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An assessment of different scoring systems in cirrhotic patients undergoing nontransplant surgery

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Abstract

BACKGROUND: Determining surgical risk in cirrhotic patients is difficult and multiple scoring systems have sought to quantify this risk. The purpose of our study was to assess the impact of Childs-Turcotte-Pugh (CTP), Model of End-Stage Liver Disease (MELD), and MELD-Sodium (MELD-Na) scores on postoperative morbidity and mortality for cirrhotic patients undergoing nontransplant surgery.

METHODS: We performed a single-center retrospective review of all cirrhotic patients who underwent nontransplant surgery under general anesthesia over a 6-year period of time to analyze outcomes using the 3 scoring systems.

RESULTS: Sixty-four cirrhotic patients (mean age, 57 y; 62 men) underwent nontransplant surgery under general anesthesia. A CTP score of ≥7.5 was associated with an 8.3-fold increased risk of 30-day morbidity, a MELD score of ≥14.5 was associated with a 5.4-fold increased risk of 3-month mortality, and a MELD-Na score ≥14.5 was associated with a 4.5-fold increased risk of 1-year mortality. Emergent surgery, the presence of ascites, and low serum sodium level were associated significantly with morbidity and 1-year mortality.

CONCLUSIONS: The major strengths of the 3 scoring systems are for CTP in estimating 30-day morbidity, MELD for estimating 3-month mortality, and MELD-Na for estimating 1-year mortality. Published by Elsevier Inc.

Estimating surgical risk in cirrhotic patients is a multifaceted and potentially difficult endeavor. It requires the consideration of various factors including severity of liver disease, urgency and type of surgery, type of anesthesia, and co-existing medical illness. Historically, the Childs-Turcotte-Pugh (CTP) classification has been used to assess liver dysfunction and predict surgical morbidity and mortality. Developed in 1964 by Child and Turcotte,[1] the CTP scoring system was an empirically derived formula used to risk-stratify patients undergoing portosystemic surgery. It was modified in 1972 by Pugh et al[2] to substitute prothrombin time for nutritional status. Currently, it is based on 5 parameters and patients are placed into 1 of 3 classes. Since its inception, the CTP scoring system has been used for a

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variety of purposes including preoperative assessment for liver transplantation, transjugular intrahepatic portosystemic shunt placement, and medical therapy. It also has proven useful for predicting postoperative outcome.[3,4]

However, there are several shortcomings of the CTP system. First, 2 of the 5 parameters (ascites and encephalopathy) are subject to interobserver variability. Second, the CTP classification divides patients more broadly into 1 of only 3 classes and cannot distinguish further among patients within a single class who still may have very different risk profiles. Third, the system is limited in its discriminatory capacity. For example, a bilirubin level of 4 and 20 are assigned the same number of points, although these drastic differences in laboratory values may have a much greater clinical significance. These shortcomings have led to the search for a more desirable disease severity scoring system.

Model of End-Stage Liver Disease (MELD) initially was developed and validated in a heterogeneous group of patients with chronic liver disease who underwent elective transjugular intrahepatic portosystemic shunt procedures.[5] Subsequently, MELD was validated as an accurate survival predictor in a broader subsets of patients with chronic liver disease.[6] Because of the inadequacy of the CTP scoring system in prioritizing patients for liver transplantation, MELD emerged as a more reliable replacement. This was instituted formally in February 2002 after a large study showed the superiority of MELD in predicting 3-month mortality for patients on the waiting list.[7]

Based on its effectiveness in transplant patients, there have been attempts to apply this system to the assessment of surgical risk in patients with liver disease. Three of 4 studies validated the usefulness of MELD in predicting surgical mortality in cirrhotic patients.[8–11] However, these studies did not assess surgical morbidity. In addition, evidence suggests that a revised MELD formula incorporating serum sodium level is superior when compared with the original model.[12] The current study was designed to assess the association of CTP, MELD, and MELD-sodium (MELD-Na) with postoperative morbidity and mortality for cirrhotic patients undergoing nontransplant surgery.

Methods

By using the computerized database at the Veterans Affairs Medical Center in East Orange, NJ, patients coded for an admitting diagnosis of cirrhosis (International Classification of Diseases, 9th revision, codes 571.2, 571.5, and 571.6) from January 1999 to January 2005 were identified. Within this group, all patients who underwent nontransplant surgical procedures under general anesthesia were included in the study. Both emergent and elective procedures were analyzed. Individual records were reviewed and information pertaining to demographic data, type and urgency of the procedure, cause of cirrhosis, history of cancer, and documented cardiac and/or pulmonary disease was collected. The cancer group included patients who underwent surgeries specifically for malignancy and those with a diagnosis of cancer who had surgery for unrelated conditions (eg, laparoscopic cholecystectomy in a patient with untreated prostate cancer). Intra-abdominal and thoracic surgeries were grouped together and compared with all other types of procedures. Preoperative laboratory and clinical data were used to calculate a CTP, MELD, and MELD-Na score for each case. Death within the first 30 days was categorized as both a morbidity and a 3-month mortality. Three-month mortality was chosen to account for prolonged (>1 mo) postoperative hospital courses that resulted in death. One-year mortality was examined as an indicator of longer-term outcomes.

The primary end points were 30-day morbidity, 3-month mortality, and 1-year mortality. Morbidity was defined very broadly to include wound infections, cirrhotic complications, bleeding, infectious complications, and metabolic complications. Descriptive statistics were used to describe the study population and continuous variables are shown as mean ± standard deviation and dichotomous variables are presented as percentages. The cut-off value of each scoring system was determined by a receiver operating characteristic curve (ROC). The data then were analyzed using multivariate logistic regression to compare the cut-off points of the 3 scoring systems and the subsequent association in the primary end points. To determine the effect of hyponatremia on outcomes, the lower limit of normal was set at 135 mEq/L. The significance level for a type I error was set at .05 and all significance tests were 2-sided. Statistical analysis was performed using PASW 18.0 (SPSS; Chicago, IL). The Veterans Administration New Jersey Healthcare System Institutional Review Board approved this investigational protocol.

Results

Sixty-four cirrhotic patients (mean age, 57 y; 62 men) underwent nontransplant surgery under general anesthesia. Most patients were CTP class A or B. Outcomes are summarized in Table 1. The mean CTP, MELD, and MELD-Na scores of the population were as follows: 8.1 ± 1.1 (range,

Table 1 Surgical outcomes

	Total (n = 64)	Morbidity (n = 28)	Mortality at 3 mo (n = 7)	Mortality at 1 y (n = 17)
CTP class A	23	7 (30)	0 (0)	2 (9)
CTP class B	31	13 (42)	3 (10)	8 (26)
CTP class C	10	8 (80)	4 (40)	7 (70)
Emergent	10	9 (90)	2 (20)	6 (60)
Ascites	34	21 (62)	6 (18)	14 (41)

Number of patients (percentages) shown.

Ascites = ascites present on physical examination and/or imaging studies; emergent = emergency surgery performed; morbidity = postoperative complications or death within 30 days.

Table 2 Multivariable Analysis of Overall Outcome Predictors

		Morbidity		1-year Mortality	
Variable	Number	*P* Value	Hazard ratio (95% CI)	*P* Value	Hazard ratio (95% CI)
CTP A	7	0.392	0.61 (0.19 – 1.91)	0.085	0.23 (0.04 – 1.22)
CTP B	13	*	*	*	*
CTP C	8	0.05	45.5 (0.99 – 30.9)	0.03	5.7 (1.18 – 27.45)
MELD	64	0.033	1.10 (1.01 – 1.21)	0.234	1.06 (0.96 – 1.18)
MELD-Na	64	0.009	1.10 (1.02 – 1.18)	0.038	1.10 (1.01 – 1.20)
Sodium†	64	0.031	1.16 (1.01 – 1.33)	0.034	1.25 (1.02 – 1.53)
Emergent	10	0.011	16.6 (1.92 – 143.34)	0.023	5.25 (1.26 – 21.93)
Ascites	34	0.003	5.3 (1.76 – 15.97)	0.019	4.55 (1.28 – 16.12)

CTP = Childs-Turcotte-Pugh; MELD = Model of End-Stage Liver Disease. MELD-Na = Model of End-Stage Liver Disease – Sodium.
*The omitted category is CTP B. All interpretations are relative to the omitted category. CTP A is not statistically different from CTP B.
†Inverse applied: for every 1 point decrease in sodium, the odds of a patient experiencing morbidity or 1-year mortality increases by the factor shown.
Emergent: emergency surgery performed. Ascites: ascites present on physical exam and/or imaging studies.

7–12), 13.1 ± 5.5 (range, 6–30), and 14.3 ± 6.9 (range, 6–35), respectively. The mean serum sodium level was 137 ± 4.1 mEq/L (range, 127–147 mEq/L), with 26.1% of patients being hyponatremic, and ascites was present in 34 (53%) individuals. The 30-day morbidity was 44% (28 patients). A total of 40 complications, including 5 deaths, were noted during the first 30 postoperative days. Infectious complications made up 35% (14 events) of the morbidities. Three-month mortality and 1-year mortality were 11% (7 patients) and 28% (18 patients), respectively.

The CTP classification showed statistically significant associations with 30-day morbidity and 1-year mortality for CTP class C patients. The morbidity (including deaths within 30 days of surgery) was 30%, 42%, and 80%, and the 1-year mortality was 9%, 29%, and 70% for CTP classes A, B, and C, respectively. CTP classes A and B were not statistically different but CTP class C patients were more likely to experience morbidity ($P = .05$) and 1-year mortality ($P = .03$) than CTP class B patients. For 30-day morbidity, the optimal cut-off points showed that CTP scoring had the highest sensitivity whereas MELD-Na had the highest specificity. When using the cut-off points in multivariate analysis, only CTP scoring above the cut-off point was found to have a statistically increased association with 30-day morbidity (odds ratio, 8.3; 95% confidence interval [CI], 2.4–29.2; $P < .01$), with 86% sensitivity and 58% specificity. When analyzing the 3-month mortality, the ROC showed similar sensitivities and specificities among the 3 scoring systems at 71% sensitivity and 63% to 68% specificity, but MELD scoring was the only one that trended toward a statistically increased risk on multivariate analysis and was associated with a 5.4-fold increased risk (95% CI, .9–30.6; $P = .056$). The final primary end point, 1-year mortality, was analyzed in a similar manner. CTP scoring had the best sensitivity at 78% compared with 67% in the MELD scoring systems, whereas MELD-Na showed the best specificity at 70% compared with MELD (63%) and CTP (46%). By using the ROC, a MELD-Na score greater than 14.5 was the only scoring system associated with a statistically significant 4.5-fold increased risk of 1-year mortality (95% CI, 1.4–14.6). Multivariate analysis showed an increased risk of morbidity and mortality with MELD-Na scoring, hyponatremia, emergency surgeries, and ascites (Table 2). With this association, a predicted probabilities curve was developed based on MELD-Na and showed a linear increase in the 1-year mortality rate with increasing preoperative MELD-Na scores (Fig. 1). This can be used to determine 1-year mortality based on the preoperative MELD-Na score as a continuous variable.

In addition to the association of the primary scoring systems to end point outcomes, this study also found that emergent surgery, the presence of ascites, and low serum sodium level were associated significantly with morbidity and 1-year mortality. Of the patients with complications, 75% (21 of 28) had ascites and 62% (21 of 34) of the patients with ascites had complications. The presence or absence of ascites was the most significant variable in association with both morbidity and 1-year mortality. None of

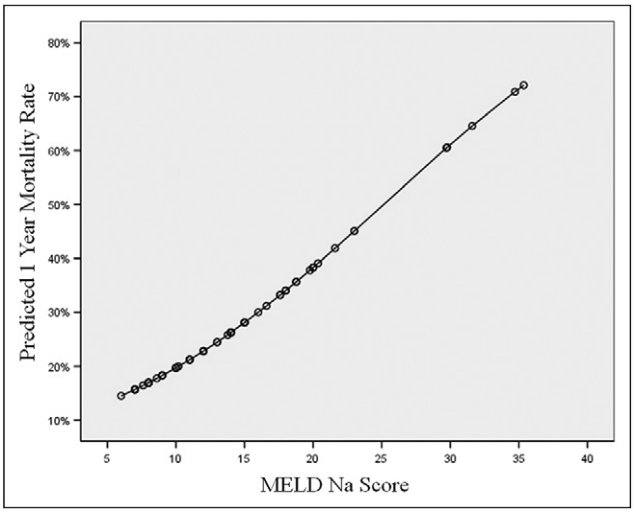

Figure 1 Predicted probabilities curve demonstrating the linear association with MELD-Na scoring and increased 1-year mortality.

the aforementioned differences achieved statistical significance for 3-month mortality. Higher-risk procedures, specifically intra-abdominal and thoracic surgeries (analyzed as a group), were not associated with worse outcomes in this study population. All other preselected variables including race, etiology of cirrhosis, history of cancer, cardiac disease, and pulmonary conditions did not show statistical significance in association with morbidity or mortality.

Comments

In this group of 64 cirrhotic patients who underwent nontransplant surgery, each of the different scoring systems showed strengths in determining the primary end points. Overall, the CTP scoring system showed the best sensitivity in all primary outcomes and the MELD-Na score had the highest specificity. The CTP classification also was associated with an 8-fold increased risk of 30-day morbidity. CTP is a well-established indicator of postoperative mortality. In studies by Garrison et al[3] and Mansour et al,[4] perioperative mortality rates after abdominal surgery were 10%, 31%, and 76%, and 10%, 30%, and 82% in cirrhotic patients who were CTP class A, B, and C, respectively. In our study, 1-year mortality rates for all types of surgery were 9%, 29%, and 70% for CTP class A, B, and C, respectively. Of note, the morbidity of surgery in this group was substantial, reaching 30%, 42%, and 80% for CTP class A, B, and C.

Despite the time-honored effectiveness of CTP in predicting outcome in nontransplant surgery, MELD proved superior in predicting mortality for transplant patients, with a 5.4-fold increase in 3-month mortality, and subsequently was applied to patients with liver disease undergoing nontransplant procedures. Suman et al[8] examined the use of MELD in 44 cardiac surgery patients. The investigators showed an association between MELD score, CTP score, and 3-month mortality. However, a MELD cut-off value for safely performing cardiac surgery could not be identified. In a study of 40 cirrhotic patients, Farnsworth et al[9] noted a good correlation between CTP classification and MELD scores in predicting mortality, especially in patients undergoing emergent surgery. Northup et al[10] examined nontransplant mortality after 140 surgical procedures performed in cirrhotic patients. MELD score was a good predictor of 30-day mortality for all procedures and for the intra-abdominal surgery subgroup. Finally, a report by Befeler et al[11] concluded that a MELD score of 14 or greater should be considered as a replacement for CTP class C as a predictor of very high risk for abdominal surgery.

Although it does have certain benefits, perhaps MELD is not the ideal system for transplant prioritization. Many pretransplant deaths occur in individuals with low MELD scores and recent evidence suggests that MELD does not apply to all patients, especially those with ascites. In a study of 507 cirrhotic patients, only persistent ascites and low serum sodium level were independent predictors of mortality for patients with a MELD score less than 21.[13] In analyzing our 1-year outcomes, a MELD-Na score greater than 14.5 was associated with a 4.5-fold increased risk of mortality. Furthermore, MELD-Na can be used as a preoperative marker for determining the 1-year mortality rate after nontransplant surgery in a predictable and linear manner (Fig. 1). Low serum sodium level alone, a variable highly associated with ascites, has been evaluated as a predictor for mortality. A review of 513 patients found that serum sodium level less than 126 mEq/L was a strong independent predictor of mortality.[14] A prospective analysis based on a multicenter database of 753 patients with end-stage liver disease showed that incorporating serum sodium level into the MELD formula (MELD-Na) provided a more accurate survival prediction than MELD alone.[12] Low serum sodium level is an even better predictor of mortality for those cirrhotic patients with low MELD scores and incorporating low serum sodium level into the model improves its predictive ability.

The results of this study indicated several strengths to incorporating serum sodium level into the MELD model and improving its ability to predict surgical morbidity and mortality in our group of cirrhotic patients. In addition, serum sodium and ascites themselves were effective independent predictors of surgical outcome. More than half (53%) of the patients in this study had ascites and this variable strongly correlated with morbidity and mortality. This may help explain why MELD did poorly and why MELD-Na did better in predicting surgical outcome for these patients. This also may explain why the CTP classification remains a powerful tool in evaluating liver disease severity, particularly for CTP class C patients. It incorporates 2 complications of portal hypertension: ascites and encephalopathy. Ascites in this study was evaluated by computed tomography or ultrasound, modalities that easily can determine if ascites is absent, minimal, or moderate.[15] With imaging of the abdominal cavity seemingly ubiquitous, the categorization of fluid in the abdominal cavity is hardly subjective. Encephalopathy did not figure significantly in our population. Of all the cirrhotic patients who underwent surgery, only 1 patient had clinical evidence of encephalopathy. Thus, CTP remains an important prognosticator with less subjectivity based on current imaging modalities.

Although CTP showed significant associations with surgical 30-day outcomes in our analysis, MELD-Na is an attractive adjunct that deserves further consideration. To place MELD-Na in perspective of current studies, a MELD-Na score of 20 was associated with a 6% risk of death within 6 months of registration, a score of 30 was associated with a 16% risk, and a score of 40 was associated with a 37% risk.[12] In our study, MELD-Na had the greatest increased risk of 1-year mortality, with MELD-Na cut-off values for 3-month morbidity and 1-year mortality both at 14.5.

Most importantly, our study showed that each of the 3 scoring systems has its own strengths and weaknesses, some of which are time dependent. When attempting to analyze and estimate the increased postoperative risk in managing these

patients, each scoring system should be used. Looking at short-term perioperative outcomes alone, this study supports that CTP scoring is the most beneficial whereas MELD is superior at the 3-month mark. However, when looking at 1-year outcomes, MELD-Na appears to be the most accurate scoring system for estimating risk and outcomes.

This investigation was limited because of its sample size and in the retrospective design of the study. Furthermore, as seen in the present study, most patients in the United States undergoing liver transplant have a MELD score less than 24,[16] potentially making MELD less applicable to patients with higher scores. However nontransplant surgery in cirrhotic patients frequently is avoided rather than embraced, making it difficult for single institutions to amass considerable numbers of patients. Our closed system managed with detailed electronic medical records allowed for longer and more complete follow-up evaluation than most other studies analyzing this patient population.

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Discussion

Dr Steven Beyersdorf (Spokane, WA): Dr Causey and colleagues have asked a key clinical question, can I safely operate on a patient with cirrhosis? To answer this question, his group has presented a retrospective review of 64 cirrhotic patients accumulated over a 6-year period at a single Veterans Administration Medical Center who underwent a nontransplant operation under general anesthesia. The authors have applied the Childs-Turcotte-Pugh, MELD, and MELD-Na scores to this patient cohort to determine the accuracy of each in predicting the acute postoperative morbidity and mortality, as well as the 3-month and 1-year mortality.

The majority of this patient group (84%) was either Child's class A or B. The authors categorized death within the first 30 days as both morbidity and 3-month mortality. Dr Causey has shown again that cirrhotic patients undergoing major operations have a high postoperative morbidity, 44%, and a nearly 8% thirty-day mortality in this study. The authors found that the Child-Turcotte-Pugh score was the most accurate at predicting acute postoperative morbidity/mortality while the MELD-Na scores were most accurate at predicting 1-year survival. Multivariate analysis of the 3 scoring systems revealed statistically significant cut-off points of 7.5 for 30-day morbidity for the Child's score, and 14.5 for the MELD-Na score for 1-year mortality. Along these lines, the presence of ascites was the most significant factor associated with postoperative morbidity/mortality. Of the patients with complications, 75% had ascites.

I understand the reasoning for grouping the acute postoperative morbidity and 3-month mortality together, but I wonder if the traditional 30-day mortality does not truly represent the risk for the surgical event while 3-month mortality represents the underlying liver disease. Cirrhotic patients with surgical conditions may not even be referred for evaluation. This study indicates that ascites and hyponatremia are the key clinical conditions affecting recovery. Should we only be looking at these 2 elements to determine operative risk?