: Awesome. What's a fun fact about yourself?

Heather: Oh, well, you guys already know that. I sing. I sing and I write songs.

Monee: If you've been following the Curbsiders social media feed during SHM in real time, you will get a glimpse of that. Due to copyright reasons, we will not be posting it. She will not be able to sing for us today, but has a gorgeous falsetto, I have to say.

Heather: [laughs]

Rahul: Heather was also in a band.

Heather: I was in a band.

Monee: Okay.

Rahul: Yeah.

Monee: What kind of band?

Heather: We did a little bit of everything. [crosstalk] original stuff. This is when I was a medical student and graduate student.

Monee: Awesome.

Heather: Yeah.

Monee: All right. That's awesome. Okay, well, we are going to close out, I guess, those are close out kind of. Yeah, Austin picks of the week. Meredith, what you got?

Meredith: Oh, I have to go first?

Monee: Yeah.

Meredith: I know what yours is, so I have to come up with something different. I'll stick with the same food theme though.

Monee: Okay.

Meredith: Okay. I know we've talked about tacos as a whole, but I'm going to go with breakfast tacos. They're hard to find outside of Texas, but they're really a complete meal with eggs and bacon that I'm telling you as a vegetarian, vegetables, it's really well balanced. Some salsa, that's more vegetables.

Monee: You know how I feel about people telling me that vegetarians only eat vegetables.

Meredith: I do.

Monee: Thank you. I appreciate that.

Meredith: As we have all these chips in front of us.

[laughter]

Rahul: They came from vegetables.

Monee: Rahul, what's your Austin pick of the week before we get too far down this rabbit hole?

Rahul: Okay. So, my pick of the week is the bats. Do people know about the bats? Were you going to take that, Heather? Oh, okay. Well, I'll only say half the things I know about bats and then we can just continue a bat-themed conversation. The largest urban bat colony in the world lives under the Congress Street Bridge. They come out and fly in a huge swarm, like, an hour before sunset. If you go running down the path just below the Congress Street Bridge, you can see them. On the first night I was here, I was totally unplanned, luckily stumbled upon them. It's beautiful. It's really an experience. It's really cool. So, check out the bats.

Monee: Yeah, a little bit like *Batman* begins vibes?

Rahul: Yes. And also, a lot of like touristy rickety boats and kayaks vibes, because you can rent a kayak and sidle up underneath the bridge and watch the bats swarm. So, pretty cool.

Monee: Awesome.

Rahul: Yeah.

Monee: Heather, would you like to continue the bat talk or do you have some notes?

Heather: I hadn't seen the bats, but I was going to mention the bats, because I heard about them yesterday and was planning on going down there tonight. But I did hear a fun fact about the bats, which was if you are underneath the bats for any given period of time, you are at high risk of bat urine, not bat guano drenching you. In fact, there was an attendee that had to go home and change before dinner because that happened to her.

Monee: That's unfortunate.

Heather: Yeah.

Meredith: I like how you prefaced it as a fun fact though.

[laughter]

Rahul: It is a fun fact. Fun fact for bat year. [laughs]

Heather: Exactly. Right.

Monee: Okay. Well, so we don't end on bat year and my pick of the week-

[laughter]

Monee: -is actually, as if you've been listening know Meredith is more of a Texas local and spent a lot of time in Austin. So, she took me on a wonderful tour of Austin things one of the evenings we were here. Deliciously yesterday had this thing called Amy's Ice Cream and it was delicious. I had a very basic flavor, cookies and cream, but it was really good. I can't explain why it's better than most cookies and cream, but it is. So, yeah, we're going to close that with some cookies and cream, which is the only ice cream anyone should ever eat. Okay, I think we are ready to talk about some studies.

Rahul: So, this is going to be a recap of the update in hospital medicine for 2022 that Heather and I just finished giving. The first paper that we're going to talk about is the EMPULSE trial. This was a paper by Voors and colleagues that was in a March 2022 issue of Nature Medicine. The question that this study was asking was whether or not SGLT2 inhibitors, specifically empagliflozin should be started during a hospitalization for acute heart failure. So, what was compared in this study? Adults hospitalized with acute heart failure were randomized to either empagliflozin 10 milligrams daily or placebo to be started during a hospitalization for an exacerbation.

The primary outcome in this study was clinical benefit at day 90. This was a composite outcome that included all the usual stuff, mortality, exacerbations, and also symptom improvement. The topline findings in this study was that patients who were randomized to empagliflozin were 36% more likely to have clinical benefit at day 90. This was really driven by greater improvement in symptoms and greater diuretic responsiveness. So, what questions can we answer for you about that?

Meredith: So, I read this study and listened to you guys give this talk and you talked a little bit about it, but I wanted you to explain the win ratio, because this was the strangest thing I had ever seen. I felt like I was watching ESPN baseball and they came out with this random statistic.

Monee: Like, the wild card round or something.

Meredith: Yeah. And so, I just was curious, like, is that really a valid measure and going through that a little bit?

Rahul: Of course, I am happy to talk about the little bit that I know about the win ratio. So, my understanding of why do this as opposed to something simpler is that it allows you to compare components of a composite outcome where there's a hierarchy to them, so that the order of occurrence of the outcomes matters, because you're only going to ask about symptom improvement in this study if patients didn't have an exacerbation and didn't die from any cause. So, what this allows you to do is to, in a more granular way than just using a hazard ratio for a composite outcome.

The intent is that this allows you to do a head-to-head comparison between every patient in one group and every patient in every other group to ultimately arrive at that distribution that we showed during the talk of where does the benefit to a drug come from. This is what showed us that at least from empagliflozin, the benefit really is driven by symptom improvement. So, that's my understanding. There's a little bit more that we talked about in the talk and I welcome if listeners know more things and have easy ways to understand it, let us know on Twitter because this is something we all struggled to wrap our heads around.

Monee: No. As you're describing it, I'm going to have to think about it more, but I'm really envisioning like, "Does anyone play Mortal Kombat," where they have the two people that you're playing the video game with and they have their ratings for everything? At the end you can see which one should win based on the ratings, like, agility and quickness and strength and all that stuff? Maybe just me.

Rahul: I played a lot of Mortal Kombat. I did not recall that part of the game at all. I remembered the punching, but I think that's a perfect analogy for the win ratio. I love it.

Monee: Cool. I think that was really the biggest question we both had when we were talking about that one.

Rahul: Yeah. So, the takeaway on that, it's just basically a way to use a composite outcome where you care about the relative importance or the hierarchy between those things. So, in this study, they prioritize the mortality benefit, highest. That was the first question that was asked. Then after that, exacerbations were the next kind of item. If no member of a pair died, then they moved on to ask, "Well, did anyone in the pair have an exacerbation?" If the answer to that was no, then they asked who had a better symptom improvement. So, it incorporates that order of importance.

Monee: Did they ask the follow-up questions, like, if there was mortality as yes, you don't go to two and three?

Rahul: That's right.

Meredith: Okay.

Rahul: In any given head-to-head, if the patient who got the placebo died, that counts as a win for empagliflozin. If neither patient died, then they went on to ask the question, "Did you have an exacerbation?" If the patient who was on, say, empagliflozin had an exacerbation, that's a win for placebo. So, you have to survive-- Not survive, you have to make it through each outcome in order to make it to that last outcome of symptom improvement. So, saying that empagliflozin improved symptoms means that it was among people who also did better with survival and exacerbation.

Monee: So, those who did not die.

Rahul: Correct.

Meredith: Okay. I think we can go to the next one because the next one you're going to talk about, I think, goes nicely with us talking about EMPULSE too.

Rahul: Sure. So, this was a paper by Mullins and colleagues and this was in a September 2022 issue with the New England Journal of Medicine. The question that the ADVOR trial was asking was, does adding acetazolamide to loop diuretics lead to faster decongestion in heart failure? What was compared in this study, patients were randomized one to one to get either IV acetazolamide or a placebo in addition to a standardized protocol of diuresis using loop diuretics. The topline finding in this study was that patients who were randomized to

acetazolamide were 46% more likely to be euvolemic at day 3. This was an absolute difference of about 12% or a number needed to treat of eight.

Monee: Can you talk a little bit about the congestion score and how clinically relevant that may or may not be?

Rahul: Yeah. So, the primary outcome in this study was assessed by a congestion score. This was a score from 0 to 10 that was kind of a composite of different physical exam findings. This included edema, ascites, and pleural effusion. The scores were assessed by cardiologists who were trained in this method. A notable omission is that weight was not a part of this and assessment of the jugular vein was not a part of the congestion score. So, in terms of clinical relevance, it doesn't incorporate some pieces that I think we are used to using to track patient's volume status. But in terms of applicability, there's a lot of variability in weight measurements. We know how difficult it can be to weigh patients who aren't able to stand. We know that jugular vein assessment is also something that's got a lot of variability to it. So, the intent with using the components of the congestion score was that it was hoped that this would be something that was reproducible and subject to less ascertainment bias.

Meredith: So, they didn't include the SGLT2 because of timing. But when I look at this one, coupled with EMPLUSE or frankly all of the SGLT2 studies that have come out in the last couple of years, how do you actually in practice apply the acetazolamide and the SGLT2?

Rahul: Yeah, this is a really important question, Meredith. All the cardiologists I've spoken to about this have been a little underwhelmed and they've basically said that every study of, is better diuresis better has shown that better diuresis is better.

[laughter]

Rahul: So, that's not really going to surprise anybody. I do think the big unknown that remains to be seen with the applicability of this trial is whether or not the same effect size is going to be seen in patients who are already getting action at that part of the nephron, because EMPULSE really suggested that it's probably some type of diuretic augmentation that's responsible for that symptom benefit. So, in the modern era, where all patients with heart failure are going to be on SGLT2s, whether this effect size that we saw in a naive population from acetazolamide is going to translate that remains to be seen.

Meredith: I guess, just like out of curiosity, has it changed your practice? Like, are you gung-ho on the acetazolamide and then starting the SGLT2 later?

Rahul: Can I tell you, I have been looking for the opportunity to try this and it has not presented itself yet chiefly because everyone has been on SGLT2s. What this study did persuade me of at least is that augmentation of diuresis in patients who are not diuretic resistant is probably safe. That is a question that comes up all the time, whether patients whose output is slowing down, should we start metolazone or chlorthalidone in these patients. This study, in my view, gave me some evidence to make me feel like that strategy is going to be safe.

Meredith: Okay. And then once again, I think hospitalists are all about the heart failure. So, I think that you guys had one other heart failure study?

Monee: We're going to round out our heart failure with strong HF with a pun of we're bringing it home strong. Heather, would you mind telling us a little bit about it?

Heather: No, I'd love to. This was a paper that answered the question is rapid up titration of guideline-directed medical therapy for acute heart failure, safe and effective. It was

published in The Lancet in November of 2022 and got a lot of people's attention frankly. What this paper did was they enrolled about 1,100 patients who were admitted with heart failure and had within 72 hours of admission and then were not on guideline-directed medical therapy two days prior to discharge. And so, about 1,100 patients were enrolled and they were either provided usual care, we know what usual care looks like or high intensity care.

What's tricky about the high intensity care group is that they had multiple visits, one, two, three, and six weeks, where they saw the care team given an exam, had laboratory data. The goal with that group was to get them up to speed with full optimal doses of guideline-directed medical therapy, ACEs, ARBs, beta-blockers, or MRA, all of them. And so, what the authors found was that the primary outcome, which was a composite measure of 180-day all cause death or heart failure readmissions was actually lower in the high intensity care group. So, it actually worked. It was 15.2% versus 23.3% in the usual care group. Also, these patients had a lot better relief of their symptoms quite a bit at 90 days. It's interesting to note that they were on lower doses of diuretics as well. So, they were on the GDMT full doses and lower doses of diuretics.

So, SGLT2 inhibitors were not included in this study either, similar to the diuretic study that we talked about. The number of visits post discharge is excessive and I don't know that all of our systems could handle that. It's pretty labor intensive. But overall, to me, I thought that this was a really well-done study that answered one of my questions and things that I would actually shame residents into, like say, "Look, you don't have to start everything before they leave. Gosh, what are you doing?" Then cardiology is telling them something else. And so, to me, I was like, "All right, maybe the cardiologists know what they're talking about here."

Monee: Yeah, there're a couple of thoughts. The first was and you pointed this out in your talk, which was the optimal doses for these things are a lot higher than I would have thought. I think that's probably what gives us a lot of pause. I think Meredith and I talk about this a fair amount, like, anecdotally, we feel like sometimes maybe it's just in our heads that certain patients come back when they've been on all these meds with things that were maybe like, "Oh, were they syncable because we started all these meds and stuff like that?" I think those doses might be part of that too. I don't know. What are your thoughts on that one?

Heather: I 100% agree. I can't remember the last time I saw somebody on 40 mg of lisinopril, which is the one that I care the least about. The 200 of metoprolol, did you see that one?

Monee: Yeah.

Heather: I think that's nutty. I think what made me feel a little bit better about this was that these outcomes still hold true with only just over half of patients at optimal doses. So, half of the other patients that they did include were on less-than-optimal doses, probably for all the things that you're imagining might happen when you start those doses. And so, it made me think this was still applicable to all of them, although it wasn't 100% of people on those doses.

Meredith: They were uptitrating them over those visits. So, it's not like they left the hospital necessarily on 40 of lisinopril, 200 of meto, they got uptitrated over that six-week process-

Heather: -in optimal doses. The first move at up titration of all of those meds was made in the hospital. They don't really get into the intervals, or like the increments that they went up, or if they switched from one to another, if they went up on all three at the same time. They don't have that granularity in the study. Again, as you also saw that probably two weeks, not

everybody was up to optimal doses, it took up to 90 days. So, that was their goal, but they got there by 90 days.

Meredith: Yeah. I feel like looking at all three of these studies, the ultimate endpoint is that we all should just be more aggressive with what we're doing. I think that's been theme over heart failure trials over the last few years at least and we all just need to grow up and be comfortable. [laughs]

Monee: If you're not watching video, currently I have my hand over my face and have like I'm trying to peek through the one, because that's how I feel when I'm sending some-

Heather: It's scary.

Monee: -of the patients home on all these medications.

Heather: It's scary, for sure.

Monee: They're terrifying.

Heather: Right. Well, I will say that this is big news, because last year at a heart failure update at SHM, which was a brilliant heart failure cardiologist. Her parting message was, "You don't have to start all these at the same time. You guys worry about it too much." I think that now we're seeing that in all three of these cases, it probably is helpful and even helping patients feel better. I think that's the other novel thing we thought about this was that, symptoms, patient reported outcomes were actually part of two of these important trials and happened to be the driving factor in the SGLT2 inhibitor trial. So, I love that.

Meredith: So, talked a little bit about heart failure and by a little bit a lot of it.

Monee: As we should, we're hospitalists.

Meredith: We'll switch gears a little bit and go into actually the perioperative landscape and some of the studies you guys talked about in that field. So, Heather, do you want to start us off with going through-- we're all in disagreement on how to say this, if it's CRYSTAL, CRYS-TAL.

Monee: High price bubbly guys, come on.

Heather: [laughs]

Meredith: We'll go with CRYSTAL for now.

Heather: That's how I've been saying it. So, yeah, I'm happy to cover this trial. This was a pretty high-profile trial that asked the question if aspirin is aspirin monotherapy for VTE prophylaxis-

Meredith: Awesome.

Heather: -as effective as low molecular weight heparin after total hip and knee arthroplasty. It was published in JAMA and came out in August of 2022. There was a ripple effect across the perioperative community really paying close attention to this. I'll just say that aspirin is-- There were two or three papers that covered aspirin this year. So, it was exciting. This group looked at patients were randomized-- actually, hospitals were randomized to either give aspirin after surgery or enoxaparin and given it for total hips or knees for 35 and 14 days respectively.

Then they looked at their primary outcome as 90-day symptomatic VTE with secondary outcomes of 90-day death, readmissions, and a number of other things, major bleeding, etc.,

and what the study authors found in the end was that there was actually-- It was a non-inferiority trial for aspirin. Aspirin indeed did not achieve non-inferiority, but there was a statistically significant lower rate of symptomatic VTE in the low molecular weight heparin group, 1.8% versus 3.5%. These were mostly lower extremity below knee DVTs in this study and no differences in mortality, major bleeding, or any of the other secondary outcomes. So, I think to us it was a well-designed study that really hadn't been done before.

Some of the trials that have been done with aspirin as DVT prophylaxis, which is a very, very common practice, had really wonky lead in periods of another anticoagulant, like, 5 to 10 days of low molecular weight heparin or rivaroxaban. "Oh, and then now you can start aspirin." And then they're saying, "Aspirin is non inferior." Unfortunately, that's not how it's being used. It's being used as monotherapy.

Meredith: I feel like comanaging with orthopedics, the data seems different for some reason, because they love the aspirin.

Heather: They do.

Meredith: I often feel like medicine doesn't love the aspirin as much. They definitely did a little bit better with the low molecular weight heparin, but just curious on how to rationalize through that. It sounded like during your talk, you guys were still leaning towards in your higher risk patients keeping with the low molecular weight.

Heather: Yeah, orthopedists are very passionate about aspirin.

Meredith: They are.

Heather: They are. They study it. A lot of the studies that were not debunked, so to speak, but that were downplayed because of this study. The study authors wrote very fervent responses to this and challenged some of the methodology. When in truth, it's a very well-designed trial. The orthopedists really love aspirin for a number of reasons besides VTE prophylaxis. There's a lot of observational studies. They're not great data, but they think that they lead to fewer joint infections, less stiffness afterwards. And so, they look at aspirin for a number of different reasons. It's also easy and cheap. So, those are the major arguments.

I think the best thing that we can do in our role as hospitalists is really speak reason and ask people to risk stratify and say, "Look, we're fine with aspirin. It works well, but it doesn't work as well in patients at higher risk." So, in the confusion around aspirin, there were a number of other trials. Metric being one of them in lower extremity fracture. It's actually extremity fracture to be totally honest. It was a study that looked and showed that their primary outcome was 90-day mortality, and they showed no differences between aspirin and low molecular weight heparin. I think it was low molecular weight heparin, right?

The problem was these were young patients. They were trauma patients. They had upper and lower extremity fractures. So, this was not hip fracture. I think it's really, really important that we don't interpret that study as, "Oh, it's okay to give our hip fracture patients aspirin." It may be, but that is not what they were looking at. There was a sub population that were hip fractures, but it ends up being confusing. I know when you're trying to sift through this data, you want a one-word answer, yes or no. Do I give them aspirin? It's not that easy.

Monee: Well, and I think what complicates that even further and you mentioned this, which was the international consensus meeting on the VTE guidelines recommended aspirin, and then you mentioned some stuff that's coming down the pipeline. So, I was wondering if you could maybe speak to that.

Heather: Yeah, that's a frustrating recommendation. Let me just say that.

Monee: [laughs]

Heather: It's gone back and forth in the guidelines. We had the ACCP guidelines in 2012 and then I think ASH came out with the guidelines. It always says one or the other, maybe okay, but this guideline last year was like whole hog, aspirin is great, strong recommendation, and all your patients, even the sick ones. So, I thought it was a little over the top, but we do have these new trials are coming up to, I think, in excess of 20,000 patients. They're going to enroll their randomized trials looking at both aspirin with a lead in period and without a lead in period. of rivaroxaban to compare aspirin monotherapy and aspirin with riva to just see if that's the EPCAT III. The PEPPER trial is simply looking at aspirin monotherapy versus rivaroxaban monotherapy for VTE prophylaxis, and low-dose warfarin as if, I guess, somebody somewhere still uses that. So, those will be really robust and I think we'll have a good answer finally.

Rahul: I totally agree with this interpretation of the CRYSTAL trial. It was very clear that low molecular weight heparin was superior to aspirin monotherapy. But I will just point out, the professional society guidelines from 2022 were published before these results were available. So, like, what we've seen in other situations, for example, the WATERFALL trial, it's possible that these data reflect new knowledge that hasn't yet had a chance to be incorporated into professional society guidelines. As a generalist nonexpert, I rely on guidelines to have a recommendation for what to do in most situations. What I take from this is is that people should be having risk stratification discussions with patients and decision-making should be individualized around a patient's particular risk for VTE in deciding, whether to use aspirin or low molecular weight heparin.

Meredith: Awesome. So, I think those are all my questions. Do you have any?

Monee: No.

Meredith: So, we can go ahead and switch then to near and dear to my heart some periop gabapentin discussion?

Heather: Uh-huh. Absolutely. Is it really near and dear to your heart?

Meredith: I love pain management.

Heather: Oh, you do? Well, I love old people.

Meredith: Okay.

Heather: So, this was going to work out well.

Monee: I feel like a friendship has just been born.

[laughter]

Heather: In fact. Yeah. So, this is a study that looked at whether or not the routine use of gabapentin after major surgery in older adults causes harm, is it safe, etc. It came out in JAMA Internal Medicine in September of 2022. I think it's important to delineate for those of you out there who don't do a lot of perioperative medicine that gabapentin is increasingly being utilized in multimodal pain control regimens. That often is seen in elective orthopedic surgery, it's seen in enhanced recovery after surgery protocols, etc. So, it's being lumped in with opiates, Tylenol, and gabapentin, and a number of other agents. It's been done in a sweeping way where they're not thinking about who they're giving it to. We know as

internists that older folks have different responses to some of these medications and gabapentin is no exception.

So, this group did a retrospective cohort study. They looked at about 238,000 patients who had undergone surgery from 2009 to 2018 and were over the ages of 65 and they compared. Actually, they had the propensity match, these patients, but they compared patients who had received gabapentin in postop day zero to two as a new medicine to them, they couldn't have been on it before versus those who did not receive that. Their primary outcome was delirium. Again, because this is a database study, they had to use a validated claims-based algorithm to identify delirium. They also looked at antipsychotic use, which can predict delirium as well as pneumonia and in-hospital death.

They found that, overall, not surprisingly, there's about a 30% increase in delirium rates in patients who were getting gabapentin after surgery. So, 3.4% versus 2.6%. There were also very small, but statistically significant increases in antipsychotic use and increased rates of pneumonia in this same population. So, I think, to me, this was one of those thank you for telling me what we already know studies. It just gives you a little bit of something to send in an email to the orthopedists, but I was happy to see this study. I think better data is probably needed overall for us to make a huge change.

Meredith: Yeah, and you already said this, but I just want to highlight it. The study was really looking at people who are not on gabapentin already, but not the 95% of our patients who are somehow already on gabapentin when they come in, not always [crosstalk]

Heather: Which is really sad. I didn't mention that a lot of people who get these surgeries and are placed on gabapentin are actually still on them three months after their surgery, which is ludicrous, because that is not how it's been studied. But that is one of those unintended downsides to just routinely prescribing these meds.

Monee: This is like a complete zag from what you guys just talked about. I think I have an idea of why, but they pick pneumonia, which I found to be random. Is this assuming that it costs aspiration or this is just me being like, I don’t, yeah.

Heather: I thought the same thing. There's nothing wrong with you. I thought the same thing. If you dig into the paper, the presumption is that you're going to have more aspiration in a delirious patient. And so, that's why they picked that. But you can imagine, it is like often left field. The vast majority of these patients were elective surgery, remember? So, they're not going to be coming to the ED with a potential infection. So, it would be unusual for you to develop pneumonia unless potentially you had some microaspiration.

Meredith: Yeah. They excluded anyone who was needing the gabapentin for another reason too, like, during the stay?

Heather: Yes, they did.

Meredith: Okay. Anything else, Dr. Amin?

Monee: No, that pneumonia thing was just bothering me.

Heather: [laughs]

Monee: Thank you for validating my confusion. I very much appreciate it.

Meredith: I'll just highlight it. I feel like I've gone to a couple of the pain talks too during this conference and that's also been the resounding message that we're prescribing gabapentin a lot in our patients. But whether the data is really all there for-

Heather: Exactly.

Meredith: -all of the indications is up in the air?

Heather: Well, there're consensus pain guidelines by American Pain Society. Those guidelines will talk about NSAIDs and say, "These are indicated in certain types of perioperative pain, etc." Then they have a caveat, but come at risk for patients with AKI or they say, "Be careful and choose your selection." They don't do that with gabapentin. They do that for opiates, they do it for NSAIDs. Gabapentin is like a free for all. It's like, "Hey, it's great. No harm, no foul." I think just exercising a little caution is what we're asking for, we're not saying don't give it.

Monee: You're describing, I feel like the way we talked about tramadol for a while.

Heather: Exactly. Yeah.

Monee: I remember when I was in med school dating myself, where everybody got tramadol, because it was not opiates and stuff.

Heather: Totally.

Monee: Here we are talking about gabapentin in a similar way, I feel. So, I don't know.

Meredith: So, at the talk I was just at, gabapentin is the second most prescribed medication at the speaker's hospital and the first is tramadol.

Rahul: Wow.

Meredith: [laughs]

Heather: Probably, behind those, there's some nefarious advertising somewhere that's making that happen.

Meredith: Yeah.

Monee: I wouldn't know anything about that.

[laughter]

Meredith: All right. So, we can, I guess, switch gears. We're going to take a left turn, I think, a little bit and talk a little bit about the WATERFALL study.

Heather: I have to admit, when I first saw this study, I was like, "Ah, IV fluids." It's just such minuscule sort of stuff that the more I dug into it, the more impactful I realized this study was going to be. So, WATERFALL looked at aggressive versus moderate fluid resuscitation strategies in patients with acute pancreatitis. As we all know, tons of papers are coming out with comparing a lot of fluid versus a little fluid. This seemed to be yet another one, but particularly important because guidelines have recommended, we essentially flood our patients in the first 24 hours. There's no secret about it. It's like 8 to 12 liters if you do the math and the AGS guidelines.

So, what these guys did was, they took two fluid resuscitation strategies, the aggressive and moderate, and patients who came to the ER within 24 hours of symptom onset of pancreatitis were randomized into one of two fluid strategies. Now, they were excluded if they were already showing signs of moderate to severe pancreatitis like AKI, or respiratory failure, or other kind of more serious signs. In the aggressive arm, they got about a liter and a half bolus and 200 an hour or so of fluids. In the moderate arm, they only got a bolus if they were deemed by exam and laboratory findings to be hypovolemic. So, some of them

didn't even get a bolus, and then they received about 100 an hour. I'm just rounding up for the audience here.

Then they looked at their primary outcome was whether or not patients progressed to moderate to severe pancreatitis. Those were things like creatinine over 2, local complications, persistent hypotension despite IV fluids. So, those were signs and symptoms of severe pancreatitis. They also looked at a lot of other secondary features like organ failure, ICU admission symptoms, etc. They monitored really closely volume status here. It was a safety outcome that they were wedded to following.

So, this study was actually stopped prematurely before I get to the primary and secondary outcomes, because the safety outcome noted a much greater difference than they anticipated in volume overload. So, the aggressive arm, one in five patients were volume overloaded 20.5%, whereas in the moderate resuscitation strategy, it was 6.3%. So, they only stopped it at a total enrollment of like 250 patients, and it was delayed to go up to 750. So, it may be underpowered for the other findings, but suffice it to say that neither fluid strategy came out ahead in the primary and secondary outcomes, which were progression to severe pancreatitis or respiratory failure or necrotizing pancreatitis.

So, in fact, it looked like the aggressive arm, again, was performing much, much worse in all of those categories. And so, the authors concluded that there doesn't seem to be a benefit from using an aggressive fluid strategy. In fact, there may well be harm. We just haven't shown it definitively here and that there is certainly a risk of volume overload in these patients.

Meredith: Yeah, I think this was what-- I know the heart failure stuff is getting all the hype right now, but this was one of my favorite studies, because I feel like the, not guideline, but the adage you learned during training was, "Keep giving them fluids. It's okay if they end up intubated," all of these things. But in your heart, you're like, "It feels like we're doing harm in a way." And so, this, I feel like was just such a question that I've had for such a long time that they did a really great job at addressing and answering.

Heather: Yeah.

Monee: Even one of our first episodes that we did was pancreatitis, we didn't go into specifics of how much, but I do remember our guest, Dr. Sharzehi mentioning like, "Just keep giving them fluids." This is well after that episode aired, but I do remember that just like we learned in training. So, it's just like you were saying about the last one, it proves something that we've all been thinking for a while.

Heather: Right, for sure.

Rahul: It is in the ACG guidelines to aggressively fluid resuscitate people. So, it is important anytime you're talking about deviating from what's in the professional society guidelines to make sure that we have a good justification for that. I think in this case, the recognition that the evidence base for aggressive fluid resuscitation was actually really limited. It was mostly animal studies. The hypothetical benefit of preventing regional pancreatic hypoperfusion was the justification given for aggressive fluid resuscitation. So, I view this as a natural extension, a natural update to the existing guidelines. We have better data now to suggest a change in practice. So, it's important to pay attention to what's in the guidelines, but I think in this case, we have better evidence and a good reason to consider a moderate resuscitation strategy.

Meredith: I think the other thing that's important was how they set up the study, like, the patients in the moderate group were still-- It could get a bolus if they were deemed

hypovolemic. You thought that they really needed more fluids and everything like that. So, the way it was set up still like -- Even the moderate group still got a fair amount of fluids. I think at the 48 hours, they're still at 5 liters compared to 7.

Heather: Exactly. This was, I think, one of the safety checkpoints that they were doing, like, they did it at 3, 6, 9 hours. Each one of those timeframes, they could have increased the fluids or decreased them based on volume status and other safety measures. And so, we can't do that with all of our patients, but it's reassuring that we're not missing something here. I was going to say that the guidelines-- I love the guidelines, but they're from 2013. Come on, GI. Get out of bed. There's also acute pancreatic-- There's like a pancreatitis guidelines also from 2013.

Meredith: I think that's how they ended this paper too that they were like, "This study is helpful, but there're so many other spaces we could start looking at for pancreatitis on therapeutics and stuff like that,-'

Heather: Right. Yeah, exactly.

Meredith: -which is true, because it's fluids, NPO and [crosstalk]

Monee: You said at the beginning when at your talk that we literally have no treatment for pancreatitis.

Meredith: [giggles] No, we don't.

Rahul: Prevention.

[laughter]

Monee: Sometimes, it cannot be helped. So, we had one last one that we wanted to go over regarding PICC lines and midlines, which is, I know, hot topic of debate all the time. So, please fill us in.

Rahul: Absolutely. So, we reviewed a paper that was by Lakshmi Swaminathan and colleagues in the January 2022 issue of JAMA Internal Medicine. This paper basically asked the question, "Are midlines better than PICCs, peripherally inserted central catheters?" The way that this study was carried out was the authors did a retrospective cohort study that compared patients who had midline catheters placed against patients who had PICC lines placed for the specific indications of difficult venous access or among people who needed IV antibiotics for up to 30 days after discharge. The primary outcome in this study was major complications within 30 days and this was a composite of symptomatic upper extremity DVT or PE, bloodstream infection, or catheter occlusion.

The top line findings in this study were that among patients with those indications, PICC lines were associated with twice the odds of major complications as midlines. In looking at the specific outcomes, the odds of bloodstream infection were about four times higher with PICC lines, the odds of occlusion were about two times higher with PICC lines compared with midlines. There wasn't a compelling difference in DVTs because the number of events in both groups was overall similar. But in terms of that composite outcome, by day 3, it looks like much higher odds in patients who got PICC lines.

Meredith: So, when they did any of the adjustments, was it based on the fact that midlines tend to be in there for a shorter time, so therefore would have less of these complications or adjust for that so that we're really going off of the length of the catheter itself?

Rahul: Yeah, this is a really important question. The authors accounted for that difference in catheter lifetime in their analysis. The main analysis just used a count of outcomes, which is indicated by the fact that they used an odds ratio. But one of the secondary outcomes was doing the primary analysis, but accounting for the difference in catheter days. And so, that's where we had something that I addressed in the talk, which I'm not going to spend too much time on here. You can read the paper and tweet at us if anyone disagrees. But there was a secondary outcome in this study that suggested that PICC lines were associated with fewer DVTs than midlines. But that was, I think, fully explained by the fact that PICC lines stayed in so much longer. What the authors didn't report was the number of DVTs per patient or per catheter. That would have been an useful way to disentangle that. It did report outcomes in terms of catheter days and there was not a dramatic difference in the outcome of DVTs in standardized catheter days.

Meredith: Then the only other thing I had seen when I looked at this paper too is, it may not be necessarily relevant. I just didn't know why there was, like, a big racial difference between who got PICC lines and who got midlines?

Heather: Yeah. No, I don't have a good explanation for that, apart from to say that it does highlight one of the critical limitations of retrospective cohort studies, which is when you're not randomizing patients to the two comparisons, you run the risk of an imbalance of both measured and unmeasured confounders. So, it's not unusual to see differences in things totally unrelated to the exposure of interest, in this case, things like race and ethnicity. Asking the question, could any of those differences actually account for the outcomes that we observe. That's a really important learning point when you're thinking about evaluating retrospective cohort studies. I don't have a good answer for why that would have been the case here, but you bring up an important point that I want listeners to think about.

Meredith: Okay, awesome. So, I think we should actually go to the most important study you guys presented. Since we're at SHM and we're all a bunch of hospitalists, I think this was really practice changing for me.

Heather: [laughs]

Monee: I have to say, I have not been so excited to talk about a paper in so long.

[laughter]

Monee: Listeners, what you'll know is that Meredith is the study junkie, and I'm the Sideshow Bob making jokes about pop culture all the time. And so, I'm just saying that this is a big effing deal, what we're about to talk about.

Meredith: [laughs] Yeah, I won't spoil it too much, but one paper talking about how people or how individuals not in healthcare really are perceiving hospitalists.

Heather: Yeah. So, this is a paper that looked at the general public's understanding. I should qualify general public by saying the Minnesota general public's understanding of medical roles and hierarchy. By medical roles, what does a specialist do were basically the questions. They did their study at a county fair. They basically grabbed people who were walking by a study booth about 200 adults over 18 who said that they had no medical or nursing background. They gave all the respondents 14 questions that were sentence completion and they basically asked, "What does a specialist do?" In other words, hospitalists are doctors who take care of ____.

Then the second part of this was taking all the team members of an academic medical team, like, medical students, residents, interns, attending, and ranking them in order from least to

the most experienced. What they found was that of the 14 subspecialties that they looked at, the hospitalists were only recognized by about 31% of people.

Rahul: Oh.

Heather: [laughs]

Monee: It wasn't the worst though, guys.

Heather: It wasn't. It gets worse. Nephrologist was the absolute worst. We were like number 11, I think, out of 14. So, pretty bad with a couple of well-known, well-treated specialists at the top, dermatologists and cardiologists were like over 90% recognized. The funny things about this article for many of us who read it were that some of the wrong answers that were most commonly written down included nephrologists care for the dead and internists care for insides.

Monee: Yes.

Rahul: That's not wrong.

Heather: Yeah.

Meredith: [laughs]

Monee: No, it's not.

Meredith: That's right.

Monee: I would be remiss if I did not shout out my brother, who is a nephrologist. Sorry, Akash.

Heather: Taking care of dead people.

Meredith: [laughs]

Heather: Thank you for the work you do.

Monee: [crosstalk].

Meredith: [laughs]

Heather: I love nephrologists, just to clarify.

Monee: As do I, morally obligated.

Heather: They are good people and we need them frankly. Some people thought that hospitalists actually care for the hospital building, which was especially troubling for us.

Meredith: Not totally wrong all the time though.

[laughter]

Heather: I take out my own garbage.

Monee: When I'm in public, well, I mention that I'm a hospitalist in settings where there are no other healthcare workers, I literally get, "Is that a thing?"

Meredith: [laughs]

Monee: "Yes, it is a thing."

Heather: 20 years running.

Rahul: Okay. So, it was also a little disappointing in terms of provider experience, what people knew about it. Attending physicians were only recognized as the most senior members of the team 27% of the time. Maybe not surprising, because it's in the name. Senior residents were most frequently categorized as the most experienced members of the team.

Meredith: I actually did not find that part is surprising, because I have definitely had patients who are I had-- When I first came out of training and I was like, "I'm the attending." They're like, "What is that?" And so, then I switched to saying a supervising physician for the team, and that computes much better for patients.

Heather: Meredith, you didn't say inpatient boss?

Meredith: No, but that was a good suggestion for other publicists.

Heather: [laughs]

Monee: PR. My residents actually will introduce me as the boss lady, sometimes. I find it to be the most effective-- [crosstalk]

Heather: Honestly. Yeah.

Monee: Especially as women in medicine.

Heather: Yeah, you cannot soft pedal it, can you?

Monee: No.

Heather: Otherwise, they're like, "Well, surely she's going to take my pulse" or something.

Meredith: Which sometimes I do as well.

[laughter]

Meredith: So, yeah, I think the summary from that was, outside of hospital medicine, maybe needing to get a new publicist that we need to probably be doing a little bit better job at actually communicating what our role is and not assuming everyone knows what a hospitalist is.

Monee: Definitely.

Heather: Yeah, totally agree.

Monee: Definitely, 100%. Okay, well, Rahul, Heather, we've taken so much of your time. We are so, so grateful that you were able to give us this glorious hour of your time. Were there any things that you wanted everyone to take home or do you feel like we nailed it?

Heather: I think one of the take homes that were talking about was, literature can be fun. Don't be afraid of it. Everybody can understand it. Sometimes, you need to break it down.

Rahul: 100%. The other thing that I took away from this experience was seeing firsthand just how much of a group activity critical appraisal is. Reading things with other people, talking with your friends and colleagues about things you're reading, that's really the only way to learn things you don't know and expand your knowledge base. So, don't be intimidated by trying to keep up with the literature. It's easier if you do it with other people.

Meredith: Literature with friends.

Heather: [laughs]

Meredith: It could be the new book club for doctors.

Rahul: I love that.

Monee: I was literally going to say, book club.

[laughter]

Monee: Okay. All right. No, again, thank you so much, and we will hopefully be able to get Heather on here for something else down the line. Very much enjoyed this time.

Heather: Thank you.

Meredith: This has been another episode of The Curbsiders bringing you a little knowledge food for your brain whole.

Monee: Yummy.

Meredith: Still hungry for more?

Monee: Yep.

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A special thanks to me and Meredith for writing and producing this episode, as well as the whole team with Curbsiders. Our technical production is done 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 Monee Amin.

Meredith: And I've been Meredith Trubitt in case you didn't know. Thank you and goodnight.

[music]

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