



# Meeting Report

**THE 2025 NATIONAL DIALOGUE ON HEPATORENAL SYNDROME WITH ACUTE KIDNEY INJURY (HRS-AKI)**

# Introduction

On July 16, 2025, the American Liver Foundation and the National Kidney Foundation convened the 2025 **National Dialogue on Hepatorenal Syndrome with Acute Kidney Injury (HRS-AKI)**.

HRS-AKI is a rare but serious condition with a mortality rate of 50% 90 days post-diagnosis. [1] It is most common in people with advanced cirrhosis, particularly those with ascites. Higher AKI stage and lack of complete treatment response are associated with worse outcomes.

The 2025 *National Dialogue* brought together leading clinicians, people with HRS-AKI, public sector representatives, and innovators to discuss strategies to improve outcomes for patients with HRS-AKI. It was the second convening of its kind, following a similar initiative held in 2019. While important progress has been made since that meeting – most notably, FDA approved the first treatment indicated for HRS-AKI in 2022 – continued work is needed.

With a program designed around the patient journey, participants at this meeting reflected on recent advances, challenges, and opportunities in HRS-AKI diagnosis, treatment, and management.

## **2025 HRS-AKI National Dialogue goals were to:**

- Reflect on recent advances, challenges, and opportunities in HRS-AKI diagnosis, treatment, and management via interactive presentations, discussion, and consensus-building exercises;
- Discuss strategies to improve outcomes for patients with HRS-AKI; and
- Inform a comprehensive action plan to raise visibility of challenges surrounding HRS-AKI, engage stakeholders to form solutions, and, ultimately, improve care.



## **Avenues for Improving Patient Care and Outcomes**

Key Themes from National Dialogue Discussions

Participants converged on a series of specific avenues for action for improving patient care and outcomes in HRS-AKI through discussions interspersed throughout the meeting. Key themes included:

- The importance of early diagnosis and response in improving outcomes;
- The need for better tools to identify at-risk patients and facilitate diagnosis;
- The importance of disease awareness education to facilitate early identification and appropriate medical response, especially amongst advanced practice providers, hospitalists, and intensivists and clinicians at community hospitals; and
- How adoption of a Model for End-Stage Liver Disease (MELD) score lock could protect organ waitlist status for terlipressin responders and partial responders.

Detailed summaries of the meeting presentations and discussions follow.

# Meeting Presentations and Discussion

## OPENING REMARKS

The American Liver Foundation’s Heidi Daniels opened the meeting by welcoming participants and expressing appreciation for their presence.

### The Lived Experience of HRS-AKI

Remarks from an HRS-AKI survivor, Catherine Nelson, were shared at the beginning of the meeting to ground discussions in real-world, lived experience. These remarks conveyed the gravity of the condition and the urgency of diagnosis and medical response.

Catherine Nelson shared her personal journey through a cirrhosis diagnosis and HRS-AKI, describing a difficult period when her health deteriorated no matter how well she managed her diet and exercise. As she was waiting for a liver transplant – having taken all of the steps needed to be approved for the transplant – she found herself in and out of the hospital with encephalopathy and ever-worsening kidney function, surrounded by loved ones who were, in her words, on “death watch.” After several months, Ms. Nelson enrolled in the CONFIRM trial and was treated with terlipressin. A little less than a month later, she received her liver transplant that has ultimately allowed her to regain her life activities.

At the end of her remarks, Ms. Nelson commented on the importance of persistence and value of research, noting that one of the doctors at her clinical site had been involved in researching terlipressin for 15 years. Addressing the gathered clinicians, she noted, “the things you can do today may not make an impact today, but they are certainly going to impact the future patients that have these diseases. And it’s really important that you keep doing what you’re doing.”

### Goals of the 2025 National Dialogue

Stephanie Cogan of the National Kidney Foundation next spoke to the history of the National Dialogue and the goals of the 2025 meeting. The first HRS-1 National Dialogue was held in 2019 and centered on gaps in care; the need for better, faster diagnosis; and the need for heightened awareness. Since then, a drug therapy for HRS-AKI, terlipressin, has been approved by the US Food and Drug Administration (FDA) and come to market. With this advance, the important questions now, as Ms. Cogan put it, are about how far the needle has moved, how to overcome continuing gaps in care, and to encourage better collaborative, multidisciplinary care.

### Evolution of the HRS-AKI Environment

*Dr. Andrew Allegretti, Director of Critical Care Nephrology, Massachusetts General Hospital Associate Professor of Medicine, Harvard Medical School*

Dr. Andrew Allegretti next gave a primer on the evolution of the HRS-AKI environment. While AKI in cirrhosis is common, HRS-AKI as currently defined is rare, but very serious, with a mortality rate around 50% at 90 days – which is, importantly, a marked improvement from the historical rate of 90% mortality in untreated HRS.[1,2] Dr. Allegretti also touched on the history of HRS, changes in the diagnostic criteria over time, treatment and transplant, and ongoing work and challenges.

**Diagnosis:** Changes in the diagnostic criteria over time have enabled more patients to access therapies, but also have complicated diagnosis. This presents a particular challenge for clinicians who are not expert in HRS to diagnose the syndrome.

**Treatment:** Because liver disease is the underlying cause of HRS, a liver transplant is the ultimate treatment for HRS. However, multiple vasoconstrictors are used for HRS reversal, some off-label, with different advantages and disadvantages in terms of accessibility, administration, and effectiveness. Terlipressin is the sole therapy indicated for HRS. While these treatments do not have a significant impact on mortality, they can serve as a bridge to organ transplant.[3]

**Clinical Research:** Terlipressin became available in the US following the phase 3 CONFIRM trial. Clinical research on potential new treatment options continues.[4] One phase 2 clinical trial (on OCE-205, a V1a partial agonist) has been completed, and another for a combination therapy approach with terlipressin and R2R01 (a relaxin receptor agonist) is underway.

**Ongoing Work and Challenges:** Issues identified include evidence-based refinement of guidelines; optimization of patient selection for medical therapies; strategies for incentivizing drug development in HRS; broader clinician education; achieving recognition of the burden of HRS in transplant allocation; and better integration of the patient voice.

## FRAMING THE UNMET CLINICAL NEED IN HRS-AKI: BEDSIDE VIEWS

In the next component of the convening, the *National Dialogue* turned to a series of interactive presentations from clinicians representing a series of medical specialties with expertise in HRS-AKI.



### Protocol To Precision: The Evolving Diagnosis Of HRS

Mitra K. Nadim, MD, FASN, Professor of Clinical Medicine, Director, Critical Care Nephrology, Keck School of Medicine, University of Southern California

Dr. Nadim covered the evolution of the definition of AKI as well as changes in HRS-AKI diagnostic criteria, noting key differences between 2015 guidelines from the International Club of Ascites and recommendations from a 2023 joint meeting of the International Club of Ascites (ICA) and the Acute Disease Quality Initiative (ADQI). [5,6] She also spoke to the likelihood of improved outcomes from earlier initiation of terlipressin and the potential of biomarkers to identify at-risk patients, noting that NGAL is the best-studied biomarker and approved for clinical use in Europe and parts of Asia, but not in the US. [7–9] Dr Nadim then called for moving away from rigid criteria and a diagnostic framework that diverges from multidisciplinary approaches and shifting to a more personalized approach to AKI management, tailored to each patient’s AKI phenotype, emphasizing physiologically guided fluid management, timely reassessment, and patient safety. Finally, she urged that, considering the multidisciplinary complexity of HRS-AKI, future consensus meetings on HRS-AKI should include nephrologists and intensivists, key stakeholders in managing AKI and fluid balance in critically ill patients with cirrhosis.



### **Before The Diagnosis: Patients At Risk**

*HoChong Gilles, DNP, FNP-BC, AF-AASLD, Program Director, Central Virginia Veterans Affairs Health Care System, Assistant Director of GI Research, Richmond Institute for Veterans Research*

Dr. Gilles began her presentation by discussing the increasing burden of cirrhosis in the US and precipitating factors for development of HRS.[10] Now that there are effective therapies for people with chronic viral hepatitis, alcohol use and metabolic dysfunction-associated steatohepatitis (MASH) are becoming increasingly significant contributors to cirrhosis. Additional risk factors for HRS-AKI were noted, including kidney-related factors, cardiovascular status, concurrent co-morbidities, volume depletion, nephrotoxic agents, and hypotension or shock.[6] Dr. Gilles also described challenges to early diagnosis, noting in particular, the diagnostic complexity of kidney injury in the setting of cirrhosis and difficulties in training providers outside academic and specialized tertiary or transplant centers. There is a need to raise awareness and educate hospitalists, intensivists, and advanced practice providers to increase their clinical suspicion and knowledge in this area. She encouraged caution in judgments exclusively based on anticipated transplant eligibility and remarked on concerns about underutilization of palliative care. Ultimately, she believes that a stronger consensus on diagnostic criteria would aid in clinician-focused educational efforts and improved decision-making to accurately diagnose HRS and offer evidenced-based treatment, in conjunction with appropriate referrals to transplant centers. At the end of her remarks, Dr. Gilles shared a kidney-liver health assessment framework (Nadim, et al.) and underscored the need for a holistic approach that considers such factors as social determinants of health, access issues, and caregiver support. [6]



### **HRS-AKI: After the Admission**

*Pratima Sharma, MD, MS, Professor of Medicine, Division of Gastroenterology and Hepatology; Scientific Director, Transplant Center, University of Michigan, Ann Arbor; Clinical Investigator, Health Services Research; Staff Physician, Veterans Administration Medical Center, Ann Arbor, Michigan*

Alcohol-related liver disease has become the number one indication for liver transplantation, and, with COVID, alcohol use disorder has increased significantly along with alcohol-associated hepatitis (AH). Dr. Sharma opened her presentation with a case study of a 34-year-old female who presented to the emergency department with AH, was treated with corticosteroids and offered substance use disorder (SUD) treatment but declined. The patient presented again two weeks later in a worsened state with acute kidney injury. The stakes are higher for these patients and time is of the essence: the worse the AKI stage, the lower the probability of survival. Dr. Sharma discussed the importance of correctly phenotyping patients, and the use of biomarkers and fluid challenges in doing so. She also spoke to how point-of-care ultrasound can guide fluid management and then urged – as others had as well – early intervention with terlipressin when appropriate because it improves the response rate. [11] The associations between ACFL3 and poor response to terlipressin and respiratory failure were covered as well. [12] Dr. Sharma then discussed the need for collaborative multidisciplinary management before returning to the case discussed

earlier – who would not have benefitted from terlipressin – and that patient’s candidacy for early liver transplant. Like Dr. Gilles, Dr. Sharma encouraged early transfer to tertiary care centers because it improves the odds for patients, since these centers are more likely to have terlipressin and patients can be concomitantly evaluated for transplantation. She also reiterated that liver transplant is the only avenue that offers survival benefits. [13] Renal replacement therapy (RRT) can be a bridge to early liver transplant and recovery, allowing time for SUD treatment with some patients.[14] Concluding takeaways from Dr. Sharma reinforced that HRS-AKI management is a “team sport,” the importance of involving all stakeholders early, the need to discuss liver transplant candidacy when someone is hospitalized for HRS-AKI, and recommended use of RRT on a case-by-case basis.



### Multidisciplinary Approach to the Management Of HRS-AKI In Patients Ineligible for Liver Transplantation

*Kevin R. Regner MD, MS, FASN, Professor of Medicine & Interim Chair, Department of Medicine, Medical College of Wisconsin*

Dr. Regner’s presentation focusing on patients ineligible for liver transplantation encompassed a second case study and discussion of prognoses and goals of care, medical management, dialysis considerations, and palliative care integration. He described the case of a 40-year-old woman with decompensated alcohol-associated cirrhosis with several complications and a diagnostic evaluation consistent with HRS-AKI who had been evaluated for liver transplantation at multiple transplant centers and deemed ineligible. Dr. Regner described how nephrology was consulted to initiate dialysis, and then articulated three scenarios for cirrhotic patients with HRS-AKI deemed ineligible for liver transplantation: they may be (1) critically ill with multiple organ failure, (2) “stable” and responsive to vasoconstrictor therapy, or (3) “stable” and unresponsive to vasoconstrictor therapy.

#### Dr. Regner outlined critical elements of the goals of care conversations:

- Multidisciplinary clinical team, patient, and family should be **aligned on prognosis and expectations;**
- **Early, honest conversations** with clarity about which clinician will lead the discussion;
- **Clarify prognosis and burdens of therapeutic options; and**
- **Explore values and care preferences.**

Subsequently, he delved into the prognoses for non-transplant candidates (see callout) with HRS-AKI and considerations for vasoconstrictor therapy use, dialysis, and palliative care. Quality of life considerations are especially important with dialysis as many patients have poor functional status and the treatment burden is high. [15–17] For patients who are

#### Survival Rates for People with HRS-AKI Who Are Not Liver Transplant Candidates

##### Without a liver transplant:

- Median survival of ~2 weeks untreated
- 90-day mortality may exceed 60%, even with treatment

##### With vasoconstrictor therapy:

- Recovery of kidney function in ~30-40% (e.g., with terlipressin)
- Variable but limited impact on survival

##### With Dialysis:

- 90-day mortality >70%
- Does not alter disease trajectory; carries high risk of complications

References [4,20–22]

not transplant candidates, he encouraged early palliative care consultation, clarification of care goals, feasibility, risks, and assessment of short-term, non-kidney related prognosis. [18]

In his discussion of palliative care and hospice, Dr. Regner urged palliative care consults in parallel with consideration of dialysis. Multiple patient- and provider-related factors can inhibit early palliative care measures and advance care planning discussions: including, for the former, poor understanding of disease trajectory and hepatic encephalopathy; and, for the latter, unclear criteria for palliative care, conflation of palliative care with end-of-life care, the perception that palliative care is mutually exclusive to disease modifying treatments, and insufficient time for complex discussions. [17,19]

The talk concluded with a return to the patient case whose goals of care were prolonging life, returning home, and avoiding dialysis, and who was administered terlipressin and albumin for treatment of HRS-AKI. She remained alive and dialysis free eight months after her initial admission, but has had three subsequent admissions for terlipressin treatment.

Dr. Regner's take-home messages were that:

- HRS-AKI in non-liver transplant candidates has a **very poor prognosis**;
- Vasoconstrictor therapy can improve renal function but **rarely alters long term survival**;
- Dialysis should be **selectively considered** with clear goals as it is a **high burden, low benefit intervention** in this context;
- **Early, clear goals-of-care** conversations are essential;
- **Palliative care** should be engaged early; and
- How to handle **recurrent HRS-AKI** in patients ineligible for liver transplantation.



### Challenges Faced by Patients With HRS-AKI In Transplant

*Kavish Patidar DO, Sherrie and Alan Conover Center for Liver Disease & Transplantation, J.C. Walter Jr. Transplant Center, Houston Methodist Hospital*

Dr. Patidar was the final meeting speaker and opened with an introduction to liver allocation policies in the US. He briefly described the Model for End-Stage Liver Disease (MELD) that is used to prioritize patients for transplants and introduced acuity circles which aim to reduce variation in medium MELD at transplant among geographic regions, reduce pre-transplant deaths, increase pediatric transplantation, and reduce geographic variation in medical urgency scores. Having provided this introduction, Dr. Patidar then focused on three overarching challenges relevant to transplant-eligible patients with HRS-AKI:

#### Challenge 1: Organ Allocation

The impact of acuity circles on transplant rates has varied by region: most have had a decrease in liver transplant rates because livers were allocated to higher-MELD score regions. Regardless, the MELD score system poses a particular challenge in HRS-AKI because it underestimates mortality risk and patients who respond to treatment for HRS-AKI may lose their priority on the transplant waiting list. [20] There are currently no specific MELD score exception criteria for HRS-AKI. Clinicians also need to determine how to balance the competing needs of patients with acute and chronic liver failure, and whose MELD scores are not reflective of mortality risk.

## Challenge 2: Timing Of Liver Transplant

There is a window of reversibility for kidney function, but each day of pre-liver transplant RRT increases the risk of renal non-recovery after transplant. [21] Earlier transplant can reduce the likelihood of progression to dialysis dependence and need for simultaneous liver-kidney transplantation. However, recent research indicates that patients with creatinine-driven MELD scores have both increased transplant waitlist mortality and decreased liver transplant rates. [22] Additionally, kidney function at the time of transplant predicts survival time post-transplant, and worse function is associated with higher risk for post-transplant kidney failure. [23,24] Finally, liver graft quality needs to be balanced with donor risk factors. Machine perfusion of liver grafts can improve liver quality and accelerate transplantation.

## Challenge 3: Ethical Considerations

Five broad ethical considerations were raised: justice and fairness, beneficence versus utility, stewardship of scarce organs, non-maleficence and justice, and socioeconomic access barriers. (See table)

Ethical Considerations for Liver Transplantation in People with HRS-AKI	
CONSIDERATIONS	IMPLICATIONS
<p><b>Justice and fairness</b> MELD underestimates mortality in HRS-AKI and patients may be at a disadvantage to their counterparts</p>	Currently policy may not be equitable to reflect urgency of transplant need
<p><b>Beneficence versus utility</b> Terlipressin can reverse HRS-AKI and treatment may delay listing or prioritization for transplant due to MELD decrease</p>	Decision-making may favor not treating vs. improved patient outcomes
<p><b>Stewardship of scarce organs</b> Some patients with HRS-AKI may be listed for simultaneous liver-kidney transplant versus liver transplant alone</p>	Creates tension between individual benefit and population-level equity
<p><b>Non-maleficence and justice:</b> HRS-AKI is potentially reversible, but predicting recovery after liver transplantation is difficult</p>	May cause harm by over or under-treating; uncertainty may bias clinicians inappropriately
<p><b>Socioeconomic and access barriers:</b> Patients with HRS-AKI often face socioeconomic challenges, and these barriers may delay diagnosis, treatment, and liver transplant evaluation</p>	Systemic disparities may lead to poorer outcomes independent of medical severity

## Future Directions

Dr. Patidar raised four questions in closing:

1. Can we improve risk stratification and MELD accuracy for patients with HRS-AKI?
2. How can we optimize timing and treatment decisions?
3. Can the allocation policy be reformed for equity for patients with HRS-AKI?
4. Can we enhance current policies with regards to liver transplant alone or simultaneous liver-kidney transplant in HRS-AKI patients?

## AVENUES FOR ACTION: KEY THEMES FROM DISCUSSIONS

Participants converged on a series of specific challenges to and opportunities for improving patient care and outcomes in HRS-AKI in discussions interspersed throughout the meeting.

### ➤ **The Importance of Early Diagnosis and Response, and the Need for More Robust Consensus on Diagnostic Criteria**

As noted throughout, early diagnosis and medical response improve outcomes and can reduce suffering for people with HRS-AKI. However, there are several barriers to earlier diagnosis ranging from disease awareness to the diagnostic complexity of HRS-AKI. Debates about the syndrome's definition and diagnostic criteria further complicate efforts to increase disease awareness and timely diagnosis, as well as decision-making about referrals from non-transplant centers to transplant centers. Continued efforts to promote early diagnosis as well as consensus-building on definitions were encouraged.

### ➤ **The Need for Better Tools to Identify At-Risk Patients and Facilitate Diagnosis**

Multiple tools were discussed for identifying at-risk patients and streamlining diagnosis. Participants raised the possibility of integrating prompts into electronic health record systems to bring attention to at-risk patients. There also was discussion about the use of biomarkers and, specifically, the use of Neutrophil Gelatinase-Associated Lipocalin (NGAL) test, with participants noting the inherent challenges of the assay's limited indication in the US.

### ➤ **Education for Clinicians Who May Encounter HRS-AKI Patients, but Don't Have Much Familiarity with the Syndrome**

Many participants agreed that educational efforts to expand clinician awareness of HRS-AKI and its treatment could aid in earlier identification and treatment and support improved outcomes. Proposed topics included AKI risk in cirrhosis, acute or chronic liver failure (especially for advanced practice providers, hospitalists, intensivists, and community hospital HCPs more generally); effective interventions; and timing for referral to tertiary care centers (for community hospitals).

### ➤ **Adoption of a MELD Score Lock to Protect Organ Waitlist Status for Terlipressin Responders and Partial Responders**

Implementing a MELD score lock for patients with HRS-AKI could address tensions between treating HRS-AKI and organ transplant prioritization. Score locks have been adopted in some European countries.

## CLOSING: A RETURN TO THE PATIENT EXPERIENCE

The meeting closed with remarks from another survivor of HRS-AKI, Jay Beyer-Kropuenske. He shared his harrowing experience of a dozen hospitalizations, and the transformation that came with HRS-AKI treatment and a simultaneous liver-kidney transplant. Mr. Beyer-Kropuenske concluded the meeting by thanking participants for their dedication to improving care and outcomes for people with this syndrome.

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## ADDITIONAL RESOURCES

For a digital copy of this report and resources for people at risk of or experiencing HRS-AKI, visit the American Liver Foundation's Hepatorenal Syndrome webpage at <https://liverfoundation.org/liver-diseases/complications-of-liver-disease/hepatorenal-syndrome/>. Additional resources available on that webpage include a printable one-pager with information about HRS-AKI, risk factors, and questions that people at risk for HRS-AKI can ask their health care professionals, as well as a journal to help track important medical information and navigate HRS-AKI.

## MEETING ATTENDEES

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<b>Stephanie Cogan</b>	National Kidney Foundation
<b>Giuseppe Cullaro, MD</b>	Columbia University
<b>Heidi Daniels</b>	American Liver Foundation
<b>Alyssa Davenport</b>	Global Liver Institute
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