Evaluation of Therapy for Hepatorenal Syndrome in Non-Intensive Care Unit Patients: A single-center retrospective chart review

Hanna Bronz, PharmD Candidate 2025[1], Dean Van Loo, PharmD[2]
(1) Ferris State University College of Pharmacy, Grand Rapids, MI
(2) Pharmacy Practice, Ferris State University College of Pharmacy, Grand Rapids, MI

Introduction

- Hepatorenal syndrome (HRS) is a diagnosis of exclusion that identifies the renal consequences of severe liver disease.
- In combination with albumin fluid replacement, current guidelines favor the use of vasopressors such as terlipressin and norepinephrine.
- The combination of midodrine and octreotide is an alternative regimen that has also been recommended; however, guidelines favor reserving it for instances where terlipressin or norepinephrine are not feasible, as it is accepted to be less effective.
- Norepinephrine is limited by the requirement of intensive care unit (ICU)-level monitoring for administration. In contrast, terlipressin does not require ICU-level monitoring and is globally accepted as the most effective therapy for HRS, but is relatively new to the market in the United States and is not on formulary at the site of this analysis.

Objective

- To understand the nature and frequency of treatment approaches for HRS and associate them with outcomes of interest.

Study design

- Retrospective chart review of 80 patients in 66 unique encounters associated with hepatorenal syndrome between 8/1/2019 and 8/1/2024.

Methods

- **Patient Identification:** ICD-10 code for HRS (K76.7) diagnosis in EHR.

Inclusion Criteria	Exclusion Criteria
• At least 18 years old • Diagnosis of hepatorenal syndrome • Clinical or imaging evidence of ascites	• Patients 17 years of age or younger • Pregnancy • Hemodialysis • Patients who were admitted to the ICU within 48 hours of general admission • Patients who were directly admitted to the ICU • Patients who died within 48 hours of admission

- **Data Collection:** Following patient identification, all encounters were independently reviewed by the primary investigator (PI) to ensure adherence to inclusion/exclusion criteria. Laboratory results were pulled from the time of first INR within the encounter or the result immediately prior to the INR if it was not evaluated in the same result set. Model for End-Stage Liver Disease-Sodium (MELD-Na) scores were calculated for each patient encounter by the PI.

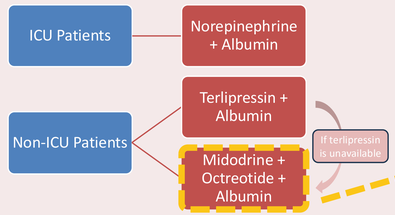
MELD-Na Components	MELD-Na	90-day Mortality Estimate
• Dialysis in the past week? (Y/N) • Creatinine • Bilirubin • INR • Serum Sodium	<17	<2%
	17-20	3-4%
	21-22	7-10%
	23-26	14-15%
	27-31	27-32%
	≥32	65-66%

Patient Demographic	Study Population
Patients, N	66
Unique Encounters, N	80
Age (years)	56.9 (28-93)
Female sex, N (%)	30 (37.5)
Causes of Liver Cirrhosis, N (%)	
Non-Alcoholic Fatty Liver Disease	18 (22.5)
EtOH Associated Liver Disease	63 (78.8)
SCr (mg/dL)	2.2 (0.4-6.0)
Serum Na (mmol/L)	130.8 (111-142)
Total Bilirubin (mg/dL)	7.6 (0.3-37)
Albumin (g/dL)	2.8 (1.5-4.6)
INR	1.8 (1-3.4)
MELD-Na Score	27 (6-40)

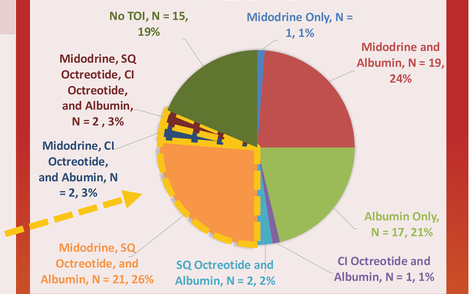
Hospital Stay Data	Study Population
Length of Stay (days)	9.9
30-Day Readmission, N (%)	
Yes	29 (36.3)
No	19 (23.8)
No (due to death)	24 (29.7)
No (lost to follow-up)	8 (10.0)
Average Days to Readmission	80.4
90-Day Mortality, N (%)	
Yes	33 (41.3)
No	28 (35.0)
Unknown (lost to follow-up)	19 (23.8)
Expired at Time of Chart Review, N (%)	
Yes	43 (53.8)
Presumed/Lost to Follow-up	19 (23.8)

Summary of Guideline-Preferred Therapies

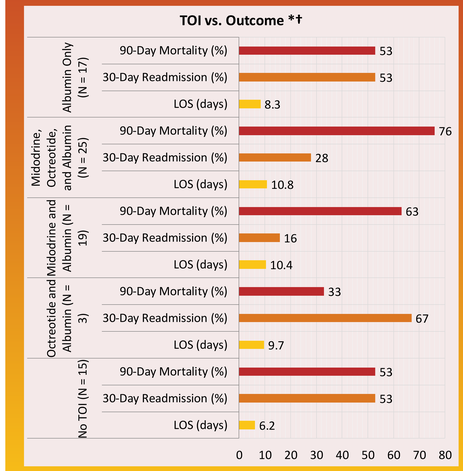
The American College of Gastroenterology (2022)[1]
American Association for the Study of Liver Diseases (2021)[2]
European Association for the Study of the Liver (2018)[3]



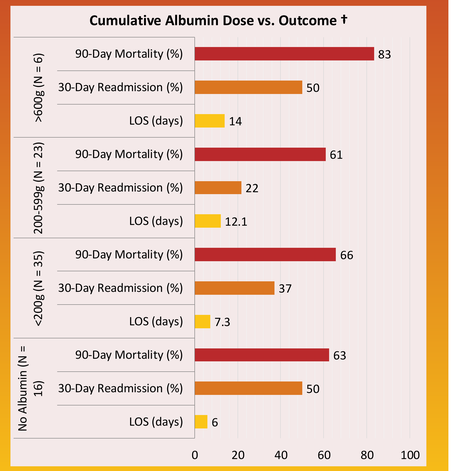
Therapies of Interest (TOI) Combinations



TOI vs. Outcome *†



Cumulative Albumin Dose vs. Outcome †



* Octreotide includes continuous infusion (CI) and subcutaneous (SQ)
† 90-day Mortality includes patients who were lost to follow-up or presumed dead

Results

- **19% of patients received no therapies** that would be guideline-recommended for HRS in the non-ICU setting.
- **32% of patients received the guideline-recommended combination** of midodrine, octreotide (CI or SQ), and albumin in combination.
- Patients in this analysis have an **average estimated 90-day mortality of 27-32%** (based on calculated MELD-Na score), but a **confirmed 90-day mortality of 41.3%**. If including patients who were lost to follow-up, this rate could be **as high as 65.1%**.
- **30-day readmission rates were 36.3%**, but if including patients who were lost to follow-up, this rate could be **as high as 46.3%**.
- As **number of TOIs** increased, length-of-stay and 90-day mortality also increased.
- TOI combinations **not including midodrine** had higher 30-day readmission rates.
- Patients who received **>600 g of albumin total** had highest 90-day mortality rate.
- Patients who received **200-599 g of albumin total** had the lowest 30-day readmission rate.

Limitations

- Numerical changes in renal function required to diagnose HRS were not independently assessed by the PI, but rather relied on the presence of an ICD-10 code for HRS.
- This patient population is small, inherently unstable, and medically complex which complicates retrospective analysis.
- Patients who were lost to follow-up were analyzed as “presumed dead” which may inflate the 90-day mortality rate.
- Admission to the ICU was not assessed, but is an outcome that is high-yield for patients and health-systems.
- Patients who did not receive inpatient dialysis were presumed to have not received dialysis within the past week.

Next Steps

- Evaluation of the association between TOI combinations and admission to the ICU and/or eventual need for a norepinephrine infusion would be relevant and could help measure the utility of terlipressin in this institution’s patient population.

Conclusion

- Most patients (64%) in this analysis did not receive the guideline-directed combination of midodrine, octreotide, and albumin.
- Most patients (80%) received albumin, but our analysis did not illustrate a notable dose-response relationship that would favor the use of increased cumulative doses of albumin.

References and Disclosures

These authors have declared no potential conflicts of interest.

Contact information: Hanna Bronz – bronzh@ferris.edu

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