Portal Hypertension

An Underestimated Entity?

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Objective: The aim of this study is to evaluate portal hypertension as an independent risk factor in general surgical procedures.

Background: Data on the impact of portal hypertension in general surgical outcomes has been limited. Published literature has focused mainly on its effect in liver surgery. The Child Pugh score and Model for End Stage Liver Disease are utilized for surgical risk assessment in liver disease but they do not accurately reflect degree of portal hypertension.

Methods: From 2005 to 2012, patients with esophageal varices (EV) in the National Surgical Quality Improvement Program (NSQIP) formed the portal hypertension cohort, and were case matched to patients without esophageal varices (NEV) based on sex, age, surgery type, and year of operation. Thirty day mortality and morbidity were analyzed using generalized estimating equations for binary outcomes. EV patients were also dichotomized by Model for End Stage Liver Disease (MELD) score ($\leq$15 vs >15) and compared with NEV patients.

Results: One thousand five hundred and seventy-four EV patients were matched to 3148 NEV patients. In multivariable analysis, EV patients had a 3.01 higher odds of 30 day mortality ($P < 0.001$) and 1.28 higher odds of complications ($P < 0.001$) compared with NEV patients. EV patients with MELD >15 had 4.64 higher odds of death within 30 days ($P < 0.001$) and had 1.75 higher odds of complications within 30 days ($P < 0.001$) compared with NEV patients; EV patients with MELD 15 or less had 1.95 higher odds of 30 day mortality ($P < 0.001$) compared with NEV patients.

Conclusions: Portal hypertension is associated with a significant mortality and morbidity risk in general surgery, and should not be underestimated even in patients with MELD 15 or less where the early mortality risk remained significant.

Keywords: esophageal varices, general surgery, morbidity, mortality, portal hypertension

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There are limited data on the impact of portal hypertension in general surgical outcomes. Published literature has focused mainly on its effect in liver surgery.[1,2] Portal hypertension has been reported to be associated with an increased morbidity and mortality after hepatic resections, specifically in the setting of cirrhosis.[1] In terms of nonhepatic general surgical procedures, studies have been very limited, concentrating on surgical risk stratification based upon the degree of cirrhosis without specifically examining the role of portal hypertension. Postoperative mortality rates in cirrhotic patients undergoing general surgical procedures have been reported to range from 8.3% to 25%, compared with the 1.1% mortality associated with the noncirrhotic patient.[3,4] Both the Child Pugh classification and the Model for End Stage Liver Disease (MELD) score are currently utilized as the prognostic indicators of postsurgical outcomes in cirrhotic patients.[5] However, the Child Pugh score is not a good predictor of postoperative 30 day mortality and its usefulness has been limited due to the subjective nature of some of its parameters such as the degree of ascites and encephalopathy.[6,7] More recently the MELD score has been proposed as a more objective predictor of the mortality risk for general surgical procedures carried out in patients with cirrhosis.[4,6] MELD was initially developed as a model predictive of the 3 month survival for patients undergoing an elective transjugular portosystemic shunt (TIPS) based on 3 easily measurable parameters: the serum International Normalized Ratio (INR), total bilirubin, and creatinine levels.[8] Although the MELD score is recognized as an independent prognostic predictor of mortality in cirrhotic patients, it does not reflect the degree of portal hypertension.[9] With the MELD score being increasingly utilized as a parameter to assess the risk of complications with general surgical procedures in cirrhotics,[6,10] portal hypertension has not been evaluated as a separate independent measure of surgical risk in patients undergoing nontransplant and nonhepatic general surgical procedures. The objective of this study was to examine whether portal hypertension played a role in the risk stratification and the outcomes of general surgical procedures, and whether its effect was significant even in the setting of a low MELD score.

METHODS

This study was a retrospective cohort study approved by Penn State College of Medicine Institutional Review Board (IRB).

Data Source

Data for this study was obtained from the National Surgical Quality Improvement Program (NSQIP) for the time period extending from 2005 to 2012 inclusive. NSQIP is a peer controlled and validated database, which includes preoperative risk factors, intraoperative variables, and 30-day postoperative mortality and morbidity outcomes for patients undergoing major surgical procedures. It was initially developed in response to a mandate by Congress in the mid-1980s requiring the Veterans Health Administration to report risk adjusted outcomes for its patient population compared with the national average. Over time, the database evolved to allow its use in the private sector and the data are collected by a trained Surgical Clinical Reviewer from patient medical charts, and not insurance claims.[11]

Study Population

We searched the NSQIP database for the presence of portal hypertension. The NSQIP database does not include cirrhosis as a variable but it does include 2 indirect parameters of liver disease and portal hypertension: ascites and esophageal varices (EV).

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We opted not to utilize ascites as a variable, given the well described interobserver variability in assessing ascites[8] and the fact that the NSQIP database includes causes of ascites unrelated to portal hypertension (eg, malignant ascites secondary to peritoneal carcinomatosis).

The presence of esophageal varices, which is documented in the NSQIP database, was felt to truly represent significant portal hypertension. Unlike the study by Bruix et al,[1] we did not have hepatic venous gradient measurements to determine the degree of portal hypertension. However, esophageal varices develop to decompress the hypertensive portal venous system and return blood to the systemic circulation. Portal pressure is determined by the product of portal flow volume and resistance to outflow from the portal vein. Esophageal varices thus occur when the pressure gradient between the portal and hepatic veins is 10 mm Hg or more. Their presence therefore reflects a significant hepatic venous gradient and, accordingly, portal hypertension.[12,13]

All patients with documented esophageal varices in the NSQIP database from 2005 until 2012 formed the cohort labeled EV in this study. Because the focus of the study was on general surgical procedures, patients with current procedural terminology (CPT) codes corresponding to liver resections (CPT codes: 47120, 47122, 47125, 47130, 47135) and portal-systemic shunt procedures (CPT codes: 37145, 37160, 37180, 37181) were excluded from the analysis. Patients with category III CPT codes were also excluded. Liver transplant procedures are not included in the NSQIP database.

Liver resections were excluded because portal hypertension has already been shown to impact hepatectomy outcomes with possible changes in intrahepatic portal venous hemodynamic physiology and an increased risk of postoperative liver dysfunction.[1,2,14–18] Portal systemic shunt procedures were also excluded because they are carried out to treat portal hypertension with the end point of normalization of portal pressures on completion of the operation, thus removing the overall impact of elevated portal pressures on postoperative outcomes.

In this study, patients with documented presence of EV were case matched to noncirrhotic patients without esophageal varices (cohort labeled NEV) using a greedy matching algorithm.[19] Two NEV patients were exactly matched to each EV patient based on gender, age, type of surgery, and year of operation. Type of surgery was derived from CPT codes and included the following categories: intraabdominal (CPT codes 40490–49999), musculoskeletal (CPT codes 20000–29999), cardiovascular (CPT codes 33010–37799), urologic (CPT codes 50010–53899, 54000–55899, 55970–55980, 56405–58999), thoracic (CPT codes 30000–32999, 39000–39599), neurologic (CPT codes 61000–64999), and miscellaneous/other surgeries (CPT codes 10040–19499, 38100–38999, 59000–59899, 60000–60699, 65091–68899, 69000–69979).

Study Outcomes

The outcome variables for this study were death within 30 days of surgery and any complication within 30 days of surgery. Patients with any of the following complications provided by NSQIP were classified as having a complication: superficial surgical site infection (SSI), deep incisional SSI, organ space SSI, pneumonia, urinary tract infection, neural deficit (peripheral nerve injury), deep vein thrombosis, wound disruption, pulmonary embolism, failure to wean from ventilator (>48 hours), progressive renal insufficiency (no dialysis), acute renal failure requiring dialysis, stroke/CVA with deficit, coma more than 24 hours, myocardial infarction, transfusion within 72 hours postoperatively, sepsis, or septic shock.

Covariates

The following patient characteristics collected at the time of surgery and provided by NSQIP were examined in this study: diabetes, functional status prior to surgery, chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD), hypertension, acute renal failure, dialysis, disseminated cancer, steroid use for chronic condition (within 30 days of surgery), weight loss more than 10% (within 6 months of surgery), preoperative systemic sepsis, transfusion more than 4 units PRBCs (within 72 hours before surgery), emergency or nonemergency case, ASA classification, and active alcohol use. Cardiovascular disease was indicated for patients who had any history of myocardial infarction, angina, cardiac surgery, peripheral vascular disease, transient ischemic attack, cerebrovascular accident/stroke, or rest pain/gangrene. MELD scores were calculated for EV patients. MELD score is not included in the NSQIP database, but the laboratory test results that comprise the score (total serum bilirubin, INR, and serum creatinine) are included. The MELD score was calculated for all patients in the EV group who had all 3 laboratory test results.

Statistical Analysis

Statistical analysis was conducted using methods appropriate for the correlation among matched sets of patients. In univariate analysis, death and complications within 30 days were compared between EV and NEV patients using Mantel-Haenszel χ^2 tests.[20] The Mantel-Haenszel test controls for matching by constructing individual tables of group (EV vs NEV) by outcome (yes vs no) for each matched cluster and combining estimates across clusters. Mantel-Haenszel tests were also used to compare patient characteristics between groups.

In multivariable analysis, the study outcomes were compared between EV and NEV patients using multivariable logistic regression models estimated via generalized estimating equations (GEE) that adjusted for all patient characteristics. GEE is an approach to account for correlation among matched sets of patients, and estimates the average response in the population. The working correlation matrix was set as exchangeable. Variables used in matching were also included in the model. Patients with a missing value on any variable in the model were excluded from final analyses. Adjusted odds ratios (aOR) and their 95% confidence intervals (CIs) were reported from these models.

In a subgroup analysis, MELD scores were calculated for all patients in the EV group with laboratory test results for bilirubin, INR, and serum creatinine. The EV group was dichotomized by MELD score ($\leq$15 vs >15). Death and complications within 30 days were compared for 3 groups: NEV patients, EV patients with MELD score 15 or less and EV patients with MELD score more than 15. EV patients with missing MELD scores were excluded from these models. Mantel-Haenszel tests and multivariable logistic regression models estimated via GEE were also used as above.

RESULTS

A total of n = 1578 patients met the inclusion criteria for this study and had documented EV in the NSQIP database from 2005 to 2012. These patients were matched to 2 controls from a pool of 1,477,673 NEV patients. Matching was completed for 1574 of 1578 EV patients; the 4 EV patients without matches were excluded from the analysis. Thus, the final data set for analysis contained N = 1574 EV patients matched to 3148 NEV patients.

The distribution of variables used in matching is shown by study group in Table 1. As specified by the matched design of the study, the distributions were equal between groups for age, sex, type of surgery, and year of surgery. The median age at surgery was 58 years and 66% were male. The majority of surgeries (76%) were intraabdominal.

TABLE 1. Distribution of Variables Used in Matching

	EV (N = 1574)	NEV (N = 3148)
Age		
n	1574	3148
Mean (SD)	58.5 (12.11)	58.5 (12.11)
Median	58.0	58.0
Range	(18.0–90.0)	(18.0–90.0)
Sex		
Female	532 (33.8%)	1064 (33.8%)
Male	1042 (66.2%)	2084 (66.2%)
Type of surgery		
Intra-abdominal	1192 (75.7%)	2384 (75.7%)
Musculoskeletal	98 (6.2%)	196 (6.2%)
Cardiovascular	127 (8.1%)	254 (8.1%)
Urologic	12 (0.8%)	24 (0.8%)
Thoracic	25 (1.6%)	50 (1.6%)
Neurologic	11 (0.7%)	22 (0.7%)
Miscellaneous/other	109 (6.9%)	218 (6.9%)
Year of operation		
2005	45 (2.9%)	90 (2.9%)
2006	169 (10.7%)	338 (10.7%)
2007	248 (15.8%)	496 (15.8%)
2008	289 (18.4%)	578 (18.4%)
2009	255 (16.2%)	510 (16.2%)
2010	301 (19.1%)	602 (19.1%)
2011	153 (9.7%)	306 (9.7%)
2012	114 (7.2%)	228 (7.2%)

Patient characteristics are shown in Table 2. The EV group had a significantly higher prevalence of diabetes mellitus ($P < 0.001$), poorer functional status ($P < 0.001$), history of acute renal failure ($P < 0.001$), an increased requirement for dialysis 2 weeks prior to surgery ($P < 0.001$), a higher ASA score ($P < 0.001$), alcohol consumption ($P < 0.001$) and more than 10% body weight loss in the last 6 months prior to surgery ($P < 0.001$). EV patients also had a significantly higher rate of preoperative systemic sepsis compared with their NEV matched counterpart ($P < 0.001$), and a significantly higher transfusion rate of more than 4 units PRBCs in the 72 hours preoperatively ($P < 0.001$).

In univariate analysis, the EV cohort had a higher 30 day mortality rate (15.7% vs 4.1%, $P < 0.001$) and a higher rate of complications (38.8% vs 23.4%, $P < 0.001$). A total of 303 patients (6%) had a missing value for at least one of the variables included in the model and were therefore excluded. In multivariable analysis(Table 3), EV patients had a 3.01 higher odds of death within 30 days (aOR = 3.01, 95% CI: 2.27–4.00, $P < 0.001$) and 1.28 higher odds of complications within 30 days (aOR = 1.28, 95% CI: 1.09–1.50, $P < 0.001$) compared with matched NEV patients, after adjusting for all other variables in the model. Emergency procedures were associated with 1.40 higher odds of mortality ($P = 0.018$) and 1.27 higher odds of complications ($P = 0.009$). Other variables strongly associated with an increased odds of death within 30 days of surgery were poorer functional status, presence of cancer, ASA classification (score of 4/5 vs 1/2) and sepsis. Functional status, sepsis, and high ASA classification were also strongly associated with higher odds of complications within 30 days. Of these parameters, the presence of EV, poor functional status and sepsis are typical presentations of significant liver disease.

When year of operation was examined, a significantly higher odds of any complication within 30 days was observed in more recent years (aOR = 2.03 for 2011 vs 2005, 95% CI: 1.24–3.31, $P = 0.005$; and aOR = 2.10 for 2012 vs 2005, 95% CI: 1.25–3.55, $P = 0.005$), although no such trend was reflected in terms of 30 day mortality.

TABLE 2. Patient Characteristics

	EV (N = 1574)	NEV (N = 3148)	*P*
Diabetes			<0.001
No	1112 (70.6%)	2520 (80.1%)	
Yes (oral or insulin)	462 (29.4%)	628 (19.9%)	
Functional status prior to surgery			<0.001
Missing	4 (%)	0 (%)	
Independent	1175 (74.8%)	2773 (88.1%)	
Partially dependent	225 (14.3%)	199 (6.3%)	
Totally dependent	170 (10.8%)	176 (5.6%)	
History of severe COPD			0.07
No	1422 (90.3%)	2893 (91.9%)	
Yes	152 (9.7%)	255 (8.1%)	
Cardiovascular disease			0.23
No	1304 (82.8%)	2648 (84.1%)	
Yes	270 (17.2%)	500 (15.9%)	
Hypertension requiring medication			0.41
No	742 (47.1%)	1522 (48.3%)	
Yes	832 (52.9%)	1626 (51.7%)	
Acute renal failure within 24 h prior to surgery			<0.001
No	1506 (95.7%)	3096 (98.3%)	
Yes	68 (4.3%)	52 (1.7%)	
Dialysis within 2 wk prior to surgery			<0.001
No	1489 (94.6%)	3070 (97.5%)	
Yes	85 (5.4%)	78 (2.5%)	
Disseminated cancer			0.49
No	1506 (95.7%)	3025 (96.1%)	
Yes	68 (4.3%)	123 (3.9%)	
Steroid use for chronic condition			0.043
No	1467 (93.2%)	2980 (94.7%)	
Yes	107 (6.8%)	168 (5.3%)	
>10% loss body weight in last 6 mo			<0.001
No	1429 (90.8%)	2971 (94.4%)	
Yes	145 (9.2%)	177 (5.6%)	
Transfusion >4 units PRBCs in 72 h presurgery			<0.001
No	1432 (91%)	3087 (98.1%)	
Yes	142 (9%)	61 (1.9%)	
Preoperative systemic sepsis			<0.001
Missing	7 (%)	30 (%)	
No	1195 (76.3%)	2606 (83.6%)	
Yes	372 (23.7%)	512 (16.4%)	
Emergency case			<0.001
No	1091 (69.3%)	2425 (77%)	
Yes	483 (30.7%)	723 (23%)	
ASA classification			<0.001
Missing	1 (%)	4 (%)	
1-No disturb	3 (0.2%)	109 (3.5%)	
2-Mild disturb	131 (8.3%)	1177 (37.4%)	
3-Severe disturb	898 (57.1%)	1500 (47.7%)	
4-Life threat	495 (31.5%)	341 (10.8%)	
5-Moribund	46 (2.9%)	17 (0.5%)	
EtOH > 2 drinks/day in 2 wk presurgery			<0.001
Missing	0 (%)	257 (%)	
No	1399 (88.9%)	2761 (95.5%)	
Yes	175 (11.1%)	130 (4.5%)	

TABLE 3. Odds Ratios for Death and Complications Within 30 Days Estimated by GEE

	Death Within 30 days		Complications Within 30 days	
Variable	**Odds ratio (95% CI)**	***P***	**Odds ratio (95% CI)**	***P***
EV (vs NEV)	3.01 (2.27–4.00)	<0.001	1.28 (1.09–1.50)	0.003
Age, 10-yr increase	1.37 (1.20–1.56)	<0.001	1.09 (1.02–1.17)	0.009
Sex (M vs F)	1.02 (0.76–1.37)	0.91	0.97 (0.83–1.14)	0.73
Type of surgery				
Intra-abdominal	(ref)		(ref)	
Musculoskeletal	0.61 (0.36–1.05)	0.07	0.83 (0.59–1.17)	0.29
Cardiovascular	0.84 (0.50–1.40)	0.51	0.65 (0.49–0.86)	0.003
Other	0.55 (0.31–0.98)	0.043	0.68 (0.51–0.90)	0.006
Year of operation				
2005	(ref)		(ref)	
2006	0.40 (0.19–0.83)	0.015	1.50 (0.93–2.42)	0.09
2007	0.33 (0.16–0.69)	0.003	1.08 (0.68–1.71)	0.75
2008	0.37 (0.19–0.74)	0.005	0.96 (0.60–1.52)	0.85
2009	0.45 (0.22–0.90)	0.025	1.10 (0.69–1.75)	0.69
2010	0.36 (0.18–0.72)	0.004	1.51 (0.96–2.37)	0.08
2011	0.43 (0.20–0.93)	0.032	2.03 (1.24–3.31)	0.005
2012	0.57 (0.26–1.26)	0.17	2.10 (1.25–3.55)	0.005
Diabetes	0.76 (0.57–1.02)	0.067	1.16 (0.98–1.39)	0.09
Functional status				
Independent	(ref)		(ref)	
Partially dependent	2.37 (1.68–3.34)	<0.001	1.89 (1.50–2.38)	<0.001
Totally dependent	3.85 (2.63–5.66)	<0.001	3.31 (2.42–4.53)	<0.001
COPD	1.32 (0.91–1.90)	0.14	0.93 (0.72–1.21)	0.61
CVD	0.88 (0.63–1.23)	0.46	0.95 (0.77–1.17)	0.63
Hypertension	1.02 (0.78–1.34)	0.86	0.92 (0.79–1.08)	0.31
Acute renal failure	1.84 (1.07–3.16)	0.027	1.87 (1.13–3.11)	0.015
Dialysis	1.72 (1.01–2.93)	0.045	1.28 (0.87–1.90)	0.21
Cancer	3.41 (2.21–5.25)	<0.001	1.51 (1.13–2.03)	0.006
Steroid use	1.54 (1.01–2.34)	0.047	1.25 (0.93–1.67)	0.14
Weight loss >10%	1.60 (1.03–2.49)	<0.001	1.31 (0.99–1.74)	0.06
Sepsis	2.84 (2.12–3.81)	<0.001	1.70 (1.40–2.07)	<0.001
Transfusion	0.93 (0.62–1.39)	0.72	1.68 (1.18–2.41)	0.004
Emergency	1.40 (1.06–1.86)	0.018	1.27 (1.06–1.51)	0.009
ASA classification				
1–2	(ref)		(ref)	
3	2.94 (1.51–5.71)	0.002	1.72 (1.40–2.11)	<0.001
4–5	7.27 (3.66–14.5)	<0.001	2.98 (2.29–3.89)	<0.001
Alcohol use	1.11 (0.71–1.74)	0.63	1.19 (0.89–1.58)	0.23

MELD Analysis

A subgroup analysis was also carried out based on MELD score. A total of 1291 EV patients (82%) had preoperative bilirubin, INR and creatinine laboratory test results and therefore a MELD score was calculated. Fig. 1 shows the distribution of MELD scores within the EV cohort. The median MELD score was 12 (interquartile range, 9–16), with 930 EV patients having MELD 15 or less (72%) and 361 EV patients having MELD more than 15 (28%).

Univariate analysis based on stratifying the EV group by MELD scores indicated that EV patients with MELD more than 15 had a higher death rate within 30 days (33%) compared with EV patients with MELD 15 or less (8%) and NEV patients (4%). Similarly, the complication rate (within 30 days) was higher for patients with EV and MELD more than 15 (60%) versus EV patients with MELD 15 or less (32%) and NEV patients (23%). All differences with respect to mortality and complications between each group were statistically significant ($P < 0.001$ for all).

Table 4 shows the multivariable analysis when stratifying the EV group by MELD score and adjusting for patient characteristics. Compared with NEV patients, EV patients with MELD more than 15 had 4.64 higher odds of death within 30 days (aOR = 4.64, 95% CI: 3.20–6.72, $P < 0.001$) and EV patients with MELD ≤15 had 1.95 higher odds (aOR = 1.95, 95% CI: 1.36–2.79, $P < 0.001$). For complications, EV patients with MELD more than 15 had 1.75 higher odds of complications within 30 days (aOR = 1.75, 95% CI: 1.32–2.32, $P < 0.001$) compared with NEV patients. However, the odds of complications within 30 days was not statistically different for EV patients with MELD 15 or less compared with NEV patients (aOR = 1.20, 95% CI: 0.99–1.45, $P = 0.07$).

DISCUSSION

Much of the literature examining general surgical risk in patients do not specifically examine the role of portal hypertension on surgical outcomes.[2,3,6,10,21] To our knowledge, this is the largest cohort of patients with documented evidence of portal hypertension (EV: n = 1574) as defined by the presence of esophageal varices, pair matched to a reference group without portal hypertension (NEV: n = 3148), that has been analyzed to evaluate the impact of portal hypertension on early postoperative morbidity and mortality after general surgical procedures.

The results of our study indicate that the presence of portal hypertension plays a significant role in the postoperative outcomes after general nonhepatic and nontransplant surgeries. The EV patients in our study experienced significantly higher 30 day mortality (15.7%

TABLE 4. Odds Ratios for Death and Complications Within 30 Days Estimated by GEE With MELD Used to Stratify EV Group

	Death Within 30 d		Complications Within 30 d	
Variable	**Odds Ratio (95% CI)**	***P***	**Odds Ratio (95% CI)**	***P***
Group				
NEV	(ref)		(ref)	
EV with MELD ≤15	1.95 (1.36–2.79)	<0.001	1.20 (0.99–1.45)	0.07
EV with MELD >15	4.64 (3.20–6.72)	<0.001	1.75 (1.32–2.32)	<0.001
Age, 10-yr increase	1.40 (1.20–1.62)	<0.001	1.10 (1.02–1.18)	0.56
Sex (M vs F)	0.97 (0.71–1.34)	0.87	0.95 (0.81–1.12)	0.56
Type of surgery				
Intra-abdominal	(ref)		(ref)	
Musculoskeletal	0.66 (0.36–1.19)	0.17	0.79 (0.55–1.12)	0.18
Cardiovascular	0.80 (0.47–1.35)	0.40	0.56 (0.42–0.75)	<0.001
Other	0.51 (0.25–1.01)	0.05	0.65 (0.48–0.88)	0.005
Year of operation				
2005	(ref)		(ref)	
2006	0.42 (0.19–0.91)	0.027	1.60 (0.97–2.63)	0.06
2007	0.34 (0.15–0.74)	0.007	1.19 (0.73–1.91)	0.49
2008	0.41 (0.20–0.87)	0.020	1.05 (0.65–1.70)	0.85
2009	0.48 (0.23–1.02)	0.06	1.17 (0.72–1.89)	0.53
2010	0.40 (0.19–0.82)	0.013	1.68 (1.05–2.69)	0.030
2011	0.42 (0.18–0.99)	0.047	2.17 (1.29–3.63)	0.003
2012	0.54 (0.22–1.29)	0.16	2.49 (1.45–4.28)	0.001
Diabetes	0.76 (0.56–1.03)	0.08	1.18 (0.98–1.42)	<0.001
Functional status				
Independent	(ref)		(ref)	
Partially dependent	2.21 (1.52–3.22)	<0.001	1.78 (1.40–2.27)	<0.001
Totally dependent	3.54 (2.33–5.38)	<0.001	3.07 (2.21–4.27)	<0.001
COPD	1.68 (1.14–2.45)	0.008	1.02 (0.77–1.34)	0.90
CVD	0.96 (0.67–1.37)	0.81	1.04 (0.83–1.29)	0.77
Hypertension	1.12 (0.84–1.50)	0.44	0.93 (0.79–1.10)	0.42
Acute renal failure	1.60 (0.86–2.97)	0.14	1.99 (1.11–3.57)	0.020
Dialysis	1.18 (0.63–2.22)	0.60	1.25 (0.80–1.97)	0.33
Cancer	3.81 (2.42–6.00)	<0.001	1.59 (1.17–2.15)	0.003
Steroid use	1.66 (1.07–2.58)	0.025	1.28 (0.95–1.73)	0.11
Weight loss >10%	1.64 (1.05–2.57)	0.029	1.30 (0.97–1.75)	0.08
Sepsis	2.72 (1.97–3.74)	<0.001	1.70 (1.39–2.09)	<0.001
Transfusion	1.10 (0.73–1.68)	0.64	1.77 (1.21–2.61)	0.004
Emergency	1.32 (0.96–1.80)	0.08	1.23 (1.02–1.48)	0.032
ASA classification				
1–2	(ref)		(ref)	
3	3.14 (1.52–6.50)	0.002	1.66 (1.34–2.05)	<0.001
4–5	6.67 (3.17–14.0)	<0.001	2.85 (2.15–3.78)	<0.001
Alcohol use	1.36 (0.84–2.21)	0.21	1.30 (0.96–1.75)	0.09

vs 4.1%, $P < 0.001$) and a higher rate of complications (38.8% vs 23.4%, $P < 0.001$). The multivariate analysis results also show that EV was associated with a 3.01 higher odds of death within 30 days and 1.28 higher odds of complications within 30 days compared with matched NEV patients. Interestingly, there was a significantly higher rate of complications within 30 days in more recent years, which could reflect a possible tendency to perform more complex cases over time, although this was not accompanied by a concomitant increase in the 30 day mortality. Emergency operations were significantly higher in the EV group (Table 2; 30.7 EV vs 23% NEV, $P < 0.001$), and were correlated with a worse outcome. Emergency procedures were associated with 1.40 higher odds of mortality ($P = 0.018$) and 1.27 higher odds of complications ($P = 0.009$) (Table 3).

Liver resections were excluded from this study as portal hypertension has already been shown to be associated with poorer outcomes, especially within the setting of cirrhosis, and changes in intrahepatic portal venous hemodynamic physiology are also thought to play a role in the development of liver failure.[1,2,14–18] However, portal hypertension in general surgical procedures not involving liver resection has been poorly studied. Surgical risk stratification in patients with liver disease has classically been based on the Child Pugh classification or the MELD score. The usefulness of the Child Pugh score has been limited by the subjective nature of some of its variables such as the degree of ascites and encephalopathy.[6,7] Conversely, the MELD score does not examine any component of portal hypertension and is limited to 3 variables: total bilirubin, INR, and serum creatinine, which may be altered from nonhepatic causes.

Our results suggest that in current surgical practice there is already a preselection of low MELD patients for general surgical procedures as depicted in the Figure 1 histogram. Although a significantly higher 30 day postoperative mortality was seen in EV patients with a higher MELD score (MELD > 15), our results show that EV patients with a MELD score 15 or less also had a significant mortality risk with a 1.95 higher odds of death within 30 days, and a trend toward increased complications within 30 days (aOR = 1.20) compared with NEV patients.

Indirect characteristics of advanced liver disease and cirrhosis, measured by some co-morbidities were more common in EV

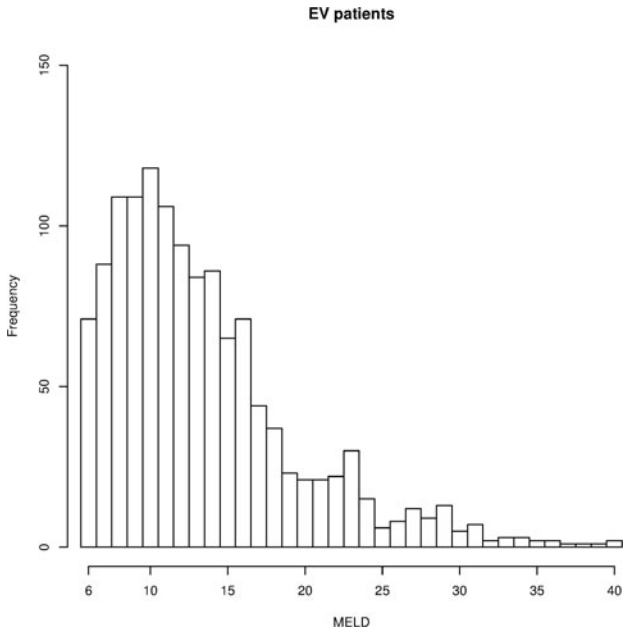

FIGURE 1. EV patients MELD distribution histogram.

patients as shown in Table 2. The EV group had a significantly higher prevalence of diabetes mellitus, poorer functional status, acute renal failure, a greater requirement for dialysis 2 weeks prior to surgery, a worse ASA score, a history of alcohol consumption, and a more than 10% body weight loss in the last 6 months prior to surgery, all of which tend to be associated with liver disease. EV patients also had a significantly higher rate of preoperative systemic sepsis, a complication typically seen in cirrhotics, compared with their matched NEV patients, and the presence of EV was also associated with a significantly higher transfusion rate of more than 4 units PRBCs in the 72 hours preoperatively.

However, although these characteristics were an indirect reflection of possible advanced liver disease and cirrhosis, a weakness of this study is that cirrhosis is not a variable collected within the NSQIP database. Furthermore, this is a retrospective cohort study using existing data, limiting our ability to control for other covariates that might contribute to increased risk of death or other complications. Additionally, significant portal hypertension can be present in the absence of esophageal varices and although ideally one would like to study patients with direct portal pressure measurements based on a hepatic venous gradient, such measurements are invasive and not routinely carried out preoperatively. Other manifestations of portal hypertension such as encephalopathy and ascites are very subjective. Encephalopathy is not a parameter collected in the NSQIP database, although ascites is a variable that is followed but NSQIP includes causes of ascites unrelated to portal hypertension such as malignant ascites secondary to peritoneal carcinomatosis, and therefore the latter was excluded from the analysis. In spite of these weaknesses, however, there are no other studies to our knowledge that have examined such a large case matched cohort of patients with documented portal hypertension (EV = 1574; NEV = 3148), and the significant impact of portal hypertension alone on early postoperative morbidity and mortality was clearly seen in our study when EV patient outcomes were compared with the case matched NEV cohort.

Although in current practice MELD is being used to assess surgical risk, the results of this study indicate that MELD is not the only parameter that should be examined in the evaluation of preoperative risk in patients with liver disease. Portal hypertension alone appears to be an important parameter in the evaluation of surgical risk factors. Given the significantly higher early mortality and increased risk of complications associated with portal hypertension, we feel that it should be included in the preoperative assessment of surgical risk of general surgical patients. The presence of portal hypertension can be evaluated through preoperative endoscopy, or by the direct measurement of the hepatic venous gradient. Our study clearly shows that portal hypertension should not be underestimated even in the well compensated patient with cirrhosis with a low MELD, and accordingly referral to experienced tertiary centers with expertise in portal hypertension and advanced liver disease may be an important consideration.

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