



MEDICAL SCHOOL
UNIVERSITY OF MICHIGAN

Postoperative Hepatic Encephalopathy in Patients with Cirrhosis

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INTRODUCTION

Background

Hepatic encephalopathy (HE) is a common complication of decompensated cirrhosis, affecting 40-50% of patients with cirrhosis and 23,000 patients annually.^{1,2} Due to its high incidence, HE is a condition seen and managed by internists, subspecialists, and surgeons.

There are numerous known factors that can precipitate episodes of HE in patients with cirrhosis, such as gastrointestinal bleeds, infections, changes in stool consistency, and medications.² As such, due to the variety of changes and events that occur while patients are hospitalized, HE is a common hospital complication.

A routine reason for admission in patients with cirrhosis (as well as for patients in the general population) is recovery after a surgical procedure. Although many postoperative periods are unremarkable and patients are discharged on time, complications that arise negatively affect patient outcomes and prolong their hospital stay.

Hepatic encephalopathy can be a complication that affects surgical patients' postoperative courses, and it is likely that the nature of surgery and postoperative management places patients at an increased risk of developing HE.

Hypothesis

In postoperative patients with cirrhosis, we hypothesize that many aspects of the postoperative period differ from the patients' baselines, whether it be energy expenditure for healing, medication changes (antibiotics, analgesics, sedatives, etc.), postoperative ileus, or activity level, and these changes may precipitate episodes of HE.

Furthermore, we hypothesize that differences in postoperative patient management, such as lactulose dosing and narcotic prescription, may contribute to differences in patient outcomes.

OBJECTIVES

Aims

The aims of this project are to:

- Determine the incidence of postoperative HE development in patients with cirrhosis undergoing non-liver surgeries,
- Determine the timing and dose of lactulose administration, whether it be preoperatively or postoperatively, that is associated with a lower likelihood of developing HE in these patients,
- Determine factors associated with development of HE postoperatively in patients with cirrhosis undergoing non-liver surgeries, and
- Determine differences in length of stay amongst patients who do and do not develop postoperative HE.

METHODS

Study Design

Population: Patients 18 years and older with cirrhosis admitted to Michigan Medicine between 01/01/2009 and 01/01/2019 for postoperative recovery after surgery.

Patients will be excluded if they are undergoing a liver-related surgery, such as liver transplantation, liver resection, ablation of any portion of the liver, transjugular intrahepatic portosystemic shunt placement, or operations that modify the biliary tree.

Data Collected

Baseline Information

- Demographics: age, sex, race/ethnicity, body mass index (BMI)
- Baseline labs: AST, ALT, alkaline phosphatase, albumin, total bilirubin, creatinine, CBC, INR
- Medications: home medications

Pre- and Postoperative Information

- Medications: inpatient medications and changes to medications while admitted, HE-related therapies (lactulose, rifaximin, etc.)
- Type of surgery performed
- Onset of HE: descriptions from clinician notes

Data Regarding Clinical Status of Liver Disease

- Disease severity scoring: MELD, CCI, ASA classification
- Exposure: history of ascites, history of hepatic encephalopathy, prior TIPS procedure, history of varices

Definitions

Cirrhosis

- Historical biopsy showing cirrhosis at any time in the past.
- Clinical decompensation
- Imaging showing a cirrhotic-appearing liver with associated signs of portal hypertension including splenomegaly, varices, or thrombocytopenia (platelet <100k in the absence of other causes)

Hepatic Encephalopathy (HE)

- Altered mentation
- Reversible with lactulose
- Documented in MiChart

Outcome Measures

- Incidence of HE amongst postoperative patients
- Timing and dose of lactulose associated with a lower likelihood of developing HE
- Factors associated with developing HE in this patient population
- Length of stay of patients who develop HE versus patients who do not

RESULTS

While still undergoing analysis, of the 580 patients that met criteria for the study, 40 (6.9%) developed HE postoperatively. Patients who developed HE tended to have a longer length of stay, higher in-hospital mortality, and higher preoperative Charlson Comorbidity Index and Mayo 30-day mortality risk.

	Developed HE			Did Not Develop HE		
	# of Patients	Frequency (%)	Median ± IQR	# of Patients	Frequency (%)	Median ± IQR
Demographics						
All	40	100.0%		540	100.0%	
Age						
Sex (% male)	22	55.0%		337	62.4%	
Race						
— African American	2	5.0%		47	8.7%	
— AI or AN	1	2.5%		4	0.7%	
— Asian	0	0.0%		2	0.4%	
— Caucasian	36	90.0%		459	85.0%	
— Unknown/Other	14	35.0%		28	5.2%	
BMI						
Baseline Laboratory Values						
WBC		6.8 ± 5.4			6.6 ± 4.5	
HGB		10.8 ± 3.7			11.5 ± 3.5	
PLT		98 ± 90			129 ± 100	
Na		136 ± 6			138 ± 5	
Cr		1.09 ± 0.51			0.96 ± 0.62	
Albumin		3.0 ± 0.6			3.6 ± 1.0	
Bilirubin, total		1.7 ± 2.2			0.9 ± 1.0	
INR		1.3 ± 0.3			1.1 ± 0.3	
Home Medications						
Lactulose	22	55.0%		99	18.3%	
Rifaximin	16	40.0%		40	7.4%	
Preoperative Medications						
Lactulose	10	25.0%		23	4.3%	
— Total Dose		70 ± 74			40 ± 70	
Rifaximin	6	15.0%		14	2.6%	
Diuretics	2	5.0%		21	3.9%	
Nonselective Beta Blockers	1	2.5%		5	0.9%	
Postoperative Medications						
Lactulose	14	35.0%		44	8.1%	
— Total Dose (24hr postop)		5 ± 40			20 ± 40	
— Total Dose (48hr postop)		50 ± 115			40 ± 45	
Rifaximin	11	27.5%		26	4.8%	
Opioids	25	62.5%		352	65.2%	
Acetaminophen	8	20.0%		240	44.4%	
NSAIDs	3	7.5%		56	10.4%	
Anti-psychotics	0	0.0%		0	0.0%	
Benzodiazepines	7	17.5%		61	11.3%	
Cirrhosis Details						
Etiology						
— Alcohol-related	15	37.5%		187	34.6%	
Complications						
— Hx of Ascites	31	77.5%		327	60.6%	
— Hx of Varices	28	70.0%		172	31.9%	
— Hx of HE	29	72.5%		260	48.1%	
— Hx of TIPS	6	15.0%		54	10.0%	
Disease Severity Scoring						
— MELD-Na		15.8 ± 10.1			10.1 ± 8.0	
— CCI		8 ± 4			5 ± 6	
— ASA classification		4 ± 1			3 ± 1	
— 30-day Mortality Risk (Mayo)		12% ± 21%			6% ± 9%	
Surgery Details						
Scheduled (%)	12	30.0%		292	54.1%	
Type of Surgery						
— Abdominal	0	0.0%		70	13.0%	
— Abdominal, Nonbowel	11	27.5%		182	33.7%	
— Cardiac	12	30.0%		79	14.6%	
— Head & Neck	4	10.0%		31	5.7%	
— I&D	0	0.0%		5	0.9%	
— IR Biopsy	1	2.5%		1	0.2%	
— OB	0	0.0%		1	0.2%	
— Orthopaedic	7	17.5%		103	19.1%	
— Spine	0	0.0%		24	4.4%	
— Thoracic	0	0.0%		15	2.8%	
— Vascular	5	12.5%		29	5.4%	
Hospital Course						
LOS		26 ± 25			7 ± 9	
In-hospital Mortality	8	20.0%		22	4.1%	
Incidence of HE	40	6.9%		N/A	N/A	
Time to HE (days)		4.0 ± 8.3			N/A	
Duration of HE (days)		4.0 ± 3.0			N/A	

CONCLUSIONS

The incidence of postoperative HE, at least within this health system, was determined over the past decade.

Development of HE was associated with worse outcomes and is a potential area for future interventions.

Further conclusions are forthcoming as the rest of data undergoes analysis.

LIMITATIONS

This study was performed with a single health system's population, limiting its generalizability to the larger population.

Other factors may also contribute to the differences in lengths of stay, in-hospital mortality, and other outcomes.

In the 10-year period, the number of patients that developed HE was on the lower end for statistical analysis, but many calculations are still able to be carried out.

LESSONS LEARNED

Starting this research study from beginning (drafting the IRB) to performing data extraction and analysis, and now moving into the stage where a manuscript will be drafted has been an enriching experience. I was not prepared for how much time data collection for an initial patient population of more than 1000 would require, but now that it has been completed, we are ready to complete the data analysis. To continue to propel the project forward, we will draft the manuscript, submit it for publication, and begin any interventions/changes we realize from the data analyzed. For future students considering a retrospective chart review project, I would highly recommend leveraging the power of two university resources – Data Direct and EMERSE – both of which were incredibly handy for a targeted chart review with many variables.

DISCLOSURES

The authors have no disclosures to report.

REFERENCES

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