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Acute Kidney Injury in Cirrhosis: Multidisciplinary Decision-Making

Announcer:
Welcome to CME on ReachMD. This activity, titled “Acute Kidney Injury in Cirrhosis: Multidisciplinary Decision-Making” is jointly provided by CiME and NKF and is supported by an educational grant from Mallinckrodt Pharmaceuticals. Before starting this activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives. Here’s your host, Dr. Nancy Reau.

Dr. Reau:
This is CME on ReachMD, and I’m Dr. Nancy Reau, Professor of Internal Medicine and Section Chief of Hepatology at Rush University Medical Center in Chicago. Joining me to discuss considerations for diagnosing and treating acute kidney injury, or AKI for short, in patients with cirrhosis are doctors Kevin Regner, Andrew Allegretti, and Ram Subramanian.

Dr. Regner is Professor of Medicine, Division of Nephrology and Interim Chair of the Department of Medicine at the Medical College of Wisconsin in Milwaukee.

Dr. Regner, thanks so much for being here today.

Dr. Regner:
Happy to be here.

Dr. Reau:
And Dr. Allegretti is the Director of Critical Care Nephrology in the Division of Nephrology at Massachusetts General Hospital and an Assistant Professor of Medicine at Harvard Medical School.

Dr. Allegretti, it’s great to have you here.

Dr. Allegretti:
It’s a pleasure to be here. Thanks.

Dr. Reau:
And finally, Dr. Subramanian is a Professor of Medicine and Surgery at Emory University as well as the Medical Director of Liver Transplantation, and Director of Liver Critical Care Services at Emory Transplant Center in Atlanta, Georgia.

Dr. Subramanian, welcome to you.

Dr. Subramanian:
Glad to be here.

Dr. Reau:
So, we’re going to start with some pretty hard questions, and I want to hear a lot of dialogue. We’re going to start with you, Dr. Allegretti. Can you give us an overview of the different etiologies of AKI in patients with cirrhosis?

Dr. Allegretti:
Sure. This one, hopefully, is not a hard question. So, our group just published a paper on this topic. We took 11 different centers from across the US and looked at exactly this question. What kind of AKI are we seeing in the hospital in these patients with advanced liver disease? And the breakdown, at least in our experience, in the United States, was predominantly prerenal injuries.

So, this would be a functional kidney injury that reverses with fluid resuscitation. Only about 1 in 8 patients had hepatorenal syndrome, AKI, or HRS, which, in part, is the nature of the disease. It's a bit more uncommon. It is a diagnosis of exclusion, which I'm sure we'll get into in a bit, and then a larger percent, maybe 30% or so, acute tubular necrosis. So, this would be some kind of ischemic or nephrotoxic kidney injury with a smaller percentage of other etiologies like glomerulonephritis and urinary obstruction and things like that, making up a small minority of the remainder.

Dr. Reau:
Now, how about if we turn to the intensive care unit. Is that still going to be true in the ICU?

Dr. Allegretti:
I think when you think about the intensive care unit, and you've got a group of patients who are more hemodynamically unstable, inherently, those patients are going to be more likely to have ischemic and nephrotoxic injuries like ATN. So, I think you would expect a higher percentage of patients with ATN and a lower percentage of those functional injuries, such as prerenal injury, which should respond to the standard fluid challenges that we give.

And hepatorenal syndrome, which by definition should not have things like severe shock or other reasons for kidney injury, of which acute tubular injury or acute tubular necrosis would qualify. So, I think you see a much higher percentage of ATN. This is, of course, depending on the location you're practicing, the threshold to get into your ICU, how sick the patients are, whether they're in mental system failure, but I think that's a fair assumption across the board.

Dr. Reau:
So, Dr. Subramanian, I'll kind of take you to the next level, which is asking: how does a patient with cirrhosis usually end up in the ICU?

Dr. Subramanian:
So, the decompensated cirrhotic patient is exquisitely sensitive to develop organ failures in multiple organ systems. So, imagine a sick cirrhotic patient in the emergency room on the floor. They're at risk for hepatic encephalopathy, that'll require urgent transfer to the ICU for intervention, for protection. They can develop shock requiring vasopressors. They can develop acute kidney injury that's going to require urgent dialysis. And then, you're familiar with the variceal bleed that requires urgent resuscitation?

So, they're multiple reasons that the cirrhotic patient can have a need to be admitted and managed in the ICU setting.

Dr. Reau:
Yeah. So, that management process in this person with multi-organ failure generally is more than just the head of the ICU or ICU team. How do you approach that multi-shared experience?

Dr. Subramanian:
That's a great question. So, I think the processes in the inpatient's hospital need to be well-oiled to make sure the patient's taken care of well. So, you can imagine a sick cirrhotic patient on a regular floor bed who's initially stable on presentation, but they can then develop multiple organ failures we spoke about. So, I think there needs to be the right clinician, a nurse in training, and awareness on the regular floor bed to understand how tenuous these patients are and have an early response system.

And so, in our hospital, for example, and many other hospitals, I'm sure, we typically initiate a code MET, which means that there is an acute deterioration. And all the providers get involved in stabilizing the patient and calling the ICU to transfer in an expeditious fashion so that you can optimize the management. And as you know, that first hour or first couple of hours when they decompensate is crucial to have successful resuscitation in these patients.

Dr. Reau:
And then, do you have multi-disciplinary rounds after the patient's been admitted to the ICU?

Dr. Subramanian:
Yeah. So, great question. I think it's emphasize an important point. In our hospital, for example, we have the hepatologist, the transplant surgeon, their transplant candidate, and the intensivist. And the intensive care group gather together to discuss the management strategy for the patient, and that really helps us tailor their therapy. And also think about what needs to be done to think about transplant as an eventual option.

Dr. Reau:
So, Dr. Regner, let's take a hypothetical complicated patient; we'll try to make this even more granular. This is a person with cirrhosis, has a history of varices, maybe a variceal bleed in the past, has had ascites, and is admitted because there's concern for an infection, sepsis. This patient is looking poorly, and that's your suspicion. In this context, you know that their baseline renal function used to have a creatinine of 1, and now it's 1.6. How do you approach that patient?

Dr. Regner:
Sure. So, we've identified that this patient with decompensated cirrhosis has AKI, so the next step is to perform a comprehensive clinical assessment to identify a specific cause of AKI that we can treat. So, we would perform our clinical exam and history, but we would also use renal imaging, urinalysis, urinary biomarkers, if available, and then urine microscopy to try to narrow down the cause of AKI.

If, during that evaluation, we don't find a specific cause of AKI, the next step would be to move on to risk factor modification. So, we would want to withdraw any diuretics or nephrotoxic agents. We would want to treat any infections. So, for example, spontaneous bacterial peritonitis, and then we would want to consider the use of volume expansion if the patient is volume-depleted or if we're unsure of what their volume status is.

And so, those are the main steps: identify AKI, perform a comprehensive clinical assessment to identify specific cause, and then perform risk factor modification, and consider volume expansion.

Dr. Reau:
Excellent. Sounds simple, but not so, right? So, let's talk about volume expansion.

Dr. Subramanian, this is controversial, right? We seem to like albumin, but this may not be our only choice. How do you bring everyone together, and how do you pick one of these products?

Dr. Subramanian:
It's a great question. So, as a general intensivist, I use crystalloid, and that's the general of teaching is: you initially start with crystalloids if you have a patient with shock, for example, for volume resuscitation. But I think this growing awareness amongst various provider phenotypes and albumin, in addition to being a volume expander, also has the added capability of decreasing the cytokine storm surge, especially in liver disease and decompensated cirrhosis.

So, it'd work sort of in two-prong fashion with respect to stabilizing the hemodynamic parameters. So, for those reasons, I think there is added value to thinking about albumin as your choice of volume resuscitation instead of a crystalloid, especially as you are putting this in the context of acute kidney injury.

Dr. Reau:
So, Dr. Allegretti, we talked about the importance of a urine analysis. What are you looking for, and what are you going to do with that information?

Dr. Allegretti:
So, I think when you're thinking about urinalysis or urine microscopy, whether it be a manual review by a nephrologist under the microscope or even the automated cell count that will give you cells and casts and different types of characteristics that the computer will generate. I think it's just like anything else in the diagnostic approach to these complicated patients. It can be a piece of the puzzle and a valuable objective piece of data but shouldn't tell the whole story.

So, I think the hallmark when we think of urine microscopy is whether there are granular or muddy brown casts, which would be more supportive of a diagnosis of ATN than, say a functional injury like prerenal injury or hepatorenal syndrome. That being said, there's a gradation between hepatorenal syndrome and acute tubular necrosis, in particular. These are very difficult diagnoses to make to distinguish from each other, and they're treated very differently: one with vasoconstrictors and one with more supportive care and maybe a more volume-restrictive strategy.

So, I think it's useful to have that information, but by no means is the urinalysis the complete story. The presence of granular casts doesn't prove a diagnosis of ATN, nor does the absence of it prove a diagnosis of hepatorenal syndrome. In fact, some of the guidelines put forth by the International Club of Ascites specifically state that you should not use urine microscopy as the only reason to make this diagnosis, nor should it on its own; it rule out a diagnosis of hepatorenal syndrome, especially in a population of cirrhosis that has high bilirubin excretion and altered bile salt metabolism.

These things are renally cleared. They can cause bilirubin of bile cast, a so-called cholemic nephrosis that has been referenced before,

which is another added insult and may or may not be contributing to a patient's injury. And they may not have one diagnosis or the otherby the presence of urinalysis. So, I think it's a nice piece of information that we can use, but, just like anything else, there's no one single diagnostic test that you can use to make a diagnosis of HRS. So, one piece of the puzzle is my short answer.

Dr. Reau:
So, you're telling me we still have to look at the patient?

Dr. Allegretti:
Yeah. I think it's just as important as anything else.

Dr. Reau:
So, let's build on that a little bit. You have a patient; creatinine is not responding to the albumin resuscitation, you have no cast in the urine, we will take out the controversial maybe cast and maybe still hepatorenal syndrome, and you do get imaging, and there's no obstruction. So, I think that although we see that rarely is still important to not miss something that would require very different management.

Are there still other things in the differential that we would want to consider?

Dr. Allegretti:
Yeah, for sure. I think when we started this discussion, we talked about the main hemodynamic reasons for AKI in cirrhosis, prerenal injury, hepatorenal syndrome, and acute tubular necrosis. Again, hepatorenal syndrome and acute tubular necrosis can present very similarly. I think the main distinguishing feature between the two is really a history or a clinical objective sign of tubular damage. Now, you might use microscopy as part of that, but historically, we've relied on things of presence of shock, exposure to nephrotoxins, like, aminoglycoside or iodinated contrast. Things that would be more likely to cause an ATN.

So, I think you take that piece of information and the history, and you insert that. In the absence of those things, you're still evaluating for things like hematuria and proteinuria, perhaps not hematuria, that's secondary to a Foley catheter placement but may be more indicative of a chronic glomerular or an acute glomerulonephritis. These are all things we have to make and take into account. The diagnostic criteria, I think, are very good for hepatorenal syndrome and helping us rule out other causes of AKI.

So, if you start with those criteria, whether you're using the ASLD or the International Club of Ascites, there are many different criteria out there. There all about the same with regards to evaluate for other causes of AKI and try to remove those for the differentia. And so, that's where the volume challenge comes from to rule out prerenal injury, looking for proteinuria or evidence of structural or parenchymal kidney injury. And then, from there, you can make your best educated guess of what's driving the injury.

Dr. Reau:
Thank you. That's a very eloquent way of trying to make something clearer that's not always clear.

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Nancy Reau, and today I'm speaking with doctors Kevin Regner, Andrew Allegretti, and Ram Subramanian about strategies for diagnosing and managing acute kidney injury in cirrhosis.

Dr. Subramanian, will make your patient a little more simple. We're going to label them as hepatorenal syndrome, AKI, and, traditionally, we might have started midodrine and octreotide on this individual, but there's been a very significant shift in our guidelines now. This is no longer considered first-line therapy. Can you tell us what is first-line and why that shift occurred?

Dr. Subramanian:
So, the latest guidelines, especially in the US now, recommend terlipressin as the initial agent of choice for the treatment of HRS-AKI. The Europeans have been using terlipressin as first-line therapy for almost 2 decades. We have documentation of great efficacy in reversing HRS-AKI. And the ample data would support that as well. You have almost a 50% reversal rate of HRS-AKI, especially if treated early compared to midodrine-octreotide.

So, I think based on all the historical evidence from Europe and the more recent evidence that we have, terlipressin should be the first-line agent for the treatment of HRS-AKI instead of midodrine-octreotide.

Dr. Reau:
So, Dr. Regner, I'll turn to you. We have had terlipressin now, not as long as Europe, but it's not brand, brand new. Are there still barriers in access? How challenging is it to get your hands on this drug when you want to use it?

Dr. Regner:
Yeah, I think there's a couple of considerations there. First is cost. Let's think about that. Yes, a new drug might be more expensive than previously available non-FDA-approved alternatives. But we have to integrate the cost of the drug as well as the cost of preventing

dialysis, preventing an ICU admission, being able to treat the patient on the floor, avoiding central lines. And so, it's important for us, when we think about cost, to integrate the entire cost of care for a patient with HRS-AKI.

With respect to safety considerations, we have to avoid the use of terlipressin in patients who are hypoxic because of the risk of worsening respiratory failure. We should avoid the use in patients who've got acute on chronic liver failure grade 3 because they are at higher risk of developing respiratory failure. And we have to closely monitor patients for the development of intervascular volume overload, in which case, we might need to temporarily stop or reduce the use of terlipressin and manage their volume by reducing albumin and actually considering using diuretics. So, those are a few of the considerations.

Dr. Reau:
Well, thank you. So, Dr. Allegretti, let's say our patient was started on terlipressin, no barriers, creatinine at baseline was 1, we initiated therapy at 1.6; you want to know where you're coming in, and now, after 4 days, we're at 1.3. What do I do with my terlipressin? Now, can I stop it? Everything is great now?

Dr. Allegretti:
Alternately better. The lower the better when it comes to creatinine, in general. So, I think the question of when to deem a successful treatment when using terlipressin is a really important one. There's kind of two schools of thoughts: the North American trials, in particular, which used older definitions of hepatorenal syndrome closer to the HRS type 1 definition where you started with a creatinine in the 2s, and you had to get below 1.5. And those were the study endpoints using that, in particular, the CONFIRM trial, the most recently published and largest of the bunch.

So, the treatments success was having two consecutive creatine values below 1.5 after starting from a creatinine of above 2.25, for example. However, we know more information than an absolute value of creatinine nowadays, and the guidelines have modulated and been adjusted to take that into account. If you have happen to know a patient's baseline creatinine, meaning their outpatient baseline, what their usual creatinine is prior to admission, prior to the insult that we're treating. I think it's very reasonable to follow the guideline approach, which is to treat within 0.3 mg of their baseline, which would be defined as a complete response to therapy. This has been shown in some European data as well as they've had more experience with the agents as compared to those practicing in the United States.

In this case, if we went from 1.6 to 1.3, we're both below 1.5 and within 0.3 mg/dL of a baseline, but you can also argue the flipside while we've only gone0.2 below 1.5. So, is there a magic number? Something magical about 1.5? No, I don't think so. I think you're trying to optimize kidney function, and the creatinine happens to be the best representation of that. It does take a little bit of clinical judgment.

You have to be comfortable with knowing what the label of terlipressin says and what the institutional guidelines are, and you always want to follow that. But if you happen to know that this patient can get lower, say their baseline creatinine was 0.6, it would make sense to me to treat a little closer to that; as long as there's no side effects, you're not apposing or delaying therapy in any other direction. I think that makes sense to me, and that's, generally, how I practice. But each case has to be individualized because these patients are so unique and so difficult to manage.

Dr. Reau:
Thank you.

Dr. Regner, our patient with HRS recovers, and now they are back in the hospital with another episode. Is there anything you would do differently? Or?

Dr. Regner:
So, I think, again, if they come back with another episode of AKI, we have to go through that whole evaluation process again. But if we diagnose them with HRS-AKI again, it is reasonable to treat them with another course of terlipressin for up to another 14 days.

Dr. Reau:
So, Dr. Allegretti, in the ICU, your patient's coming in; are you typically finding that your patient was placed on terlipressin, or might they still be getting octreotide and midodrine?

Dr. Allegretti:
I think, even in our work at academic center or liver transplant center, I think there's still a large percentage of patients who are being started with midodrine-octreotide first; I think old habits are hard to break. I think it's what people are generally and have been generally comfortable with. And this is a new therapy. We're still in the early part of the adoption curve, and many clinicians may not have had it on opportunity even now, a couple years into its approval to have the opportunity to use terlipressin.

So, I do think it's important to acknowledge that midodrine-octreotide; while not being on label number one, they just don't work as well as terlipressin. So, if you have a candidate for terlipressin with hepatorenal syndrome, you should be starting with that because, as Ram mentioned earlier, the earlier we start therapy, the more likely you are to reverse it. So, in general, we're seeing a mix, and I hope, over time, we'll see less midodrine-octreotide and more terlipressin for those patients with tried-and-true hepatorenal syndrome.

Dr. Reau:
Thank you. So, Ram, in the ICU norepinephrine is also an option because if you don't have access to midodrine or octreotide, and you don't have access to terlipressin, our guidelines really do push toward norepinephrine. But you might access to both. Is there ever a time when you would use both of these together?

Dr. Subramanian:
So, we typically don't use them both together. Remember, they both are vasoconstrictor agents, so you have to be careful about the potential adverse effects. So, using them together with respect to splanchnic circulation. But going back to your question, so imagine a patient coming into the ICU. If they are already developing shock, and you're going to place a central line in, which you don't need for terlipressin, terlipressin can be administered peripherally, as we know. But if the patient is in shock and is getting a central line in, in those cases we typically move towards norepinephrine as a single agent in order to treat the shock as well as HSR-AKI. So, in sort of in that context, I think it has utility just to go with the norepi option.

Now, if the patient is coming in with purely HRS-AKI, and does not have a central line, there I think there is an option to use terlipressin as your first-line. With the caveats Dr. Regener mentioned about checking the boxes regarding hypoxemia, checking the box regarding advanced ACLF grade, especially at ACLF grade 3, is a relative contraindication, so we have to be careful about the potential barriers to terlipressin in that context.

Dr. Reau:
Thank you.

So, Dr. Regner, your patient has hepatorenal syndrome, and you're treating them; is there ever a time when you would go back and think about additional renal pathology, and how would you evaluate that? And what would you do?

Dr. Regner:
Yeah. So, you can imagine a scenario where a patient with cirrhosis comes in with acute kidney injury and no urine is available, and you begin your treatment for HRS, and a few days later, urine becomes available to perform urinalysis or microscopy, and you find evidence of tubular injury on the urine microscopy. That might cloud the picture a little bit. But if we go back to what Dr. Allegretti said about some of the caveats with respect to the interpretation of urine microscopy in the scenario, I think it's at that point that you have to judge how the patient is responding to whatever interventions you're performing.

So, if you're treating the patient with vasoconstrictors and IV albumin and they're responding, perhaps you just continue on that course. But, if you have a patient that you're treating with vasoconstrictors and they're not responding, and now you have this urine microscopy showing tubular injury, perhaps that's telling you that's more what the etiology is and perhaps you need to back off on the vasoconstrictors.

Dr. Reau:
Thank you.

So, Dr. Allegretti, even making this a little more complicated, so much of our patient population with cirrhosis has metabolic syndrome, and certainly diabetes and hypertension drive underlying kidney disease; how do you approach those individuals with underlying CKD that now have worsening of a kidney function in the background of cirrhosis?

Dr. Allegretti:
That's a great question, and I'll see your complication, and I'll raise you on more. So, before I even jump into CKD, I think it's important to set up two things: one, there's the type of CKD that can be associated with portal hypertension, refractory ascites, and HRS. We might call that HRS-CKD a natural progression of decompensated cirrhosis that, at some point, may lead to HRS-AKI, but even in the background, may have a smoldering sort of rise in creatinine that we would consider functional with a preserved kidney.

There's a whole other brand of CKD, that sometimes is referred to as organic or parenchymal. But some underlying associated metabolic disease, most commonly in our world where we have a lot more MASH cirrhosis or an aging population of cirrhosis, we'll see diabetic or hypertensive-related chronic kidney disease, which is very common in the general population. This could even be a little bit of smoldering glomerular disease, IgA nephropathy being common in advanced liver disease as well as far as glomerulonephritis goes.

So, there're two kinds of very different types of CKD to think about: one, you can imagine like an HRS-CKD may be amenable to treatment like you would an AKI with vasoconstrictors, albumin support as you're trying to restore profusion to the kidney to reverse that injury. Whereas obviously, if you have some underlying parenchymal injury, that's not going to respond in the same way.

But the population of CKD to second point within the liver population is, I think, evolving. We are seeing the population age, and in some of the older trials, particularly the trials around terlipressin, we didn't really have a definition for CKD, and we still don't have a great one for HRS-CKD. It's sort of like the subacute version of HRS, where these very strict guideline and strict sort of parameters for HRS-AKI doesn't really exist for HRS-CKD except to say this is kidney injury that's been going on for somewhere around 90 days, right? Like that's the kind of the magic number for chronic in our world.

So, a lot of those patients either weren't included in or weren't even considered in some of the older terlipressin trials, even though they may have had CKD when we were using absolute creatinine thresholds. And, in fact, we have another paper that is recently in press that showed that patients with underlying CKD, in general, did a little bit better than those with just isolated AKI. And now, whether that's because they're a different phenotype, they have a different etiology of cirrhosis, their degree of liver disease is not quite as severe as those with a more fulminant severe AKI in the absence of the CKD.

Remember, AKI is defined by a change in number. So, if you start at 1.8 or a 2, you only need to go up a little bit more to get into the hospital, perhaps to a 2.5, where that's a small relative change, but the absolute number is high and that may help triage someone into the hospital.

So, it's a really complicated question. I think there's a lot more to learn about this population both in terms of diagnosing, understanding the epidemiology, and as well as what management decisions we want to make different between the two. Obviously, you're not trying to treat someone with an underlying diabetic nephropathy down to normal because you're never going to get there, and that can be a really hard thing to distinguish on clinical presentation.

Dr. Reau:
Thank you.

So, Dr. Subramanian, your patient with hepatorenal syndrome, is really at high-risk for liver-related complications. In many of these, if transplant is an option that's the ideal endpoint is transplant. The worse your kidney function, the higher your score to get a transplant. So, how do you negotiate this now with your surgical team, trying to want to improve your renal function knowing that it might also lower the priority of your patient that would like to go to transplant?

Dr. Subramanian:
This is a very interesting question. And it's stirring up a lot of debate I'm sure at my center and I'm sure across the country. As you know the MELD score includes the creatinine. And if the patient with HRS-AKI responds to terlipressin the creatinine will come down, therefore the MELD will come down. And as you stated, that will decrease their priority for transplantation.

So, this is going to be an issue. Does it create a disincentive in certain transplant centers to reverse the HRS-AKI? With the right intention that, the ultimate fix is liver transplantation, and that's the ultimate fix for HRS-AKI. So, this is going to be an area of debate. We know that in Europe, certain countries have created a MELD lock system. IEU captured the MELD before you treat with terlipressin so that the patient retains their priority on the weight list. And then, you optimize kidney function before they see transplantation, which, as you know, improves perioperative renal function, even post-transplant renal function.

So, that's the ideal state, but I think, in the US we are not there yet. So, as we have this new drug, relatively new drug, terlipressin, we have to be careful about how we utilize this in the context of prioritizing for liver transplantation. I think that's going to be an important debate that we need to, as a medical community, come together.

Dr. Reau:
Is there a MELD threshold where you would not give terlipressin?

Dr. Subramanian:
So, this again is a moving target, in my opinion, and a MELD of 35 would be a number which is high enough in certain parts of the country where there's a high probability of urgent or quick transplantation. So, in those cases, you can think about not treating and then just waiting for life-saving transplant, which will reverse the HRS-AKI. That's a rough rule of thumb. I think different parts of the country have different cut-offs that would prioritize liver transplant, so we have to be careful about that.

I think the other point that needs to be made is with the use of DCD Organization after cardiac death organs. We are seeing an increase in the organ supply and patients getting transplanted with lower MELDs. So, for example, at our center pre-DCD, we had to wait for a

MELD of 30/35 before we transplanted. Now, we're transplanting MELDs in the 20s. So, that needle has moved as well with respect to where patients are getting transplanted as far as the MELDs score is concerned.

So, lot of moving parts, and so we have to be careful about incorporating all these issues as we think about doing right for the patient.

Dr. Reau:
Right. And iit's important to emphasize that the studies have suggested that the healthier the kidneys are at the time of transplant, the better the renal outcome is post-transplant. So, even if you have HRS-AKI, which might be reversed with transplant, if you had healthier kidneys going in, you're going to still do better.

Dr. Subramanian:
That's a great point. Yeah.

Dr. Reau:
I'm going to turn to even a more controversial concept, and that's alcohol-associated hepatitis. So, in this syndrome, a very rapid, aggressive, alcohol-related injury, where the patient is acutely ill and often succumbs to their disease quite quickly, renal failure, HRS-AKI, with progression to renal failure, is very common. Our sobriety rules are changing for this syndrome. Sometimes, these patients might be inappropriate or too sick for even terlipressin, so that you're now discussing management. How do you approach that patient?

Dr. Subramanian:
That's a great question. And, again, centers across the US, as you mentioned, are changing the paradigm regarding consideration for liver transplant in the setting of acute alcoholic hepatitis. So, I'll share with you, sort of, my center's perspective, and I think this hopefully mirrors most other centers.

Since we are not waiting for sustained alcoholic sobriety before we offer them transplants, so, for example, if a young hepatitis patient gets admitted to the ICU. You know that with non-transplant care, the mortality is really high. So, therein lies the value offering them lifesaving liver transplant. Now, if they have AKI in that context, and we think there is an opportunity to bridge that patient to temporary stabilization with a goal to eventually transplant them in the very near future, that will be a scenario where I would advocate for the patient receiving lifesaving renal replacement therapy.

As we buy time for us to assess the patient and, therefore, stabilize them, the medical status so that we can then think about lifesaving transplant. So, I think the changing paradigm, with respect to transplant for acute alcoholic hepatitis, should make us re-think the pros and cons of offering dialysis support in the short-term.

Dr. Reau:
Thank you.

So, Dr. Regner, you've a sick individual who now has renal failure, needs dialysis, but is not a transplant candidate right now; what do you consider for that patient? How are you going to approach them? And when would dialysis not be an option? And when would dialysis still potentially be an option?

Dr. Regner:
Right. I think the question there is, are they not a transplant candidate now? Or they never will be a transplant candidate? For those patients who are not yet a transplant candidate now, of course, I think we would all agree that we should probably be as aggressive as possible with our medical therapies and dialysis as a bridge towards transplantation, getting them through the evaluation process, getting them through the psychosocial evaluation or whatever other treatments they need.

For those patients who have been deemed not a transplant candidate at all, I think that becomes a little bit more complicated. And most of us would approach this from a standpoint of we would be willing to provide that patient with a time-limited trial of dialysis just to see how they tolerated this because their AKI or renal failure may have occurred in the setting of an infection or some other reversible decompensation. In which case, they might, from a hemodynamic standpoint, tolerate dialysis more effectively and be able to make it a little bit longer on dialysis.

But sometimes these patients are so sick there's nothing reversible. Their blood pressure is low, and they don't tolerate hemodialysis at all. And it's in that short, time-limited period that we can give the patients, their families, and other providers a little bit of a window into what we might expect, and whether it's even feasible to perform dialysis both in the hospital, much less outside of the hospital. So, that's how we kind of approach that in the short-term.

Dr. Reau:
Thank you.

Well, we have covered a lot today. And so, I'm going to turn to each one of you for some closing thoughts as we understand that the concept of identification and treatment of acute kidney injury in patients with cirrhosis has really changed.

So, Dr. Regner, any remaining challenges or anything else you want to address?

Dr. Regner:
Yeah. No, I think the most important thing that the field is thinking about nowadays is can we identify AKI earlier in the course of the disease so we can implement treatment. For example, vasoconstrictor therapy for HRS-AKI earlier because the thought is if we can treat earlier the response rate is going to be that much higher. So, I think we just need to be very aggressive in our evaluation and early management of these patients.

Dr. Reau:
Dr. Allegretti?

Dr. Allegretti:
This is a really important topic in a very sick patient population. The patients rapidly evolve, and I think we can do better in every aspect of the game. I think we can, to Dr. Regner's point, get better at diagnosis. I don't think we should be satisfied with current treatments, and I think we should push forward and try new therapies and try to optimize the use of the existing therapies we have.

And I think for those of us who aren't hepatologists, and even those who are hepatologists, this is a multi-disciplinary illness. And the more you learn about, including the things outside your specialty, the better off you will be at taking care of these patients. And with the rapidly changing demographics of liver disease and the rapidly changing treatments we have for them, it's a full-time job. So, a lot more time and effort is always appreciated for this population.

Dr. Reau:
Excellent.

And Dr. Subramanian?

Dr. Subramanian:
Just to add to those thoughts, the one thing that I keep emphasizing to trainers and learners is AKI in cirrhosis can be multi-factorial. And therein lies the multi-disciplinary approach to care. We have to have a broad differential diagnosis and also think about, from a therapeutic standpoint, target different aspects or different phenotypes of AKI. So I look forward to further advances my colleagues have mentioned.

Dr. Reau:
Wonderful. And so, ultimately, we still do have to look at our patients.

These have been really great insights for us to think about as we come to the end of today's program. I really want to thank my guests for helping us better understand how we can collaborate to diagnose and manage acute kidney injury in cirrhosis.

Dr. Regner, Dr. Allegretti, and Dr. Subramanian, it was great speaking with all of you today.

Dr. Renger:
Thanks for having us.

Dr. Allegretti:
Thanks so much.

Dr. Subramanian:
Thank you.

Announcer:
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