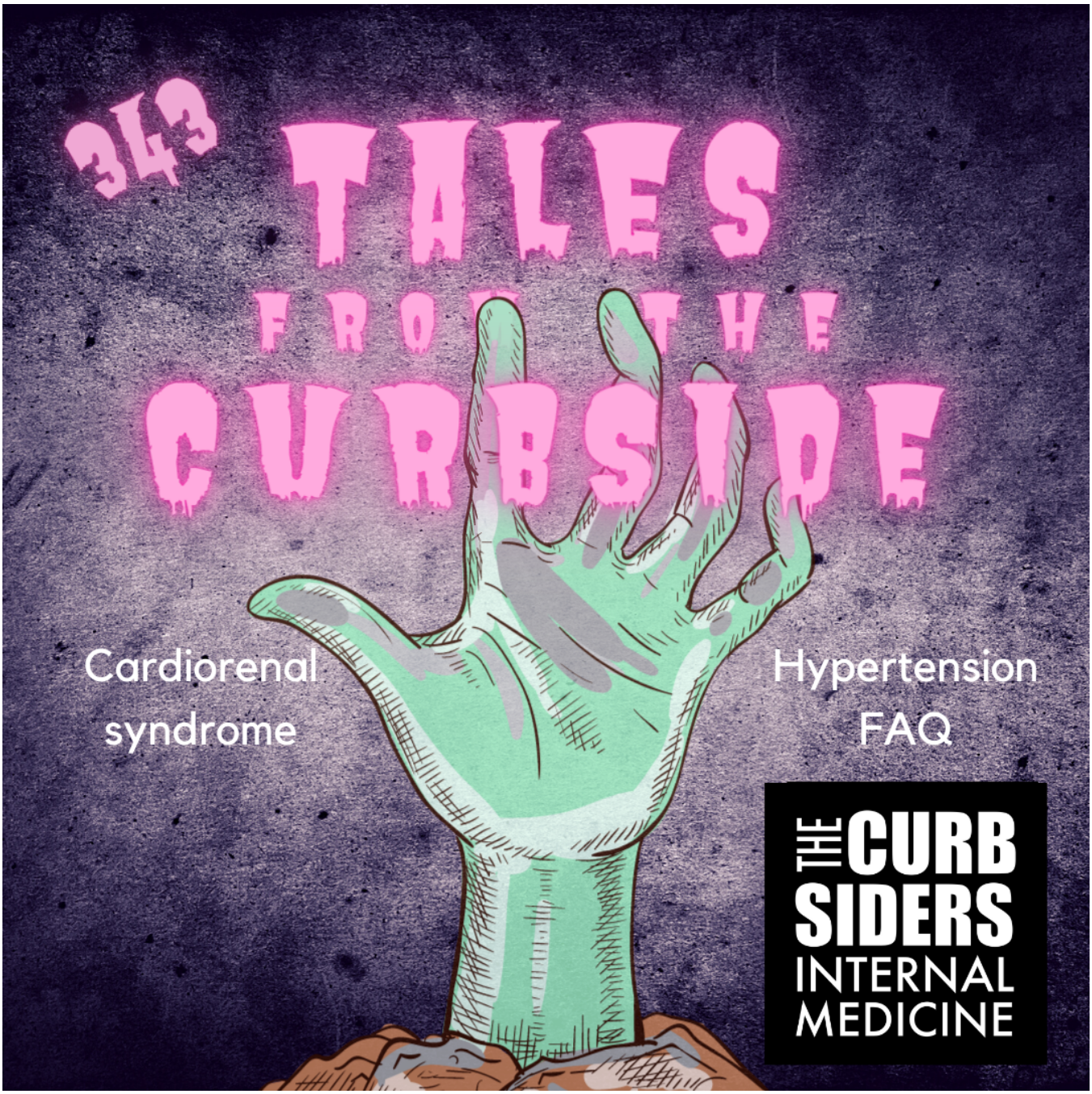
#343 Hypertension FAQ and Cardiorenal: A rapid review (TFTC)



[The Curbsiders Podcast theme]

Matthew: Welcome back to The Curbsiders. I'm Dr. Matthew Watto. Here with my great friend, Dr. Paul Nelson Williams. Paul, how are you doing tonight?

Paul: I've never been better, Matt. How are you doing?

Matthew: Paul, it's a weeknight.

Paul: [laughs]

Matthew: We both had full days in clinic and now, we're recording podcast. What could be better?

Paul: I'm spending time with my friend. We're talking about diuretics. This is the drill.

Matthew: Yeah. So, today, this is one of the episodes where for your space learning, we're going to talk about two great recent episodes, one on hypertension, some frequently asked questions with Dr. Jordana Cohen and another on cardiorenal syndrome from NephMadness featuring two great guests, Dr. Joel Topf and Dr. Sadiya Khan. And on this episode, Paul, we're just going to go through our favorite pearls. I'll remind the audience that on the shorter episodes, we typically don't make them available for CME, but the individual episodes we're talking about, we're both available for CME, so, you can go back and claim credit for those. And Paul, I think I'm forgetting to do this. Can you tell the audience-

Paul: [laughs]

Matthew: -in case they haven't listened before, what is it that we do on The Curbsiders?

Paul: I was going to throw it in, medicine podcast [unintelligible [00:01:17] experts.

Matthew: [laughs]

Paul: We are *the* internal medicine podcast. We use expert interviews to bring you clinical pearls and practice changing knowledge. We already told you who we are. The experts will be talking about our evening, you will not hear from them tonight. We're just recapping these amazing episodes that I just had a chance to relisten to recently. And as much as I hate the sound of my own voice, they're both fantastic episodes. So, it was nice to go back and revisit them.

Matthew: First up, number 321, hypertension FAQ with Dr. Jordana Cohen and this was with production and graphics by the great Malini Gandhi, who is just an up and coming medical student, Paul, probably, going to take over the world someday.

Paul: Wunderkind, I might say. Yeah.

Matthew: Yes, wunderkind. There you go. Paul, to start off the diagnosis of hypertension seems easy, right? Just slap a blood pressure cuff on there and then if its high, person has hypertension. What's your approach to this in the office and what are some pitfalls for the audience?

Paul: Yeah. No, you nailed it. Just a thigh cuff for every arm, ideally over top of a coat and hopefully, a cigarette in the other hand.

Matthew: [laughs]

Paul: No, we spent a lot of time talking about blood pressure measurement, because that's the right thing to do. Matt, I think you've raised this point a bunch of times is that, we lean so heavily on the SPRINT trial as guiding how we're treating patients these days. But the study measurements and the way they did those things are different a lot than what we do in the clinic. They use these automated measurements that were done three times, then averaged out, and then the patients weren't spoken to, and it was very regimented, as opposed to a lot of clinic blood pressures, which I think and I love this term that Dr. Cohen referred to as a casual blood pressure where say, the patient comes in, perhaps, the medical assistant is asking them questions as they take the blood pressure without measuring the arm. Perhaps, the legs are crossed, perhaps the patient's just eaten, perhaps they're talking, perhaps their back is not supported, there's lots of ways where things can go south, you can get maybe suboptimal numbers, I might call them.

Matthew: Yeah, and that's why the USPSTF, Dr. Cohen, all experts recommend now confirming with a home blood pressure reading to try to make sure that you're not just capturing this casual blood pressure that looks high and it's not really high at home. So, I love that and now, I always make sure to try to confirm, and we'll talk about this a little bit later, but they're either a home blood pressure monitor, where the patient checks themselves. You got to instruct them how to do it. Back supported feet on the floor, arm supported, appropriate sized cuff on the upper arm, and ideally, Dr. Cohen said she likes to take at least a couple readings over three days, usually the average of two readings in the morning and two readings in the evening over three days, at least six values to determine what you're going to do.

I've actually taken to trying to get extra readings before I make changes in blood pressure readings, because a lot of times someone's nervous, they're running late to the appointment, or they're just nervous about seeing a physician, and the blood pressure is running high. So, I really have tried to get extra data and tried to get the best readings possible to make my decisions about blood pressure medications.

Paul: Yeah, I don't know, if you've had a similar experience. But even for me, sometimes, what I will do is, I'll leave the patient sit when I get their paperwork together, and gather things as I'm getting there to go pack it together, I'll come back, and then remeasure the blood pressure after they've been sitting quiet in a room by themselves. The difference between that and the triage measurement is often striking and it's almost always uniformly lower.

Matthew: Right.

Paul: So, I think that just speaks to the importance of different environments and checking different context to make sure you have the right number.

Matthew: Yeah, which is probably why the hypertensive urgency, whatever that trial was from the ER, where they just let someone rest in a quiet room for 30 minutes and recheck the blood pressure-

Paul: [laughs] Yeah.

Matthew: -that did the job most of the time. But patients can go to validate *bp.org*, which is a website that is Dr. Cohen is involved with and our past guests also had mentioned and that's a place you can just look to see which blood pressure cuffs are recommended. And then the 24-hour ambulatory blood pressure monitor, I know some primary care offices are set up to send patients home with those. Personally, usually I've had to send people to either cardiology or nephrology to get that done. I'm not sure for you, Paul, if you have any tricks to getting a 24-hour monitor.

Paul: No, this remains a unicorn to me. It's something that I would like to exist, but I still haven't actually seen it myself.

Matthew: I used to get them all the time in a previous job and it's great. It gives you this like, how often are they in the red, how often are they in the green, and you can see it graphed out over time, so that way you can see if they're a non-dipper, are they higher when-

Paul: Exactly.

Matthew: -they're sleeping, or during the day, all that thing. It's great.

Paul: Well, this might be the time to talk about now. I think the other benefit of having home blood pressure readings, whether it's 24-hour blood pressure monitor or just out of office blood pressure measurement done with a home cuff that has been validated. Are there other classes of hypertension that do potentially diagnose that you have to have these home measurements? You have to have other office readings to see if you can make the measurements. So, obviously, talking about white coat hypertension, but then also masked hypertension. So, maybe I'll actually ask you to talk a little bit about both those things.

Matthew: Well, I'll take white coat hypertension, which Dr. Cohen said, "Classically, for her it's an older woman who's coming into the office and she thinks maybe, it's arterial stiffness and when they're a little nervous, their blood pressure spikes. But at home, she doesn't do home readings and typically, their blood pressure will be okay." You can have white coat hypertension and sustained hypertension, where you're on medicine for blood pressure, blood pressure is good at home, but in the office, it is really high or just someone who has normal blood pressure at home, not on any medicine, but in the office it's high and we do need to take that seriously. It does confer some increased risk, but not as much as someone who has sustained high blood pressure all the time. But Paul, what's the opposite of white coat hypertension and who gets that?

Paul: Yeah. We're taking normal hypertension out of the equation or treated hypertension. The other class is masked hypertension, which I forget exists sometimes.

Matthew: Yeah.

Paul: Trainees often do, too. I think Dr. Cohen said this is the present in 25% of the population, some alarmingly high number that made me think I should be doing a better job thinking about it. But this is the case, where you have someone who is normotensive in the office, but then actually hypertensive at home, which is the opposite of what we-- I think we have been trained to recognize and this has-- [crosstalk]

Matthew: It's not fair that that exists.

Paul: Right. There're a couple of reasons why it may exist, but it is not benign. This does warn more aggressive risk factor modification. The person who typically gets this is someone who probably needs that risk factor modification. Typically, a man who smokes tobacco, so the classic one, but then also alcohol use can also be a risk factor for, as well as some of the other metabolic syndromy stuff sort of impaired glucose tolerance, central obesity that kind of thing. All those things tend to lean themselves more towards masked hypertension, which you have to take seriously and you have to treat. You would never know it exists unless you have this home blood pressure reading.

Matthew: Yeah. We were talking about this earlier, I think for patients who just look like they should have high blood pressure, they have metabolic syndrome otherwise, but their blood pressure is weirdly normal in the office, that's someone I might ask to grab a couple out of the office blood pressures just to see, I have started to do that because I'm just like, “How are you not hypertensive?”

Paul: [laughs]

Matthew: You seem like you have all the risk factors. I would just recommend the audience knowing it exists is half the battle, I guess, Paul. Paul, let's say, we've made the diagnosis of high blood pressure. Now, I want to start my patient on a medication. how do you think about this classic ACE versus ARBs? I always thought they were just the same, but now, maybe we know something different. Tell the audience.

Paul: Yeah, this is one of my favorite points. For a long time, I’ve favorite ARBs over ACEs or ACE inhibitors I should say, just because I had the sense that they probably had a better side effect profile, but it turns out there was a relatively recent meta-analysis that looked at this very thing. All the things that we like ACE inhibitors for in terms of being nephroprotective and in terms of being good with systolic heart failure, ARBs do just as well, but in this meta-analysis, the ARBs were less likely to have adverse effects than the ACEs. Things like the ACE inhibitor associated cough, or angioedema, or even weirdly GI bleed, which is not one that I thought about.

Matthew: No.

Paul: It happens way more with ACE numbers than the ARBs. Now, I almost never start-- If I'm initiating a blood pressure medication, I'm thinking about angiotensin receptor blockade. It's always the ARBs now and I almost never started ACE.

Matthew: Yeah.

Paul: Yeah, and then in terms of which one to pick, I thought Dr. Cohen made some interesting points in terms of half-life and stuff. Do you remember some of her favorites?

Matthew: I do because this was so jarring to me-

Paul: [laughs]

Matthew: -because I was always just like ACEs and ARBs, just pick whichever ones covered, there's no differentiation between them. But she gave us some great pearls. Her preferred agent is olmesartan, which I will say to the audience, I know we've talked about olmesartan on the show before-

Paul: We know. [laughs]

Matthew: -only in the context of Olmesartan-induced enteropathy, which looks like celiac disease and is caused by olmesartan. I don't think it's super common, but you do need to warn patients about it. If they start to develop GI side effects or weird iron deficiency, they're losing weight unexpectedly, think about that as something going on. But olmesartan, she likes it because it's long acting and it does come in combination with amlodipine, which is a calcium channel blocker. So, that may be one of her go to meds in combination with other meds. Losartan, if you're like me, Paul, losartan, well, we're in the same state. I know you are-- The medication losartan is one of the ones that's often cheap. It's on the $4 formulary. I'm using a lot of losartan but it doesn't last a full 24 hours. Ideally, you dose it twice a day, which I was not doing before now. But sometimes, now, if I have someone on 25 or 50 of losartan and they're not getting that full coverage, then I might have them on it twice a day, which is not ideal, because you want once a day medication.

Paul: That's exactly my practice. Especially, if I have someone who's maybe just a little bit suboptimally controlled rather than increasing the dose of losartan to 50 milligrams, I'll just use say, 25 twice daily, and just take advantage of that, and use the way it's supposed to be used.

Matthew: Yeah. And then valsartan is the other one, Paul, that's on all the $4 formularies, and that seems to come in a lot of the combination pills. That one, she said, “The duration is not the problem there. It's the potency.” For the audience watching at home, Paul and I recording, but we also have two cats who are in the studio with Paul. So, Paul, is that Ally or Bella that's causing a problem or are they fighting?

Paul: No, that's Bella just passing out in the background.

Matthew: Okay.

Paul: It’s fine. It just adds-- Yeah.

Matthew: It's a great environment for the podcast. Paul's cats are always recording with us and I don't think we shoutout to them enough. Paul, back to valsartan.

Paul: [laughs]

Matthew: Valsartan, less potent. So, just be aware. Losartan, not lasting a full 24 hours, valsartan less potent, and Dr. Cohen said, if she has her druthers, olmesartan or even on Twitter afterwards, someone else asked her, she said, “telmisartan, candesartan, some of these other agents that have just better pharmacology and are a little more potent.” You can use those if you can get them and they're reasonably priced.

Paul: I think the other reason if I remember correctly and correct me if I'm wrong that she likes olmesartan is, because it's available in combination with calcium channel blocker which is a combination she likes, which might be a good chance for us to talk about. I know you have a very specific approach in terms of combination meds. I think you're a new convert now.

Matthew: Yeah, I think where this came from Paul is, I know the geriatricians have known this for a while that using two meds in and low dose can give you nice control and less side effects. My approach has been typically, I'll start a two meds at a quarter dose. Say 2.5 of amlodipine and 10 of benazepril, or take your ACE or ARB, whatever you're going to start them on, and start them both at a quarter of the maximum dose. If it's a person who's older, more frail, and you're just worried about how strong the medication is going to be for them or I might start two medications in combination at a half the maximum dose because you really get most of the bang for your buck at that half dose of the medication going up to the maximum dose of any blood pressure medication often has diminishing returns and they're more likely to get side effects, especially with amlodipine the edema is dependent based on the dose.

That's how I've started. Most of the time now, if someone's really far off target, if they're 20 points above goal, I'm going to start them on two medicines in combination right from the get go rather than start just one agent and take six months to get them to go. I'll try to get them to go right away with a low-dose combination. What about you, Paul? What do you do?

Paul: Yeah, you've talked me into it. I probably have a very similar approach. I will say that I probably actually will still do individual medications. Then once I find the sweet spot, I might switch over to the combination tablet. Yeah, no, I agree. I'm much less likely to try to max out one therapy in hopes of getting someone there unless they're really, really close because as you say the side effects tend to manifest more than the benefits do at the high doses.

Matthew: Treating blood pressure, I think what you really get into it, it's managing diabetes. There's more than one right answer, there's definitely some wrong answers, but starting someone over 100 of chlorthalidone and not checking a metabolic panel that would certainly be reckless. But I think most of

the time, you have some time to figure it out, make some changes. I always tell patients, most patients in the SPRINT trial, most patients in general just need two medications to get them at the goal blood pressure. That's why knowing that information and knowing that the low-dose combination works well. That's where I've gone to. In general, Paul, we know that lower is better. We're moving more and more towards these lower blood pressure goals. Certainly, if you can get there with a reasonable amount of medications, the patient's tolerating it without side effects. I'm trying to go for that 130/80 goal for most of my patients now.

Paul: Yeah. I think one of the places where this came up is talking about blood pressure management in younger patients, which I think we see more and more often.

Matthew: Yeah.

Paul: I think with the new ACC guidelines, there's the class 1 hypertension where you calculate their 10-year risk using the risk calculator. But of course, that's only made for patients between the ages of 40 and 70. And so, we have this non-applicable group to even use that with and what do you do with these younger patients who nevertheless meet the criteria for hypertension. Dr. Cohen made the point that she, as far as we can tell and most of these, as you say, lower is better, and it just prevents more longer-term outcomes. She said, "No one's going to run this study on 30-year-olds [chuckles] with antihypertensives and following them out for 30 years." It's not something that you're going to see.

But probably, tighter control over a longer period of time is going to prevent more cardiovascular bad outcomes. She has this conversation with younger patients says, "Listen, the evidence is a little bit sparse, but if it was me, I would probably want tighter blood pressure control," and then has the conversation moving forward like that. This is probably another group. I'll probably be more aggressive moving forward, or at least having more forward moving discussion about blood pressure control rather than just checking in perpetuity, which had been my MO up until this point.

Matthew: Right. Yeah, because there's all this inertia if someone's not yet on a med or someone's on a med, and you keep getting back those blood pressures in 140 range/high 80s or 90s, and you're just like, "Ah, it's probably fine. I'll just keep it riding." But I do think, especially if I think someone's high risk, I try to be more aggressive, especially if they're okay with starting a medication and there're not lifestyle changes we can make to get the blood pressure where we need to be. So, I have become more aggressive about treating blood pressure. Of course, with close monitoring and making sure that I think the patient can handle the stricter target.

Paul, we dd talk about one other thing that this is a quick point to make, she mentioned that hydrochlorothiazide, probably a lot of the times we're dosing it incorrectly. It comes in combination pills many times in a 12.5 milligram dose and she said that's practically a homeopathic dose for a lot of patients, probably, 25 milligrams is a starting dose of hydrochlorothiazide for the majority of patients. What about chlorthalidone, Paul? I know this is a medicine you love and this is not quite as straightforward.

Paul: Yeah, no, chlorthalidone, it is a medicine I love. It is pretty potent and you do run the risk, particularly of hypokalemia, which I've seen, if you're not careful. It's something and we've talked with Dr. Topf about this too. Once you started, you should probably do fairly close follow up in terms of just checking electrolytes and making sure that everything's where it's supposed to be. But that's one that probably you'd be better off maybe even starting at 12.5 as opposed to hydrochlorothiazide, I think I'm not sure.

Matthew: Yeah.

Paul: But I seem to remember being told that the dosing of those two is equivalent. Like 25 of hydrocortisone is the same as 25 of chlorthalidone.

Matthew: No.

Paul: That seems to not actually be the case.

Matthew: Yeah.

Paul: Yeah.

Matthew: Yeah, and she made a point, it's more potent, so typically I almost think of chlorthalidone is being twice as potent. Essentially, chlorthalidone, unfortunately, it doesn't seem to come in a 12.5 milligram tablet. Most of the time, you either have to tell the patient to cut a 25 milligram chlorthalidone in half and take half a tablet every day or you could tell them it's so long acting, you could actually tell them to start off with 25 every other day, and then you could always go to daily if you decide you want to increase the dose, but that would be the same effective dose if you did 25 every other day instead of half a tablet a day. So, chlorthalidone is definitely one that I've been using a lot more of. I wish it came in more combinations and that's probably the limitation I think for it being used more often. Yeah, go on.

Paul: I was going to say, let me employ one of your teaching methodologies as it transitions forward if you're okay. Since we're talking about chlorthalidone, this feels the right chance to say, if you have someone chlorthalidone-- Now, let me say this a different way. If you have a patient with chronic kidney disease, I've been taught that chlorthalidone is completely off the table, it is not even going to affect the parts that it needs to affect. You may as well not even use these thiazide diuretics in chronic kidney disease. They are in fact worthless and there's probably no recent data to even support their use. Is that correct, Matt?

Matthew: I love that this is catchy gone, Paul. It's such a great teaching method.

Paul: [laughs] It feels great.

Matthew: Because that would be wrong. Of course, the CLICK trial came out in late 2021, I believe. It was by Agarwal, et al. We talked about this with Dr. Cohen and this was also covered, I believe in the Digest, our newsletter. Chlorthalidone, actually was effective in lowering blood pressure. I think it

lowered blood pressure by about 10 points in these patients with CKD. They found it was safe to do this. We're still waiting for long-term outcomes data from this, but patients with CKD, they tend to be a little volume overloaded, and it makes sense that this would work, and help to control the blood pressure.

In the CLICK trial. I think something probably 60% of patients were already on a loop diuretic. Even if they were already on a loop, it was okay to do this. What Dr. Cohen made the point of is like, “Yes, you can use it especially if you're not a goal and you're thinking okay, this person is on an ACE or an ARB. What's my next agent? You can use diuretics in patients. You just have to monitor them.” She likes as far as loop diuretics go, so chlorthalidone to be the thiazide diuretic that to go to. Loop diuretic, she mentioned torsemide 20 milligrams is probably her go to because it's a longer acting loop and it could be dosed once a day as opposed to bumetanide or furosemide, which have to be dosed twice a day. I would consider all these in play now for my patients with stable CKD, where I'm trying to get better blood pressure control especially if they have edema, I think then it makes sense. But Paul, what about ACEs and ARBs? How can we use those in CKD? Because surely that sounds way too dangerous.

Paul: It's funny. I was going to turn that around and ask you that, too.

Matthew: [chuckles]

Paul: First of all, I just want to make the point that Dr. Cohen, I think used the term wildly underutilized in terms of diuretics and chronic kidney disease. But yeah, no, I was going to ask you, did you say a chronic kidney disease patient on an ACE or an ARB? Surely, that is malpractice-

Matthew: [laughs]

Paul: -because that's the medication that will send them screening over in end-stage renal disease, and you'll probably end up starting hemodialysis shortly thereafter. Perhaps, you misspoke.

Matthew: I didn't-- [crosstalk]

Paul: [crosstalk] ACEs and ARBs in chronic kidney disease.

Matthew: I did not. I thought this was crazy. Part of the case we gave her was patients on hydralazine and betablockers and she's like, “Actually, I don't like hydralazine. It can actually worsen edema, it can make the blood pressure more labile.” So, it's not her choice. She actually tries ACEs and ARBs and you would expect a creatinine bump of up to 30% and that's okay if it happens. Paul, talking a little bit about the physiology here, the physiology is that essentially you are taking away some of that hyperfiltration, you're relaxing the outflow from the glomerulus, so that you're getting a little bit less of that hyperfiltration taking some of the stress off of it. You'd expect with that decreased filtration that you'd have a little bit of increase in creatinine and that's okay.

If the increase is more like 50%, you got to think about bilateral renal artery stenosis and maybe those are patients that is not a good choice for, but creatinine bump up to 30% is okay. Paul, what about

hyperkalemia, though? How can we handle that because I'm worried about hyperkalemia by patients with CKD, if I'm using an ACE and an ARB?

Paul: I think is a valid concern, especially depending on what combination of diuretics you have those patients on. But Dr. Cohen makes the point that patients with chronic kidney disease, probably tolerate a little bit of a higher potassium than patients who do not have chronic renal insufficiency. She allows a K of up to 5.5. She's fairly comfortable with letting patients ride it. She doesn't panic until over five and a half, I think if I remember her potassium threshold. So, good medications nephroprotective. If you see the expected increase in creatinine that actually means they're working the way they're supposed to keep an eye on the K as long as it's less than five and a half, you're probably doing the right thing, if I followed what she was telling us.

Matthew: Yeah, that's exactly it. This was great. She gave us very clear targets, and parameters, and gave us license, Paul with close monitoring to use some medications because for CKD, I was just completely at a loss. I had all these patients I was seeing with CKD, and I wasn't really sure what's next, and you can't always just rely on a specialist to take care of them. I like to know what to do myself. Paul, I actually think for interest of time, let's move on to the next episode, which is number 326 cardiorenal syndrome. This was part of NephMadness, as I said with the great Dr. Joel Topf, a nephrologist and Dr. Sadiya Khan, a cardiologist, and with graphics and production again and by Malini Gandhi, wunderkind Malini Gandhi.

Paul, to start us off here, the pathophysiology of cardiorenal syndrome, I always thought it was this poor forward flow, but actually, it turns out that venous congestion, this venous back pressure on the kidney is actually, that seems to be more important because the cardiac index is often normal in these patients or not poor enough to explain the rise in creatinine in cardiorenal syndrome. So, venous congestion, which is going to speak to the treatment, which is diuretic therapy. This was surprising to me. Paul, you probably already knew all this.

Paul: No, I had not and it was exciting to hear frame it that way, because also Dr. Topf makes the point, good news because if you're talking about poor forward flow, then we're in pressor land that now we're outside of the realm of things that I am or inotropes I should say, and now, we're outside the realm of things I'm comfortable messing around with.

Matthew: Right

Paul: But venous congestion. internist do that all day long.

Matthew: Yeah.

Paul: It's just a matter of fixing that, then we then we actually have an answer for that.

Matthew: Right.

Paul: This was an exciting way for me to think about it and it makes more sense. In retrospect, I'm thinking of all the patients that I've treated for heart failure by decongesting them very aggressively.

Matthew: Yeah, if patients are frankly hypotensive, obviously, that's going to affect the kidneys, but that's not what we're talking about. We're talking about the patient that presents with decompensated heart failure and their creatinine's up, they're not hypotensive. This is believed to be the mechanism. And then, Paul, we talked about permissive hypercreatinemia, which I think is the main take home point of this is that, that creatine bump that we all fear when we're diuresing somebody with acute decompensated heart failure is expected, we should expect it and actually it doesn't mean we're done. Because I don't know about you, but at some point in my career I was taught, "Diurese them until they're creatinine bumps, then stop and you're done." But what did Dr. Khan and Dr. Topf tell us about that?

Paul: Well, I think one of the things that I appreciate it was thinking about creatinine is almost analogous to hemoglobin. I think we're used to seeing volume contraction, where the hemoglobin goes up as you diurese someone. You're just like, well, this is contraction. But you can see the same thing with your creatinine. Someone who comes in congested volume overloaded might have this artifactually low creatinine if I'm understanding correctly, and then as you diurese all the extra volume off, then you're actually seeing them approach, which is probably closer to their true creatinine. So, I found that a little bit reassuring.

Then, more to the point, I think that you're making is that the number itself is not probably what you should be fixating on is, how are they feeling, are they doing better, how's their breathing, do they just overall—what does their JVP look like? clinically, how are they doing? It seems more and more important that you actually drive these patients out appropriately, and get them all the way back to their baseline, and not 75% of the way, because the patients that you don't finish the job are the ones that probably come back to the hospital. So, not getting quite so excited about the creatinine and getting more excited about their actual clinical status.

Matthew: The evidence or this clinically, the dose trial, they actually showed improved outcomes. When they did a postdoc analysis, they saw that the patients who actually had a creatinine bump seemed they had better outcomes and the speculation was probably, because we did a better job diuresing these patients and that's why those patients did better. We need to get these patients decongestant. Use your clinical exam and a bunch of other things. Don't just look at the creatinine and say, I'm done.

Then Paul, the other thing that they mentioned is that if the patient's not hypotensive, you don't necessarily need to stop the ACE, the ARB, the SGLT2 inhibitor, if someone comes in with a slight creatinine bump, and they have heart failure, and they've been already on these medicines at baseline. Clinical picture, look at their blood pressure, look at the creatinine, and all that stuff. But you don't necessarily have to stop these and if you are going to stop them, make sure your resume them on discharge, because these medicines are very important in the long-term and that's a common mistake that both of our guests mentioned that they see made.

Paul: Yeah, Joel made the point and just saying it explicitly, if someone is coming in with this picture that we're describing, where their volume overloaded, we know the problem. This is not prerenal azotemia. They are volume congested. So, there's no reason to stop the ACE or the ARB. You need to do the thing which is decongest them, unless, of course the blood pressure is not tolerating their antihypertensives.

Matthew: And part of a topic that goes along hand in hand with this is this concept of diuretic resistance, which Joel told us about way back on Episode 31, Diuretics and Leg Cramps, Paul. This is where we talked about pickle juices. It's a Curbsiders' classic.

Paul: I have used that successfully for multiple patients-- [crosstalk]

Matthew: Yeah. Basically, Dr. Topf's approach to diuretic resistance is, when you're giving a diuretic to a patient with heart failure you really want to assess the response to that dose that you gave, because for loop diuretics, there is a threshold that you have to meet. For IV versions, it should be within minutes, certainly, within 30 minutes that they start to put out urine if you hit the right dose. If you're giving it orally, it should be within hour, two hours depending on the agent. I don't wait six hours, I go back, and I ask in 30 minutes, if it's IV or I go back in an hour or two if it's given orally, and I check like, "Have you been making urine?" Patients should be complaining about their urine output, Paul, if you're adequately diuresing them. So, that was one of the main things. Make sure you hit the threshold.

Paul: It's such an important point. If you have someone who's not making urine with 40 milligrams of furosemide, doing 40 milligrams furosemide twice daily is still not going to achieve what you're trying to do. You have to get them peeing and then you can increase the frequency.

Matthew: Yep. Step one, meet the threshold. Step two, if you meet the threshold, but you're still not meeting your overall output goals for the day, you are not taking enough weight off, then increase the frequency to two or three times a day or you might even put them on a drip. And Paul, what was the point of the drip? I haven't used those as often, but I know Dr. Topf gave us some great points about that.

Paul: Yeah, if we get to drip planned, I'm at the point where I probably called in the cavalry at this point.

Matthew: Yeah.

Paul: But some are bolder than others. But the point that doctor taught me about the drip is, there's nothing magical in the mode of delivery other than the fact that can get the patients to a much higher dose of diuretic, I think was his point. I think it's not so much the fact that it's just continuous, but the fact that you're receiving these higher doses that are hard to achieve with the intermittent dosing if I'm understanding his point correctly.

Matthew: Yeah. Then if you've met their threshold, you've increased the frequency, you're still not hitting your goals, then we're in sequential nephron blockade territory, Paul, where you're adding on things like a thiazide diuretic to block a different part of the nephron. Other things you can think about

are acetazolamide, the mineralocorticoid receptor antagonist like spironolactone or the newer SGLT2 inhibitors, which I haven't seen used as much in the hospital, but Dr. Khan was saying, she's in a very specialized practice for heart failure. She was mentioning that she has seen them started on inpatients during their stay as part of the sequential nephron blockade.

Paul: Right. She did make the point that's typically instead of getting the patients out the door on a good guideline directed regimen. So, it started inpatient appropriately, but probably not as part of the acute decompensation treatment if one would think [crosstalk]

Matthew: Yeah, that's a good point, that's a good point. Yeah, I should have made that distinction as well for the SGLT2s, but the rest of them would be the thiazides, the acetazolamide, the MRAs those were definitely part of the inpatient. And then, Paul, what's the big gun one? I have not seen this done in the wild.

Paul: [laughs]

Matthew: I only just learned about this when reviewing for NephMadness, this hyper diuresis, Paul. What is that about and have you seen it done?

Paul: I have neither seen it nor will be bold enough to try it myself.

Matthew: [laughs]

Paul: Maybe it'll be the standard of practice someday-- [crosstalk]

Matthew: Not going to that on an outpatient in clinic? [chuckles]

Paul: Yeah, sure. Why not? Step one, start my infusion clinic, step two, start with hyperdiuresis, and step three, wait for the subpoena.

Matthew: [laughs]

Paul: But the idea is that you give these patients hypertonic saline, while still giving them the loop diuretic and the idea, there's some hand wavy stuff and I think Joel would forgive me for saying that about maybe resetting the thermostat or turning off the renin-aldosterone-angiotensin system, but just confusing the body enough that it starts responding to diuretic treatment was how I conceptualize it. So, some people have looked at it, but I think it was an Italian study, Joel was saying.

Matthew: Yeah, I don't remember the country the study was from. We'll put some links in the show notes here. But it has been looked at-

Paul: I'm 90% sure.

Matthew: -and I'd be curious, people on Twitter, have you seen people using hypertonic saline as a Hail Mary for patients with acute decompensated heart failure? I'm sure there's some people out there in the audience who have seen this in the wild. I just haven't seen it. I thought it was super cool. Paul, I guess, the last thing about diuretics that is probably worth mentioning, bumetanide versus furosemide, any differentiation there that you wanted to point out to the audience?

Paul: Yeah, the age-old battle. It's hard to know. I think there's probably some institutional variation. I tend to see people reach for furosemide a little bit more frequently than it seems to be changing over the past five years or so. But for no good reason that I can tell furosemide in terms of oral bioavailability is wild. It's anywhere between 10 and 90 something percent. It is not very consistent as opposed to bumetanide, which has fairly high bioavailability that is consistent. If you're worried about particularly someone who has HFpEF or is someone who's holding on to their fluid in their abdomen, which I think we see a fair amount of time and have underlying gut edema, that might be a better choice because of the better bioavailability.

Then, the other point is that bumetanide, the levels are not quite as dependent on GFR. You can make sort of minor dose adjustments as opposed to these big swings you have to take with furosemide. It's just a little bit less nerve racking to deal with in my estimation. I think those are probably the two big points. In IV land probably, this stuff doesn't matter as much because the bioavailability is a non-issue. From an oral outpatient regimen, those are probably the big-- [crosstalk]

Matthew: Yeah, if you have the right patient, and they're in heart failure, and they're on furosemide, and you're trying to keep them out of the hospital, maybe switching to bumetanide, might be something you can try. And then, Paul to bring it home, I think the last point we want to make is just a quick one about cardiac biomarkers. Because Paul, I'm going to use my fame teaching method where I say the wrong thing-

Paul: [laughs]

Matthew: -and then you correct me.

Paul: Great,

Matthew: Paul, I don't pay any attention to the troponin or the BNP in patients with CKD because that's just meaningless. You can't really interpret it. How do you approach it?

Paul: No, I've made this joke before, but it's one of my favorite things is to check a lab that you'll then completely disregard and just explain with some hand wavy stuff. It drives me nuts. This is my own personal hobbyhorse. I appreciate bringing this up. When someone has an elevated troponin in the setting of chronic kidney disease and it's just waved away is like, well, they have CKD. So, of course, they have an elevated troponin, which if you take three steps back is just an absurd thing to say. You can make the point that that is probably nothing immediately intervenable. These are not someone who needs to be rushed off to the cath lab necessarily.

But it's also not meaningless. It's a poor prognostic indicator. We know that patients with chronic kidney disease, cardiovascular diseases is the major cause of death in these patients. I think it's helpful in terms of least risk stratifying. You should take it seriously, even if you may not be doing something exciting like wheeling through doors into the cath lab or something like that. You should still pay attention and pay notice to them. That's my thought about troponin. I think BNP, I know sometimes they're often discounted in terms of patients' chronic kidney disease that BNP might also be chronically elevated. How do you approach that? How do you deal with this chronic elevation that you sometimes see? Does that make [crosstalk] or how do you use it.

Matthew: I didn't have a great approach to this beforehand. I often would expect it to be elevated and not be surprised when I see an elevated number. Dr. Khan mentioned that she actually likes to look at the relative change compared to prior values that she has and she finds that helpful. I think that's probably the way that I'll be using it. It is for my patients with CKD just looking at this relative change in it. We're not suggesting people trend this during a hospitalization to figure out when the person's decongested. I wish it worked that way. It doesn't work that way, but it is-- [crosstalk]

Paul: But nothing does.

Matthew: It could be helpful to see the relative change from prior times when the patient was maybe doing better. But that's it. A lot of cardiology tonight, Paul. A lot of great pearls. People can go back and listen to the full episodes if they haven't heard them, because certainly, we couldn't do them go over every single thing, but this is just a little taste of what those episodes were like.

Paul: They were so good. Everybody, I cannot stress how much I hate the sound of my own voice and I hear the things I say I'm like, "What a pretentious--?" [crosstalk]

Matthew: [laughs]

Paul: The episodes are so great, the guests are so knowledgeable, and the teaching points, they make are so solid. It really is worth a listen, if this was helpful to you.

Matthew: And with that, Paul, will you take us to an outro?

Paul: Happy to do so. This has been another episode of The Curbsiders, bringing you a little knowledge food for your brain whole.

Matthew: Yummy.

Paul: [laughs] Great. A little bit too much confidence really.

Matthew: [chuckles]

Paul: Get your show notes at *thecurbsiders.com*. While you're there, 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.

Matthew: And we're committed to high value, practice changing knowledge. We want your feedback. You can subscribe, rate, and review us on Apple Podcasts, or on Spotify, or you can send an email to *thecurbsiders@gmail.com*. Reminder, that most episodes are available for CME, the two individual episodes we talked about number 321 and number 326 have individual CME available for them. I'd like to give a special thanks to our producer for this episode Dr. Malini Gandhi, who did both of the episodes we talked about, and to the production team at Pod Paste, who produced and edited this episode. Elizabeth Proto runs our social media, and of course, the great, Stuart Brigham composed our theme music. Paul, with all that until next time, I've been Dr. Matthew Frank Watto.

Paul: Oh, spectacular as always, Dr. Watto. And as always, I remain Dr. Paul Nelson Williams. Thank you and goodbye.

[music]

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