

Clinical Study

Sicker Patients for Liver Transplantation: Meld, Meld Sodium, and Integrated Meld's Prognostic Accuracy in the Assessment of Posttransplantation Events at a Single Center from Argentina

Federico Piñero,^{1,2} Sebastián Marciano,^{1,2} Alejandra Villamil,^{1,2}
Juan Bandi,^{1,2} Paola Casciato,^{1,2} Omar Galdame,^{1,2} Sergio Giannasi,³
Eduardo de Santibañes,² and Adrian Gadano^{1,2}

¹ Hepatology Unit, Hospital Italiano de Buenos Aires, Avenida Presidente Perón 1500, Derqui, B1629HJ Buenos Aires, Argentina

² Liver Transplant Unit, Hospital Italiano de Buenos Aires, Avenida Presidente Perón 1500, Derqui, B1629HJ Buenos Aires, Argentina

³ Adult Intensive Care Unit, Hospital Italiano de Buenos Aires, Avenida Presidente Perón 1500, Derqui, B1629HJ Buenos Aires, Argentina

Correspondence should be addressed to Federico Piñero; fedepinero@gmail.com

Received 23 May 2013; Accepted 21 August 2013

Academic Editors: A. D. Hess and A. Jaramillo

Copyright © 2013 Federico Piñero et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. MELD or MELD sodium promotes sicker patients for earlier liver transplantation (LT); the balance between pre- and post-LT outcomes is still controversial. **Aim.** To compare MELD and related scores' risk assessment of short-term morbidity and mortality after LT. **Methods.** We included only transplanted cirrhotic patients from 6/2005 to 6/2010 ($N = 152$). Immediate pre-LT MELD, integrated MELD (iMELD), and two MELD sodium formulas "MELD Na1" and "MELD Na2" were calculated. **Results.** Pre-LT scores for nonsurvivors were higher than those for survivors: MELD (28 ± 8 versus 22 ± 7 , $P = 0.005$), MELD Na1 (33 ± 8 versus 27 ± 10 , $P = 0.039$), and iMELD (51 ± 6 versus 46 ± 8 , $P = 0.018$). Patient survival assessment was performed by AUROC analysis (95% CI): MELD 0.694 (0.56–0.82; $P = 0.006$), MELD Na1 0.682 (0.56–0.79; $P = 0.046$), MELD Na2 0.651 (0.54–0.76; $P = \text{NS}$), and iMELD 0.698 (0.593–0.80; $P = 0.022$). Patients with MELD ≥ 25 points had longer intensive care stay (mean 10 versus 7 days, $P = 0.015$) and longer mechanical ventilatory support (5.4 versus 1.9 days, $P = 0.022$). **Conclusions.** The addition of serum sodium to MELD does not improve assessment of mortality after LT. Patients with higher MELD may preclude higher morbidity after transplantation.

1. Introduction

Organ shortage and waiting list mortality have focused increased attention on improving liver transplants candidates' stratification. In recent years there has been increasing debate concerning the most appropriate allocation system of organs for liver transplantation. The Model for End-Stage Liver Disease (MELD) score [1] which is a numerical scale, ranging from 6 (less ill) to 40 (gravely ill), has been adopted as the allocation system in the United States in 2002. Argentina has been the second country in the world to adopt this score for organ allocation in July 2005. The MELD score accurately predicts short-term waiting list mortality in approximately

80% of patients with cirrhosis [2]; however, there are approximately 15–20% of patients that are not correctly categorized by MELD [3]. This is why several studies in an attempt to improve MELD's waiting list performance proposed the addition of other variables such as serum sodium and age to the formula [4, 5].

At the same time, the precise relationship between severity of illness at transplantation and outcome after LT is unclear. There is a need for better pretransplant predictors of pre-LT and post-LT outcomes. It has been argued that the use of MELD or related scores to prioritize patients could result in a decrease in posttransplant survival, as sicker patients will have priority for transplantation. However, neither MELD

nor other related pre-LT scores were designed to predict short-term survival following liver transplantation (LT). As these scores favor sicker patients, they may imply greater morbidity and mortality and may generate excessive health-care costs and possible therapeutic futility of transplantation [6].

A number of recent studies have demonstrated that the MELD score obtained immediately prior to transplantation is also associated with post-transplant patient survival. Lower survival rates in patients with higher MELD scores have been assessed before [7, 8]. However, the performance of MELD in prediction of post-LT events has been explored with poor results [7–14]. Outcomes after transplantation depend on a number of pre- and post-LT factors, which include both recipient and donor fitness, surgeon's skills, and transplant unit team's experience. A comparative analysis of prediction of mortality and morbidity following LT between MELD and related scores (MELD sodium, integrated MELD) has not been assessed before. The aim of this study was to compare the performance between MELD, MELD sodium (MELD-Na), and integrated MELD (iMELD) in assessment of morbidity and mortality during the first 90 days following liver transplantation at a single liver transplant center from Argentina.

2. Patients and Methods

We performed a retrospective single center analysis from 255 adult patients (≥ 18 years) who consecutively underwent liver transplantation at the Hospital Italiano from Buenos Aires between June 1, 2005, and June 30, 2010. Subjects included in the study were adult cirrhotic patients who underwent a first liver transplant with a deceased donor. Exclusion criteria for the analysis were transplanted patients for ALF, tumors, retransplantation, or with living donor in order to avoid confounding variables on survival.

Laboratory values obtained immediately before the time of transplantation were used for our analysis. Variables analyzed included age, gender, weight (kg), presence of pre-LT diabetes mellitus, HCV status, creatinine, prothrombin time, INR, total bilirubin, serum sodium, use of renal replacement therapy prior to transplantation (RRT), and the immunosuppression regimen. Presence of moderate-severe ascites, hepatic encephalopathy, or history of variceal hemorrhage was included for the analysis. Mild or severe pre-LT hyponatremia was identified when serum sodium was <130 or <126 mEq/L, respectively. Renal function was assessed by pretransplant serum creatinine and calculated glomerular filtration rate (GFR) by MDRD (Modification of Diet in Renal Disease study) [16]. We also included data from donors (age, sex, weight, height, and laboratory values) and from cold and warm ischemic times.

Post-transplant variables recorded were total blood product consumption during the first 48 hrs, major infections, length of hospital and critical care stay, days of assist mechanical ventilation (AMV) from surgery, and hospital readmissions during the first 90 days following LT. Total blood product consumption was calculated as the sum of total blood unit requirement of red cell (1 unit = 300 mL), platelets (1 unit = 1200 mL), and plasma (1 unit = 200 mL). Major

infection was considered when a site of infection was suspected (confirmed or not with positive cultures), antibiotic treatment was implemented, and prolonged hospitalization or rehospitalization was required. Length of hospital stay was calculated from the date of transplantation until discharge while length of critical care stay from day of transplantation until discharge from ICU. The duration of assist mechanical ventilation (AMV) was calculated in days. If weaning from AMV was done after 12 hrs of surgery it was cataloged as 1 day of AMV.

Immediate pretransplant scores were calculated by the following formulas according to the laboratory values closest to the time of transplantation. The MELD-Na was calculated using two methods, calling them *MELD Na1* [4] and *MELD Na2* [15].

- (i) *MELD*: $9.6 \times \log_{10}(\text{Creat mg/dl}) + 3.8 \times \log_{10}(\text{tot bil mg/dl}) + 11.2 \times \log_{10}(\text{RIN}) + 6.4$.
- (ii) *MELD-Na1*: $\text{MELD} + 1.59 \times (135 - \text{patient's serum sodium mEq/L})$. For patients with serum sodium above 135 mEq/L, it was equated to 135.
- (iii) *MELD-Na2*: $\text{MELD} - \text{serum sodium} - [0.025 \times \text{MELD} \times (140 - \text{serum sodium})] + 140$. For patients with serum sodium above 140 mEq/L, it was equated to 140.
- (iv) *Integrated MELD score (iMELD)*: $\text{MELD} + (\text{age} \times 0.3) - (0.7 \times \text{serum sodium}) + 100$.

Initial immunosuppression included methylprednisolone 1200 mg during the first 24 hrs after transplant, followed by Tacrolimus (Tac) or Cyclosporine A (CsA) with or without mycophenolate sodium/mophetil (MMF). Tac and CsA target trough levels during the first year following LT were 8–12 ng/mL and 250–300 ng/mL, respectively. Monoclonal antibody induction (Basiliximab) use depended on individual patient clinical criteria. Mammalian target inhibitors (mTOR), sirolimus or everolimus, use or switching from calcineurin inhibitors (CNI) to mTOR was evaluated on a case-by-case basis by the transplant team.

Our primary outcome was mortality and morbidity following 90 days of LT. Morbidity was evaluated with length of hospital stay and intensive care unit (ICU), days of assist mechanical ventilatory support (AMV), total blood products consumption, hospital readmissions, and major infections.

3. Statistical Analysis

Categorical variables were expressed as percentages, and continuous variables are represented as means plus standard deviations (95% CI). Univariate and multivariate linear regression analysis were performed in order to identify variables related to the primary outcomes; all univariate variables with P values <0.10 were considered for multivariate analysis. Independent variables associated with mortality were identified with a P value <0.05 . The global ability for each pre-LT score to distinguish between patients who were dead or alive at 3rd month after transplantation was evaluated with the area under the receiver operating characteristic

curve (AUROC) or c-statistic (sensitivity/specificity). The c-statistic reported corresponds to the area under the curve with a value of 0.5 corresponding to no apparent accuracy and a value of 1.0 corresponding to a perfect accuracy. Statistical analyses were performed with SPSS software (SPSS version 17.0 for Windows; SPSS Inc., Chicago, IL).

4. Results

From 255 adult transplanted patients, 152 cirrhotic patients who underwent liver transplantation with a deceased donor were included for the final analysis. Patients transplanted for ALF ($n = 26$), tumors ($n = 37$), retransplantation ($n = 24$), kidney-liver transplantation ($n = 6$), or with living donors ($n = 10$) were excluded. Mean patient age was 52.5 years, 59% were male, and HCV was the single most common etiology (23.6%), followed by alcoholic (19.7%) and cryptogenic cirrhosis (11.8%). Mean donor age was 40.3 years, mean donor BMI was 26 kg/m², and 25.8% of the graft had >30% biopsy confirmed macrosteatosis. Mean and SD of the different scores were MELD 23 ± 9 , MELD Na1 28 ± 13 , MELD Na2 26 ± 9 , and iMELD 47 ± 16 (Table 1).

Overall patient and graft survival at 3 months were 90.1% and 88%, respectively. Fifteen patients died with a mean survival of 17 days. Multiorgan failure ($n = 6$) and sepsis ($n = 5$) were the main causes of death. Mean total blood products requirement during the first 48 hours of LT was 45.8 units, while mean length of hospital, ICU stay, and AMV duration was 20.7, 7.7, and 2.6 days, respectively. Hospital readmission was required at least once in 34.2% of the study population, and 35.5% had a major infectious event following 90 days after transplantation.

Variables that were statistically related with patient survival on univariate analysis are shown in Table 2. Among the scores analyzed, a significant difference was found between patients who survived and died at 90 days after LT among MELD (survivors 22 ± 7 versus nonsurvivors 28 ± 8 , $P = 0.005$), MELD Na1 (27 ± 10 versus 33 ± 8 , $P = 0.039$), and iMELD (46 ± 8 versus 51 ± 6 , $P = 0.018$). No significant difference was found in MELD Na2 score.

None pretransplant score statistically correlated with length of hospital stay and prolonged AMV; only iMELD correlated significantly with ICU stay ($P = 0.048$, $R = 0.16$). In a subanalysis, patients with MELD ≥ 25 points took longer intensive care stay versus MELD < 25 (mean 10 versus 7 days, $P = 0.015$) and prolonged AMV (5.4 versus 1.9 days, $P = 0.002$). There was significant correlation ($R = 0.3$ – 0.5) between consumption of blood products and all pre-LT scores (none better than other). Patients with MELD > 30 had a trend to require more blood products during surgery (43 ± 37 versus 58 ± 36 units, $P = 0.05$). Hospital readmission and major infection rates after LT were not accurately predicted by any MELD related score.

Furthermore, serum sodium did not impact on patient survival as continuous or categorical variable. Renal function assessed by GFR-MDRD predicted survival (GFR alive 74.8 ± 35 versus dead 51.4 ± 25 mL/min, $P = 0.014$). Donor characteristics and surgery times (CIT and WIT, total surgery time)

TABLE 1: Characteristics of cirrhotic patients who underwent liver transplantation ($N = 152$).

Parameter	$N = 152$
Age (yr)	52.5 ± 11
Male gender (%)	59.3
Hepatitis C (%)	23.6
DM* (%)	14.4
Child pugh	10.5 ± 4
MELD	23 ± 9
MELD Na1	28 ± 13
MELD Na2	26 ± 9
iMELD	47 ± 16
Total bilirubin (mg/dL)*	10 ± 7
INR*	2.17 ± 1.8
Creatinine (mg/dL)*	1.2 ± 0.49
GFR-MDRD mL/min*	72 ± 23
Hyponatremia < 130 mEq/L* (%)	17.7
Hyponatremia < 126 mEq/L* (%)	5.9
Hypernatremia > 145 mEq/L* (%)	1.9
Ascites* (%)	76.9
Hepatic encephalopathy* (%)	58.5
Donor age	40 ± 26
Donor BMI	26 ± 4
Donor natremia (mEq/L)	151 ± 11
Donor macrosteatosis $> 30\%$ (%)	25.8
CIT (minutes)	467 ± 67
Surgery time (minutes)	318 ± 38
WIT (minutes)	52 ± 4
RRT after LT (%)	3.9
Total blood products (units)	45 ± 38
Monoclonal antibodies induction (%)	25
HAT (%)	3.9
PVT (%)	0.65
Biliary complications (%)	9.8

Note. Normal values: creatinine 0.6–1.1 mg/dL, serum sodium 135–145 mEq/L. *Pre-LT variables.

BMI: body mass index; CIT: cold ischemic time; DM: diabetes mellitus before LT; GFR-MDRD: glomerular filtration rate calculated by Modification of Diet in Renal Disease equation; HAT: hepatic artery thrombosis after liver transplantation; MELD: Model for End-Stage Liver Disease: $9.6 \times \log_{10}(\text{Creat mg/dL}) + 3.8 \times \log_{10}(\text{tot bil mg/dL}) + 11.2 \times \log_{10}(\text{RIN}) + 6.4$; MELD Na1: MELD sodium 1: MELD + $1.59 \times (135 - \text{patient's serum sodium mEq/L})$; MELD Na2: MELD sodium 2: MELD - Na - $[0.025 \times \text{MELD} \times (140 - \text{Na})] + 140$; iMELD: integrated MELD: MELD + $(\text{age} \times 0.3) - (0.7 \times \text{Na p}) + 100$; INR: international normalized ratio; WIT: warm ischemic time; RRT: renal replacement therapy; total blood products: total blood products consumption during the first 48 hrs after Liver Transplantation; monoclonal antibodies induction: use of Basiliximab (20 mg day 0 and 20 mg day 4); PVT: portal vein thrombosis after LT.

as continuous or discrete variables had no impact on patient and graft survival.

Independent variables related to patient survival on logistic regression multivariate analysis were MELD ($P = 0.006$), MELD Na1 ($P = 0.046$), integrated MELD ($P = 0.022$), pre-LT total bilirubin ($P = 0.006$), INR ($P = 0.043$),

TABLE 2: Variables associated with risk of mortality at 3 months following LT. Univariate logistic regression analysis.

Parameters	Survivors <i>n</i> = 137	Nonsurvivors <i>n</i> = 15	<i>P</i> value
Total bilirubin (mg/dL)*	9 ± 9	16 ± 10	0.005
INR*	2.1 ± 0.9	2.7 ± 1.3	0.03
Creatinine (mg/dL)*	1.1 ± 0.7	1.5 ± 0.7	0.07
GFR-MDRD (mL/min)*	75 ± 35	51 ± 25	0.01
Hyponatremia <130 mEq/L (%)*	16.7	26.6	0.34
Hyponatremia <126 mEq/L (%)*	6.5	0	0.31
Hypernatremia >145 mEq/L (%)*	0.7	13.3	0.0009
Total blood products (units)	41 ± 33	83 ± 51	<0.0001
Monoclonal antibodies induction (%)	22.6	46.6	0.02
Mean ICU stay (days)	7	13	0.001
Mean AMV (days)	2	5	0.05
Female gender (%)	37.9	66.6	0.03
RRT after LT	2.2	20	0.0008
Child pugh	10 ± 2	11 ± 1	0.08
MELD	23 ± 7	28 ± 8	0.005
<i>MELD Na1</i>	27 ± 10	33 ± 8	0.03
<i>MELD Na2</i>	25 ± 7	29 ± 5	0.06
iMELD	46 ± 8	51 ± 6	0.01
MELD <20 (%)	36.5	6.6	0.02
MELD >30 (%)	15.3	40	0.01

Note. Normal values: creatinine 0.6–1.1 mg/dL, serum sodium 135–145 mEq/L. *Pre-LT variables. Continuous variables are shown as mean ± standard deviation (SD).

AMV: assisted mechanical ventilation; BMI: body mass index; CIT: cold ischemic time; DM: diabetes mellitus before LT; GFR-MDRD: glomerular filtration rate calculated by Modification of Diet in Renal Disease equation; HAT: hepatic artery thrombosis after liver transplantation; MELD: Model for End-Stage Liver Disease: $9.6 \times \log_{10}(\text{Creat mg/dL}) + 3.8 \times \log_{10}(\text{tot bil mg/dL}) + 11.2 \times \log_{10}(\text{RIN}) + 6.4$. *MELD Na1*: MELD sodium 1: $\text{MELD} + 1.59 \times (135 - \text{patient's serum sodium mEq/L})$; *MELD Na2*: MELD sodium 2: $\text{MELD} - \text{Na} - [0.025 \times \text{MELD} \times (140 - \text{Na})] + 140$; iMELD: Integrated MELD: $\text{MELD} + (\text{age} \times 0.3) - (0.7 \times \text{Na p}) + 100$; INR: international normalized ratio; WIT: warm ischemic time; RRT: renal replacement therapy; total blood products: total blood products consumption during the first 48 hrs after liver transplantation; monoclonal antibodies induction: use of Basiliximab (20 mg day 0 and 20 mg day 4); PVT: portal vein thrombosis after LT.

GFR-MDRD ($P = 0.015$), total blood products consumption ($P \leq 0.0001$), pre-LT hypernatremia ($P = 0.0009$), and the need for renal replacement therapy after transplantation ($P = 0.0008$) (Table 3).

ROC Curves (AUROC). The corresponding AUROC (95% CI) for assessing patient survival were MELD 0.694 (0.56–0.82), *MELD Na1* 0.682 (0.56–0.79), *MELD Na2* 0.651 (0.54–0.76), and iMELD 0.698 (0.593–0.80). Best cut-off values of sensibility and specificity for each score were MELD >25, *MELD Na1* >30, *MELD Na2* >27, and integrated MELD >47 (Figures 1(a)–1(d)).

5. Discussion

We have compared MELD and related scores (MELD sodium, integrated) in predicting morbid-mortality at three months after transplantation in order to identify which of these scores would predict better survival following transplantation. Our data clearly shows that addition of sodium or age to MELD formula does not improve the model's performance in patient survival assessment following liver transplantation.

The allocation of organs for sicker patients for earlier transplantation can reduce mortality on waiting list, but it may preclude lower survival following LT or ultimately leading to higher morbidity and transplantation costs [6]. MELD score has been implemented to identify those patients with a high short-term waiting list mortality in order to achieve liver transplantation earlier [2, 17]. However, neither MELD nor related scores (MELD sodium, integrated MELD) were created for assessing post-LT events. Assuming similar pretransplant power of *c*-statistic (AUROC) for survival on waiting list among MELD and related scores, the higher *c*-statistic for survival after transplantation among these scores, the less futile the categorization of patients for transplantation.

Previously published data have described that MELD score has a poor prognostic accuracy for assessing survival following LT [6, 7]. Another group compared MELD versus Child for the same purpose favoring the first one (*c*-statistic < 0.7) [9, 18]. Some authors stated that a MELD score >25 has AUROC of 0.54 and 0.55 for predicting patient survival following 3 and 12 months of transplantation [19], while other groups behalf similar survival prediction (AUROC of 0.58,

TABLE 3: Independent variables associated with risk of mortality at 3 months following LT. Multivariate logistic regression analysis.

Variable (Mean \pm SD or %)	Survivors <i>n</i> = 137	Nonsurvivors <i>n</i> = 15	<i>P</i> value
MELD	23 \pm 7	28 \pm 8	0.006
<i>MELD Na1</i>	27 \pm 10	33 \pm 8	0.046
iMELD	46 \pm 8	51 \pm 6	0.022
Total bilirubin (mg/dL)*	9 \pm 9	16 \pm 10	0.006
INR*	2.1 \pm 0.9	2.7 \pm 1.3	0.043
GFR-MDRD (mL/min)*	75 \pm 35	51 \pm 25	0.015
Total blood products (units)	41 \pm 33	83 \pm 51	<0.0001
Hyponatremia >145 mEq/L*	0.7	13.3	0.0009
RRT after LT	2.2	20	0.0008

Note. Normal values: creatinine 0.6–1.1 mg/dL, serum sodium 135–145 mEq/L. *Pre-LT variables. Continuous variables are shown as mean \pm standard deviation (SD).

DM: diabetes mellitus before LT; GFR-MDRD: glomerular filtration rate calculated by Modification of Diet in Renal Disease equation; MELD: Model for End-Stage Liver Disease: $9.6 \times \log_{10}(\text{Creat mg/dL}) + 3.8 \times \log_{10}(\text{tot bil mg/dL}) + 11.2 \times \log_{10}(\text{RIN}) + 6.4$. *MELD Na1*: MELD sodium 1: MELD + $1.59 \times (135 - \text{patient's serum sodium mEq/L})$; *MELD Na2*: MELD sodium 2: MELD - Na - $[0.025 \times \text{MELD} \times (140 - \text{Na})] + 140$; iMELD: Integrated MELD: MELD + $(\text{age} \times 0.3) - (0.7 \times \text{Na p}) + 100$; INR: international normalized ratio; BMI: body mass index; CIT: cold ischemic time; WIT: warm ischemic time; RRT: renal replacement therapy; total blood products: Total Blood Products Consumption during the first 48 hrs after liver transplantation; monoclonal antibodies induction: use of Basiliximab (20 mg day 0 and 20 mg day 4); HAT: hepatic artery thrombosis after liver transplantation; PVT: portal vein thrombosis after LT.

0.67, and <0.61) [20]. Most of these studies did not include a pure cohort of cirrhotic patients.

We evaluated not only the prediction of MELD (AUROC of 0.694) but also when serum sodium (*MELD Na1* 0.682, *MELD Na2* 0.651) and age (iMELD 0.698) were added to the model. In order to answer our first question, the addition of serum sodium or age did not improve MELD score accuracy for assessing survival after transplantation. The AUROC for each score in our cohort were relatively close to 0.7 and higher than data published before; perhaps this was because we included only patients with “own MELD” and excluded patients with MELD exception points, tumors, retransplantation, or acute liver failure. Among MELD sodium formulas (*MELD Na1* and *MELD Na2*), we believe that different results observed were due to different cut-off reference of serum sodium coupled with different correction factors [4, 15]. Our first conclusion is that MELD and related scores are almost close to be good predictors of survival after transplantation, and the addition of serum sodium or age does not improve MELD's score assessment. Categorization of patients with MELD sodium formulas may not improve overall results after transplantation. However, it can be argued that MELD sodium identifies patients with low MELD score (<20) with dilutional hyponatremia who are at increased risk of short-term mortality. These patients may have better survival following liver transplantation than those with high MELD score without hyponatremia. However, our data

indicates that patients with higher MELD sodium score (*MELD Na1* > 30, *MELD Na2* > 27) have higher chance of mortality after transplantation. In our study population, moderate and severe hyponatremia did not implicate more risk of death, but there was association with graft loss (data not shown). Consistent with previously published data [21, 22], pretransplant hyponatremia had an independent role of risk in both patient and graft survival in our cohort.

In terms of hospital and critical care stay, Foxton et al. [6] from the King's College Hospital, London, UK, demonstrated that patients with MELD score >24 or with refractory ascites had significantly higher longer post-LT ICU stay and total post-LT hospital stay. In addition, they had significantly increased ICU cost. In our cohort, none of the scores statistically correlated with length of hospital stay; however, integrated MELD predicted better length of ICU. In a sub-analysis, patients with MELD ≥ 25 required prolonged ICU stay and AMV. In a series from Canada [23] MELD score did not correlate with blood product requirement during liver transplantation. In our study all the included scores correlated with blood product consumption during the first 48 hrs of surgery. Those patients with MELD >30 required more blood products during the first 48 hrs of surgery.

We recognized some limitations of our study because, firstly, it was limited to patients undergoing LT at a single center and it may not be representative of practice patterns in other liver transplant centers. Secondly, it is a retrospective cohort analysis, and further follow-up was not analyzed. Furthermore, our results would only have to be taken into account for cirrhotic patients and not the whole liver transplant patients. Finally, although including all the liver transplant patients may have increased the discriminative ability of the model we tried to identify accuracy of MELD and related scores in prediction of post-LT events in a more homogeneous group of patients in order to avoid the impact of random variation. The small sample size might decrease the power to detect differences in post-LT events between MELD and related scores. Additionally, we did not assess liver transplantation costs among MELD scores although we knew that these data would have been of interest.

In summary, our data suggests that morbid-mortality may be close to be predicted by MELD and related scores. However, MELD or related scores are still far away from a perfect model. It seems that sicker patients may have reduced survival and higher morbidity after transplantation. Liver transplantation costs may be higher for those patients with higher MELD scores, and this must be taken in consideration. In our analysis, the c-statistic of MELD and related scores for post-transplant survival has been close to 0.7. This could involve, first, that, although MELD score was created for pretransplant setting, it is close to predict post-LT events. Secondly, the addition of variables to MELD such as serum sodium or age does not produce a net improvement. Overall, based on our results we can say that patients with higher MELD score require greater care in the immediate post-operative period and therefore may have increased morbidity and probably greater risk of mortality. We reaffirm the need for an objective prognostic model, easily reproducible in the clinical setting, to assess probability of survival in order to

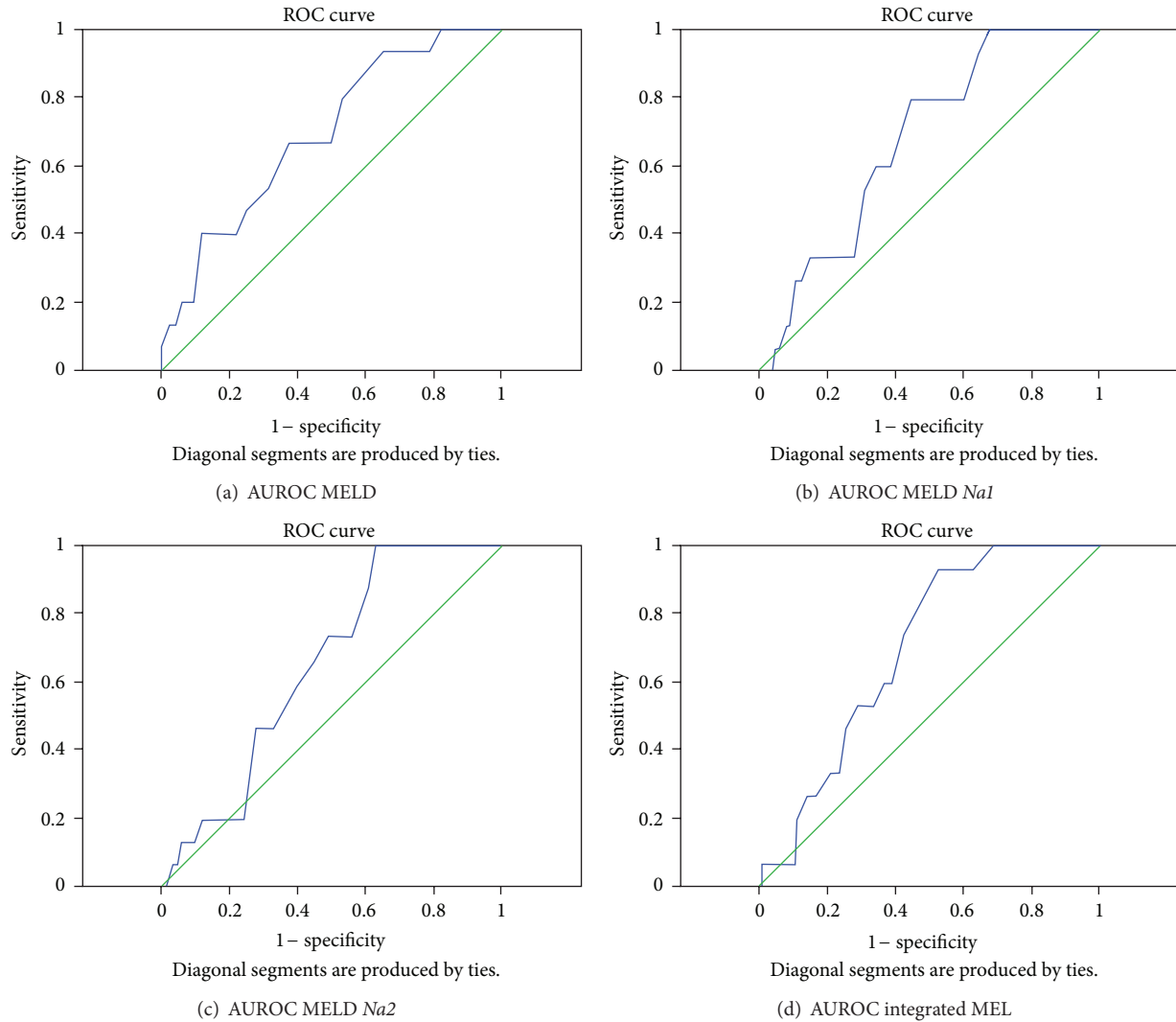


FIGURE 1: AUROC curves analyzing 3 months after liver transplant patient survival. (a) Receiver operating characteristic (ROC) curve for 3 months after transplant survival ranked on the basis of pretransplant MELD score. The c -statistic was 0.694 (0.56–0.82); $P = 0.014$. Best cut-off of sensibility and specificity for MELD is >25 . (b) Receiver operating characteristic (ROC) curve for 3 months after transplant survival ranked on the basis of pretransplant MELD sodium 1 score [4]. The c -statistic was 0.682 (0.56–0.79); $P = 0.021$. Best cut-off of sensibility and specificity for MELD $Na1$ is >30 . $MELD Na1$: MELD sodium 1: MELD + $1.59 \times (135 - \text{patient's serum sodium mEq/L})$. (c) Receiver operating characteristic (ROC) curve for 3 months after transplant survival ranked on the basis of pretransplant MELD sodium 2 score [15]. The c -statistic was 0.651 (0.54–0.76); $P = 0.05$. Best cut-off of sensibility and specificity for MELD $Na2$ is >27 . $MELD Na2$: MELD sodium 2: MELD – Na – $[0.025 \times \text{MELD} \times (140 - \text{Na})] + 140$. (d) Receiver operating characteristic (ROC) curve for 3 months after transplant survival ranked on the basis of pretransplant MELD sodium 2 score [5]. The c -statistic was 0.698 (0.593–0.80); $P = 0.012$. Best cut-off of sensibility and specificity for iMELD is >47 . iMELD: integrated MELD: MELD + $(\text{age} \times 0.3) - (0.7 \times \text{Na p}) + 100$.

avoid futile categorization on waiting list and thus better resource utilization after LT.

Abbreviations

LT: Liver transplantation
 MELD: Model for End-Stage Liver Disease
 MELD $Na1$: MELD sodium 1
 MELD $Na2$: MELD sodium 2
 iMELD: Integrated MELD
 ICU: Intensive care unit

AMV: Assist mechanical ventilatory support
 MDRD: Modification of Diet in Renal Disease
 GFR: Glomerular filtration rate
 PNF: Primary nonfunction
 HAT: Hepatic artery thrombosis
 PVT: Portal vein thrombosis
 BMI: Body mass index
 CIT: Cold ischemic time
 WIT: Warm ischemic time
 RRT: Renal replacement therapy
 ALF: Acute liver failure.

Funding

Authors of this paper have received no grant or funding from any agency in the public, commercial, or not-for-profit sectors and have no conflicts of interest to disclose.

References

- [1] P. S. Kamath, R. H. Wiesner, M. Malinchoc et al., "A model to predict survival in patients with end-stage liver disease," *Hepatology*, vol. 33, no. 2, pp. 464–470, 2001.
- [2] E. Cholongitas, L. Marelli, V. Shusang et al., "A systematic review of the performance of the Model for End-Stage Liver Disease (MELD) in the setting of liver transplantation," *Liver Transplantation*, vol. 12, no. 7, pp. 1049–1061, 2006.
- [3] D. M. Heuman, S. G. Abou-Assi, A. Habib et al., "Persistent ascites and low serum sodium identify patients with cirrhosis and low MELD scores who are at high risk for early death," *Hepatology*, vol. 40, no. 4, pp. 802–810, 2004.
- [4] S. W. Biggins, W. R. Kim, N. A. Terrault et al., "Evidence-based incorporation of serum sodium concentration into MELD," *Gastroenterology*, vol. 130, no. 6, pp. 1652–1660, 2006.
- [5] A. Luca, B. Angermayr, G. Bertolini et al., "An integrated MELD model including serum sodium and age improves the prediction of early mortality in patients with cirrhosis," *Liver Transplantation*, vol. 13, no. 8, pp. 1174–1180, 2007.
- [6] M. R. Foxton, M. A. B. Al-Freah, A. J. Portal et al., "Increased model for end-stage liver disease score at the time of liver transplant results in prolonged hospitalization and overall intensive care unit costs," *Liver Transplantation*, vol. 16, no. 5, pp. 668–677, 2010.
- [7] W. R. Kim, R. H. Wiesner, P. S. Kamath et al., "Prediction of liver transplant outcome using the MELD scale," *Transplantation*, vol. 71, supplement 1, p. 284, 2001.
- [8] H. Y. Yoo and P. J. Thuluvath, "Short-term postliver transplant survival after the introduction of MELD scores for organ allocation in the United States," *Liver International*, vol. 25, no. 3, pp. 536–541, 2005.
- [9] A. Lally, A. Nixon, D. Lewis et al., "MELD, CTP and region 1 CMSS equally predict post liver transplant patient survival," *Hepatology*, vol. 34, article 290, 2001.
- [10] S. Saab, V. Wang, A. B. Ibrahim et al., "MELD score predicts 1-year patient survival post-orthotopic liver transplantation," *Liver Transplantation*, vol. 9, no. 5, pp. 473–476, 2003.
- [11] H. Y. Yoo and P. J. Thuluvath, "Short-term postliver transplant survival after the introduction of MELD scores for organ allocation in the United States," *Liver International*, vol. 25, no. 3, pp. 536–541, 2005.
- [12] K. V. N. Menon, S. L. Nyberg, W. S. Harmsen et al., "MELD and other factors associated with survival after liver transplantation," *American Journal of Transplantation*, vol. 4, no. 5, pp. 819–825, 2004.
- [13] N. M. Desai, K. C. Mange, M. D. Crawford et al., "Predicting outcome after liver transplantation: utility of the model for end-stage liver disease and a newly derived discrimination function," *Transplantation*, vol. 77, no. 1, pp. 99–106, 2004.
- [14] A. Habib, I. Duorchik, J. Ahmad et al., "MELD as predictor of post-transplantation," *Hepatology*, vol. 40, article 261, 2004.
- [15] W. R. Kim, S. W. Biggins, W. K. Kremers et al., "Hyponatremia and mortality among patients on the liver-transplant waiting list," *The New England Journal of Medicine*, vol. 359, no. 10, pp. 1018–1026, 2008.
- [16] E. Rodrigo, G. Fernández-Fresnedo, J. C. Ruiz et al., "Assessment of glomerular filtration rate in transplant recipients with severe renal insufficiency by Mankivell, Modification of Diet in Renal Disease (MDRD), and Cockcroft-Gault equations," *Transplantation Proceedings*, vol. 35, no. 5, pp. 1671–1672, 2003.
- [17] P. S. Kamath and W. R. Kim, "The model for end-stage liver disease (MELD)," *Hepatology*, vol. 45, no. 3, pp. 797–805, 2007.
- [18] R. S. Brown Jr., K. S. Kumar, M. W. Russo et al., "Model for end-stage liver disease and child-turcotte-pugh score as predictors of pretransplantation disease severity, posttransplantation outcome, and resource utilization in united network for organ sharing status 2A patients," *Liver Transplantation*, vol. 8, no. 3, pp. 278–284, 2002.
- [19] N. M. Desai, K. C. Mange, M. D. Crawford et al., "Predicting outcome after liver transplantation: utility of the model for end-stage liver disease and a newly derived discrimination function," *Transplantation*, vol. 77, no. 1, pp. 99–106, 2004.
- [20] M. Jacob, L. P. Copley, J. D. Lewsey et al., "Pretransplant MELD score and post liver transplantation survival in the UK and Ireland," *Liver Transplantation*, vol. 10, no. 7, pp. 903–907, 2004.
- [21] M. F. Dawwas, J. D. Lewsey, J. M. Neuberger, and A. E. Gimson, "The impact of serum sodium concentration on mortality after liver transplantation: a cohort multicenter study," *Liver Transplantation*, vol. 13, no. 8, pp. 1115–1124, 2007.
- [22] B. C. Yun, W. R. Kim, J. T. Benson et al., "Impact of pretransplant hyponatremia on outcome following liver transplantation," *Hepatology*, vol. 49, no. 5, pp. 1610–1615, 2009.
- [23] L. Massicotte, D. Beaulieu, J.-D. Roy et al., "MELD score and blood product requirements during liver transplantation: no link," *Transplantation*, vol. 87, no. 11, pp. 1689–1694, 2009.

