RESEARCH **ORIGINAL ARTICLE**

Predictors and Outcomes of Intraoperative Blood Transfusion in Cirrhotic Veterans

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ABSTRACT

BACKGROUND - Cirrhotic patients are at increased risk of morbidity and mortality following any surgical procedure. One of the independent predictors of adverse outcomes is intraoperative transfusion (IOT). In this study we examine the profile of cirrhotic patients requiring IOT to determine its predictors.

METHODS- The Veterans Affairs Surgical Quality Improvement Program (VASQIP) was utilized to identify all patients with cirrhosis and ascites who underwent any non-liver transplant procedures from 2008 to 2015. Univariate and multivariate regression were used to identify predictors of increased risk of IOT and associated outcomes.

RESULTS- A total of 1,957 cirrhotic patients were identified, of which only 358 (18.8%) required IOT ≥1 unit. IOT group were older, more frail, higher Model for End-stage Liver Disease (MELD) score, anemic (hematocrit <30%), hypoalbuminemic. This group also had more emergent procedures, higher rates of preoperative sepsis, longer operative time, longer postoperative length of stay, and higher morbidity and mortality rates. On multivariate logistic regression, pancreatic resections, open hernia repair, anemia, gastric resections, hypoalbuminemia, acute renal failure, emergency procedure, preoperative sepsis, and preoperative weight loss >10% were significant predictors of IOT.

CONCLUSION - IOT in cirrhotic patients is associated with worse outcomes. Pancreatic procedures, open hernia repair, and gastric resection were associated with increase IOT. This aid in preoperative planning and blood products preparation.

KEYWORDS - Transfusion; Operative; Cirrhosis; Outcomes; Veterans.

INTRODUCTION

The prevalence and burden of chronic liver disease and cirrhosis have been on the rise, with an increase of 59% between 2001 and 2013 in the Veterans Affairs (VA) healthcare system [1]. This trend is attributed to multiple factors, including the worsening of non-alcoholic liver disease, alcohol use, and obesity [1]. It is well supported in the literature that this population is at increased risk of adverse effects following any surgical intervention, with mortality reaching 45% in non-hepatic procedures [2,3].

About 10% of cirrhotic patients will require surgical intervention at some point, and this number will increase due to improved survival [3]. These procedures include cholecystectomy, hernia repair, and colectomy [4–6]. Multiple factors were identified that predict poor outcomes including high Model for End-stage Liver Disease (MELD) score, emergency surgery, hypoalbuminemia, perioperative blood product transfusion [7,8]. Application of minimally invasive approaches in cirrhotic patients showed advantageous outcomes with shorter length of stay (LOS), lower intraoperative transfusion as well as lower morbidity and mortality in selected patients [4,9]. Coagulopathy of the end stage liver disease is a complex process not simply explained by decrease in anticoagulant and procoagulant factors [10].

Due to paucity of data on intraoperative blood transfusion in cirrhotic patients undergoing general surgical procedures other than liver transplant surgery, we aimed to explore and identify the predictors of IOT in this population of patients using the Veterans Affairs Surgical Quality Improvement Program (VASQIP) database.

METHODS

VASQIP is a robust database, established in 1991 in 44 veterans affairs medical centers (VAMC), and extended to include 123 centers later on [11]. We inquired this database for patients who underwent non-liver transplant abdominal procedures between 2008-2015.

Liver cirrhosis is captured automatically in the VASQIP database based on the presence of peritoneal fluid on physical exam or imaging, along with documentation of active or history of liver disease [12]. Data collected included demographics, preoperative comorbidities, operative details, and 30 and 90-day postoperative outcomes. 30-day morbidity were defined as occurrence of at least one complication within 30 days from the procedure. The VASQIP can capture up to 28 different postoperative events as complications. Model for End-stage Liver Disease (MELD) score was calculated using preoperative results of serum total bilirubin, international normalized ratio (INR), and serum creatinine, using the following formula: 11.2 × loge (INR) + 3.78 × loge (serum bilirubin [mg/dL]) + 9.57 × loge (serum creatinine [mg/dL]) + 6.43 [13]. Any patient's laboratory value <1 was given the value of 1. MELD score was classified into: mild (≤8), moderate (9-16), and severe (≥17), to correlate with Child-Turcotte-Pugh score classes A, B, and C, respectively [14,15].

The 5-item modified frailty index (mFI) was calculated for each patient by adding the preoperative variables which are: chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), not independent functional status, hypertension on medications and diabetes mellitus. The score ranges between 0 and 5. Then it was categorized into three groups: 0, 1, and +2 [16]. This study was approved by the Institutional Review Board of our institution, and due to the retrospective and de-identified nature of the data, patient consent was waived.

For categorical clinical and demographic variables, the chi-square test was utilized, and two-sided unpaired Student's t-test or Mann–Whitney U test were used for continuous numerical variables as appropriate. Multivariate logistic regression adjusting for demographics, comorbidities, and other preoperative factors was used to analyze postoperative outcomes. P <0.05 was considered statistically significant. Statistical analyses and nomogram construction were carried out using SPSS version 25.0 (IBM Corp. Armonk, NY) and Stata version 14.2 (Stata Corp. College Station, TX).

RESULTS

A total of 1,957 cirrhotic patients were included in the analysis, 18.8% of patients required IOT ≥1 unit. Patients' demographics and preoperative characteristics are summarized in Table 1. IOT group were older, more frail (modified frailty index (mFI) +2), had higher MELD scores, were anemic (hematocrit <30%), and were hypoalbuminemic (<3.5 g/dL). This group also had more emergent procedures, higher rates of preoperative sepsis, longer operative time, longer postoperative length of stay (LOS), and higher morbidity and mortality rates, as listed in Table 2.

On multivariate logistic regression, pancreatic resections, open hernia repair, anemia, gastric resections, hypoalbuminemia, MELD score >8, acute renal failure, emergency procedure, preoperative sepsis, and preoperative weight loss >10% were significant predictors of IOT (Table 3). A significant linear correlation was found between MELD score and number of intraoperative transfused blood units (R2 Linear = 0.032).

DISCUSSION

The incidence of liver cirrhosis is increasing worldwide [1,17,18]. It is well reported in the literature that these patients suffer from worse outcomes compared to non-cirrhotic patients. Multiple factors affect surgical outcomes, one of those is IOT [7]. Utilizing the VASQIP database, we compared the profiles and outcomes of cirrhotic patients who required IOT in general surgery procedures over the period of 8 years.

Coagulopathy of the end stage liver disease is a complex process not simply explained by alterations in anticoagulant and procoagulant factors, along with thrombocytopenia which put these patients at increased risk for intraoperative bleeding and requiring transfusions [10,19]. Multiple studies explored the predictors of blood loss in patients undergoing liver transplant and hepatectomies [20,21]. No studies explored that in other general surgery procedures as listed in our study.

In this report, we are able to identify certain surgical procedures that caried higher risk of IOT including gastric resection, pancreatic surgery and open hernia repair. Other predictors include Hypoalbuminemia, anemia, weight loss >10%, emergency surgery, preoperative sepsis, acute renal failure, similar to what reported previously [22]. We found a linear correlation between MELD score and number of transfused units intraoperatively. Minimally invasive approaches are shown to be associated with less intraoperative blood loss.

Our study has its not without limitations. As a retrospective analysis of clinical database, data lacked certain points regarding preoperative factors that may have affected selecting the surgical approach including previous abdominal surgery, severity of ascites, as well as important postoperative complications, most notably decompensated liver failure. Additionally, there is a potential for selection bias. Also, given the nature of the VA patient population, which is mainly male and elderly, our findings may not be generalizable to other patient populations. Further data is needed to build a predictive model to estimate the number of required blood products to aid in perioperative management of these patients.

In conclusion, cirrhotic patients undergoing general surgical procedures are at high risk of worse outcomes, particularly if they require IOT. Certain risk factors can help identify these patients and may aid perioperative decision-making regarding blood products preparation and capability to accommodate that.

AUTHORS' CONTRIBUTIONS

Study conception and design: AS
Acquisition of data: AS
Analysis and interpretation of data: AS
Drafting of manuscript: AS, AP
Critical revision: KS

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DISCLOSURES

Drs. A Shahait, A Pearl and Dr. K Saleh have no conflicts of interest or financial ties to disclose.

DISCLAIMER

The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States Government.

Table 1. Acute Kidney Injury Cast Scoring Index (CSA). The approach to viewing the slide was to search for casts (GCs or ECCs), then view the entire slide. Granular cast index. GC = Granular casts; ECC = epithelial cell casts; LPF = low-power field (×10). The table is adapted from Chawla et al. Nephron Clin Pract 2008;110:c145–c150.

	All n= 1,957	With intraoperative blood transfusion n=358 (18.8%)	Without intraoperative blood transfusion n=1,589 (81.2%)	P-value
Age (years), mean ± SD	63.5 ± 10.8	65.1 ± 11.5	63.2 ± 10.6	**0.002**
Age ≥ 65 years, n (%)	769 (39.3)	175 (47.6)	594 (37.4)	**<0.001**
Sex (male), n (%)	1,910 (97.6)	358 (97.3)	1,552 (97.7)	0.661
ASA class, n (%)				<0.001
1 or 2	73 (3.7)	2 (0.5)	71 (4.5)	
≥3	1,884 (96.3)	366 (99.5)	1,518 (95.5)	
BMI (kg/m2), mean ±SD	26.6 ± 6.3	26.9 ± 7.8	26.5 ± 5.9	0.381
Obesity (BMI ≥30), n (%)	127 (6.5)	27 (7.3)	100 (6.3)	0.686
Underweight (BMI <18.5), n (%)	486 (24.8)	94 (25.5)	392 (24.7)	0.686
Emergency, n (%)	895 (45.7)	228 (62.0)	667 (42.0)	**<0.001**
Preoperative Sepsis	481 (24.6)	166 (45.1)	315 (19.8)	**<0.001**
Current smoker, n (%)	852 (43.5)	144 (39.1)	708 (44.6)	0.059
Current alcohol use, n (%)	290 (14.8)	57 (15.5)	233 (14.7)	0.688
Independent functional status, n (%)	1,249 (63.8)	154 (41.8)	1,095 (68.9)	**<0.001**
Modified 5-point frailty index, n (%)				**<0.001**
0	337 (17.2)	31 (8.4)	306 (19.3)	
1	649 (33.2)	102 (27.7)	547 (34.4)	
+2	971 (49.6)	235 (63.9)	736 (46.3)	
Preoperative comorbidities, n (%)				
CHF	128 (6.5)	33 (9.0)	95 (6.0)	**0.037**
Hypertension on medications	1,313 (67.1)	260 (70.7)	1,053 (66.3)	0.107
Diabetes mellitus	482 (24.6)	98 (26.6)	384 (24.2)	0.323
COPD	474 (24.2)	100 (27.2)	374 (23.5)	0.142
Chronic Steroid use	94 (4.8)	29 (7.9)	65 (4.1)	**0.002**
Weight loss >10%	384 (19.7)	105 (28.7)	279 (17.6)	**<0.001**
Dialysis	104 (5.3)	36 (9.8)	68 (4.3)	**<0.001**
Acute renal failure	123 (6.3)	53 (14.4)	70 (4.4)	**<0.001**
MELD score, mean ± SD	9.5 ± 2.7	10.5 ± 3.2	9.3 ± 2.4	**<0.001**
Mild (≤8)	645 (33.0)	90 (24.5)	555 (34.9)	
Moderate (9-16)	1,090 (55.7)	230 (62.5)	860 (54.1)	**0.001**
Severe (≥17)	222 (11.3)	48 (13.0)	174 (11.0)	
Sodium	136.7 ± 4.9	137.0 ± 4.9	136.7 ± 4.8	0.213
Anemia (Hematocrit <30%), n (%)	521 (26.6)	214 (58.2)	307 (19.3)	**<0.001**
Hypoalbuminemia (<3.5 g/dL), n (%)	1,435 (73.3)	329 (89.4)	1,106 (69.6)	**<0.001**
Thrombocytopenia (<150×109/L), n (%)	735 (37.6)	141 (38.3)	594 (37.4)	0.739

Abbreviations: SD: Standard Deviation; ASA: American Society of Anesthesiologists; BMI: body mass index.; CHF: Congestive Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; MELD: Model for End-stage Liver Disease

Table 2. Unadjusted analysis of operative and postoperative mortality, LOS, and morbidities.

	All n= 1,957	With intraoperative blood transfusion n=358 (18.8%)	Without intraoperative blood transfusion n=1,589 (81.2%)	P-value
Operation duration (hours), mean ± SD	1.9 ± 1.4	2.8 ± 1.7	1.8 ± 1.2	**<0.001**
Postoperative LOS (days), median (Interquartile range)	9.0 (14)	15.0 (20.0)	8.0 (11)	**<0.001**
Approach				**<0.001**
Laparoscopic	344 (17.6)	32 (8.7)	312 (19.6)	
Open	1,613 (82.4)	336 (91.3)	1,277 (80.4)	
Procedures				**<0.001**
Open gastric resection	21 (1.1)	11 (3.0)	10 (0.6)	
Open small bowel resection	91 (4.6)	14 (3.8)	77 (4.6)	
Open partial colectomy	422 (21.6)	140 (38.0)	282 (17.7)	
Laparoscopic partial colectomy	164 (8.4)	29 (7.9)	135 (8.5)	
Open total colectomy	54 (2.8)	28 (7.6)	26 (1.6)	
Laparoscopic total colectomy	3 (0.2)	0 (0.0)	3 (0.2)	
Other major abdominal procedures	371 (19.0)	85 (23.1)	286 (18.0)	
Open liver resection	13 (0.7)	6 (1.6)	7 (0.4)	
Laparoscopic liver resection	6 (0.3)	0 (0.0)	6 (0.4)	
Open cholecystectomy	133 (6.8)	28 (7.6)	105 (6.6)	
Laparoscopic cholecystectomy	135 (6.9)	3 (0.8)	132 (8.3)	
Pancreatic resection / necrosectomy	13 (0.7)	10 (2.7)	3 (0.2)	
Diagnostic laparoscopy	7 (0.4)	0 (0.0)	7 (0.4)	
Open hernia repair (inguinal/ventral/ umbilical)	495 (25.3)	14 (3.8)	481 (30.3)	
Laparoscopic hernia repair	29 (1.5)	0 (0.0)	29 (1.8)	
30-day mortality, n (%)	360 (18.4)	117 (31.8)	243 (15.3)	**<0.001**
90-day mortality, n (%)	562 (28.7)	166 (45.2)	396 (24.9)	**<0.001**
6-month mortality, n (%)	656 (33.5)	185 (50.3)	471 (29.6)	**<0.001**
1-year mortality, n (%)	802 (41.0)	211 (57.3)	591 (37.2)	**<0.001**
Morbidity, n (%)	650 (33.2)	203 (55.2)	447 (28.1)	**<0.001**
Surgical complications, n (%)				
Superficial SSI	55 (2.8)	9 (2.4)	46 (2.9)	0.638
Deep SSI	29 (1.5)	9 (2.4)	20 (1.3)	**0.089**
Organ space SSI	64 (3.3)	20 (5.4)	44 (2.8)	**0.010**
Reoperation	3431(16.9)	104 (28.3)	227 (14.3)	<0.001
Wound dehiscence	45 (2.3)	15 (4.1)	30 (1.9)	0.012
Bleeding requiring ≥4 units postoperatively	32 (1.6)	23 (6.3)	9 (0.6)	<0.001
Medical complications, n (%)				
Pneumonia	142 (7.3)	47 (12.8)	95 (6.0)	<0.001
Myocardial infarction	3 (0.2)	2 (0.5)	1 (0.1)	0.034
Reintubation	133 (6.8)	47 (12.8)	86 (5.4)	<0.001
Failure to wean off ventilator	308 (15.7)	121 (32.9)	187 (11.8)	<0.001
Renal failure	49 (2.5)	20 (5.4)	29 (1.8)	<0.001
Urinary tract infection	52 (2.7)	15 (4.1)	37 (2.3)	0.060
Deep venous thrombosis	20 (1.0)	9 (2.4)	11 (0.7)	0.003
Pulmonary embolism	16 (0.8)	3 (0.8)	13 (0.8)	0.996

Abbreviations: SD: Standard Deviation, LOS: Length of Stay; SSI: Surgical Site Infection.

Table 3. Multivariate logistic regression for predictors of intraoperative blood transfusion.

	OR	CI 95%	P-value
Hypoalbuminemia	2.19	1.46-3.28	**<0.001**
Anemia (hemoglobin <10 g/dL)	4.36	3.32-5.72	**<0.001**
Weight loss > 10%	1.48	1.09-2.00	0.013
Emergency procedure	1.82	1.37-2.37	<0.001
Preoperative Sepsis	1.75	1.29-2.37	<0.001
Acute renal failure	1.85	1.13-3.01	0.014
Operation time	1.47	1.32-1.64	<0.001
MELD Score			
9-16	1.8	1.14-2.85	0.012
≥17	3.3	1.08-9.87	0.036
Laparoscopic approach	0.42	0.29-0.63	<0.001
Procedure			
Open gastric resection	3.07	1.00- 9.41	0.050
Pancreatic resection / debridement	34.12	6.34-183.76	<0.001
Open hernia repair	15.40	5.08-46.67	<0.001

Abbreviations: OR: Odds Ratios; CI: Confidence Interval; Model of End-Stage Liver Disease

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