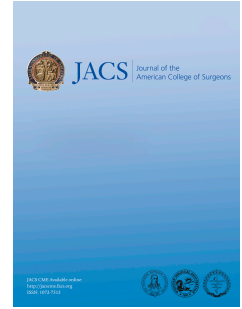


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George A. Taylor, MD, MS, Alexander M. Fagenson, MD, Lindsay E. Kuo, MD, MBA, FACS, Henry A. Pitt, MD, FACS, Kwan N. Lau, MD, FACS

PII: S1072-7515(20)32529-1

DOI: <https://doi.org/10.1016/j.jamcollsurg.2020.11.020>

Reference: ACS 10152

To appear in: *Journal of the American College of Surgeons*

Received Date: 29 November 2020

Accepted Date: 30 November 2020

Please cite this article as: Taylor GA, Fagenson AM, Kuo LE, Pitt HA, Lau KN, Predicting Outcomes of Surgery in Patients with Liver Disease: Albumin-Bilirubin Score vs Model for End-stage Liver Disease-Sodium Score *Journal of the American College of Surgeons* (2021), doi: <https://doi.org/10.1016/j.jamcollsurg.2020.11.020>.

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Predicting Outcomes of Surgery in Patients with Liver Disease: Albumin-Bilirubin Score vs Model for End-stage Liver Disease-Sodium Score

George A Taylor, MD, MS^a, Alexander M Fagenson, MD^a, Lindsay E Kuo, MD, MBA, FACS^a, Henry A Pitt, MD, FACS^b, Kwan N Lau, MD, FACS^a

^aDepartment of Surgery, Lewis Katz School of Medicine Temple University Hospital, Philadelphia, PA

^bRutgers Cancer Institute of New Jersey, New Brunswick, NJ

Drs Taylor and Fagenson contributed equally to the manuscript.

Disclosure Information: Nothing to disclose.

Disclaimer: The American College of Surgeons NSQIP and its participating hospitals were the source of the data used in this study. The analyses, conclusions, and opinions presented in this study were derived solely by the authors and have not been verified or supported by the ACS, NSQIP, or any of its participating hospitals.

Selected for the 2020 Southern Surgical Association Program.

Corresponding author and request for reprints:

Kwan N Lau, MD, FACS

Department of Surgery, Lewis Katz School of Medicine Temple University Hospital

3401 N Broad Street, Philadelphia, PA 19140

Email: kwannang.lau@tuhs.temple.edu

Phone: 215-707-3626

Fax: 215-707-7514

Brief Title: Albumin-Bilirubin and Surgical Outcomes

ABSTRACT

Background: The Albumin-Bilirubin score (ALBI) has recently been shown to have increased accuracy in predicting post-hepatectomy liver failure and mortality compared to the Model for End Stage Liver Disease (MELD). However, the utilization of ALBI as a predictor of postoperative mortality for other surgical procedures has not been analyzed. The aim of this study is to measure the predictive power of ALBI compared to MELD-sodium (MELD-Na) across a wide range of surgical procedures.

Study Design: Patients undergoing cardiac, pulmonary, esophageal, gastric, gallbladder, pancreatic, splenic, appendix, colorectal, adrenal, renal, hernia, and aortic surgery were identified in the 2015-2018 ACS-NSQIP database. Patients with missing laboratory data were excluded. Univariable analysis and receiver operator characteristic (ROC) curves were performed for 30-day mortality and morbidity. Areas Under the Curves (AUC) were calculated to validate and compare the predictive abilities of ALBI and MELD-Na.

Results: Of 258,658 patients, the distribution of ALBI Grade 1, 2, 3 were 51%, 42%, and 7%, respectively. The median MELD-Na was 7.50 (IQR: 6.43-9.43). The overall 30-day mortality rate was 2.7%, while overall morbidity was 28.6%. Increasing ALBI Grade was significantly associated with mortality (ALBI Grade 2 OR 5.24, $p < 0.001$; ALBI Grade 3 OR 25.6, $p < 0.001$) and morbidity (ALBI Grade 2: OR 2.15, $p < 0.001$; ALBI Grade 3: OR 6.12, $p < 0.001$). On ROC analysis, ALBI outperformed MELD-Na with increased accuracy in several operations.

Conclusion: ALBI score predicts mortality and morbidity across a wide spectrum of surgical procedures. When compared to MELD-Na, ALBI more accurately predicts outcomes in patients undergoing pulmonary, elective colorectal, and adrenal operations.

ABBREVIATIONS / ACRONYMS:

AAA, Abdominal aortic aneurysm

ACS, American College of Surgeons

ALBI, Albumin-Bilirubin Score

AUC, Area Under the Curve

CABG, Coronary artery bypass grafting

INR, International Normalized Ratio

MELD-Na, Model for End-stage Liver Disease-sodium score

NSQIP, National Surgical Quality Improvement Program

OR, Odds ratio

ROC, Receiver Operating Characteristic

INTRODUCTION

Surgical patients with liver disease have higher rates of morbidity and mortality than those without liver disease.¹⁻⁵ Multiple studies examining wide ranges of non-hepatic general surgical procedures have demonstrated that outcomes are worse for patients with clinical signs of liver disease, such as ascites or encephalopathy.^{4,6-8} Several clinical and laboratory-based scoring systems have been developed to identify patients at risk for poor outcomes due to their underlying liver disease. The first widely accepted scoring system was the Child-Pugh-Turcotte (CPT) score, whose combination of subjective clinical findings and objective laboratory data identifies cirrhotic patients at high risk for procedural complications.^{7,9} Given the subjective drawbacks of the CPT score, the Model for End-stage Liver Disease (MELD) was developed to objectively define the severity of liver disease.^{10,11} Since 2002, MELD has been used for organ allocation in liver transplantation due to its objectivity and reproducibility.^{12,13} The MELD score has recently been updated to include serum sodium levels (MELD-Na), leading to more accurate mortality prediction.¹⁴⁻¹⁶ MELD-Na has been regarded as the most useful system in predicting outcomes in patients with⁸ and without liver disease.^{17,18}

In the last decade, the Albumin-Bilirubin score (ALBI) was developed to assess liver function and patient survival in patients with hepatocellular carcinoma utilizing only serum albumin and bilirubin.¹⁹ Recent investigations in the outcomes of liver transplantation have shown ALBI to be a better predictor of postoperative liver failure and survival than MELD.^{20,21} Furthermore, ALBI has been found to be a better predictor of post-hepatectomy bile leak,²² liver failure, and mortality when compared to MELD.²³ As the recent focus of the ALBI score has been its validation in liver surgery, this study sought to directly compare the predictive ability of ALBI and MELD-Na in morbidity and mortality for patients undergoing non-hepatic surgery.

METHODS

Study Population

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Participant Use Files from 2015-2018 were combined into one dataset. Current Procedural Terminology (CPT) codes were used to query this dataset for patients undergoing major thoracic or abdominal surgeries. The following procedures were included: coronary artery bypass grafting (CABG), lung resection, esophagectomy, gastrectomy, cholecystectomy, pancreatectomy, splenectomy, appendectomy, colectomy, proctectomy, adrenalectomy, nephrectomy, umbilical hernia repair, ventral hernia repair, open abdominal aortic aneurysm (AAA) repair, and endovascular aortic aneurysm repair (EVAR). The predictive ability of ALBI in hepatectomy was reported previously; thus, liver resections were not included in this study.²³ A full list of CPT codes for each procedure can be found in eTable 1.

Patients were included if they had laboratory testing within 30 days preoperatively, and if both ALBI and MELD-Na scores could be calculated. Due to differences in emergent presentations, the procedures of CABG, colectomy, and open AAA repair were divided into emergent and elective cases. Furthermore, patients with strangulated umbilical or ventral hernias were examined in subset analyses. Due to the de-identified nature of the NSQIP data, Institutional Review Board approval was not required.

ALBI and MELD-Na Scores

ALBI scores were calculated using the formula: $(\log_{10} \text{bilirubin} \times 0.66) + (\text{albumin} \times -0.085)$, where total bilirubin was measured in $\mu\text{mol/L}$ and albumin in g/L .¹⁹ As has been previously described, ALBI was stratified into three grades: Grade 1 (≤ -2.6), Grade 2 (-2.6 to -1.39), and Grade 3 (> -1.39).²⁴ ALBI Grades 2 and 3 were classified as high-risk patients.²⁴

MELD-Na scores were calculated using the formula: $(0.957 \times \ln(\text{creatinine mg/dL}) + 0.378 \times \ln(\text{total bilirubin}) + 1.120 \times \ln(\text{INR}) + 0.643) \times 10$, where total bilirubin is measured in mg/dL; \ln is natural logarithm; and INR is International Normalized Ratio.^{16,25} To calculate MELD-Na, modifications instituted by UNOS/OPTN in 2016,¹⁶ and successfully employed in a NSQIP study by Abbas et al., were used to avoid high MELD-Na scores in patients with hyponatremia but otherwise normal liver function.²⁵ MELD-Na ≥ 10 patients were categorized as high-risk.²²

Surgical Outcomes

Overall morbidity and mortality were the primary outcomes of this study. Morbidity was defined as development of any NSQIP-tracked complication, which include superficial surgical site infection, deep surgical site infection, organ space surgical site infection, wound dehiscence, pneumonia, unplanned reintubation, pulmonary embolism, failure to wean off the ventilator after 48 hours, progressive renal insufficiency, acute renal failure, urinary tract infection, cerebrovascular accident or stroke, cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction, bleeding requiring blood transfusion, deep vein thrombosis, sepsis, septic shock, and unplanned return to the operating room. Mortality was defined as death within 30 days of the operation.

Statistical Analyses

Descriptive statistics were first used to determine the preoperative characteristics of the cohort. Continuous variables were examined as median and interquartile range (IQR). Categorical variables were examined as total count (n) and percentage of the overall cohort. Univariable logistic regression analyses were conducted to determine the likelihood of overall morbidity and 30-day mortality with increasing ALBI grade for the entire cohort. Receiver operating characteristic (ROC) curves were generated for 30-day mortality and overall

morbidity. For the cohort as a whole as well as for each procedure, ALBI and MELD-Na scores were analyzed as continuous variables. To examine the predictive ability of ALBI and MELD-Na in morbidity and mortality, the area under the curve (AUC) was calculated from these ROC curves for both scoring systems, overall and for each procedure. The scoring systems were considered acceptable predictors of morbidity or mortality if the AUC was ≥ 0.6 , and excellent if the AUC was ≥ 0.7 .²⁶ Paired-sample design analysis was performed to directly compare the AUC of the ALBI curve to that of the MELD-Na curve, overall and for each procedure. Statistical analyses were carried out using SPSS (version 26, release 26.0.0.0, IBM Corporation, Armonk, NY, USA). A p-value of ≤ 0.05 was used to determine statistical significance in each analysis.

RESULTS

Patient Demographics

The overall cohort included 258,568 patients. The median age was 60 years old (IQR 47 to 71). Females comprised 50% (n=129,957) of the patients, and 70% (n=182,083) were white (eTable 2). Median body mass index (BMI) was 28.2 (IQR 23.2 to 33.05), and over half of the patients had an American Society of Anesthesiologists (ASA) class of 3 or higher (60%, n=154,200). The median ALBI score was -2.61 (IQR -2.96 to -2.11). In terms of grading, 51.8% (n=131,464) of the cohort were classified as ALBI Grade 1, 42% (n=109,689) Grade 2, and 6.8% (n=17,505) Grade 3. The median MELD-Na score was 7.5 (IQR 6.43 to 9.43), and 78% (n=202,236) of the patients had a MELD-Na score <10 . The median preoperative serum albumin was 3.8g/dL (IQR 3.3 to 4.2), while the median preoperative serum total bilirubin was 0.6 (IQR 0.4 to 0.9). The most common procedure performed in this study was colectomy, which comprised 30% (n=77,343) of the cohort, followed by cholecystectomy (22%, n=55,886), and

appendectomy (13%, n=24,152) (Table 1). The procedures with the fewest patients included splenectomy (0.6%, n=1,617) and adrenalectomy (0.4%, n=943).

MELD-Na and ALBI Scores

The highest median MELD-Na scores per procedure were those of splenectomy and open AAA repair, both at 8.5 (Table 1). The lowest median MELD-Na score by procedure was 6.7, for adrenalectomy. The highest median ALBI score by procedure was -2.3, for both cholecystectomy and splenectomy. The lowest median ALBI score was -2.9, for adrenalectomy. CABG, colectomy, and open AAA repair were subdivided into emergent and elective operations. Although the emergent procedures were performed less frequently than the elective procedures, the median MELD-Na and ALBI scores were higher in each emergent group. Emergent CABG median MELD-Na and ALBI scores were 7.6 and -2.6, respectively; emergent colectomy median scores were 9.8 and -2.0, respectively; and emergent open AAA repair median scores were 10.22 and -2.2, respectively. Emergent colectomy had the highest proportion of ALBI Grade 3 patients (24%, n=4,498). Furthermore, the subsets of patients with strangulated hernias had higher median MELD-Na and ALBI scores than the patients who underwent elective herniorrhaphy, for both umbilical hernia repair (8.0 and -2.7 versus 7.5 and -2.8, respectively), and ventral hernias (7.5 and -2.7 versus 7.3 and -2.8, respectively).

Outcomes

The distribution of 30-day morbidity and mortality for all patients, and for each procedure, is presented in Table 2. Overall morbidity rate for the entire cohort was 29% (n=74,077). The morbidity rate varied widely by procedure, ranging from 12% for umbilical hernia repair to 82% for open AAA repair. In the emergent cases, higher morbidity rates were observed when compared to the same procedure performed electively: colectomy (68% vs. 35%)

and AAA repair (93% vs 73%). However, this difference was not observed for CABG (64.5% vs 67.1%). The 30-day mortality rate for all patients was 2.7% (n=6,952). Similar to morbidity, mortality varied widely by procedure, from 0.3% for appendectomies to 17% in open AAA repair. Higher mortality rates were observed in emergent cases than in elective cases for CABG (4.0% vs 2.2%), colectomy (17% vs. 2.5%), and open AAA repair (31% vs. 6.0%).

ALBI versus MELD-Na as Predictors of Mortality

By univariable regression analysis, increasing ALBI score was associated with a greater likelihood of mortality in the overall cohort (ALBI Grade 2: OR 5.24, 95% CI 4.86 – 5.65, $p < 0.001$; ALBI Grade 3: OR 25.50, 95% CI 23.54 – 27.62, $p < 0.001$; Figure 1A). On ROC analysis, both scoring systems were excellent predictors of mortality: the ALBI AUC was 0.80 for the overall cohort, whereas that of MELD-Na was 0.79 (Table 3). This difference was statistically significant ($\Delta AUC = 0.01$, $p < 0.001$; Figure 2A), indicating that ALBI has better predictive ability than MELD-Na for mortality in the entire population of 258,658 patients.

For each procedure, ALBI was statistically similar or superior to the MELD-Na in predicting mortality for all but one procedure. Specifically, ALBI was a significantly better predictor of mortality than MELD-Na for lung resections ($\Delta AUC = 0.07$, $p = 0.009$; Figure 2B and Table 3), elective colectomy ($\Delta AUC = 0.05$, $p < 0.001$; Figure 2C and Table 3), and adrenalectomy ($\Delta AUC = 0.25$, $p = 0.008$; Figure 2D and Table 3). One exception was emergent colectomy, in which both scoring systems were excellent predictors of mortality, but ALBI was statistically inferior to MELD-Na ($\Delta AUC = -0.02$, $p < 0.001$).

ALBI versus MELD-Na as Predictors of Morbidity

Univariable regression analysis demonstrated that increasing ALBI score was associated with an increasing likelihood of experiencing morbidity in the cohort (ALBI Grade 2: OR 2.15,

95% CI 2.12 – 2.19, $p < 0.001$; ALBI Grade 3: OR 6.12, 95 % CI 5.92 – 6.33, $P < 0.001$; Figure 1B). ROC analysis demonstrated that both ALBI and MELD-Na had good predictive ability for overall morbidity: the ALBI AUC was 0.66 and MELD-Na was 0.63 for the overall cohort, which was a statistically significant difference ($\Delta AUC = 0.03$, $p < 0.001$; Table 4)

The AUCs calculated from the ALBI and MELD-Na ROC curves for morbidity as well as the paired-sample comparisons, for each procedure and overall, are presented in Table 4. Similar to mortality, ALBI was statistically similar or superior to the MELD-Na in predicting morbidity for each procedure. Specifically, ALBI outperformed the MELD-Na in lung resections ($\Delta AUC = 0.05$, $p < 0.001$), gastrectomy ($\Delta AUC = 0.03$, $p = 0.004$), splenectomy ($\Delta AUC = 0.04$, $p = 0.002$), colectomy overall ($\Delta AUC = 0.03$, $p < 0.001$), elective colectomy ($\Delta AUC = 0.05$, $p < 0.001$), proctectomy ($\Delta AUC = 0.03$, $p = 0.019$), adrenalectomy ($\Delta AUC = 0.09$, $p = 0.001$), and ventral hernia repair ($\Delta AUC = 0.01$, $p = 0.040$).

DISCUSSION

In this analysis of the 2015-2018 NSQIP database, the Albumin-Bilirubin score (ALBI) predicted both 30-day mortality (AUC = 0.80) and morbidity (AUC = 0.66) among a wide range of surgical procedures. Increasing ALBI grade was associated with a greater likelihood of mortality (Grade 2: OR 5.24, 95% CI 4.86 – 5.65, $p < 0.001$; Grade 3: OR 25.50, 95 % CI 23.54 – 27.62, $p < 0.001$) as well as overall morbidity (Grade 2: OR 2.15, 95% CI 2.12 – 2.19, $p < 0.001$; Grade 3: OR 6.12, 95 % CI 5.92 – 6.33, $P < 0.001$). In addition, paired-sample analyses of the areas under the ROC curves demonstrated that ALBI was more accurate than the updated Model for End-stage Liver Disease (MELD-Na) in predicting both mortality ($\Delta AUC = 0.01$, $p < 0.001$) and morbidity ($\Delta AUC = 0.03$, $p < 0.001$). ALBI also was a better predictor of mortality than MELD-Na for lung resections, elective colectomy, and adrenalectomy. Furthermore, ALBI was a

better predictor of morbidity for lung resections, gastrectomy, splenectomy, colectomy, proctectomy, adrenalectomy, and ventral hernia repair.

Surgery in patients with liver disease carries an increased risk of morbidity and mortality, especially in patients with more advanced disease.¹⁻⁷ Thus, a reliable and objective scoring system is needed for effective risk stratification. The CPT, MELD, and MELD-Na scores all have been shown to be effective in predicting surgical morbidity and mortality.^{7,8,11} However, studies comparing scoring systems have shown that each model has its advantages and deficiencies, resulting in attempts to modify the equations or switch to new models.^{8,10,20-22} The ALBI score is the latest model to continue this trend. ALBI improves on prior iterations of liver disease scores by utilizing only two objective findings: serum albumin and bilirubin levels.¹⁹ Recently, ALBI has been shown to be better than MELD in predicting mortality and procedure-specific complications in hepatectomy.^{22,23} However, a direct comparison between ALBI and MELD-Na has not been performed in the vast majority of non-hepatic operations.

Cardiothoracic procedures in the current study included coronary artery bypass grafting (CABG) and lung resections. Liver disease has been associated with an increased risk of complications among cardiac surgery patients, and MELD has been described as a predictor of morbidity and short-term mortality.^{3,27,28} In the current study, ALBI was an adequate predictor of mortality (AUC = 0.68), and slightly outperformed MELD-Na (AUC=0.65). In emergent CABG, ALBI was a better predictor of mortality when compared to MELD-Na (AUC = 0.70 vs. 0.60), but these differences were not statistically significant. For pulmonary resections, liver disease confers an increased, but acceptable, risk for complications in Child's A patients, but neither MELD nor ALBI have been studied.^{29,30} In this study, ALBI was a better predictor than MELD-Na of 30-day mortality (AUC = 0.77 vs 0.70, p=0.009) and overall morbidity (AUC = 0.63 vs

0.58, $p < 0.001$) for lung resections. For both cardiac and lung surgery, ALBI should be compared to the current Society of Thoracic Surgeons risk models.

Foregut procedures including esophagectomy and gastrectomy were examined in this study. For esophagectomy, ALBI was an acceptable predictor of mortality (AUC = 0.66), but not of morbidity (AUC = 0.57) and was statistically equivalent to MELD-Na for both mortality (Δ AUC = 0.05, $p = 0.420$) and morbidity (Δ AUC = 0.02, $p = 0.172$). A MELD greater than 9 in patients undergoing esophagectomy has been associated with anastomotic leak ($p = 0.016$) and worse 5-year survival ($p = 0.007$).³¹ Gastrectomy is considered safe with an acceptable risk profile in Child's A patients³² and can even be performed safely laparoscopically in Child's B patients.³³ Interestingly, ALBI grade has recently been associated with gastric cancer recurrence following gastrectomy³⁴ as well as tolerance to adjuvant chemotherapy.³⁵ However, surgical morbidity and mortality have not been directly assessed with ALBI. In this study, ALBI was an excellent predictor of mortality (AUC = 0.79), an acceptable predictor of morbidity (AUC = 0.67), and outperformed MELD-Na in morbidity (Δ AUC = 0.03, $p = 0.004$). With the rising incidence of non-alcoholic fatty liver disease, targeted evaluation of bariatric surgery using MBSAQIP data is warranted to evaluate the predictive ability of ALBI in weight-loss procedures.³⁶

With respect to pancreatic surgery, MELD-Na ≥ 11 has recently been shown to be associated with higher risk of mortality (OR = 2.07, $p < 0.001$) but not morbidity ($p = 0.501$).²⁵ The current analysis confirmed these observations and found no significant differences between ALBI and MELD-Na. Interestingly, ALBI has recently been shown to be a good prognostic score for advanced pancreatic cancer survival.³⁷ Regarding cholecystectomy, a recent NSQIP study demonstrated that the inclusion of ascites with MELD in multivariable regressions yielded higher odds ratios for both composite complications and mortality than MELD alone.³⁸ The

current study found ALBI and MELD-Na to be similar predictors of mortality (AUC = 0.80 vs 0.80) and morbidity (AUC = 0.65 vs 0.66). Splenectomy has generally been regarded as safe and feasible in cirrhotic patients, especially when done laparoscopically, albeit with an increased rate of complications compared to those without cirrhosis.³⁹ For splenectomy, the current study found that ALBI and MELD-Na were similar predictors of mortality (AUC = 0.78 vs 0.78), but ALBI was superior to MELD-Na in predicting morbidity (AUC = 0.73 vs 0.69, $p=0.002$). These findings may warrant the use of ALBI prior to splenectomy in patients with liver disease.

Laparoscopic appendectomy has been shown to have higher rates of mortality when performed in patients with cirrhosis.⁴⁰ However, a paucity of data exists regarding risk stratification equations. In the present study, both ALBI and MELD-Na were excellent predictors of mortality (AUC = 0.85 vs 0.83), and acceptable predictors of morbidity (AUC = 0.66 vs 0.66). For colectomy, MELD-Na > 9 has been associated with an increased likelihood of any complications (OR = 1.3, $p<0.01$) and mortality (OR = 2.7, $p<0.01$).¹⁷ In the current study, ALBI and MELD-Na predicted mortality accurately (AUC = 0.80 vs 0.80, $p=0.486$). However, ALBI was superior to MELD-Na in predicting morbidity (AUC = 0.70 vs 0.67, $p<0.001$). On subset analysis, ALBI outperformed MELD-Na for elective colectomy in both mortality (Δ AUC = 0.05, $p<0.001$) and morbidity (Δ AUC = 0.05, $p<0.001$). In addition, a prior study using the colectomy-targeted NSQIP dataset showed that increasing MELD-Na also was predictive of anastomotic leak.⁴¹ Therefore, ALBI should be further investigated with respect to colectomy-specific outcomes.

To date, only a few case reports describe adrenalectomy in the setting of liver dysfunction.^{42,43} In the current analysis, ALBI was excellent in predicting mortality (AUC = 0.86) and was superior to MELD-Na (Δ AUC = 0.25, $p=0.008$). ALBI also was superior to

MELD-Na in predicting morbidity (AUC = 0.68 vs. 0.59, $p = 0.001$). Accurate prediction of outcomes in patients with portal hypertension and retroperitoneal varices is important, and ALBI may be a simple way to make this assessment. For nephrectomy, ALBI and MELD-Na were equivalent in predicting morbidity ($\Delta\text{AUC} = 0.01$, $p=0.279$) and mortality ($\Delta\text{AUC} = 0.03$, $p=0.377$) with AUCs somewhat better for mortality (0.76 and 0.73) than for morbidity (0.67 and 0.66). Of note, albumin-to-alkaline phosphatase ratio also may predict outcomes in patients undergoing nephrectomy.⁴⁴

With respect to ventral hernias, Schlosser et al recently utilized NSQIP to demonstrate that increasing MELD-Na was associated with an enhanced risk in ventral hernia repair in non-cirrhotic patients.¹⁸ In the current study, both ALBI and MELD-Na were excellent, but statistically similar in predicting mortality in these cases ($\Delta\text{AUC} < -0.01$, $p=0.998$). For morbidity in ventral hernia, ALBI was acceptable and outperformed MELD-Na ($\Delta\text{AUC} = 0.01$, $p=0.040$). In umbilical herniorrhaphy, both ALBI and MELD-Na were excellent and statistically similar in predicting both mortality ($\Delta\text{AUC} = -0.02$, $p=0.208$) and morbidity ($\Delta\text{AUC} < 0.01$, $p=0.197$). Of note, both ALBI and MELD-Na also were equivalent when predicting outcomes in patients with strangulated ventral or umbilical hernias.

Liver disease has been shown to increase the risk of complications in elective AAA repair.³ The current analysis found similarly high rates of mortality and morbidity in these patients. However, ALBI and MELD-Na were only acceptable in predicting outcomes for open AAA repair, whether performed emergently or electively. As open AAA is associated with increased morbidity and mortality, cardiovascular risk may be more important than the risk associated with underlying liver disease. For EVAR, where morbidity and mortality are much

lower, both ALBI and MELD-Na were better at predicting mortality than in predicting morbidity, but again were not statistically different.

This study has several limitations. The patient data analyzed herein comes from a heterogeneous set of participating hospitals (722 in 2018), which may limit the generalizability of these results. Additionally, NSQIP only captures 30-day morbidity and mortality, so longer-term complications with these procedures are not represented in this study. While NSQIP does track several of these procedures in targeted datasets with more detailed variables such as procedure-specific pre-, intra-, and postoperative care, these data and outcomes were not evaluated in the current study. Also, this study focused on mortality and overall morbidity and did not report individual outcomes. Another drawback to this study is the lack of a timeframe placed on the variable “currently on dialysis.” Thus, patients may be listed as on dialysis, but the acuity of their dialysis dependence is unknown. This factor may have negatively impacted the calculation of the MELD-Na scores. Finally, the low percentage of patients with ascites in this study (1.3%) may indicate a selection bias against patients with severe liver disease, thus limiting the population of patients with overt liver dysfunction.

CONCLUSIONS

In this large cohort analysis, ALBI was an excellent predictor of morbidity and mortality in a wide variety of non-hepatic operations. Furthermore, ALBI outperformed MELD-Na in predicting 30-day mortality for lung resections, elective colectomy, and adrenalectomy. ALBI also was a better predictor of morbidity for lung resections, gastrectomy, splenectomy, colectomy, proctectomy, adrenalectomy, and ventral hernia repair. Future investigation into procedure-specific complications using procedure-targeted data is warranted to further clarify the predictive ability of ALBI.

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Table 1. Distribution of Model for End-stage Liver Disease-Sodium Score and Albumin-Bilirubin Score for All Procedures

Procedure	Patients, n (%)	MELD-Na, median (IQR)	ALBI, median (IQR)	ALBI grade 1, n (% row)	ALBI grade 2, n (% row)	ALBI grade 3, n (% row)
Overall	258,658 (100)	7.5 (6.4 – 9.4)	-2.6 (-3.0 to -2.1)	131,464 (50.8)	109,689 (42.4)	17,505 (6.8)
CABG	5,929 (2.3)	7.5 (6.4 – 9.1)	-2.6 (-2.8 to -2.3)	2,820 (47.6)	3,049 (51.4)	60 (1.0)
Emergent	550 (0.2)	7.6 (6.4 – 9.3)	-2.4 (-2.7 to -2.1)	170 (30.9)	370 (67.3)	10 (1.8)
Elective	5,379 (2.1)	7.5 (6.4 – 9.0)	-2.6 (-2.9 to -2.3)	2,650 (49.3)	2,679 (49.8)	50 (0.9)
Lung resection	9,737 (3.8)	6.8 (6.4 – 8.2)	-2.8 (-3.1 to -2.6)	6,992 (71.8)	2,599 (26.7)	146 (1.5)
Esophagectomy	1,595 (0.6)	7.0 (6.4 – 7.7)	-2.8 (-2.9 to -2.5)	1,013 (63.5)	560 (35.1)	22 (1.4)
Gastrectomy	3,086 (1.2)	7.5 (6.4 – 8.7)	-2.5 (-2.9 to -2.0)	1,404 (45.5)	1,429 (46.3)	253 (8.2)
Cholecystectomy	55,886 (21.6)	7.5 (6.4 – 10.0)	-2.3 (-2.8 to -1.8)	20,019 (35.8)	30,549 (54.7)	5,318 (9.5)
Pancreatectomy	20,470 (7.9)	7.5 (6.4 – 9.4)	-2.7 (-3.0 to -2.2)	10,984 (54.7)	7,931 (38.7)	1,555 (7.6)
Splenectomy	1,617 (0.6)	8.5 (7.3 – 11.2)	-2.3 (-2.8 to -1.8)	553 (34.2)	881 (54.5)	183 (11.3)
Appendectomy	34,152 (13.2)	7.5 (6.5 – 9.0)	-2.8 (-3.1 to -2.5)	23,900 (70.0)	9,983 (29.0)	359 (1.1)
Colectomy	77,343 (29.9)	7.6 (6.4 – 9.8)	-2.4 (-2.9 to -1.9)	31,958 (41.3)	37,261 (48.2)	8,124 (10.5)
Emergent	18,991 (7.3)	9.8 (7.5 – 16.1)	-2.0 (-2.5 to -1.4)	3,806 (20.0)	10,687 (56.3)	4,498 (23.7)
Elective	58,352 (22.6)	7.5 (6.4 – 8.9)	-2.6 (-2.9 to -2.1)	28,152 (48.2)	26,574 (45.5)	3,626 (6.2)
Proctectomy	3,913 (1.5)	7.1 (6.4 – 8.2)	-2.8 (-3.0 to -2.4)	2,470 (63.1)	1,328 (33.1)	115 (2.9)
Adrenalectomy	943 (0.4)	6.7 (6.4 – 8.4)	-2.9 (-3.1 to -2.6)	690 (73.2)	238 (25.2)	15 (1.6)
Nephrectomy	11,192 (4.3)	7.5 (6.4 – 9.6)	-2.8 (-3.1 to -2.5)	7,890 (70.5)	3,035 (27.1)	267 (2.4)
Umbilical hernia	7,361 (2.8)	7.5 (6.4 – 10.6)	-2.8 (-3.1 to -2.3)	4,519 (61.4)	2,321 (31.5)	521 (7.1)
Strangulated	3,360 (1.3)	8.0 (6.4 – 12.7)	-2.7 (-3.0 to -2.2)	1,827 (54.4)	1,251 (37.2)	282 (8.4)
Ventral hernia	22,416 (8.7)	7.3 (6.4 – 8.9)	-2.8 (-3.1 to -2.5)	14,950 (66.7)	7,022 (31.3)	444 (2.0)
Strangulated	9,767 (5.1)	7.5 (6.4 – 9.4)	-2.7 (-3.0 to -2.6)	5,852 (59.9)	3,657 (37.4)	258 (2.6)
AAA repair (open)	1,914 (0.7)	8.5 (7.0 – 11.7)	-2.5 (-2.8 to -2.1)	782 (40.9)	1,043 (54.5)	89 (4.6)
Emergent	792 (0.3)	10.22 (8.1 – 15.0)	-2.2 (-2.5 to -1.8)	173 (21.8)	557 (70.3)	62 (7.8)
Elective	1,122 (0.4)	7.7 (6.4 – 9.8)	-2.6 (-2.9 to -2.3)	609 (54.3)	486 (43.3)	27 (2.4)
EVAR (2018 only)	1,104 (0.4)	8.2 (7.0 – 10.7)	-2.6 (-2.8 to -2.2)	520 (47.1)	550 (49.8)	34 (3.1)

AAA, abdominal aortic aneurysm; ALBI, Albumin-Bilirubin Score; CABG, coronary artery bypass grafting; EVAR, endovascular aortic aneurysm repair; MELD-Na, Model for End-stage Liver Disease-sodium score

Table 2. Distribution of Morbidity and Mortality, Overall and for All Procedures

ALBI grade	Patients	Morbidity	Mortality
Overall	258,658 (100)	74,077 (28.6)	6,952 (2.7)
CABG	5,929 (2.3)	3,693 (66.8)	138 (2.3)
Emergent	550 (0.2)	355 (64.5)	22 (4.0)
Elective	5,379 (2.1)	3,608 (67.1)	116 (2.2)
Lung resection	9,737 (3.8)	1,953 (20.1)	136 (1.4)
Esophagectomy	1,595 (0.6)	747 (46.8)	42 (2.7)
Gastrectomy	3,086 (1.2)	1,367 (44.3)	169 (5.5)
Cholecystectomy	55,886 (21.6)	6,975 (12.5)	432 (0.8)
Pancreatectomy	20,470 (7.9)	9,687 (47.3)	321 (1.6)
Splenectomy	1,617 (0.6)	871 (53.9)	89 (5.5)
Appendectomy	34,152 (13.2)	4,730 (13.8)	102 (0.3)
Colectomy	77,343 (29.9)	33,112 (42.8)	4,641 (6.0)
Emergent	18,991 (7.3)	12,984 (68.4)	3,185 (16.8)
Elective	58,352 (22.6)	20,128 (34.5)	1,456 (2.5)
Proctectomy	3,913 (1.5)	1,724 (44.1)	49 (1.3)
Adrenalectomy	943 (0.4)	181 (19.2)	13 (1.4)
Nephrectomy	11,192 (4.3)	2,516 (22.5)	115 (1.0)
Umbilical hernia	7,361 (2.8)	856 (11.6)	95 (1.3)
Strangulated	3,360 (1.3)	506 (15.1)	73 (2.2)
Ventral hernia	22,416 (8.7)	3,540 (15.8)	236 (1.1)
Strangulated	9,767 (3.8)	1,816 (18.6)	166 (1.7)
AAA repair (open)	1,914 (0.7)	1,562 (81.6)	315 (16.5)
Emergent	792 (0.3)	740 (93.4)	248 (31.3)
Elective	1,122 (0.4)	822 (73.3)	67 (6.0)
EVAR (2018 only)	1,104 (0.4)	293 (26.5)	58 (5.3)

AAA, abdominal aortic aneurysm; ALBI, Albumin-Bilirubin Score; CABG, coronary artery bypass grafting; EVAR, endovascular aortic aneurysm repair

Table 3. Areas Under the Receiver Operating Characteristics Curves for Mortality, Using Albumin-Bilirubin and Model for End-Stage Liver Disease-Sodium Scores, Overall and for All Procedures.

Procedure	Patients, n (%)	ALBI score	MELD-Na score	Δ AUC	p Value
Overall	258,658 (100)	0.80	0.79	0.01	<0.001
CABG	5,929 (2.3)	0.68	0.65	0.03	0.360
Emergent	550 (0.2)	0.70	0.60	0.10	0.157
Elective	5,379 (2.1)	0.67	0.66	0.01	0.821
Lung resection	9,737 (3.8)	0.77	0.70	0.07	0.009
Esophagectomy	1,595 (0.6)	0.66	0.61	0.05	0.420
Gastrectomy	3,086 (1.2)	0.79	0.75	0.04	0.096
Cholecystectomy	55,886 (21.6)	0.80	0.80	<0.01	0.905
Pancreatectomy	20,470 (7.9)	0.68	0.68	<0.01	0.843
Splenectomy	1,617 (0.6)	0.78	0.78	<0.01	0.777
Appendectomy	34,152 (13.2)	0.85	0.83	0.02	0.455
Colectomy	77,343 (29.9)	0.80	0.80	<-0.01	0.486
Emergent	18,991 (7.3)	0.71	0.73	-0.02	<0.001
Elective	58,352 (22.6)	0.79	0.74	0.05	<0.001
Proctectomy	3,913 (1.5)	0.79	0.76	0.03	0.556
Adrenalectomy	943 (0.4)	0.86	0.61	0.25	0.008
Nephrectomy	11,192 (4.3)	0.76	0.73	0.03	0.377
Umbilical hernia	7,361 (2.8)	0.86	0.88	-0.02	0.208
Strangulated	3,360 (1.3)	0.81	0.85	-0.04	0.158
Ventral hernia	22,416 (8.7)	0.80	0.80	<-0.01	0.998
Strangulated	9,767 (5.1)	0.78	0.79	-0.01	0.640
AAA repair (open)	1,914 (0.7)	0.69	0.72	-0.03	0.184
Emergent	792 (0.3)	0.60	0.65	-0.05	0.062
Elective	1,122 (0.4)	0.64	0.65	<-0.01	0.923
EVAR (2018 only)	1,104 (0.4)	0.75	0.75	<0.01	0.917

AAA, abdominal aortic aneurysm; ALBI, Albumin-Bilirubin Score; AUC, area under curve; CABG, coronary artery bypass grafting; EVAR, endovascular aortic aneurysm repair

Table 4. Areas Under the Receiver Operating Characteristics Curves for Morbidity, Using Albumin-Bilirubin and Model for End-Stage Liver Disease-Sodium Scores

Procedure	Patients, n (%)	ALBI	MELD-Na	Δ AUC	p Value
Overall	258,658 (100)	0.66	0.63	0.03	<0.001
CABG	5,929 (2.3)	0.54	0.55	-0.01	0.132
Emergent	550 (0.2)	0.58	0.60	-0.02	0.429
Elective	5,379 (2.1)	0.54	0.55	-0.01	0.250
Lung resection	9,737 (3.8)	0.63	0.58	0.05	<0.001
Esophagectomy	1,595 (0.6)	0.57	0.55	0.02	0.172
Gastrectomy	3,086 (1.2)	0.67	0.64	0.03	0.004
Cholecystectomy	55,886 (21.6)	0.65	0.66	<-0.01	0.156
Pancreatectomy	20,470 (7.9)	0.59	0.55	0.04	<0.001
Splenectomy	1,617 (0.6)	0.73	0.69	0.04	0.002
Appendectomy	34,152 (13.2)	0.66	0.66	<0.01	0.458
Colectomy	77,343 (29.9)	0.70	0.67	0.03	<0.001
Emergent	18,991 (7.3)	0.68	0.67	0.01	0.094
Elective	58,352 (22.6)	0.67	0.62	0.05	<0.001
Proctectomy	3,913 (1.5)	0.61	0.58	0.03	0.019
Adrenalectomy	943 (0.4)	0.68	0.59	0.09	0.001
Nephrectomy	11,192 (4.3)	0.67	0.66	0.01	0.279
Umbilical hernia (all)	7,361 (2.8)	0.73	0.72	0.01	0.197
Strangulated	3,360 (1.3)	0.72	0.72	<0.01	0.769
Ventral hernia (all)	22,416 (8.7)	0.63	0.62	0.01	0.040
Strangulated	9,767 (5.1)	0.64	0.64	<0.01	0.705
AAA repair (open)	1,914 (0.7)	0.65	0.65	<0.01	0.587
Emergent	792 (0.3)	0.61	0.63	-0.03	0.577
Elective	1,122 (0.4)	0.58	0.58	<0.01	0.851
EVAR (2018 only)	1,104 (0.4)	0.68	0.66	0.02	0.335

AAA, abdominal aortic aneurysm; ALBI, Albumin-Bilirubin Score; AUC, area under curve; CABG, coronary artery bypass grafting; EVAR, endovascular aortic aneurysm repair

FIGURE LEGEND

Figure 1. Univariate analyses of (A) mortality and (B) morbidity stratified by albumin-bilirubin (ALBI) grades. Bars represent odds ratios, while error bars represent 95% confidence intervals. In both figures, ALBI Grade 1 is the reference score, in which the odds ratio is set to 1 by definition.

Figure 2. Select receiver operating characteristic curves comparing the predictive ability of albumin-bilirubin (ALBI) and Model for End-stage Liver Disease-sodium (MELD-Na) score in 30-day mortality. (A) Mortality for all combined cases; (B) mortality for lung resection; (C) mortality for adrenalectomy; (D) mortality for elective colectomy

Precis:

The albumin-bilirubin score (ALBI) was equivalent to or more accurate than the Model for End Stage Liver Disease (MELD-Na) in predicting mortality and morbidity in this broad analysis of the 2015-2018 NSQIP datasets. ALBI was a significantly better predictor than MELD-Na in lung resection, elective colectomy, and adrenalectomy.

Journal Pre-proof

eTable 1. Current Procedural Terminology Codes Used in this Study.

Procedure	Queried code
Coronary artery bypass grafting (CABG)	33510, 33511, 33512, 33513, 33514, 33515, 33516, 33533, 33534, 33535, 33536
Lung resection	32440, 32442, 32445, 32480, 32482, 32484, 32486, 32488, 32491, 32501, 32503, 32504, 32505, 32506, 32507, 32663, 32666, 32667, 32668, 32669, 32670, 32671, 32672
Esophagectomy	43117, 43118, 43121, 43122, 43360
Gastrectomy	43611, 43620, 43621, 43622, 43631, 43632, 43633, 43634
Pancreatectomy	48105, 48120, 48140, 48145, 48146, 48148, 48150, 48152, 48153, 48154, 48155, 48160
Cholecystectomy	47562, 47563, 47564, 47570, 47600, 47605, 47610, 47612, 47620
Splenectomy	38100, 38101, 38102, 38120
Appendectomy	44900, 44950, 44960, 44970, 44979
Colectomy	44139, 44140, 44141, 44143, 44144, 44145, 44146, 44147, 44150, 44151, 44155, 44156, 44157, 44158, 44160, 44204, 44205, 44206, 44207, 44208, 44210, 44211, 44212, 44213
Proctectomy	45110, 45111, 45112, 45113, 45114, 45116, 45119, 45120, 45121, 45126, 45395, 45397
Adrenalectomy	60540, 60545, 60650
Nephrectomy	50220, 50225, 50230, 50234, 50236, 50240, 50320, 50543, 50545, 50546, 50547, 50548, 50549
Umbilical hernia repair	49585
Strangulated	49587
Ventral hernia repair	49560, 49570, 49590, 49565, 49652, 49654, 49656
Strangulated	49561, 49572, 49566, 49653, 49655, 49657
Abdominal aortic aneurysm repair (open)	34830, 34831, 34832, 35081, 35082, 35091, 35092, 35102, 35103
Endovascular aortic aneurysm repair (EVAR)	34701, 34702, 34703, 34704, 34705, 34706

eTable 2. Patient Demographics and Preoperative Characteristics

Variable	Data, N = 258,568
Age, y, median (mean, IQR)	60 (57.91, 47–71)
Sex, f, n (%)	129,957 (50.2)
Race, n (%)	
White	182,083 (70.4)
Black	28,367 (11.0)
Asian	9,923 (3.8)
Other	38,385 (14.8)
BMI, kg/m ² , median (mean, IQR)	28.20 (28.81, 23.20 – 33.05)
ASA class 3-5, n (%)	154,200 (59.6)
Ascites, n (%)	3,258 (1.3)
Diabetes, n (%)	46,542 (18.0)
Hypertension, n (%)	123,974 (47.9)
History of severe COPD, n (%)	15,939 (6.2)
Current smoker within the last year, n (%)	47,563 (18.4)
On dialysis preoperatively, n (%)	4,269 (1.7)
Disseminated cancer	13,052 (5.0)
Steroid use preoperative, n (%)	15,960 (6.2)
Bleeding disorder	18,230 (7.0)
ALBI score, median (mean, IQR)	- 2.6 (-2.5, -3.0 to -2.1)
Grade 1, n (%)	131,464 (50.8)
Grade 2, n (%)	109,689 (42.4)
Grade 3, n (%)	17,505 (6.8)
MELD-Na Score, median (IQR)	7.5 (9.02, 6.43 – 9.43)
< 10, n (%)	202,236 (78.2)
≥ 10, n (%)	56,422 (21.8)
Preoperative laboratory data	
Platelet Count, K/uL, median (mean, IQR)	236 (248.88, 189 – 293)
Albumin, g/dL, median (mean, IQR)	3.8 (3.73, 3.3 – 4.2)
Total Bilirubin, mg/dL, median (mean, IQR)	0.6 (0.83, 0.4 – 0.9)
Creatinine, mg/dL, median (mean, IQR)	0.82 (0.7-1.0)
INR, median, (mean, IQR)	1.04 (1.11, 1.00 – 1.12)
SGOT, IU/L, median (mean, IQR)	22 (34.79, 17 – 31)
Hematocrit, %, median (mean, IQR)	38.7 (38.06, 34.3 – 42.2)

ALBI, albumin-bilirubin; ASA, American Society of Anesthesiologists; INR, international normalized ratio; IQR, Interquartile range; MELD, model for end-stage liver disease; SGOT, serum glutamic oxaloacetic transaminase.

