

Announcer: Welcome back to the Mayo Clinic cardiovascular podcast series, interviews with the experts. I'm your host, Sharonne Hayes. I'm a non-invasive cardiologist and vice chair of faculty development and academic advancement for the Department of Cardiovascular Medicine here in Rochester, Minnesota. Today I'm joined by Dr. Jacob Jentzer. Jake, who is assistant professor of medicine and chair and director of the CICU research here at Mayo Clinic in Rochester. And that's where he spends most of his clinical time in the cardiac ICU. So today, a fitting topic, recognizing shock, cardiogenic Shock. So cardiogenic shock is a major cause of death and disability for patients with acute coronary disease or cardiac disease, and early recognition of cardiac shock is essential to allow timely intervention and avoid complications. So, Dr. Jentzer is gonna share with us some of the contemporary research and evolving definitions as well as current practice that can facilitate the recognition of subtle manifestations of cardiogenic shock with the goal of improving patient outcomes. So Jake, let's start with defining cardiogenic shock for us, and why is it so important for us to be paying more attention to it now?

Dr. Jacob Jentzer: So to begin with, cardiogenic shock is a very dangerous condition with after diagnosis. The short-term mortality in about the next 30 days is often up to 40 to 50%. So it's, it's definitely a, a deadly condition or the years the definitions have evolved. The AHA definition is extremely broad to try to be inclusive and essentially says that any cardiac disorder that leads to ineffective cardiac output resulting in inadequate supply demand, a balance of oxygen to the tissues and organs despite adequate preload would qualify as cardiogenic shock. There's a lot of hemodynamic definitions that are very nuanced, and I think we've come to recognize that those are overly restrictive and there's a lot of patients out there who have early or mild forms of cardiogenic shock that are still at substantial risk, but don't meet those classic definitions.

Dr. Sharonne Hayes: So it's under recognized. I, I'm, I'm, and, and now the definitions, and I'm assuming you're gonna share with us some evidence about why finding it out early is better for our patients, but what are some of these common manifestations of cardiogenic shock that we should be looking out for?

Dr. Jacob Jentzer: So when I think of cardiogenic shock, I try to think of the cardinal manifestations that are shared by all forms of shock. And then once I recognize that that shock is present, then I try to think about is it cardiogenic or could it be a different etiology like sepsis? So the cardinal manifestations of shock all depend on recognizing tissue and organ hypoperfusion. And there's both clinical findings as well as laboratory findings that help pin down from a clinical standpoint. Some of the world's experts in shock have summarized it very, very nicely. You can look at the brain and see evidence of mental confusion or depressed mental status. You can look at the skin and see evidence of delayed capillary refill or even modeling and, and li Vito in some extreme cases. And you can look at the kidneys and see impaired kidney function or specifically low urine output. From the lab standpoint, there's a lot of different end organ manifestations that can be seen throughout the course of shock. I mentioned kidney manifestations, elevated kidney biomarkers, BUN creatinine. Also you can see evidence of liver injury. But one of the most important markers that should raise suspicion that shock might be present is an abnormal lactic acid level. And so metabolic acidosis and specifically lactic acidosis is in many ways part

and parcel of the definition. So those are the, the types of things you might see in your patient with heart disease that might lead you down a pathway to think the patient might have cardiogenic shock.

Dr. Sharonne Hayes: You've talked about all these manifestations, brain, kidney and others, but you don't talk about blood pressure. So can somebody have cardiogenic shock with a normal blood pressure?

Dr. Jacob Jentzer: So my, this is an area where a lot of experts differ. My personal belief is the answer is yes. Many patients who meet all the other definitions of cardiogenic shock, including having low cardiac output and lactic acidosis and end organ hypoperfusion, many of them actually do have initially a normal blood pressure. This has been known for quite some time dating back to some of the original clinical trials in this field. Some people prefer the term preshock, but I don't, I think preshock is a different situation where the patient is hemodynamically unstable or as some form of hemodynamic compromise, but is still able to maintain their organ perfusion. And I think that's a state that often deteriorates to shock. Now, some of my own research has suggested that patients who have hypoperfusion but are preserved blood pressure, who I call normotensive shock, have worse outcomes than those who have low blood pressure but don't have hypoperfusion. And so I call those preshock, and then the patients who have both manifestations, they're hypotensive and they have hypoperfusion, they do even worse. And most of the patients that are initially normotensive will develop a drop in their blood pressure. So the way that I view this condition is this is an early manifestation of shock where patients have some preserved compensatory mechanisms, the same, you know, cardiovascular reflexes that preserved blood pressure that are still working, but those won't work forever. And if you fail to recognize and adequately treat that patient, they typically will deteriorate and develop the classic manifestations of shock, and by then it might be too late to intervene.

Dr. Sharonne Hayes: And can you just give us, I mean, really high level, this whole, we're talking about recognition, but the importance recognition is because we actually have effective treatments that I presume if initiated early would improve outcomes. Can you tell us just a little bit about what, why we're looking and what is the important things that we're going to be doing?

Dr. Jacob Jentzer: So this is a, a very challenging area. And the reason that I say that is the majority of recent large scale randomized trials published for patients with cardiogenic shock, established cardiogenic shock actually haven't really shown a substantial improvement in outcomes. And so this is indirect evidence that perhaps we're intervening too late, and by the time a patient develops manifest cardiogenic shock to the point where they are clearly recognized and could be enrolled in a clinical trial, in some cases it's actually too late for, for standard interventions to benefit them. In general, the most reliable treatment for improving outcomes in cardiogenic shock is early revascularization for patients who have acute myocardial infarction. And so that dates back to really the first high quality randomized trial in cardiogenic shock, which was the aptly named shock trial. And so when they looked at the randomized patients to either early revascularization plus optimal medical therapy or just optimal medical therapy with or without, you know, delayed revascularization, and they found that the patients

in the early revascularization group did better, particularly over long term, and the ones that were the earliest of all had the best outcomes. So that is, again, pointing towards early action is better than late action. And there's a lot of belief in the field that as the shock state is sustained and the longer it goes on, it becomes self-perpetuating and patients often develop this downward spiral. And so at this point, there's not a clear answer for how to rescue patients from that downward spiral. There are a lot of treatments that can be used, but when they're applied broadly across populations and clinical trials, they haven't shown dramatic benefits.

Dr. Sharonne Hayes: Yeah. So I guess we'll pivot then to why it's so important to recognize and what research are you and your colleagues doing to help us better understand and recognize early signs of shock?

Dr. Jacob Jentzer: So I think, you know, the emphasis on early recognition in, in some ways is not, doesn't have the evidence base that I would like. I think that there's a lot of indirect reasons to believe that it should be true. I mean, it has face validity. The earlier you intervene in a severe illness, you know, the better the patient might do, particularly if, you know, you can see evidence that the patients develop worsening organ function when they have delayed treatment. The research that I'm doing really engages with several members of the writing group on the Sky Shock Classification Scientific statement. And so what I want to emphasize about that is it, it's a fairly new concept introduced about five years ago, and really emphasizes that patients with acute cardiovascular disease exist on a spectrum. And there are those patients who are hemodynamically stable and despite having acute cardiovascular disease, are actually doing quite well. But if something were to happen to them, they could be at risk of shock. And so the sky classification grades patients between A and e, A being the lowest risk, the at-risk patients who don't actually have shock, and then it, it goes up in a stepwise manner. B would be the patients with hemodynamic instability and pre-shock. C would be patients who have hypoperfusion and therefore shock and require an intervention more than just a little bit of fluids. D would be a patient who's deteriorating, who gets worse despite that initial intervention, and E would be a patient in extremis with severe refractory shock. And although we think of this as in a stepwise manner, it's actually a spectrum of illness. And so the hope is that as we get better at, at recognizing early shock, we can start taking action in that transition state between B, pre-shock and C classic shock, or in the earlier stages of C before you get to D and deterioration. And so I've worked with several of the experts in this field from other institutions to demonstrate that this is a very useful approach to providing risk stratification. And you can very clearly show that in lots of different populations with acute cardiovascular disease, particularly those in the, in the cardiac ICU that I care for, that there are dramatic differences in survival outcomes between these stages. And so it, it is again, indirect evidence that the patients who stabilize in the earlier or milder forms of shock do much better. And the hope is that we can act earlier to, to keep patients from progressing because we know that progressions associated with poor outcomes. And so I've, I've done a lot of outcomes research in this field. I think the next step where is where I'm hoping to collaborate with some of the researchers who have engaged in the large scale clinical trials to see whether we can actually show evidence that the treatments that were studied in those randomized trials, for example, mechanical circulatory support devices, which many people think are, are a potential, you know, next level treatment strategy for patients with cardiogenic shock. We wanna see whether

potentially using those devices earlier in the disease course might be associated with better outcomes than using them later. And so there's a lot of really exciting areas where we can expand this outcomes research and try to engage multicenter collaboration to identify better strategies.

Dr. Sharonne Hayes: Oh, well, thank you for sharing that and kind of looking toward the future. But I also know that you and the team have put into place in our own CICU some mechanisms to and systems to help us without such sort of an early warning system for shock. Can you tell people about the system as well as how it's being used and, and I, I guess what kind of validation it has?

Dr. Jacob Jentzer: Yeah, this, this is something I'm really excited about. I, I've, I've put a lot of, of my own time into it collaborating with our, our current outcomes research center here at, at Mayo Rochester, as well as some really terrific colleagues at, at Mayo Florida. So what we've actually done with, you know, as, as in many ways a labor of love is we have translated the Sky Shock Classification into our electronic health record. And so when patients at RO at Mayo Clinic are admitted to a cardiology service, they're auto-enrolled in what's called a care path. And what this does is that it takes their available health record data and it assigns them to a sky shock stage. And so hopefully most patients start and stay in stage a some of course will progress in, in either a predictable or in some cases unpredictable fashion to higher grades of shock. And what we do in Rochester is we actually work, we have a really terrific advanced practice provider team in our cardiac ICU. And when a patient outside of the cardiac ICU on one of the cardiology services triggers this sky shock alert that says, you know, hey, they may be in shock, our advanced practice providers actually go see them at the bedside. They, they collaborate with the, the primary team that's already taking care of them, and they have a structured assessment and they work with the primary team to decide whether the patient in fact does have cardiogenic shock because they could have something else that, that masquerades like sepsis. They think about what are, what is the right thing for the patient? Is that someone who probably is on the mend and really they're actually headed in the right direction and and they will do just fine in their current environment. Or is that somebody who's deteriorating, who might need escalation to the cardiac ICU? And we have order sets that can help with the evaluation and management of patients at each stage along that sky shock continuum. And so once they're in the cardiac ICU, the, you know, we still will stage them. And if we see somebody who is deteriorating, for example, if their lactic acid level is rising despite therapy, that's a big warning sign and we get alerts, I actually would get paged for that, which would give me an opportunity to work with my work with my team to figure out what more could be done for that patient. And so it's, it's really a very exciting area and we're, we're trying to determine whether this is something that could be useful outside of the confines of a cardiology practice. There's a lot of other inpatient practices that have patients that are re at risk of, of shock. There are also other healthcare facilities within the Mayo Clinic Health system where having this type of early warning system could really, improve processes of care.

Dr. Sharonne Hayes: Yeah, I can really see that one because if it was disseminated in less well resourced inpatient areas, critical access hospitals, that to be able to have that early warning system and, and get

the patients to where they might get a higher level of care. How long have you been using, how long has this process been actually been used clinically?

Dr. Jacob Jentzer: Gosh, it, it seems like it's been forever, but it certainly hasn't. I think we've, we've been going through different, as they say, alpha versions and beta versions for about three years. Yep. And so our, our contemporary version has been, was fully active for the entirety of 2023. And our hope is to use that 2023 data to allow us to improve upon the algorithm. And my own personal research is actually related to taking one step beyond early detection, and actually to identify those patients who are in stage A or stage B who are very, very numerous and most of whom do fine, but to identify those ones that are likely to progress. And so to use a predictive analytic approach using machine learning to identify those few who deteriorate so that we can potentially identify them earlier, because at least in the Mayo Clinic cardiology practice, the number of patients who meet criteria for pres shock is, is tremendous. And if we were to get an alert for every single one of those patients, it would immediately overwhelm our system. And so we don't, we don't take that step, but that means that those, that minority of those at risk and, and pres shock patients who do progress, we don't necessarily act until they already have Yeah. Evidence of shock. So the hope is that we can, you know, take advantage of some of the resources at Mayo Clinic, potentially ideally within the current outcomes research center to predict which of those few, which of those many are gonna progress. And so that's really the next step here, is to create a, a package that not only does early identification, linked into improving processes of care, but also can predict. And the hope would be that if a patient is at high risk of progression, that you could do many of the same good clinical practice steps as you might with a patient with early shock.

Dr. Sharonne Hayes: This is really, really exciting and I really wanna thank you for sharing this important problem, but also a little bit of hope in terms of being able to intervene, recognize, and intervene. So thank you very much, Jake.

Dr. Jacob Jentzer: Well, it's been a pleasure speaking with you as always. Thanks for inviting me. This is, I've enjoyed this very much as well.

Dr. Sharonne Hayes: Thank you. So this wraps up this week's inter episode of interviews with the experts, and I'd like to thank Dr. Jentzer for joining me today to discuss this important topic. We look forward to you joining us next week for another interview with an expert. Be well.