Is Model for End-stage Liver Disease 3.0 Better Than Model for End-stage Liver Disease? Evaluating the Association of Liver Disease Severity Scores With Perioperative Complications in Liver Transplant Recipients

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ABSTRACT

Background. Sequential adaptations to Child-Pugh (CP) and MELD have improved prediction of waitlist mortality in liver transplant (LT). Despite its widespread use as a prognosticator, the association between the MELD score and perioperative adverse events during LT has yet to be evaluated. this study seeks to evaluate whether advances in MELD score calculations correspondingly improve predictions for massive transfusion (MT) and renal failure.

Methods. Adult patients undergoing LT at a tertiary institution between 2015 and 2023 were enrolled. MELD, MELD-Na, MELD 3.0, and CP were calculated at time of LT. Massive transfusion (MT) was >6 units of red blood cells before hepatic artery ligation. Renal failure (RF) was defined as requiring dialysis on postoperative-day one. Area-under-the-receiver-operating-characteristic curves (AUC) was estimated for each score and outcome and compared using the DeLong method. Score performance was evaluated using receiver operator curves (ROC) with a high performing assay considered as an area under the curve (AUC) >0.800.

Results. Total 265 patients were included; 20 (7.6%) received MT, 31 (11.8%) had RF. For MT, scores performed similarly (CP 0.70 [95% CI: 0.58, 0.81]; MELD 0.69 [0.59, 0.80]; MELD-Na 0.71 [0.61, 0.81]; MELD 3.0 0.69 [0.59, 0.80]). For RF all MELD scores outperformed CP, and MELD-Na outperformed MELD 3.0 (0.58 [0.48, 0.68], 0.66 [0.55,0.77], 0.67 [0.56, 0.78], and 0.65 [0.53, 0.77]).

Conclusion. MELD 3.0 did not outperform its predecessors. MELD-Na may still have a role in assessment of perioperative complications in LT recipients as well as patients with end-stage liver disease undergoing nontransplant operations.

LIVER transplantation (LT) is a life-saving surgical procedure that requires rigorous surveillance and management before, during, and after the operating room. The demand for liver allografts continues to outpace the supply, necessitating careful choice of recipients [1]. Current criteria for organ allocation are based on disease severity and wait-list mortality; however, predicting which patients will continue to suffer high morbidity and mortality rates after and in association with LT requires additional investigation.

Previous presentations: Southwest Surgical Congress 2024.

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0041-1345/20
https://doi.org/10.1016/j.transproceed.2025.06.022

The Child-Pugh (CP) and the model for end-stage liver disease (MELD) scores are primary measures used for prioritization of LT organ allocation and have also been applied as systems for risk stratification among patients with cirrhosis. CP was the first criterion for determining transplant candidacy and remained the principal method for stratifying patients on the wait list until the introduction of the first MELD score in 2002 [2,3]. MELD was identified as a more objective measure of liver disease severity useful for predicting 3-month survival in patients with cirrhosis, as well as a more generalizable priority score for graft allocation [2,4]. Over time, MELD has been adapted to MELD-Na, and subsequently, MELD 3.0 to more accurately predict waitlist mortality and improve the disparity in organ allocation that has historically placed female recipients lower on the waiting list [5,6].

While CP and MELD scores continue to be primary prognostic factors for determining a patient's need for LT, studies have not fully defined their specific association with intraoperative and postoperative complications in LT surgery [7,8]. The most recent meta-analyses were performed prior to the introduction of MELD 3.0 and did not consider the relation of MELD and CP with other predictive factors of adverse outcome in LT, such as high intraoperative transfusion requirement and postoperative renal failure (RF) [9−12]. Thus, this study seeks to evaluate whether advances in liver disease severity scores correspondingly improve predictions for intraoperative massive transfusion (MT) and postoperative RF in LT recipients. We hypothesize that MELD 3.0 will be associated with higher predictive accuracy in intraoperative MT and RF, reflecting its improved accuracy in characterization of liver disease severity [5].

METHODS

Ethical Oversight

This study used data from an observational liver transplant database at the University of Colorado from 2015 to 2023, which was overseen and approved by Colorado Multiple Institution Review Board (IRB #15-0813). All patients signed a consent form which was explained by a member of the research staff in person. Research staff documented patient consent and inclusion in this observational study their respective electronic health record chart. Collection and storage of patient information remained HIPAA compliant, as only research staff had access to patient information, and collection of data was conducted in REDCap.

Analysis Design

We included entries that fulfilled the following criteria: recipient over 18 years old, recipient's first LT in the database, not yet on dialysis prior to LT, deceased donor recipient, did not receive tranexamic acid, and did not receive a multiorgan transplant.

Our analysis included 2 primary outcomes of interest and one secondary outcome of interest. The first primary outcome of interest was MT prior to hepatic artery (HA) ligation, defined as the volume of red blood cells (RBCs) administered within 24 hours prior to the start of the surgery and intraoperatively prior to HA clamp. The reason we used HA ligation as our data point for intraoperative blood loss was because it represents time of shunting blood from the liver which will not only decrease hepatic synthesis of proteins but also increase fibrinolysis. As such, the patient's native coagulation processes are disrupted after this time, and bleeding after HA ligation may not be directly associated with the patient's preoperative state, which was the focus of this study. We excluded the remainder of the operation in the calculation for MT to maintain results that reflected the state of the recipients' native liver without influence of the donor liver. MT was defined as more than 1800 cc or 6 units of RBCs transfused within the specified time. The other primary outcome of interest was need for dialysis during POD1 reflecting RF in the immediate postoperative period. Our secondary outcome of interest was if the patient required the intensive care unit (ICU) on POD1 to describe a more generalized outcome after LT.

Statistical Analysis

We calculated MELD, MELD-NA, MELD 3.0, and CP scores at time of LT. MELD refers to the original iteration of the score, while MELD-Na and MELD 3.0 refer to subsequent iterations, with MELD 3.0 being the most recent [4,5,13]. We summarized recipient characteristics using means or medians, standard deviations, 25th and 75th percentiles for continuous variables, and numbers and percents for categorical variables. For descriptive analysis, recipients were grouped into MELD severity categories as follows: <25, 25-35, and >35. Recipient characteristics were compared by category using ANOVA, Kruskal−Wallis test, Pearson's chi-square test, and Fisher's Exact test.

We graphed the distribution of RBC units received for all patients at the time of LT and the distribution for each MELD and CP score. We also graphed the receiver operating characteristic (ROC) curves and estimated the area under the curves (AUC) for MELD, MELD-Na, MELD 3.0, and CP scores across the following outcomes: MT, dialysis on POD1, ICU stay on POD1. We compared the AUC for the different MELD and CP scores using the DeLong, DeLong, and Clarke-Pearson method [14]. We selected optimal cut-points for each of the scores to predict each outcome using the Youden index, which indicates the values that maximize the sum of the sensitivity and specificity for a given outcome and is equal to the vertical distance from the uninformative diagonal to the cut-point.

Logistic regression models were built to evaluate whether inclusion of age, body mass index (BMI), primary diagnosis, preoperative hematocrit or preoperative platelet level improved the predictive ability of any of the scores. Inclusion of sex was also evaluated for CP, MELD and MELD-Na but not for MELD 3.0 since its formula already incorporates sex. Sex was defined as the patient's sex assigned at birth. Additionally, creatinine was excluded from the model because it is already incorporated into all MELD scores. When evaluating adjusted results, we iteratively added one factor at a time to adhere to best practices for the ratio of explanatory variables to outcomes

(MT and dialysis events) in the models; for ICU, we also assessed models with the full set of covariates since more than 100 events were observed.

All analyses were performed using SAS 9.4 software (SAS Institute).

RESULTS

Our database contained 370 records of LT occurring between 2015 and 2023. Of those, we excluded the following patients: 12 re-transplantations within the same admission as the index LT, 54 preoperative dialysis, 2 missing dialysis status, 33 living-donor recipients, 1 missing donor type, 1 received tranexamic acid, and 2 multiorgan recipients. A total of 265 recipients met the inclusion criteria. All recipients were adults with an average recipient age of 54 years old (SD = 11.2), and 39.2% were females. Median MELD scores were MELD 19, MELD-Na 22, MELD 3.0 21, and median CP was 9.0. Figure 1 shows the distribution of CP and each MELD score. Most of the patients had noncholestatic liver disease (82.6%). Additional recipient characteristic information is detailed in Table 1.

Figure 2 shows the distribution of RBC units received by LT recipients. Twenty patients (7.6%) received MT prior to HA clamp, 31 (11.8%) had dialysis on POD1, and 110 (41.8%) were in the ICU on POD1. Two patients died on the day of surgery and were excluded from the POD1 dialysis and ICU outcomes.

Figure 3 shows ROC curves and the estimated AUC with 95% confidence intervals for CP and each MELD score. The AUC for MT were CP 0.70 (95% CI: 0.58,0.81), MELD 0.69 (0.59, 0.80), MELD-Na 0.71 (0.61, 0.81), MELD 3.0 0.69 (0.59, 0.80), and there were no differences between their predictive performances (Table 2). The AUCs for POD1 dialysis were CP 0.58 (0.48, 0.68), MELD 0.66 (0.55, 0.77), MELD-Na 0.67 (0.56, 0.78), and MELD 3.0 0.65 (0.53, 0.77). All MELD scores were better than CP,

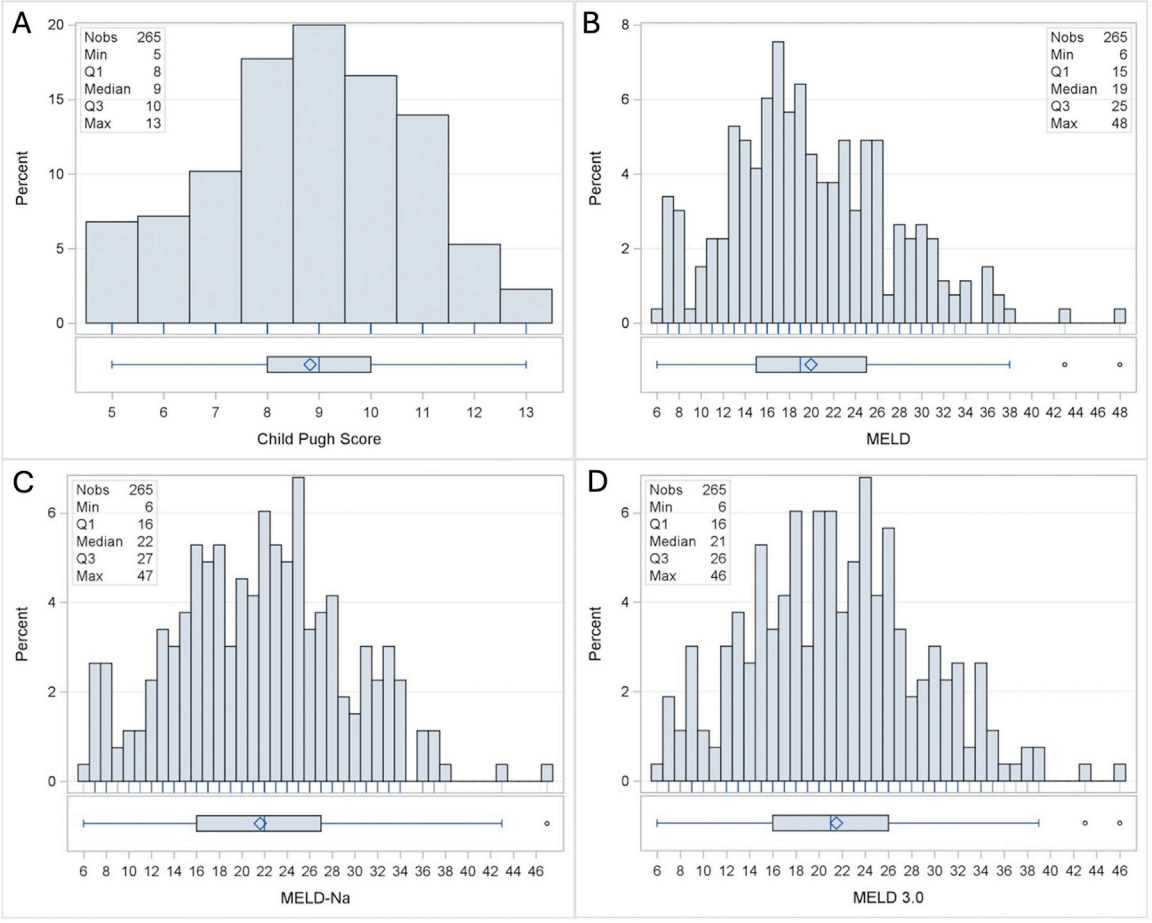

Fig 1. Distribution of liver disease severity scores. **(A)** distribution of Child Pugh scores among LT recipients. **(B)** Original MELD score distribution among LT recipients. **(C)** MELD-Na score distribution among LT recipients. **(D)** MELD 3.0 score distribution among LT recipients.

Table 1. Recipient Characteristics, Child Pugh and MELD Scores by MELD Category

Factor	Total (N = 265)	<25 (N = 194)	25-35 (N = 62)	>35 (N = 9)	*P*-value
Age	54.1 ± 11.2	56.3 ± 9.8	48.3 ± 12.4	45.9 ± 14.3	<.001*
Sex					.14‡
Female	104 (39.2)	75 (38.7)	28 (45.2)	1 (11.1)	
Male	161 (60.8)	119 (61.3)	34 (54.8)	8 (88.9)	
BMI	28.1 ± 5.0	27.7 ± 5.0	29.2 ± 5.0	31.4 ± 3.8	.016*
Primary diagnosis					
Chronic liver failure: noncholestatic Cirrhosis	219 (82.6)	160 (82.5)	50 (80.6)	9 (100.0)	.36‡
Chronic liver failure: cholestatic cirrhosis	26 (9.8)	20 (10.3)	6 (9.7)	0 (0.00)	.60‡
Race (nonexclusive)					
White or Caucasian	202 (76.2)	159 (82.0)	38 (61.3)	5 (55.6)	.001‡
Black or African American	3 (1.1)	1 (0.52)	2 (3.2)	0 (0.00)	.23§
Asian	6 (2.3)	5 (2.6)	1 (1.6)	0 (0.00)	.99§
American Indian or Alaska Native	17 (6.4)	7 (3.6)	7 (11.3)	3 (33.3)	.002§
Native Hawaiian or Other Pacific Islander	1 (0.38)	1 (0.52)	0 (0.00)	0 (0.00)	.99§
Other	47 (17.7)	29 (14.9)	16 (25.8)	2 (22.2)	.14‡
Child Pugh	9.0 (8.0, 10.0)	8.0 (7.0, 9.0)	10.5 (10.0, 11.0)	11.0 (11.0, 12.0)	<.001†
MELD	19.0 (15.0, 25.0)	17.0 (13.0, 20.0)	28.0 (26.0, 30.0)	37.0 (36.0, 38.0)	
MELD-Na	22.0 (16.0, 27.0)	18.5 (15.0, 23.0)	30.0 (27.0, 32.0)	37.0 (36.0, 38.0)	
MELD 3.0	21.0 (16.0, 26.0)	18.5 (15.0, 22.0)	30.0 (27.0, 32.0)	38.0 (37.0, 39.0)	

Statistics presented as Mean ± SD, Median [P25, P75], N (column %).
* ANOVA.
† Kruskal–Wallis test.
‡ Pearson's chi-square test.
§ Fisher's Exact test.

and MELD-Na was a better predictor than MELD 3.0 (P = .045) although the AUC estimates were similar. For prediction of POD1 ICU stay, AUCs were CP 0.54 (0.47, 0.61), MELD 0.57 (0.50, 0.64), MELD-Na 0.59 (0.52, 0.66), MELD 3.0 0.57 (0.50, 0.64). All MELD scores outperformed CP, and MELD-Na again performed significantly better than MELD 3.0 (P = .033), but the AUC estimates were similar. Otherwise, there were no significant differences between scores.

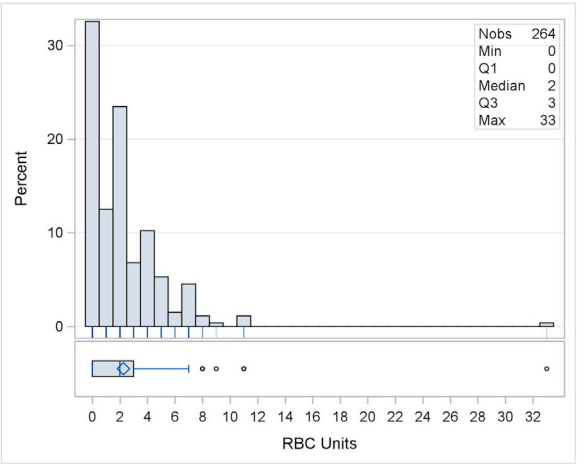

Fig 2. Units of red blood cells transfused. Percentage of subjects by number of units of red blood cells transfused during the time period between 24 h prior to surgery and clamping of the hepatic artery.

For prediction of MT, the optimal cut-points per Youden's criteria were CP 11, MELD 23, MELD-Na 18, and MELD 3.0 22. For POD1 dialysis, the optimal cut-points per Youden's criteria were CP 10, MELD 23, MELD-Na 27, and MELD 3.0 25. For POD1 ICU, the optimal cut-points per Youden's criteria were CP 10, MELD 28, MELD-Na 31, and MELD 3.0 29.

A combination of CP and preoperative hematocrit might improve prediction of MT compared to CP alone, but this did not reach statistical significance (P = .056). The inclusion of age, BMI, primary diagnosis, preoperative hematocrit, preoperative platelet level, or sex did not improve prediction of any of the scores for MT or dialysis on POD1. For prediction of POD1 ICU stay, a combination of CP and diagnosis of cholestatic cirrhosis was better than CP alone (P = .045), but the AUC remained low (0.58, 95% CI: 0.51, 0.65). Also, ICU models with all variables were significantly better than each score on its own (Table 2).

DISCUSSION

Liver risk severity scores were specifically designed to assess risk of mortality while waiting for transplantation and have been used primarily to prioritize patients in need for LT. However, liver severity scores may also be used as a proxy for risk stratification and patient management for transplant recipients. While MELD 3.0 offers decreased disparity in recipient selection and predicting pretransplant mortality, the new iteration may not outperform its predecessors in prognostication of perioperative morbidity. Given the overwhelming scarcity of liver grafts, understanding recipient perioperative morbidity and

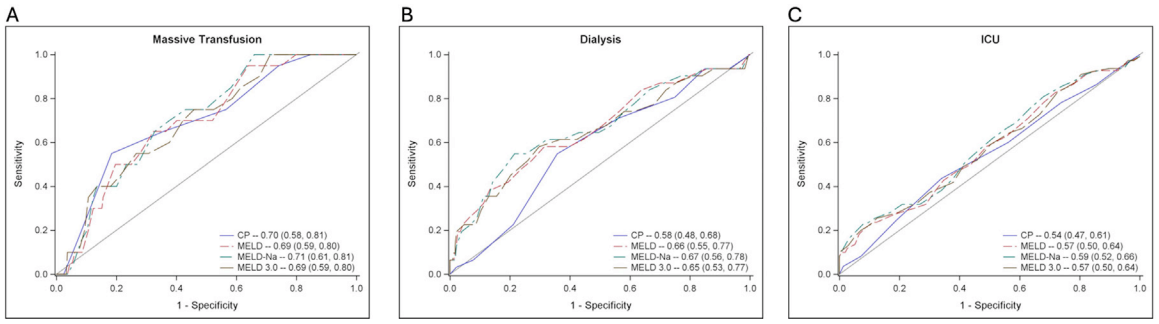

Fig 3. Receiver operator curves by outcome. **(A)** ROC plots of each liver severity score for massive transfusion outcome. **(B)** ROC plots of each liver severity score for dialysis on POD1 outcome. **(C)** ROC plots of each liver severity score for ICU stay on POD1 outcome. The solid gray line represents chance level, AUC = 0.5.

mortality is paramount to maximizing graft outcomes. Our findings suggest that MELD scores should be considered more favorably than CP in future predictive modeling of early post operative dialysis in LT, and that MELD-Na may continue to be useful for perioperative planning and care for LT recipients.

The AUCs for MELD, MELD-Na, MELD 3.0, and CP were not significantly different in their ability to predict intraoperative MT, and the addition of other preoperative factors did not improve any of the models. This was unsurprising given all scores use similar variables to characterize coagulopathy, which may account for similar predictive performance [15]. Even so, all scores provided reasonable predictive performance for MT, supporting the association between liver disease severity and coagulopathy in patients with cirrhosis [16]. Our study found that CP with the addition of preoperative serum hematocrit appeared to improve the prediction of MT, but without reaching statistical significance. This is similar to prior studies that identified preoperative serum hemoglobin to be predictive of transfusion requirements during LT [17−20]. However, in our study this was not significantly better than CP alone, perhaps due to the relatively limited timespan used in our definition of MT. Additionally, the difference attributable to using hemoglobin versus hematocrit may not be insignificant, and this analysis is limited by the absence of recipient preoperative hemoglobin from the database. Also, preoperative platelet levels were noncontributory to predictive models for MT, but are often considered by surgical and anesthesia providers during optimization for LT. Studies investigating the relationship between MELD scores and transfusion requirements in LT have been highly variable in both the definitions used for MT as well as outcomes, making comparison difficult [21,22]. In an effort to only characterize the recipient's own liver and not the effect of the donor graft, we only considered transfusion prior to HA. Other studies employed the traditional definition of MT in LT described by McCluskey as 6 units of RBCs over 24 hours after LT, but with variable time span definitions, or adopted the definition of MT from trauma literature as 10 units of RBCs over 24 hours [18,23,24]. Ultimately, CP and MELD scores provided reasonable predictive performance for MT and should be considered in future predictive models, but could benefit from separate assessment of different time points during LT, as well as a standardized definition for MT in LT. Use of other indicators of coagulopathy such as hemoglobin and the interplay of non-RBC blood product transfusion also require further investigation [19].

Measures of renal function have been identified to be crucial in predicting outcomes in patients with decompensated cirrhosis overall [25]. In our study, all MELD score types outperformed CP in predicting POD1 dialysis requirement, which may be because MELD scores include components explicitly reflective of renal function [26]. The improved predictive performance of MELD-Na compared to MELD 3.0 in anticipating RF, although small, was unexpected considering the sequential adjustments to MELD over the decades to account for renal function and volume status in patients with cirrhosis. MELD 3.0 differs from MELD-Na in that the weights of serum creatinine and serum sodium have been lessened, resulting in a scoring paradigm with improved waitlist mortality prediction that also addresses the discrepancy in organ allocation that has been disadvantageous for female recipients since MELD's inception [5,27,28]. Although the addition of sodium to MELD-Na may have been a driving force behind such sex disparities, it is possible that reducing the weight of sodium in liver severity score calculation is disadvantageous in other applications outside of estimating waitlist mortality [28]. This is because serum sodium has been identified as an independent predictor of adverse outcomes in patients with cirrhosis [29]. Recent studies investigating factors predisposing patients to post-LT acute kidney injury and dialysis requirement have suggested that the severity of the liver disease itself is associated with incidence of postoperative RF [30]. Other studies have identified an association between severe hyponatremia and incidence of renal dysfunction requiring short- or long-term replacement therapy [31]. As such, decreasing the impact of serum sodium in the calculation of MELD 3.0 may account for our findings.

In predicting the need for requirement of ICU status on POD1 after LT, MELD scores again had higher AUCs than CP but their AUCs were not significantly different from CP. This is somewhat in contrast to historical studies that identified CP to be more predictive of perioperative adverse events and mortality in patients with cirrhosis [11,12,25]. This discrepancy

Table 2. Area Under the Curve for Each Meld Score and CP Score for Each of the 3 Outcomes

	RBC >1800		POD1 Dialysis		POD1 ICU	
Model	AUC (95% CI)	Contrast *P*-value	AUC (95% CI)	Contrast *P*-value	AUC (95% CI)	Contrast *P*-value
CP	0.70 (0.58, 0.81)	Reference	0.58 (0.48, 0.68)	Reference	0.54 (0.47, 0.61)	Reference
CP + Sex	0.70 (0.58, 0.82)	.83	0.63 (0.54, 0.73)	.28	0.60 (0.53, 0.67)	.094
CP + Age	0.70 (0.58, 0.82)	.77	0.58 (0.48, 0.69)	.79	0.56 (0.49, 0.63)	.53
CP + BMI	0.72 (0.60, 0.84)	.46	0.66 (0.55, 0.76)	.22	0.56 (0.49, 0.63)	.55
CP + Noncholestatic Cirrhosis	0.71 (0.59, 0.82)	.72	0.58 (0.48, 0.69)	.82	0.55 (0.48, 0.62)	.63
CP + Cholestatic Cirrhosis	0.70 (0.58, 0.82)	.74	0.58 (0.48, 0.69)	.93	0.58 (0.51, 0.65)	.045
CP + Preop Hematocrit	0.80 (0.72, 0.88)	.056	0.67 (0.56, 0.77)	.099	0.55 (0.48, 0.62)	.65
CP + Preop platelets	0.70 (0.58, 0.81)	.8	0.57 (0.47, 0.68)	.79	0.56 (0.49, 0.63)	.49
CP + all variables	n/a	n/a	n/a	n/a	0.62 (0.55, 0.69)	.03
Meld1	0.69 (0.59, 0.80)	Reference	0.66 (0.55, 0.77)	Reference	0.57 (0.50, 0.64)	Reference
MELD1 + Sex	0.69 (0.59, 0.80)	.95	0.69 (0.59, 0.79)	.4	0.62 (0.55, 0.69)	.12
MELD1 + Age	0.70 (0.59, 0.80)	.38	0.67 (0.56, 0.78)	.5	0.60 (0.53, 0.67)	.2
MELD1 + BMI	0.73 (0.62, 0.84)	.3	0.71 (0.61, 0.81)	.21	0.58 (0.51, 0.65)	.45
MELD1 + Noncholestatic Cirrhosis	0.68 (0.57, 0.80)	.35	0.66 (0.55, 0.78)	.83	0.58 (0.51, 0.65)	.85
MELD1 + Cholestatic Cirrhosis	0.69 (0.58, 0.80)	.34	0.66 (0.54, 0.77)	.75	0.60 (0.54, 0.67)	.071
MELD1 + Preop hematocrit	0.79 (0.70, 0.87)	.13	0.68 (0.57, 0.79)	.4	0.57 (0.50, 0.65)	.87
MELD1 + Preop platelets	0.69 (0.59, 0.80)	.91	0.66 (0.54, 0.77)	.58	0.58 (0.51, 0.65)	.42
MELD1 + all variables	n/a	n/a	n/a	n/a	0.64 (0.57, 0.71)	.022
MELDNA	0.71 (0.61, 0.81)	Reference	0.67 (0.56, 0.78)	Reference	0.59 (0.52, 0.66)	
MELDNa + Sex	0.71 (0.62, 0.81)	.57	0.69 (0.59, 0.80)	.43	0.63 (0.56, 0.69)	.14
MELDNa + Age	0.71 (0.61, 0.81)	.59	0.67 (0.56, 0.78)	.66	0.61 (0.54, 0.68)	.27
MELDNa + BMI	0.75 (0.65, 0.84)	.28	0.72 (0.61, 0.82)	.24	0.59 (0.52, 0.66)	.69
MELDNa + Noncholestatic Cirrhosis	0.71 (0.60, 0.81)	.65	0.67 (0.55, 0.78)	.86	0.59 (0.52, 0.66)	.8
MELDNa + Cholestatic Cirrhosis	0.71 (0.61, 0.81)	.81	0.67 (0.55, 0.78)	.75	0.62 (0.55, 0.69)	.085
MELDNa + Preop hematocrit	0.79 (0.71, 0.87)	.12	0.68 (0.56, 0.79)	.73	0.59 (0.52, 0.66)	.5
MELDNa + Preop platelets	0.71 (0.61, 0.81)	.79	0.67 (0.56, 0.78)	.77	0.59 (0.52, 0.66)	.44
MELDNa + all variables	n/a	n/a	n/a	n/a	0.65 (0.58, 0.72)	.026
Meld3	0.69 (0.59, 0.80)	Reference	0.65 (0.53, 0.77)	Reference	0.57 (0.50, 0.64)	Reference
MELD3 + Age	0.70 (0.59, 0.80)	.87	0.65 (0.54, 0.77)	.73	0.60 (0.53, 0.67)	.26
MELD3 + BMI	0.74 (0.63, 0.84)	.18	0.70 (0.59, 0.81)	.25	0.58 (0.51, 0.65)	.64
MELD3 + Noncholestatic Cirrhosis	0.69 (0.57, 0.80)	.26	0.65 (0.53, 0.77)	.99	0.58 (0.51, 0.65)	.6
MELD3 + Cholestatic Cirrhosis	0.69 (0.58, 0.80)	.62	0.65 (0.53, 0.77)	.96	0.61 (0.54, 0.68)	.065
MELD3 + Preop hematocrit	0.79 (0.70, 0.87)	.1	0.67 (0.56, 0.78)	.37	0.58 (0.51, 0.65)	.68
MELD3 + Preop platelets	0.69 (0.58, 0.80)	.64	0.65 (0.54, 0.77)	.49	0.58 (0.51, 0.65)	.39
MELD3 + all variables	n/a	n/a	n/a	n/a	0.64 (0.57, 0.71)	.024

AUC, area under the curve; CI, confidence interval; n/a, not assessed.

DeLong *P*-values for pair-wise score comparisons.

MT outcome: CP vs MELD *P* = .93, CP vs MELD-Na *P* = .80, CP vs MELD 3.0 *P* = .94, MELD vs MELD-NA *P* = .53, MELD vs MELD 3.0 *P* = .97, MELD-Na vs MELD 3.0 *P* = .13.

Dialysis outcome: CP vs MELD *P* = .005, CP vs MELD-Na *P* = .002, CP vs MELD 3.0 *P* = .014, MELD vs MELD-NA *P* = .60, MELD vs MELD 3.0 *P* = .55, MELD-Na vs MELD 3.0 *P* = .045

ICU outcome: CP vs MELD *P* = .19, CP vs MELD-Na *P* = .06, CP vs MELD 3.0 *P* = .19, MELD vs MELD-NA *P* = .19, MELD vs MELD 3.0 *P* = .99, MELD-Na vs MELD 3.0 *P* = .033.

emphasizes the extreme importance of considering patients undergoing LT as unique from patients with cirrhosis undergoing any surgery. Of all the scores, MELD-Na yielded the best predictive performance of all score types, which again may be a product of the lower weight of serum sodium in MELD 3.0 than in MELD-Na as described earlier. These findings reflect evidence supporting the association of hyponatremia with post-LT adverse outcomes including longer ICU stays [32,33].

This study is strengthened by its prospective design and detailed transfusion data. Also, it is one of the only analyses that includes all MELD score iterations to assess perioperative relationships. Limitations include that the outcome variables assessed are subject to provider practice preferences which vary across and even within institutions, including intraoperative transfusion, intraoperative blood pressure support using vasopressor medications, and ICU admission [34]. In addition, the analyses may not have been statistically powered to address all hypotheses or account for all potential confounders, resulting in exclusion of important preoperative variables including cardiomyopathy, portal venous thrombosis, sclerosing peritonitis and hepatic venous occlusion. Also, lack of statistically significant differences may not all have been indicative of null findings. Other preoperative variables that would be important to incorporate into future studies include history of previous liver resection or hepatobiliary procedure and degree of portal hypertension. Also, we did not compare individual components of CP with different MELD scores in the predictive models. While the seminal findings of Kamath et al [35] identified that

the subjective measures of portal hypertension that differentiate the CP score did not affect the accuracy of the MELD score in predicting liver disease severity, their effects on MELD 3.0 and on predicting MT and POD1 requirement for dialysis or ICU are yet to be investigated.

In conclusion, while targeted adjustment of liver disease severity scores has improved waitlist mortality estimation, our findings indicate that MELD 3.0 is not superior to its predecessors in risk assessment for perioperative events. In fact, MELD-Na appears to maintain value in predictive modeling in LT although organ allocation is now focused on MELD 3.0. Further improvement in perioperative care of LT recipients will require a more granular understanding of the interconnected relationships between preoperative characteristics, intraoperative events and postoperative outcomes, and should continue to consider the implications of MELD-Na scores.

FUNDING

This study was supported in part by the National Heart Lung and Blood Institute: R00-HL151887. Distribution of funding included toward resident salary (MZ) and laboratory equipment for data collection.

DECLARATION OF COMPETING INTEREST

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Hunter B. Moore reports financial support was provided by National Heart Lung and Blood Institute. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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