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Preparing the Patient with Decompensated Cirrhosis for Liver Transplant: ICU Discussions, Considerations and Dialysis

Announcer:
Welcome to CME on ReachMD. This activity, titled “Preparing the Patient with Decompensated Cirrhosis for Liver Transplant: ICU Discussions, Considerations and Dialysis” 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. Brian McDonough.

Dr. McDonough:
This is CME on ReachMD. I'm Dr. Brian McDonough. Today, I'm joined by Drs. Andrew Allegretti and Ram Subramanian to discuss how we can prepare patients for liver transplants when they have acute kidney injury, or AKI for short, and decompensated cirrhosis.

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

Dr. Allegretti, thanks for being here today.

Dr. Allegretti:
Thanks so much for having me.

And Dr. Subramanian is 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, it's great to have you with us as well.

Dr. Subramanian:
Thank you for having me.

Dr. McDonough:
Let's begin with you, Dr. Subramanian. Could you tell us about the importance of kidney function in patients who are candidates for a liver transplant?

Dr. Subramanian:
So, kidney function and kidney dysfunction becomes really important as we think about patients for liver transplant. As you know, the score that we used to define disease severity and listing for transplant is the MELD, model for end-stage liver disease, score. And one of the variables in that score is the creatinine. And so, acute kidney injury, acute and chronic kidney injury, becomes a really big driver of raising the MELD score as we think about patients for liver transplantation.

And just a related issue is that kidney injury is such a major driver of liver dysfunction and associated complications. It becomes very important to have the right strategies to manage kidney injury before and after liver transplantation.

Dr. McDonough:

And staying with you for just another moment, Dr. Subramanian, when might a patient with cirrhosis or advanced stage liver disease enter the ICU? And how would you manage them?

Dr. Subramanian:
So, patients with liver dysfunction are exquisitely sensitive to developed arrangements, and these can be in different organs. So, for example, from neurologic standpoint, they can develop hepatic encephalopathy, from a cardiovascular standpoint they can develop distributive shock, from a lung standpoint they can develop acute lung injury, from a kidney standpoint they can develop severe hepatorenal syndrome that requires the need for dialysis. So, you're looking at a patient phenotype that can really deteriorate very fast on the floor and require urgent transfer to the ICU for a high level of care.

Dr. McDonough:
And when you have a difference between the ICU and the hospital floor, like you're talking about, are there differences in decision-making management in those two settings?

Dr. Subramanian:
So, it depends on the disease process and the acuity of the disease process. It really depends on, for example, if you have somebody going into severe shock or low blood pressure, that is going to be an automatic trigger to take them to the ICU for support with vasoconstrictive therapy, invasive hemodynamic monitoring. So, they'll be an example of the cardiovascular sort of phenotype.

Dr. McDonough:
Turning to you now, Dr. Allegretti. The guidelines recommend using vasoconstrictors to treat hepatorenal syndrome, AKI specifically, but are there other agents you might use in the ICU based on various factors?

Dr. Allegretti:
Yeah, it's a great question. I think when you think about these patients, there's a couple of sort of tenants that I have in mind that sort of overarch the care we're providing. First, the kidneys are an organ that follows suit to the rest of the body when there's physiologic or systemic stressors. Of course, all these patients have liver disease, but there may be other organ systems involved; circulatory dysfunction, respiratory dysfunction.

You're seeing that stress on the kidney. Hepatorenal syndrome, of course, is a liver specific influence on the kidney where change is related to portal hypertension and the hemodynamic abnormalities related to cirrhosis are causing a lack of kidney perfusion, so it makes sense to try to restore that perfusion using things like vasoconstrictors, intravenous albumin, and other hemodynamic supports. But these patients are rapidly evolving and they're often not one-problem patients, and their kidney injuries can have overlapping etiologies. Someone can start with a hepatorenal syndrome and develop an acute tubular necrosis on top of it, so you're always constantly having to reevaluate these patients in the context of where their care is in the moment, which is why they're so hard to manage.

Historically, for example, we withhold diuretics and give a volume challenge as part of the guideline driven sort of initial approach to all AKI and cirrhosis. Part of that is to rule out things like prerenal injury that will get better with fluids, as things like hepatorenal syndrome and acute tubular necrosis are not thought to be fluid responsive. But that doesn't mean you can't develop these things later on.

So, for example, if you are withholding diuretics and giving volume and the patient becomes volume overloaded, you may have to come back and give them diuretics later if they develop pulmonary edema or respiratory distress. If you are just, for example, becoming oliguric, well, you can't just say, well, maybe we should give diuretics because I want them to urinate more. You have to think about, well, are they not urinating because they've had terrible acute tubular damage, and there's ischemic injury to the kidney and they're just in a period where they can't make urine? Or do they need more kidney perfusion as in the case of hepatorenal syndrome and restoring that will help? Or maybe they've had a large-volume GI loss, and they need more fluids to compensate for that. So, you really have to assign the right treatment to the moment.

Dr. McDonough:
For those just joining us, this is CME on ReachMD. I'm Dr. Brian McDonough, and today I'm speaking with Drs. Andrew Allegretti and Ram Subramanian about preparing patients with AKI and decompensated cirrhosis for liver transplant.

So, now that we've discussed key considerations for patients who are in the ICU, let's focus on liver transplants as an approach. Coming back to you, Dr. Subramanian, what role can a patient's etiology have when making a transplant decision?

Dr. Subramanian:
So, as you think about patients for liver transplantation, the major ideologies currently in the US for liver dysfunction and cirrhosis are alcoholic liver disease and now what we're calling metabolic-associated liver disease. So, it was previously called NASH. So, those are

the major drivers of cirrhosis in the US, and now also in the world. Hepatitis C, which was a previously common ideology, is now decreased in prevalence because of the new drugs for hepatitis C.

So, those are the major ideologies of liver dysfunction. But at the end of the day, once you start developing cirrhosis and decomposing cirrhosis, the pathways start unifying where patients start showing similar symptoms of hepatic decompensation. So, imagine a patient with severe encephalopathy or severe ascites, or severe jaundice, or hepatorenal syndrome. So, once they reach a stage of advanced cirrhosis, then they start developing similar manifestations of hepatic dysfunction that then necessitate the need to consider them for liver transplantation.

Dr. McDonough:
How important is it to evaluate CKD in a patient with liver disease and AKI?

Dr. Subramanian:
So, that's a great question. I think that is becoming an important issue, especially as we try to treat acute kidney injury in the inpatient setting, both on the floor and the ICU. As I mentioned to you, one of the etiologies of cirrhosis is NASH, which is associated with the metabolic syndrome, such as diabetes and hypertension, and those are major drivers of chronic kidney disease. And Dr. Allegretti provides wisdom on this issue as well.

So, as you think about transplanting for metabolic liver disease, there is a high probability of coexisting chronic kidney disease that can come into play, and so I think that further complicates the issue as you think about managing acute kidney injury, because a lot of these patients then need to be managed for acute on chronic kidney injury. And that really can make the diagnostic work-up more challenging, and also therapeutic interventions more challenging.

Dr. McDonough:
So, I would assume the critical care teams really have to look at this, evaluate things like tubular necrosis.

Dr. Subramanian:
Correct. So, the one thing that I keep sharing with our trainees and our learners is that when you have a patient with cirrhosis coming into the ICU and you're dealing with acute kidney injury, you can have multifactorial etiologies of the acute kidney injury. And normally, when you think about taking care of these patients in the ICU, zooming in on one particular diagnosis. But these patients can have coexisting diagnoses and also you can have coexisting CKD. Classic case in point is when you have a patient with acute on chronic liver failure, and that's the other terminology we can talk about more, ACLF, and the patient is presenting with AKI, you can have one ideology being hepatorenal syndrome, or HRS-AKI as we now term it. We can also have superimposed septic AKI which will be characterized by ATM if they have an infection.

So, I think it is very important to think about dual diagnosis or multiple diagnoses as you think about acute kidney disease in these patients, so that you can tailor your therapeutic strategies accordingly. You may have to start hitting two separate pathways in order to optimally treat the patient with acute kidney injury.

Dr. McDonough:
Very individualized and complex, the treatment. Dr. Allegretti, let's explore dialysis as an option for patients who are experiencing AKI and potentially, other organ failures while awaiting liver transplant. When should we consider dialysis?

Dr. Allegretti:
So, when you think about a patient with cirrhosis or end-stage liver disease well, you can consider them for dialysis when they develop an indication for dialysis, which is not that dissimilar from the general population. There's a great pneumonic, AEIOU. This is the list of things that could be indications for dialysis; A for acidemia, E for electrolyte imbalance, I for intoxication, O for overload or volume overload, and U for uremic symptoms or severe uremia, things like pericarditis. On top of that, there are liver-specific indications for dialysis as well. So, many people know that there are other things dialyzable besides creatinine and potassium, things like ammonia. So, sometimes it may be helpful to, in addition to ammonia lowering therapies enterally, like things like lactulose and rifaximin. Dialysis will also remove ammonia and help. May potentially mitigate encephalopathy and prevent complications like cerebral edema.

Dr. McDonough:
Another idea or question. How long should transplant candidates remain on dialysis prior to a transplant, at least optimally?

Dr. Allegretti:
Yeah, this is a difficult question, but a good one. It's really hard to provide a general answer because these cases are very individualized, as we talked about earlier, and you really have to tailor it to not only the patient, but the situation you're in. My general thought as an overarching, say, thesis, is that you want to dialyze when there's an indication for dialysis, but I try not to dialyze more

than that. So, I try to use the least amount of dialysis that is necessary to provide optimal and safe care for the patient. So, for example, like, a patient who's been on dialysis for several weeks has a much less likely chance of recovering their natural kidney function, their native kidney function, after a liver transplant. And we really want that, not just because giving a combined liver-kidney transplant is a limited resource, but we want these patients to do well.

In the immediate post operative period, there's a large amount of evidence to suggest that the better your kidney function is, the less dialysis you're on, I guess, for example. The better your postoperative kidney function is, the better you will do after a liver transplant. And this is not jaw-dropping news. This is true in any large surgery. You have better postoperative outcomes, the better your creatinine is or the better your kidney function is, going into a big surgery. Your volume status is better, there's lower infections, there's better perioperative mortality, all these things are better when you have better kidney function. So, the better you can optimize that before a surgery like this, the better you are.

That being said, you want to go into the surgery as optimized as you can. So, if you're thinking about a liver transplant and you're tremendously volume overloaded and you don't think you can be able to manage that with medical management alone, diuretics and whatnot, you might want to start a little bit earlier. If your metabolics are in poor shape, you're very acidotic and you're worried about going into the operating room in that situation, and the surgery is going to be more hemodynamically unstable as a result, he may consider starting earlier. So, it's a really hard question to answer for all patients, but I think trying to be thoughtful, use a consistent and multidisciplinary approach.

So, you're talking to the transplant surgery team and the ICU team and the nephrology and the hepatology team, so you can make an informed decision on that front.

Dr. McDonough:
One other question, Dr. Allegretti. There are patients who are obviously not candidates for liver transplant. What are the options for dialysis palliative care, those sorts of things for them?

Dr. Allegretti:
That's another difficult question to answer briefly, but I'll do my best. So, obviously, when you have a transplant as an option, you're doing everything you can medically and supportively, which includes dialysis, to get them safely to transplant. Obviously, not every patient has that as an option and so you're often faced as a clinician with a difficult discussion or decision-point of what to do when you develop an indication for dialysis. I think in general, you brought up palliative care, and I think the guidelines are supportive of this, that we probably could use more palliative-based approaches and palliative care consultations in general in this population, not just because these patients are very sick and their survival may be limited, but also there's a lot of symptoms to be managed, and when you're dealing with complicated medical patients, sometimes those things fall by the wayside to a certain extent. If you're focused on managing volume and keeping a patient alive and managing encephalopathy and bleeding and all the other things that are going on with the hemodynamically unstable patient, that may fall down your list. And if you have a separate service, like a palliative care service that can focus on the patient's comfort or be an added area of support as they're sort of contemplating the next few days and their families are often involved in this, and their loved ones. I think that can be very, very helpful.

If you have a patient who's not a liver transplant candidate, it's been pretty clear in the literature, the survival is pretty poor once you start down the dialysis road. You're not fixing the liver, which is the main reason the patient is so sick to begin with. And as I mentioned earlier, the kidneys follow suit to the rest of the body. So, I think it's really important to have a thoughtful discussion about goals, about what your expectations are, why you're doing the dialysis, what you're hoping to achieve, and you have to be frank. I think, in general, we feel like the survival is pretty poor in the absence of liver transplant once you get to this phase of the natural history of illness. But there are reasons why you should and can pursue it. Certainly, many patients would be appropriate to focus on comfort-based measures and talk to them about what the end of their life is going to look like. You have to have that discussion to know what the patient's values are. But on the other hand, if you have, say, a younger patient or a patient that wasn't as prepared, you may need that time that dialysis could afford to get your affairs in order, to exhaust all therapeutic options to feel like you have done what you need to do, even if you can't modulate the end of the natural history of cirrhosis to find where you need to be, both with the patient, their family, and the overall situation.

So, one of the questions I get asked a lot is, do you offer dialysis to patients who are not liver transplant candidates? And the answer is yes, with a huge caveat that I have this conversation that we don't believe you're very likely to do well. Here are the things that we are looking for that we were worried about that might happen, and if they start to happen, we can expect things to get worse from here. And if you have that discussion in a framework, you can use a number of different ways, a time-limited trial of dialysis, you can use the best case/worst case framework that's been developed in the surgical literature to say, here's the best thing that we hope will happen, here's the worst thing that we think could happen, and here's what we think probably will happen and go from there and find a way to convey

the information. And, a thoughtful and patient-centric way, but also making sure that the care team feels like you've really conveyed the dire straits of how sick these patients are.

Dr. Subramanian:
Can I add something to Dr. Allegretti's comments?

I think one thing that we are dealing with more recently is transplanting for acute alcoholic hepatitis, which we did not do in the past. So, previously for alcoholic liver disease, we mandated 6 months of sobriety before we would consider somebody for liver transplant. But now, more and more centers across the US are offering transplants for acute alcoholic hepatitis, so imagine a 35-year-old coming into the emergency room or the inpatient floor with an alcohol binge as their first presentation to a healthcare system. Father of two, otherwise a responsible member of society. In those kind of cases, we are reconsidering the 6 months of sobriety rule, and we are thinking about on a case-by-case basis, offering transplants even within a few weeks because the mortality for that disease process is very high in the absence of transplantation.

So, I bring that up to say that, going back to Dr. Allegretti's point, in those kind of cases, if there is acute kidney injury requiring dialysis therapy, we at our center would consider, and our nephrology colleagues would consider, offering dialysis therapy with the goal that you can stabilize the acute dysfunction as you think about them for transplants urgently. So, we're talking about within a couple of weeks.

Within hemodialysis in the inpatient setting, and especially in the ICU setting, we definitely prefer continuous renal placement therapies, or CRRT, as opposed to intermittent hemodialysis, because these patients are so hemodynamically tenuous that from a safety standpoint, CRRT is definitely the mode of choice instead of intermittent hemodialysis.

Dr. McDonough:
Just to follow up on that, not to get too far afield, but this person has had – 35, alcoholic binge – they have been drinking for quite some time as well? It's not just an isolated thing?

Dr. Subramanian:
So, it varies. It varies. It could be their first There could be some chronicity to the alcohol consumption, it could be another first or second presentation after a huge alcohol binge. So, it really varies but the paradigm is definitely shifted as far as offering transplant in that phenotype of patients where we're not waiting for 6 months of sobriety and the documentation of an alcohol relapse prevention program. More and more centers are changing their philosophy about acute alcoholic hepatitis, and I think that plays into how we collaborate with our nephrology colleagues regarding offering dialysis.

Dr. Allegretti:
Yeah. To your point, when you were talking about the different etiologies of cirrhosis and the presence or absence of chronic kidney disease or CKD, I mean, the demographics are changing and they're changing pretty rapidly. There's this chronic kidney disease. CKD is a disease of aging. And as we are seeing more metabolic associated liver disease, as our supportive care is getting better, there's a huge percentage of patients with cirrhosis or end stage liver disease who are getting older whereas, say, a generation ago, they weren't making it to 70. And we are now seeing this new set of patients, this new set of complications related to that. On the other hand, we are definitely seeing a large, at least percentage increase of cases of alcohol-related liver disease, which tend to be younger, which tend to have the potential to reverse if you can maintain sobriety. And it's really hard to approach these patients with a one-size-fits-all because they are so different. I mean, how can you approach a patient with minimal comorbidities who's 35 with alcohol-related liver disease. Granted, may have the same degree of liver disease severity as a 70-year-old with diabetes and hypertension and cardiovascular disease and metabolic-associated liver disease, and maybe some chronic kidney disease. Those two patients are so very different. The system has to afford some ability to account for that, both on the individual patient level and how we advocate and allocate livers on the grander scheme. So, these are things that I expect to continue to evolve over time and makes managing this population so challenging.

Dr. McDonough:
And you both have brought up some amazing points. As a family doctor, we're seeing so many more people with what used to be called NASH. I mean, it wasn't even a consideration and now it's like, oh my gosh. And we're starting to think, where are they on that path? What's going to happen if they mix alcohol with that? What's the associated damage that can occur? So, these issues aren't going to go away. And as you both said, it's very variable.

With those closing comments in mind, I want to thank my guests for explaining how we can prepare patients with AKI and decompensated cirrhosis for liver transplant.

Dr. Allegretti, Dr. Subramanian, it was great speaking with both of you today.

Dr. Allegretti:

Thanks again.

Dr. Subramanian:
Thank you.

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