

ONLINE FIRST

The Model for End-stage Liver Disease Score

An Independent Prognostic Factor of Mortality in Injured Cirrhotic Patients

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Objective: To examine the ability of the model for end-stage liver disease (MELD) score to predict the risk of mortality in trauma patients with cirrhosis. Although cirrhosis is associated with poor outcomes after injury, the relative effect of the severity of the cirrhosis on outcomes is unclear. The MELD score is a prospectively developed and validated scoring system, which is associated with increasing severity of hepatic dysfunction and risk of death in patients with chronic liver disease.

Design: Retrospective review. The MELD score for each patient was calculated from the international normalized ratio, the serum creatinine level, and the serum total bilirubin level obtained from the patient at admission to the level 1 trauma center. The association of MELD score with mortality was assessed using logistic regression analysis.

Setting: Level 1 trauma center.

Patients: Cirrhotic patients with trauma admitted to the level 1 trauma center during the period from January 2003 to December 2009.

Main Outcome Measure: Mortality.

Results: During the 7-year study period, 285 injured cirrhotic patients were admitted. The mean (SD) age was 50.0 (10.5) years, and the mean (SD) MELD score was 11.7 (4.8) (range, 6-28). Overall, patients who died had a significantly higher mean (SD) MELD score than did survivors (14.1 [5.4] vs 11.2 [4.6]; $P < .001$). The MELD score and the injury severity score were statistically significant risk factors that were independently associated with mortality in this group of patients (the area under the curve for the model was 0.944; cumulative $R^2 = 0.545$). Each unit increase in the MELD score was associated with an 18% increase in the odds for mortality (adjusted odds ratio, 1.18 [95% confidence interval, 1.08-1.29]; $P < .001$).

Conclusion: The MELD score is a simple objective tool for risk stratification in cirrhotic patients who have sustained injury.

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PATIENTS WITH CIRRHOSIS PRESENT a unique challenge to the health care system. This is a progressive disease, complicated by a wide range of systemic abnormalities, and a major cause of death and residual disability worldwide. After injury, in particular, cirrhosis is a well-known risk factor for death.¹⁻⁷ In the

largest study of its kind to date,⁸ cirrhosis was associated with a significantly increased mortality rate and a significantly increased complication rate after injury with an adjusted odds ratio of 5.65 (95% confidence interval, 3.72-8.41; $P < .001$) and 2.05 (95% confidence interval, 1.45-

2.84; $P < .001$), respectively. For those patients undergoing emergent exploratory laparotomy, the effect was even more pronounced, with the mortality rate increasing from 15% for those without cirrhosis to 40% for those with cirrhosis. There is, however, great variation in the degree of physiologic compromise among cirrhotic patients, commensurate with the degree of liver dysfunction. The magnitude of the negative effect of cirrhosis on outcomes after injury is therefore likely to be proportional to the degree of liver dysfunction. Historically, the Child-Pugh classification system was used to quantify the severity of liver dysfunction. Although this classification system has been analyzed in 2 small series of injured patients,^{1,7} the practical application of this scoring system in the acute risk stratification of injured cirrhotic patients is difficult, par-

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ticularly for 2 of the 5 measures used to calculate this score. These require the subjective evaluation of measures that are particularly difficult to interpret in injured patients. These include (1) distinguishing encephalopathy from traumatic brain injury or the acute effects of intoxicants, (2) delineating ascites from free intraperitoneal blood secondary to injury, and (3) attempting to estimate its volume.

The model for end-stage liver disease (MELD) score, however, is a scoring system that relies on 3 simple, objective laboratory values (serum total bilirubin level, international normalized ratio [INR], and serum creatinine level) that can be obtained within minutes of a patient's arrival into the trauma resuscitation area. This scoring system was initially developed to predict 3-month mortality estimates in patients undergoing transjugular intrahepatic portosystemic shunt procedures^{9,10} and has subsequently been demonstrated to be a reliable predictive tool for all patients who have advanced liver disease regardless of the underlying etiology.¹¹ The MELD score is now widely used as an index of disease severity, for survival prediction in cirrhotic patients with complications such as infection, for surgical risk stratification, and for prioritization of organ allocation, effectively replacing the Child-Pugh scoring system.^{10,12}

The purpose of our study was to examine the ability of the MELD score to predict the risk of mortality in patients with cirrhosis who sustain traumatic injuries. Our hypothesis was that an increase in the MELD score would be associated with an increase in mortality in cirrhotic patients who have been injured.

METHODS

After approval by the institutional review board of the University of Southern California, all patients admitted to the Los Angeles County Medical Center during the period from January 2003 to December 2009 following a traumatic injury and with a secondary diagnosis of cirrhosis or chronic liver disease were retrospectively reviewed. Demographic data (including age; sex; mechanism of injury; injury severity score [ISS]; Abbreviated Injury Scale score for the body regions of head or neck, chest, abdomen or pelvis, and extremity; systolic blood pressure; and Glasgow Coma Scale score on admission) were abstracted. In addition, the first available laboratory values for serum total bilirubin level, serum creatinine level, and INR in the first 24 hours after admission were entered into a computerized spreadsheet (Microsoft Excel 2003; Microsoft Corp, Redmond, Washington), which was created for the purposes of our study.

CALCULATION OF THE MELD SCORE

The standardized United Network for Organ Sharing formula, which is the widely accepted modification of the initial score described by Malinchoc et al,⁹ was used to calculate each patient's MELD score: $0.957 \times \ln(\text{creatinine [mg/dL]}) + 0.378 \times \ln(\text{bilirubin [mg/dL]}) + 1.120 \times \ln(\text{INR}) + 0.6431$.

The score was then multiplied by 10 and rounded to the nearest whole number. The standard approach to a serum total bilirubin level or a serum creatinine level of less than 1.0 mg/dL was to round to 1.0 mg/dL in order to avoid a negative score. Likewise, serum creatinine levels exceeding 4.0 mg/dL were set to 4.0 mg/dL, and all patients undergoing dialysis prior to injury received the maximal score.

STATISTICAL ANALYSIS

Univariate analysis was conducted to compare the risk factors between patients who died and those who survived. All risk factors that were different at a $P < .20$ level were entered in a forward logistic regression to determine their independent association with mortality. The R^2 and the area under the curve for the receiver operating characteristic curve were derived to assess the strength of the association. In addition, a linear regression was utilized to examine the correlation between the independent risk factors and to assess for colinearity. All statistical analyses were performed using the SPSS for Windows, version 12.0 (SPSS Inc, Chicago, Illinois).

RESULTS

During the 7-year study period, 285 cirrhotic patients were admitted to the Los Angeles County Medical Center following a traumatic injury. The mean (SD) age was 50.0 (10.5) years; 86.3% of these patients were men, and 11.4% had sustained a penetrating injury (**Table 1**). Overall, the mean (SD) MELD score was 11.7 (4.8) (range, 6-28), with 8.8% of the patients having a MELD score of 20 or higher.

The overall mortality rate was 14.7%: 42 patients died, and 243 patients survived. We found that, compared with the patients who survived, patients who died were more likely to be 65 years of age or older (14.3% vs 4.5%; $P = .03$), were more likely to be admitted with a Glasgow Coma Scale score of 8 or less (24.4% vs 7.1%, $P = .002$), and were more likely to be more severely injured as indicated by a higher mean (SD) ISS (26.7 [10.7] vs 8.1 [7.9]; $P < .001$). In addition, the mean (SD) MELD score was significantly higher in patients who died than in patients who survived (14.1 [5.4] vs 11.2 [4.6]; $P < .001$) (Table 1).

The MELD score, an age of 65 years or older, an ISS, a Glasgow Coma Scale score of 8 or less, and an Abbreviated Injury Scale score of 3 or greater for all body regions were entered in a forward logistic regression to determine independent associations with mortality. Two factors were found to be significantly associated with mortality in this population: the ISS and the MELD score (**Table 2**). The ISS explained 48% of the variation in mortality in the studied population, and the MELD score independently contributed an additional 7% of the variation. The area under the curve for the model was 0.944 and the R^2 was 0.545, demonstrating the significance of the combination of these 2 risk factors in predicting mortality in cirrhotic patients who sustained an injury.

Further examination of the correlation between the ISS and the MELD score demonstrated that the ISS and the MELD score are indeed independent of each other. **Figure 1** is a scatterplot showing the relationship between the ISS and the MELD score. The Pearson correlation was 0.045, $P = .45$, and $R^2 = 0.002$, thus strengthening the independent association of these 2 variables with mortality.

Each unit increase in the MELD score was associated with an 18% increase in the odds for mortality (adjusted odds ratio, 1.18 [95% confidence interval, 1.08-1.29]; $P < .001$). **Figure 2** depicts the increase in the cumulative risk for death with each unit increase in the MELD score.

Table 1. Comparison of Cirrhotic Patients Who Died With Those Who Survived

| Variable | Total (n=285) | Patients Who Died (n=42) | Patients Who Survived (n=243) | P Value ^a |
|------------------------------------|----------------|--------------------------|-------------------------------|----------------------|
| MELD score, mean (SD) | 11.7 (4.8) | 14.1 (5.4) | 11.2 (4.6) | <.001 |
| ISS, mean (SD) | 10.8 (10.7) | 26.7 (10.7) | 8.1 (7.9) | <.001 |
| Age, mean (SD), y | 50.0 (10.5) | 49.8 (10.0) | 51.5 (12.7) | .33 |
| Patients, No./Total No. (%) | | | | |
| Age ≥65 y | 17/285 (6.0) | 6/42 (14.3) | 11/243 (4.5) | .03 |
| Men | 246/285 (86.3) | 36/42 (85.7) | 210/243 (86.4) | .902 |
| Sustained penetrating injury | 31/272 (11.4) | 6/39 (15.4) | 25/233 (10.7) | .414 |
| GCS score ≤8 | 27/279 (9.7) | 10/41 (24.4) | 17/238 (7.1) | .002 |
| Systolic BP <90 mm Hg | 20/280 (7.1) | 4/41 (9.8) | 16/239 (6.7) | .509 |
| AIS score ≥3 for head or neck | 60/285 (21.1) | 23/42 (54.8) | 37/243 (15.2) | <.001 |
| AIS score ≥3 for chest | 33/285 (11.6) | 16/42 (38.1) | 17/243 (7.0) | <.001 |
| AIS score ≥3 for abdomen or pelvis | 17/285 (6.0) | 6/42 (14.3) | 11/243 (4.5) | .03 |
| AIS score ≥3 for extremity | 37/285 (13.0) | 10/42 (23.8) | 27/243 (11.1) | .02 |

Abbreviations: AIS, Abbreviated Injury Scale; BP, blood pressure; GCS, Glasgow Coma Scale; ISS, injury severity score; MELD, model for end-stage liver disease.

^aP values for means were determined by use of the *t* test, and P values for proportions were determined by use of either the χ^2 test or the Fisher exact test.

Table 2. Results of a Forward Logistic Regression^a

| Regression Step | Factors Independently Associated With Mortality | OR (95% CI) | P Value | Cumulative R ² |
|-----------------|---|------------------|---------|---------------------------|
| Step 1 | Injury severity score | 1.19 (1.13-1.25) | <.001 | 0.478 |
| Step 2 | MELD score | 1.18 (1.08-1.29) | <.001 | 0.545 |

Abbreviations: CI, confidence interval; MELD, model for end-stage liver disease; OR, odds ratio.

^aVariables in the model are age (65 y vs <65 y), Glasgow Coma Scale score (8 vs >8), injury severity score, and Abbreviated Injury Scale scores (3 vs <3) for head or neck, chest, abdomen or pelvis, and extremity. The area under the curve for the model was 0.944.

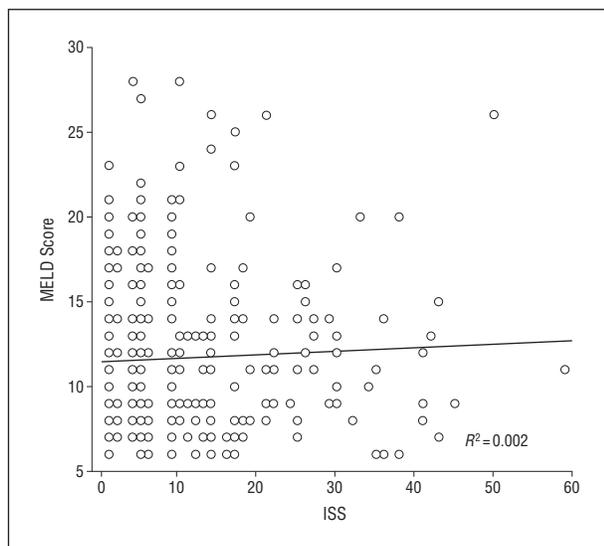


Figure 1. Correlation between the 2 independent risk factors for death: the injury severity score (ISS) and the model for end-stage liver disease (MELD) score. Pearson correlation=0.045, $R^2=0.002$, and $P=.45$.

COMMENT

For patients who have sustained an injury, the presence of cirrhosis is a major risk factor for both death and disability. This is not an uncommon problem in the gen-

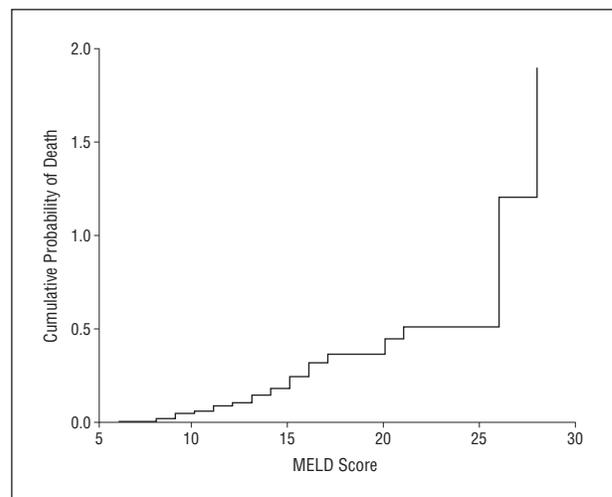


Figure 2. Cumulative probability of death with an increase in the model for end-stage liver disease (MELD) score.

eral population. The incidence of cirrhosis among trauma patients is approximately 1%, with the majority of injuries in these patients occurring as a result of blunt mechanisms, particularly falls.^{3,8} This incidence has not changed appreciably over the past decade.⁸

The negative effect of cirrhosis on outcomes, including mortality after trauma, is clear. Several large retrospective patient series^{1,3,6,8} have demonstrated an in-

hospital mortality rate that ranges from 12% to 33%. In a recent study from our institution,⁸ the mortality rate in patients with cirrhosis was significantly higher than in patients without cirrhosis, with an adjusted odds ratio of 5.65. Likewise, in a study from Morris et al,¹³ the presence of cirrhosis increased the relative odds of death by 4.5 times.

Cirrhosis, however, is a progressive disease, with a wide spectrum of physiologic abnormalities that range from mild and asymptomatic to severe with major systemic abnormalities, including alterations to the coagulation, metabolic, fluid, and electrolyte systems, all of which would be expected to decrease the ability of these patients to tolerate injury. To date, the only risk stratification system evaluated for injured cirrhotic patients has been the Child-Pugh classification system. In the 2005 study by Christmas et al,¹ 61 patients were matched 2:1 for age, sex, ISS, and Glasgow Coma Scale score. A mortality rate difference of 33% for patients with cirrhosis vs 1% for patients without cirrhosis was found. Within the cirrhotic cohort, however, a stepwise increase in mortality was seen as the Child-Pugh classification increased, progressing from 15% in class A patients to 63% in class C patients. In the study by Dangleben et al,⁶ the majority of injured cirrhotic patients who died were those who were Child-Pugh class C patients. Although the study⁶ was limited by its sample size, when a mortality prediction analysis was performed using the Trauma-Related Injury Severity Score, class C patients had a higher than predicted mortality, whereas those with less severe liver dysfunction did not.

Unfortunately, one of the practical limitations of this classification system is that the severity score calculation requires 5 component measures to be obtained (serum total bilirubin level, serum albumin level, INR, presence of ascites, and presence and extent of encephalopathy). In particular, 2 of these 5 measures are highly subjective and especially difficult to quantify in injured patients. First, it is difficult to distinguish ascites from free intraperitoneal blood or hollow viscus content. Second, the presence and extent of encephalopathy is a challenge to estimate in the face of both traumatic brain injury and the presence of intoxicants, a common problem in many trauma patients.

The MELD score, however, requires 3 simple, objective laboratory tests that can be obtained and calculated within minutes of a patient's arrival to the resuscitation area. Initially developed for estimating predicted survival in patients undergoing a transjugular intrahepatic portosystemic shunt, it is now used ubiquitously to predict outcomes in patients with liver dysfunction. It has been demonstrated to accurately predict survival in cirrhotic patients with variceal bleeding, in patients with infection, or in patients undergoing surgery and is now an important component of the recipient evaluation process for potential hepatic transplant candidates. To the best of our knowledge, however, it has yet to be evaluated in the risk stratification process for injured patients with liver dysfunction.

In our analysis, the mean (SD) MELD score of the cirrhotic patients was 11.7 (4.8) (range, 6-28). A significant proportion (8.8%) had a MELD score of 20 or

higher. The overall mortality rate of 14.7% for this patient population was in the expected range on the basis of previous data.⁸ However, when the effect of the extent of liver dysfunction, as quantified by the MELD score, was analyzed, the MELD score was found to be independently associated with mortality. As the severity of the liver dysfunction increased, with every unit increase in the MELD score, there was an associated 18% increase in the odds of death (adjusted odds ratio, 1.18 [95% confidence interval, 1.08-1.29]; $P < .001$).

Seamon et al¹⁴ have recently published a study that includes 68 trauma patients with chronic liver disease. The aim of their study was to examine whether the MELD score or the Child-Turcotte-Pugh classification was better at predicting morbidity and mortality among this population. Seamon et al¹⁴ classified their population into Child-Turcotte-Pugh classes A, B and C on the basis of their preadmission medication list. This interesting method of estimating the Child-Turcotte-Pugh classification does get around the problems inherent to using this classification system in injured patients; however, its accuracy is unknown. In addition, Seamon et al¹⁴ report that, of the 68 patients, only 49 (72%) had complete data for calculation of the Child-Turcotte-Pugh and MELD scores, and 9 (13%) were burn patients, a population with significant differences from the trauma population sustaining blunt or penetrating trauma. On the basis of this heterogeneous population, in which a significant proportion of patients had missing data with regard to the dependent variables (MELD and Child-Turcotte-Pugh scores), their analysis demonstrated that among the Child-Turcotte-Pugh classification, the MELD score, the ISS, and the Trauma-Related Injury Severity Score, only the Child-Turcotte-Pugh classification was predictive of in-hospital mortality. This is in contrast to our results, which demonstrated that the ISS and the MELD score are highly predictive of mortality in trauma patients with chronic liver disease, after adjusting for all available confounding factors. This may be due to the more homogeneous nature of our population, the significantly higher sample size, and the availability of MELD scores for all included patients.

Cirrhosis is a common comorbidity in the injured patient population and has remained so over the past decade. The identification of cirrhosis in an injured patient requires that an aggressive approach to diagnosis and management be taken so as to mitigate the direct effect of the associated physiologic abnormalities on mortality. These patients warrant aggressive monitoring and the careful selection of therapeutic interventions. At our center, all attempts are made to identify these patients as early as possible in the resuscitation phase. If this information is elicited during their prehospital care, this triggers the activation of the trauma team, with the attending surgeon present to assess the patient on arrival in the resuscitation area. Surgical care is performed with meticulous attention to detail. All patients undergo tests (eg, imaging) to catalog all injuries and are monitored in the intensive care unit with coordinated consultation with the hepatology service. This is a resource-intensive process, and an understanding of the risk profile for these

patients would allow for the selective application of this aggressive protocol to the patients that require it most.

Ours was a retrospective analysis, and all of the limitations inherent to this study design apply. In particular, all patients with cirrhosis were identified through our trauma registry. In an effort to identify these patients as early as possible so as to optimize their care, all patients at the Los Angeles County Medical Center are screened at admission, during their tertiary survey, and then throughout their hospital course for any evidence of cirrhosis by the surgical team. Data are then captured on a daily basis by a dedicated team of trauma registry nurses who screen each patient for various comorbidities and, in particular, cirrhosis (which is a mandatory data field), making the diagnosis of cirrhosis as robust as possible for any trauma system with a formal data-collection process in place. Although it is unlikely that a patient with cirrhosis was not captured, it is possible that there were patients with cirrhosis evaluated during the study period who were not included in the data set and therefore not analyzed.

Our results show that cirrhotic patients with severe traumatic brain injuries had a significant increase in mortality when compared with patients without cirrhosis. Whether this was due to the cirrhosis or to the head injury and its effect on coagulopathy could not be delineated in our study design. However, this is an important question that should be investigated further.

Although there was a significant increase in the risk of death with increasing MELD scores, no patients with scores higher than 28 were analyzed. As can be seen by this data set, this may not be clinically relevant because it is rare for such severely decompensated patients to sustain severe injury. Nonetheless, the results of our study may have been even more pronounced if data at the upper end of the MELD spectrum was available for analysis.

To the best of our knowledge, ours was the largest study to examine the risk stratification of injured patients with cirrhosis using the MELD score. In our analysis, the MELD score, an inexpensive, easy to obtain, and objective risk stratification system available early in the resuscitation phase, was able to predict outcomes independent of the injury burden sustained.

Cirrhosis is a common and highly morbid condition that requires early identification and aggressive treatment of the injured patient. The MELD score is a simple, objective tool for risk stratification in cirrhotic patients who have sustained a traumatic injury. Prospective validation of this scoring system is warranted.

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