



Outcomes in patients with portal hypertension undergoing gastrointestinal surgery: A propensity score matched analysis from the NSQIP dataset

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ABSTRACT

Background/Aim: We aim to study the impact of PH in patients undergoing gastrointestinal surgery (GI). **Methods:** We queried the ACS-NSQIP database from 2005 through 2010 for patients undergoing GI surgery with PH. Esophageal varices (EV) diagnosis was used as a surrogate of PH.

Results: A total of 192,296 patients underwent GI surgery, of which 379 had PH. Regression analyses revealed that patients with PH had a 6-fold (95% CI 4.6–7.9) increase in 30-day mortality, a 3-fold (95% CI 2.5–3.7) increase in morbidity, a 3.2-fold (95% CI 2.6–3.9) increase in critical care complications (CCC), and a 6.5-day (95% CI 5.1–7.8) increase in hospital LOS. After PSM, the impact of PH on the outcomes remained. These differences were significant regardless of the emergent or elective status of the procedure. AUC analysis demonstrated that MELD and MELDNa + score greater than 10.5 was the most predictive of peri-operative mortality in elective PH cases.

Conclusions: PH is associated with an increased risk of poor surgical outcomes in patients undergoing elective and emergent gastrointestinal surgery.

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Introduction

The incidence of Portal Hypertension (PH) has been increasing in recent years in the United States. In patients undergoing general surgery, the presence of PH has been associated with poor outcomes.^{1–4} Therefore, treatment guidelines in Europe and the United States recommend caution while selecting candidates for surgery.^{5–8}

Gastrointestinal (GI) surgery is associated with higher mortality rates compared to other intra-abdominal procedures, such as nephrectomies and cystectomies.⁹ Currently, the risk of postoperative morbidity and mortality in patients with cirrhosis is assessed using

the Child Pugh Turcotte Score (CPT) and the Model of End Stage liver disease (MELD) score.^{10–13}

Esophageal varices (EV) is one of the strongest indicators of PH and it has been used as a surrogate for PH in several previous studies.^{14–16} The aim of this study is to analyze the impact of PH in patients undergoing GI surgery in the U.S. using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database.

Methods

Patient and data collection

The ACS-NSQIP Participant Use Files (PUFs) from 2005 to 2010 were queried for all adult (>17 years-old) patients undergoing the most common gastrointestinal procedures as their primary procedure. Patients undergoing esophageal surgery, gastrectomy, hepatectomy, colectomy, appendectomy, small bowel resection, pancreaticoduodenectomy, distal pancreatectomy, hepaticojejunostomy and cholecystectomy were included. (See the appendix for a table of the included current procedural

Abbreviations: PH, Portal Hypertension; GI, Gastrointestinal; EV, Esophageal varices; LOS, Length of stay; PSM, Propensity score match; AUC, Area under the curve; MELD, Model of End Stage liver disease; CCC, Critical care complications; LOS, Length of stay; ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program; PUFs, ACS-NSQIP Participant Use Files.

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terminology (CPT) codes). Esophageal varices diagnosis was identified using NSQIP's esophageal varices field in the NSQIP PUF which requires a documented diagnosis within 6 months of surgery from an esophagogastroduodenoscopy or CT scan. EV was used as a surrogate for portal hypertension. Patients missing data on EV were removed prior to analysis.

To ensure patient privacy, NSQIP only reports "90+" for patients above the age of 89 years at the time of surgery; an age of 90 was imputed for these cases. MELD score was calculated using the formula $[9.57 \times \ln \text{ serum creatinine (mg/dl)} + 3.78 \ln \text{ serum bilirubin (mg/dl)} + 11.2 \times \ln \text{ INR} + 6.43]$ and was divided in MELD score cutoffs of 12, 15, 18 and 20 to assess risk at different score cutoffs.

Morbidity (30 days) was defined as any of the following post-operative occurrences: superficial surgical site infection, deep surgical site infection, wound disruption, transfusion, urinary tract infection, any return to the operating room (OR), and critical care complications (CCC). A CCC (30 days) was defined as any of the following postoperative occurrences: unplanned intubation or mechanical ventilation for longer than 48 h, pneumonia, sepsis, septic shock, renal failure, cardiac arrest, myocardial infarction or stroke, pulmonary embolism, deep vein thrombosis, or organ/space surgical site infection.

Statistical analyses

Preoperative and perioperative characteristics were compared between those with and without EV. Categorical variables were reported using counts (N) and column percentages were compared using chi-square or Fisher's exact tests, as appropriate. Continuous variables were tested for normality using Shapiro-Wilk test. Normally-distributed continuous variables were reported using means and standard deviations (SD) and compared using t-tests; otherwise, they were reported using medians and 25th - 75th percentiles (IQR) and compared using Mann-Whitney *U* test. Both the unadjusted and adjusted impact of EV on the 30-day patient outcomes were assessed using regression models. Logistic regression models were used for binary outcomes and general linear regression models were used for continuous outcomes. The area under the curve (AUC) was calculated to assess the MELD and

MELDNa + score that was most predictive of perioperative death (mortality within 30 days).

A propensity score match (PSM) was also used to account for observed confounding factors.¹⁷ Only cases with all necessary MELD score lab values were included. The probability of having EV was estimated using a logistic regression model with EV as the dependent variable and all variables with a bivariate p-value with EV less than 0.10 and an overall incidence greater than 0.5% as predictor variables. The PSM was done using a nearest-neighbor matching algorithm at a 1:5 treated to control ratio. The balance between EV and no EV in the resulting PSM cohort was assessed using standardized mean differences (SMD), where values less than 0.10 were not considered meaningfully different. Sepsis and functional dependence were included in the PSM model due to their clinical relevance. Outcomes in the PSM cohort were analyzed while accounting for the matched nature of the data. Conditional logistic regression models with stratification on match group were used for binary outcomes, multilevel linear models with random intercepts for match group were used for continuous outcomes, and Cox proportional hazards models with stratification on match group were used for time-to-event outcomes.

Analyses were conducted using R statistical programming language version 3.4.0 (R Core Team, Vienna, Austria). The following R packages were also used: MatchIt 3.0.1 (Ho et al.), ggplot2 2.2.1 (Wickham), survival 2.38 (Therneau), and lme4 1.1–13 (Bates et al.). Significance was set at $P < 0.01$ for bivariate comparisons and $P < 0.05$ for regression analyses.

Results

Patients' characteristics and demographics

192,296 patients that underwent gastrointestinal surgery from 2005 to 2010 were identified in the NSQIP dataset. Of those, 379 patients (0.197%) had a diagnosis of esophageal varices and PH at the time of surgery. The median age was 56.5 years, with a median BMI of 26.3 kg/m². Over 46% of these patients were obese and 41.6% were male. Patients with a diagnosis of esophageal varices were older and predominantly male (Table 1).

Table 1

Selected Baseline Characteristics in patients undergoing gastrointestinal procedures with and without portal hypertension.

| | No portal hypertension (N = 191,917) | Portal hypertension (N = 379) | P-value |
|---------------------------------------------------|--------------------------------------|-------------------------------|---------|
| Median Age (IQR), years | 56.5 (17.0) | 58.4 (14.2) | 0.0243 |
| BMI, kg/m ² Median (IQR) | 29.3 (24.4–38.9) | 27.4 (24.0–32.1) | <0.0001 |
| Male | 79,873 (41.6%) | 253 (66.8%) | <0.0001 |
| Current Smoker | 35,119 (18.3%) | 97 (25.6%) | 0.0003 |
| Treatment for Diabetes | 35,145 (18.3%) | 103 (27.2%) | <0.0001 |
| Dyspnea | 29,371 (15.3%) | 80 (21.1%) | 0.0022 |
| Functionally Dependent | 16,662 (8.7%) | 98 (25.9%) | <0.0001 |
| Ventilator Dependent | 3249 (1.7%) | 36 (9.5%) | <0.0001 |
| History of COPD | 10,153 (5.3%) | 31 (8.2%) | 0.0167 |
| Current Pneumonia | 1748 (0.9%) | 16 (4.2%) | <0.0001 |
| Ascites | 3990 (2.1%) | 155 (40.9%) | <0.0001 |
| History of CHF | 2250 (1.2%) | 12 (3.2%) | 0.0021 |
| History of MI | 1418 (0.7%) | 10 (2.6%) | 0.0006 |
| History of Angina | 1345 (0.7%) | 6 (1.6%) | 0.0530 |
| Treatment for Hypertension | 95,700 (49.1%) | 188 (49.6%) | 0.9600 |
| History of PVD | 2699 (1.4%) | 11 (2.9%) | 0.0244 |
| Acute Renal Failure | 1718 (0.9%) | 17 (4.5%) | <0.0001 |
| Currently on Dialysis | 2350 (1.2%) | 16 (4.2%) | <0.0001 |
| Impaired Sensorium | 2579 (1.3%) | 27 (7.1%) | <0.0001 |
| Open Wound/Wound Infection | 5128 (2.7%) | 25 (6.6%) | <0.0001 |
| Bleeding Disorder | 10,267 (5.3%) | 102 (26.9%) | <0.0001 |
| Transfusion ≥ 1 Unit in 72 Hours Prior to Surgery | 2170 (1.1%) | 32 (8.4%) | <0.0001 |
| Preoperative Sepsis/Septic shock | 28,080 (14.8%) | 95 (25.3%) | <0.0001 |

PVD: Peripheral vascular disease.

Table 2
Postoperative outcomes.

| | No portal hypertension (N = 191,917) | Portal hypertension (N = 379) | P-value |
|--------------------------------------------|--------------------------------------|-------------------------------|---------|
| Median Hospital Length of Stay (IQR), Days | 5 (2–10) | 11 (6–20) | <0.0001 |
| Death within 30 Days of Surgery | 6495 (3.4%) | 67 (17.7%) | <0.0001 |
| Morbidity | 47,619 (24.8%) | 191 (50.4%) | <0.0001 |
| Superficial SSI | 11,589 (6.0%) | 32 (8.4%) | 0.0636 |
| Deep SSI | 2570 (1.3%) | 9 (2.4%) | 0.1267 |
| Wound Disruption | 2620 (1.4%) | 12 (3.2%) | 0.0052 |
| Transfusion | 6010 (3.1%) | 49 (12.9%) | <0.0001 |
| UTI | 5793 (3.0%) | 21 (5.5%) | 0.0066 |
| Any Return to OR | 11,861 (6.2%) | 49 (12.9%) | <0.0001 |
| Critical Care Complications | 29,159 (15.2%) | 139 (36.7%) | <0.0001 |
| Unplanned Intubation or Vent > 48 h | 12,327 (6.4%) | 84 (22.2%) | <0.0001 |
| Pneumonia, Postop | 7011 (3.7%) | 26 (6.9%) | 0.0014 |
| Sepsis/Septic Shock | 14,259 (7.4%) | 78 (20.6%) | <0.0001 |
| Renal Failure/Insufficiency | 3027 (1.6%) | 31 (8.2%) | <0.0001 |
| Cardiac Arrhythmia, MI, or CVA | 3036 (1.6%) | 11 (2.9%) | 0.0642 |
| Pulmonary Embolism or DVT | 3841 (2.0%) | 11 (2.9%) | 0.2859 |
| Organ/Space SSI | 7251 (3.8%) | 28 (7.4%) | 0.0004 |

SSI: Surgical site infection; UTI: Urinary tract infection; OR: Operating room; MI: Myocardial infarction; CVA: Cerebrovascular accident; DVT: Deep vein thrombosis.

Over 25% of patients with PH were identified as functionally dependent and 9.5% as ventilator dependent (vs 8.7% and 1.7% $p < 0.0001$ in the non PH group). We also found a higher frequency of ascites in these patients (40.9% vs 2.1% in the non PH group, $p = 0.0001$). Acute renal failure was identified in 4.5% of the patients in the PH group, and 4.2% were on dialysis (vs 0.9% and 1.2% respectively, in the non PH group, $p < 0.0001$) (Table 1).

When comparing, diabetes mellitus and wound infections were significantly higher in the PH group (27.2% vs 18.3%, $p < 0.0001$ and 6.6% vs 2.7%, $p = 0.0001$, respectively) (Table 1). Forty-four percent of patients with PH had albumin levels lower than 3 g/dL. Liver function tests (LFTs) and renal function tests including median alkaline phosphatase (105 vs 81), bilirubin > 1 mg/dl (59% vs 16.5%), BUN > 40 (12.8% vs 3.6%), creatinine > 1.2 mg/dl (26.3% vs 13.4%), PT median (14.6 vs 12.8), PTT median (31.9 vs 29), and SGOT median (40 vs 23), were significantly higher in PH patients compared to those without PH ($p < 0.0001$), while hematological values, such as hematocrit < 30, platelets < 150, and leucocytes ≤ 4500 , were significantly lower in the PH group (24.6% vs 8.4%, 60.2% vs 6.6%, 28.3% vs 7.1%, PH group vs non PH, respectively, $p < 0.0001$). A significantly higher proportion of hyponatremia was noticed on the PH cohort (18.4% vs 9.4% non PH, $p < 0.0001$).

Operative and postoperative characteristics

The median operative time was longer in the PH group when compared to non PH patients (143 vs 134 min, respectively, $p = 0.0079$). In the PH group the most common GI procedures were colectomy 31.1%, small bowel 19.3%, cholecystectomy 17.4%, gastric 10.3%, hepatectomy 8.2%, distal pancreatectomies 4.5%, esophagus 4% appendectomy 4% hepatoicojejunostomy 4.8 and pancreaticoduodenectomies 1.1%. Sixty percent of patients with EV were classified as ASA III and 32.3% as ASA IV-V, which was significantly higher compared to those without EV ($p < 0.0001$).

Table 3
Regression results in patients with PH compared to non-PH after GI surgery all emergent and elective cases.

| Outcome | Type of Estimate | Unadjusted PH Estimate | 95% Confidence Limits | P-value |
|-------------------------|----------------------------------|------------------------|-----------------------|---------|
| 30-Day Mortality | Odds Ratio | 6.131 | (4.666, 7.935) | <0.0001 |
| Morbidity | Odds Ratio | 3.079 | (2.516, 3.767) | <0.0001 |
| CCC | Odds Ratio | 3.233 | (2.617, 3.978) | <0.0001 |
| Hospital Length of Stay | Change in Days for PH over No PH | 6.503 | (5.197, 7.808) | <0.0001 |

CCC: Critical care complications. PH: Portal hypertension.

The median hospital length of stay (LOS) was significantly longer in patients with PH (11 vs. 5 days in the non PH group, $p < 0.0001$). A 17.7% peri-operative mortality (30-days) was found within the PH cohort, whereas a smaller percentage (4.7%) was observed in the non PH group ($p < 0.0001$). Overall morbidity was higher in the PH group compared to those without PH (50.4% vs 24.8%, respectively, $p < 0.0001$). Patients with PH had significantly higher transfusion rates (12.9% vs 3.1% non PH, $p < 0.0001$) and returns to the OR (12.9% vs 6.2% non PH, $p < 0.0001$). Critical care complications were significantly higher in the PH group (36.3% vs 20.1% $p < 0.0001$), particularly unplanned intubation, sepsis, and renal failure (Table 2).

Regression analyses revealed that patients with PH had a 6-fold increase in 30-day mortality, a 3-fold increase in morbidity, and a 3.2-fold increase in CCC (all $p < 0.0001$) (Table 3).

MELD and MELDNa + score on peri-operative mortality

Seventy nine percent of the patients with esophageal varices who died within 30 days of the procedure had MELD score over 12, and 45% had a score of over 20. Ninety percent of peri-operative deaths in the cohort of patients undergoing emergent procedures had a MELD score of 12 or higher. AUC analysis demonstrated that MELD score greater than 10.5 was the most predictive of peri-operative mortality in elective PH cases with a sensitivity of 68% and specificity of 60% (AUC 0.64, CI 95%, 0.535, 0.746, OR 3.2). MELDNa+ of 10.5 was the most predictive of per-operative mortality in this cohort with a sensitivity of 73% and specificity of 0.57% (AUC 0.64, CI 95%, 0.55, 0.75, OR 3.49). (Figs. 1 and 2).

Emergent vs elective cases

Our results showed that patients undergoing emergent procedures had a higher length of stay and risk of morbidity. Patients

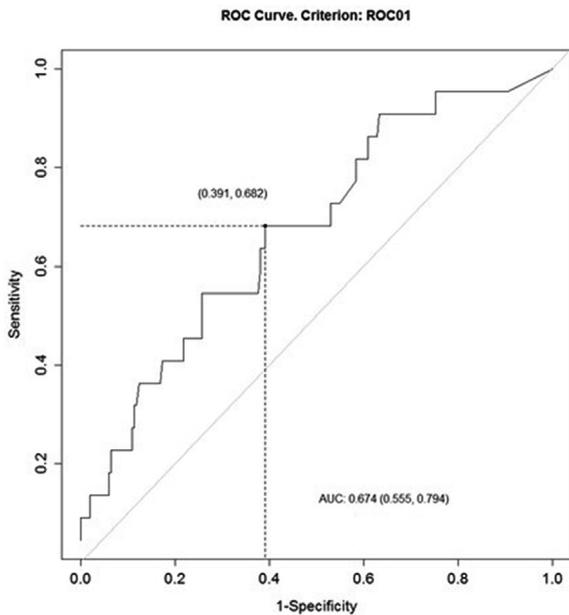


Fig. 1. Receiver operator curve (ROC) for MELD as a predictor of 30-day mortality in non-emergent patients with esophageal varices. The optimal cut-point for predicting 30-day mortality was found to be a MELD score of 10.58 which represented by the intersection of the dotted lines in the graph below.

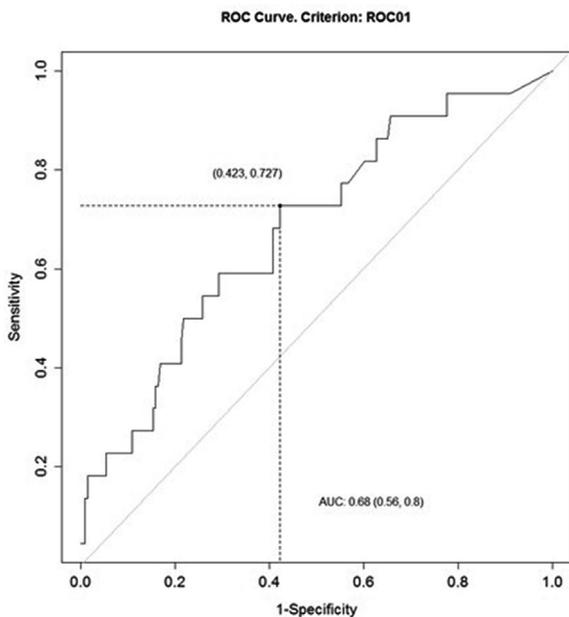


Fig. 2. Receiver operator curve (ROC) for MELD-Na as a predictor of 30-day mortality in non-emergent patients with esophageal varices. The optimal cut-point for predicting 30-day mortality was found to be a MELD score of 10.58 which represented by the intersection of the dotted lines in the graph below.

Table 4
Regression results of elective and emergent cases separately by outcome in PH cases.

| Outcome | Non-emergent | | | Emergent | | |
|-------------------------|--------------------|----------------|---------|--------------------|-----------------|---------|
| | Estimate | 95% CI | P-value | Estimate | 95% CI | P-value |
| 30-Day Mortality | OR 6.380 | (4.147, 9.398) | <0.0001 | OR 4.356 | (2.965, 6.300) | <0.0001 |
| Morbidity | OR 2.675 | (2.082, 3.426) | <0.0001 | OR 3.248 | (2.248, 4.768) | <0.0001 |
| CCC | OR 3.101 | (2.358, 4.039) | <0.0001 | OR 2.618 | (1.839, 3.730) | <0.0001 |
| Hospital Length of Stay | ^a 5.290 | (3.833, 6.748) | <0.0001 | ^a 7.282 | (4.417, 10.147) | <0.0001 |

OR: Odds ratio.

^a Change in days for PH cases over no PH cases.

with PH undergoing non-emergent procedures had a 5.2-fold increase in hospital length of stay and 2.6-fold increase in morbidity, while patients with PH undergoing emergent procedures had a 7.2-fold increase in hospital length of stay and 3.2-fold increased risk of morbidity ($p < 0.0001$). The effect of PH on mortality and morbidity was significant regardless of emergent or non-emergent status (Table 4).

Predictors of morbidity in elective cases with portal hypertension

We performed a logistic regression analysis to estimate predictors of morbidity in non-emergent cases with portal hypertension and found MELD over 18 to be the strongest predictor of overall morbidity (OR 4.633, $p = 0.02$). Other important factors included ascites, preoperative sepsis, and operative time.

Preoperative sepsis was the strongest predictor of critical care complications in patients with PH (OR 6.764, $p = 0.0009$), followed by MELD score over 18 (OR 4.55 $p = 0.038$), steroid use (OR 3.916, $p = 0.0832$), and COPD (OR 2.717, $p = 0.094$). Age at surgery, and operation time longer than 30 min increased the risk of critical care complications by 20%.

Propensity score matched analysis

We performed a 1:5 propensity score match for elective cases with all of the MELD lab values. The PSM model had EV status as the outcome and all of the following are predictors: age, sex, smoking, diabetes, dyspnea, functional dependence, ventilator dependence, pneumonia, ascites, history of CHF, history of myocardial infarction, previous cardiac surgery, renal failure, dialysis, impaired sensorium, disseminated cancer, open wound/wound infection, bleeding disorder, preoperative transfusion, radiotherapy, sepsis/septic shock, GI procedure type, ASA class, wound class, and MELD score. After the PSM, all pre- and peri-operative variables had standardized mean differences less than 0.10, suggesting no meaningful differences. Regression analyses accounting for the matched nature of the PSM cohort found that patients with PH had a 1.98-fold increase in 30-day mortality, a 1.82-fold increase in need for unplanned intubation, and a 1.94-fold increase in transfusion. There was also a 41% increase in the odds of critical care complications ($p = 0.0412$) and 35% increase in morbidity ($p = 0.0550$) in the PH group (Table 5).

Discussion

Gastrointestinal surgical interventions are the most commonly performed intra-abdominal procedures in general surgery. Previous studies have established the presence of esophageal varices as a critical surrogate of portal hypertension, which has important implications in peri-operative outcomes. Artinyan et al.,¹⁸ using the National Inpatient Sample Database, demonstrated high mortality rates in cirrhotic patients undergoing gastrointestinal resections. Kadry et al. also reported increased morbidity and mortality in patients with PH who underwent general surgery procedures.¹⁴ In

Table 5
Outcomes in the elective cases, 1:5 propensity-matched cohort. N = 1278.

| Outcome | Type of Estimate | Estimate | 95% Confidence Limits | P-value |
|-----------------------------|------------------------------------|----------|-----------------------|---------|
| Mortality within 30 Days | OR | 1.986 | (1.160, 3.400) | 0.0124 |
| Morbidity | OR | 1.349 | (0.994, 1.832) | 0.0550 |
| Critical Care Complications | OR | 1.410 | (1.014, 1.962) | 0.0412 |
| Unplanned Intubation | OR | 1.823 | (1.050, 3.164) | 0.0328 |
| Ventilator > 48 Hours | OR | 1.090 | (0.616, 1.929) | 0.7660 |
| Transfusion | OR | 1.945 | (1.208, 3.130) | 0.0062 |
| Operative Duration | Change in Minutes for PH vs. No PH | 14.349 | (-0.669, 29.367) | 0.0611 |
| Hospital Length of Stay | Change in Days for PH vs. No PH | 0.115 | (-1.768, 1.997) | 0.9051 |

PH = Portal hypertension, OR=Odds Ratio.

concordance with these findings, we observed an increased risk in overall morbidity, critical care complications, and mortality associated with the presence of EV (our surrogate for PH) in patients undergoing elective and emergency GI surgery.

Patients with PH showed higher rates of pre-operative encephalopathy, central nervous system disorders, and renal complications such as acute renal failure and dialysis, which has been tightly bound in other series to increased mortality.¹⁹ Diabetes, smoking, and cardiopulmonary co-morbidities were also significantly more prevalent in the PH group. The increased complexity in the PH group resulted in prolonged operative time due to significant coagulopathy associated with bleeding and difficult hemostasis.

Among patients with PH undergoing gastrointestinal surgery, including both elective and emergency cases, our overall analysis demonstrated 6-fold, 3-fold, and 3.2-fold increases in rates of 30-day mortality, morbidity, and critical care complications, respectively. LOS was prolonged by 6.5-fold in PH patients compared to controls.

The MELD score has been considered a strong independent factor associated with morbidity and mortality in cirrhotic patients after general surgery, with mortality rising by 2% for each point above 20.^{13,20–22} Studies have reported that MELD is a better indicator of poor peri-operative outcomes than the CTP score and ASA class in cirrhosis.^{23,24} Teh et al.,¹³ reported a 50% risk of peri-operative death in cirrhotic patients with MELD scores above 20 who underwent major digestive, orthopedic, and cardiovascular surgeries. In their regression analysis, only MELD score, ASA class, and age predicted mortality independent of the type or year of the procedure.

In our series, 40% of the patients with PH who died within 30 days after surgery had MELD greater than 20. Patients with PH were older and belonged to a higher ASA class compared to patients without PH. We found that MELD higher than 18 was the strongest independent predictor of morbidity, increasing its overall risk almost 5-fold. The most significant independent factors associated with critical care complications in our cohort were pre-operative sepsis and MELD score greater than 18, which increased patients' risk by 6.7-fold and 4.5-fold, respectively. Importantly, the calculation of area under the curve demonstrated that MELD and MELDNa + greater than 10.5 was the most predictive score of peri-operative mortality in patients undergoing complex elective gastrointestinal surgery.

Emergency surgery among cirrhotic patients conferred a high mortality risk. This is likely due to difficulties in assessing and controlling modifiable risk factors prior to surgery. A single center experience by Neeff et al.²² reported 30- and 90-day mortality rates of 20% and 30%, respectively, in cirrhotic patients undergoing abdominal surgery. They also found that MELD, CTP, ASA class, emergency operations, and cancer influenced long-term survival. Our results demonstrated that patients with PH undergoing

emergent procedures had a major increase in morbidity compared to elective cases and a significantly higher mortality compared to patients undergoing emergent cases without PH.

Due to important differences between the PH and control groups, we performed a PSM analysis adjusting for factors such as age, gender, MELD, ASA class, diabetes, cardiopulmonary co-morbidities, renal insufficiency, pre-operative sepsis/septic shock, and type of gastrointestinal procedure. Interestingly, the strong effect of PH on critical outcomes such as peri-operative mortality, critical care complications (post-operative sepsis, pneumonia, renal failure and intra-abdominal abscess), un-planned intubation, and transfusions remained after these adjustments. Importantly, mortality was still increased 2-fold and critical care morbidity by 40% after PSM analysis.

Another key, but expected finding was the greater need for transfusion in the PH group even after PSM adjustment. Previous studies have linked transfusions to higher mortality rates and higher incidence of sepsis in the peri-operative period, particularly in patients with liver diseases and cancer.^{25–27} In our series, peri-operative transfusions predicted critical care complications in patients with PH.

Our study has limitations that should be disclosed. We used EV as the only indicator of PH. Tissue biopsy and/or imaging is not available in NSQIP. Other relevant information such as spleen size, trans-hepatic pressure gradient, prophylactic antibiotics, antibiotic treatment, colon preparation practices, and culture results are not available in the database. Nevertheless, the strengths of this system includes stringent definition of the analyzed variables and homogeneous data within a fixed timeframe from multiple healthcare institutions.

Overall, our analysis suggests that patients with EV and portal hypertension have a significant increased risk of 30-day morbidity, mortality, and critical care complications after elective and emergency gastrointestinal surgery. Further prospective studies are needed to increase knowledge on the impact of PH in peri-operative and long term outcomes and help identify modifiable risk factors to improve care of patients with cirrhosis.

Author contribution

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work: FD, CG, MG, FM, LT, AD, RG
- Drafting the work or revising it critically for important intellectual content: FD, CG, MG, FM, LT, AD, RG
- Final approval of the version to be published: FD, CG, MG, FM, LT, AD, RG
- Agreement to be accountable for all aspects of the work: FD, CG, MG, FM, LT, AD, RG

Financial disclosure

None.

Conflicts of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amjsurg.2018.12.008>.

References

- Cucchetti A, Ercolani G, Vivarelli M, et al. Is portal hypertension a contraindication to hepatic resection? *Ann Surg*. 2009;250(6):922–928.
- Jang CW, Kwon HJ, Kong H, et al. Impact of clinically significant portal hypertension on surgical outcomes for hepatocellular carcinoma in patients with compensated liver cirrhosis: a propensity score matching analysis. *Ann Hepatobiliary Pancreat Surg*. 2016;20(4):159–166.
- Bruix J, Castells A, Bosch J, et al. Surgical resection of hepatocellular carcinoma in cirrhotic patients: prognostic value of preoperative portal pressure. *Gastroenterology*. 1996;111(4):1018–1022.
- Bruix J, Llovet JM. Locoregional treatments for hepatocellular carcinoma. *Baillieres Best Pract Res Clin Gastroenterol*. 1999;13(4):611–622.
- Bruix J, Sherman M, Llovet JM, et al. Clinical management of hepatocellular carcinoma. Conclusions of the barcelona-2000 EASL conference. European association for the study of the liver. *J Hepatol*. 2001;35(3):421–430.
- Bruix J, Sherman M, Practice Guidelines Committee AaFtSoLD. Management of hepatocellular carcinoma. *Hepatology*. 2005;42(5):1208–1236.
- Bruix J, Sherman M, American Association for the Study of Liver D. Management of hepatocellular carcinoma: an update. *Hepatology*. 2011;53(3):1020–1022.
- Berzigotti A, Reig M, Abraldes JG, Bosch J, Bruix J. Portal hypertension and the outcome of surgery for hepatocellular carcinoma in compensated cirrhosis: a systematic review and meta-analysis. *Hepatology*. 2015;61(2):526–536.
- Reames BN, Ghaferi AA, Birkmeyer JD, Dimick JB. Hospital volume and operative mortality in the modern era. *Ann Surg*. 2014;260(2):244–251.
- Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg*. 1973;60(8):646–649.
- Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology*. 2000;31(4):864–871.
- Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. *Hepatology*. 2001;33(2):464–470.
- Teh SH, Nagorney DM, Stevens SR, et al. Risk factors for mortality after surgery in patients with cirrhosis. *Gastroenterology*. 2007;132(4):1261–1269.
- Kadry Z, Schaefer EW, Shah RA, et al. Portal hypertension: an underestimated entity? *Ann Surg*. 2016;263(5):986–991.
- Llovet JM, Bru C, Bruix J. Prognosis of hepatocellular carcinoma: the BCLC staging classification. *Semin Liver Dis*. 1999;19(3):329–338.
- Ishizawa T, Hasegawa K, Aoki T, et al. Neither multiple tumors nor portal hypertension are surgical contraindications for hepatocellular carcinoma. *Gastroenterology*. 2008;134(7):1908–1916.
- Haukoos JS, Lewis RJ. The propensity score. *Jama*. 2015;314(15):1637–1638.
- Artinyan A, Marshall CL, Balentine CJ, et al. Clinical outcomes of oncologic gastrointestinal resections in patients with cirrhosis. *Cancer*. 2012;118(14):3494–3500.
- Thorat A, Jeng LB. Management of renal dysfunction in patients with liver cirrhosis: role of pretransplantation hemodialysis and outcomes after liver transplantation. *Semin Vasc Surg*. 2016;29(4):227–235.
- Nicoll A. Surgical risk in patients with cirrhosis. *J Gastroenterol Hepatol*. 2012;27(10):1569–1575.
- Northup PG, Wanamaker RC, Lee VD, Adams RB, Berg CL. Model for End-Stage Liver Disease (MELD) predicts nontransplant surgical mortality in patients with cirrhosis. *Ann Surg*. 2005;242(2):244–251.
- Neeff HP, Streule GC, Drognitz O, et al. Early mortality and long-term survival after abdominal surgery in patients with liver cirrhosis. *Surgery*. 2014;155(4):623–632.
- Befeler AS, Palmer DE, Hoffman M, Longo W, Solomon H, Di Bisceglie AM. The safety of intra-abdominal surgery in patients with cirrhosis: model for end-stage liver disease score is superior to Child-Turcotte-Pugh classification in predicting outcome. *Arch Surg*. 2005;140(7):650–654. discussion 5.
- Delis S, Bakoyiannis A, Madariaga J, Bramis J, Tassopoulos N, Dervenis C. Laparoscopic cholecystectomy in cirrhotic patients: the value of MELD score and Child-Pugh classification in predicting outcome. *Surg Endosc*. 2010;24(2):407–412.
- Amri R, Dinaux AM, Leijssen LCJ, Kunitake H, Bordeianou LG, Berger DL. Do packed red blood cell transfusions really worsen oncologic outcomes in colon cancer? *Surgery*. 2017;162(3):586–591.
- Aquina CT, Blumberg N, Becerra AZ, et al. Association among blood transfusion, sepsis, and decreased long-term survival after colon cancer resection. *Ann Surg*. 2017;266(2):311–317.
- Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. *J Am Coll Surg*. 2009;208(5):931–937. discussion 8–9.