Clinical and Economic Burden of Patients with HRS-AKI Treated with Current Standard of Care: Retrospective Analysis of Real-world Data 2016-2020

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Background

- Hepatorenal syndrome (HRS) with rapid reduction in kidney function in patients with advanced chronic liver disease is a rare, acute, life-threatening complication of cirrhosis and is associated with a very poor prognosis. If untreated, HRS poses a median survival time < 2 weeks and 80% mortality within 3 months[1,2]
- Prior to the FDA approval of Terlipressin in September 2022, standard of care (SOC) for HRS-AKI involved the use of vasoconstrictors and plasma volume expanders[2]
- We aimed to evaluate the effect of AKI severity on treatment (Tx) response and in-hospital mortality

Data Source & Patient Selection

- Cerner Real World Data™ (Cerner, Kansas City, MO) was used to conduct this retrospective analysis; we included adult patients with the following criteria:
  - Hospitalized for ≥48 hours with HRS (ICD-10, K76.7) between Jan. 1, 2016 — Dec. 31, 2020 and treated with midodrine/octreotide (M/O) and/or norepinephrine (NE) with a valid Tx start/stop time
  - Had a baseline serum creatinine (SCr) >1.5 mg/dL prior to or at hospitalization (with HRS diagnosis) and a post-treatment SCr value (at index hospitalization)
    - Patients who died or underwent renal replacement therapy, transjugular intrahepatic portosystemic shunt, or liver transplantation were included if death or procedure occurred >2 days after Tx initiation. In these cases, response was assessed 1 day prior to death or procedure

Outcomes of Interest

- AKI severity was determined based on KDIGO staging[3] and pretreatment SCr[4]
  - Mild AKI if pretreatment SCr <2.25 mg/ dL, moderate AKI if ≥2.25 but <3.5, and severe AKI if ≥3.5 mg/dL
- Mortality and Tx response by AKI severity, classified as:
  - Complete: Post-Tx SCr improved to ≤1.5 mg/dL
  - Partial: Post-Tx SCr showed ≥30% reduction from baseline but remained >1.5 mg/dL
  - None: Post-Tx SCr decreased by <30% from baseline

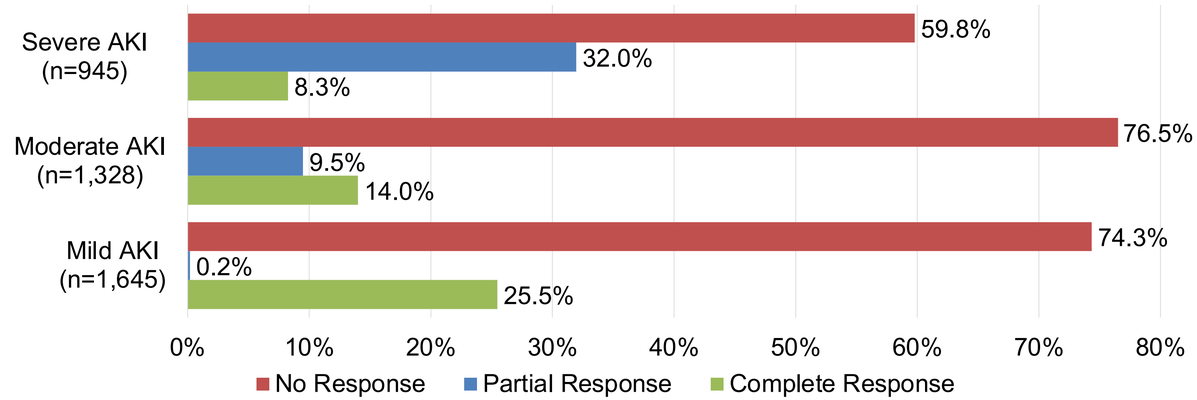
Results

Table 1. Treatment Response Population		N = 3,918
Sex, n (%)	Male	2,528 (64.5)
	Female	1,390 (35.5)
Age	Mean ± SD	59.4 ± 12.7
Ethnicity, n (%)	White or Caucasian	2,675 (68.3)
	Black or African American	275 (7.0)
	Other	968 (24.7)
Pretreatment SCr, mean ± SD, mg/dL	Mild AKI	1.9 ± 0.2
	Moderate AKI	2.8 ± 0.3
	Severe AKI	5.3 ± 1.9
Baseline SCr by KDIGO staging, mean ± SD, mg/dL	No AKI (n= 1,103)	2.8 ± 1.3
	Stage 1 or 2 (n= 2,302)	3.0 ± 1.7
	Stage 3 (n= 513)	3.3 ± 2.2
Etiology of Liver Disease, n (%)*	Alcoholic Cirrhosis/Hepatitis	1,779 (45.4)
	Viral Hepatitis	560 (14.3)
	NASH/NAFLD	1,728 (44.1)
Conditions during Hospitalization, n (%)	Sepsis	846 (21.6)
	Respiratory failure	817 (20.9)
	Fluid overload	807 (20.6)
	Pleural effusion	553 (14.1)
	Abdominal pain	354 (9.0)
	Diarrhea	199 (5.1)
	Bradycardia	123 (3.1)
	Dyspnea	89 (2.3)
	Nausea	54 (1.4)
Treatment, n (%)	M or O without NE	2,013 (51.4)
	M and O without NE	1,168 (29.8)
	NE, regardless of other vasopressor(s)	982 (25.1)

* Non-mutually exclusive; SD: Standard deviation;

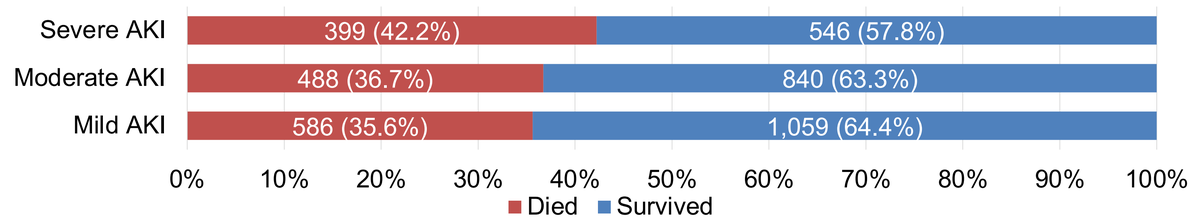
- Of 8,552 HRS-AKI patients who received SOC Tx, (non-mutually exclusive), 3,918 met inclusion criteria
  - 3,797 were excluded for baseline SCr≤ 1.5 mg/dL
  - 837 patients were excluded due to lack of post-Tx SCr, receipt of TIPS/RRT/LT within 2 days of Tx start, or death within 2 days of Tx start
- Due to lack of true baseline SCr, we were unable to determine AKI severity using KDIGO, as shown in Table 1 (e.g., no AKI with a SCr of 2.8 mg/dL)
  - Pretreatment SCrs were used to determine AKI severity (mild/moderate/severe)

Figure 1: Treatment Response by AKI Severity Based on Pretreatment SCr



- Across all patients with HRS, the complete Tx response (HRS reversal) rate was 17.4% (683 out of 3,918)
- NE was administered in 736 cases where M or O was also administered, either after M or O (n=430), concurrently with M or O Tx (n=1), or before M or O (n=305)
- A total of 817 (20.9%) patients had respiratory failure (RF) and 658 (16.8%) were placed on mechanical ventilation (MV); Out of the 817 patients with RF, 454 (55.6%) were placed on MV
- In-hospital mortality was positively correlated with AKI severity and complete Tx response (HRS reversal) was inversely correlated with AKI severity

Figure 2: In-Hospital Mortality by AKI Severity Based on Pretreatment SCr



Conclusions

- This cohort analysis of 5-year data shows that AKI severity based on pretreatment SCr is inversely correlated with complete Tx response (HRS reversal) and positively correlated with in-hospital mortality
- Findings also indicate frequent lung and airway disorders in patients hospitalized with HRS, as 16.8% required mechanical ventilation and 20.9% had respiratory failure
- Management of HRS requires early recognition of renal impairment (i.e., increased SCr), followed by timely intervention. Our Tx response analysis suggests that prior to the recent approval of Terlipressin for adults with HRS with rapid reduction in kidney function, SOC did not adequately revert HRS, as shown by a 17.4% overall complete Tx response (HRS reversal) rate among all patients with HRS

Reference: Boyer TD, Sanyal AJ, Wong F, et al. Terlipressin Plus Albumin Is More Effective Than Albumin Alone in Improving Renal Function in Patients With Cirrhosis and Hepatorenal Syndrome Type 1. Gastroenterology. 2016;150(7) (2) Flamm SL, Brown K, Wadei HM, et al. The Current Management of Hepatorenal Syndrome-Acute Kidney Injury in the United States and the Potential of Terlipressin. Liver Transpl. 2021;27:1191–1202. (3) KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120(4):c179-84. (4) Moore K, Jamil K, Verleger K, et al. Real-world treatment patterns and outcomes using terlipressin in 203 patients with the hepatorenal syndrome. Aliment Pharmacol Ther. 2020;5

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