Different Score Systems to Predict Mortality in Living Donor Liver Transplantation: Which Is the Winner? The Experience of an Egyptian Center for Living Donor Liver Transplantation

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ABSTRACT

Introduction. Many scoring systems have been proposed to predict the outcome of deceased donor liver transplantation. However, their impact on the outcome in living donor liver transplantation (LDLT) has not yet been elucidated. This study sought to assess performance of preoperative Model for End-Stage Liver Disease (MELD) score in predicting postoperative mortality in LDLT and to compare it with other scores: MELDNa, United Kingdom End-Stage Liver Disease (UKELD), MELD to serum sodium ratio (MESO), updated MELD, donor age-MELD (D-MELD) and integrated MELD (iMELD).

Methods. We retrospectively analyzed data from 86 adult Egyptian patients who underwent LDLT in a single center. Preoperative MELD, MELDNa, MESO, UKELD, updated MELD, D-MELD, and iMELD were calculated. Receiver-operator characteristic (ROC) curves and area under the curve (AUC) were used to assess the performance of MELD and other scores in predicting postoperative mortality at 3 months (early) and 12 months.

Results. Among the 86 patients, mean age 48 ± 7 years, 76 (88%) were of male sex and 27 (31.4%) had died. Preoperative MELD failed to predict early mortality (AUC = 0.63; $P = .066$). Comparing preoperative MELD with other scores, all other scores had better predictive ability ($P < .05$), with D-MELD on the top of the list (AUC = 0.68, $P = .016$), followed closely by UKELD (AUC = 0.67, $P = .025$). After that were iMELD, MESO, and MELDNa with the same predictive performance (AUC = 0.65; $P < .05$); updated MELD had the lowest prediction (AUC = 0.640; $P = .04$). Moreover, all scores failed to predict mortality at 12 months ($P > .05$).

Conclusions. Preoperative MELD failed to predict either early or 1-year mortality after LDLT. D-MELD, UKELD, MELDNa, iMELD, and MESO could be used as better predictors of early mortality than MELD; however, we need to develop an effective score system to predict mortality after LDLT.

MANY prognostic systems have been devised to predict the outcome of liver transplantation (LT). The Model for End-Stage Liver Disease (MELD) is widely used for organ allocation, but it has shown some limitations [1].

Many studies evaluated other prognostic models to either refine or improve the current MELD-based liver allocation. These studies have evaluated the effect of incorporating other variables into the model, such as serum sodium and age; MELD incorporating serum sodium (MELD-Na) [2], MELD incorporating sodium and age (iMELD) [2,3], and MELD to serum sodium ratio (MESO) [2,4]. Also, organ allocation in the United Kingdom is based on a model that includes serum sodium (United Kingdom End-Stage Liver

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Disease, UKELD) [5,6]. An updated MELD score is associated with a lower relative weight for serum creatinine coefficient and a higher relative weight for bilirubin coefficient [7]. The D-MELD, the arithmetic product of donor age and preoperative MELD, proposes donor–recipient matching [8]. All of these scoring systems have been proposed to predict the outcome of deceased donor liver transplantations (DDLT). However, their impact on the outcome in living donor liver transplantation (LDLT) has not yet been elucidated and is still a matter of controversy [9].

Egypt is a country with a heavy burden of hepatitis C virus, which is the most common cause of liver cirrhosis. Cultural barriers against cadaveric liver transplantation still exist, so LDLT has been, until now, the only available solution for patients with end-stage liver disease. Preoperative MELD is the standard score for evaluating our recipients. Patients are indicated for LDLT if the MELD score ranges between 15 and 26 (unless there is another clinical indication for transplantation). The aim of this study was to assess performance of preoperative MELD score in predicting early (first 3 months) and 1-year postoperative mortality in LDLT and to compare it with other scores: MELDNa, UKELD, MESO, updated MELD, D-MELD, and iMELD.

PATIENTS AND METHODS

Of 125 Egyptian patients who had liver transplantation in a single center (Al-Manial Specialized Hospital) for LDLT during the study period (between May 2005 and July 2013), 86 patients were included (excluding 27 pediatric cases and 12 cases with missing data). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional) and with the Helsinki Declaration of 1975, as revised in 2008 [5]. Informed consent was obtained from all patients included in the study.

Preoperative MELD, MELD-Na and MELDNa, MESO, iMELD, UKELD, updated MELD, and D-MELD were calculated in all patients according to the following formulas:

(1) MELD $9.57 \times \ln$ (creatinine (mg/dL)) $+ 3.78 \times \ln$ (bilirubin (mg/dL)) $+ 11.2 \times \ln$ (INR) $+ 6.43$

(2) MELD-Na MELD $+ 1.59 \times (135 - \text{Na (mmol/L)})$; Na range = 120–135 mmol/L

(3) MELDNa MELD − Na (mmol/L) − $(0.025 \times \text{MELD} \times (140 - \text{Na (mmol/L)}) + 140$; Na range = 125–140 mmol/L

(4) MESO (MELD/Na (mmol/L)) × 100

(5) iMELD MELD + (age (years) × 0.3) − $(0.7 \times \text{Na (mmol/L)}) + 100$

(6) UKELD $5 \times \{1.5 \times \ln$ (INR) $+ 0.3 \times \ln$ (creatinine (μmol/L)) $+ 0.6 \times \ln$ (bilirubin (μmol/L)) − $13 \times \ln$ (Na (mmol/L) + 70}

(7) Updated MELD $1.27 \times \ln (1 +$ creatinine (mg/dL)) $+ 0.94 \times \ln (1 +$ bilirubin (mg/dL)) $+ 1.66 \times \ln (1 +$ INR)

(8) D-MELD LabMELD × donor age in years

Statistical Methods

The data were coded and entered using the statistical package SPSS version 15. The data were summarized using descriptive statistics: mean, standard deviation, median, minimal, and maximum values for quantitative variables and number and percentage for qualitative values. Statistical differences between groups were tested using the χ^2 test for qualitative variables, independent samples *t* test, and ANOVA with post hoc Bonferroni test for quantitative variables. Correlations were done to test for linear relations between variables. The ability of different scores to discriminate between both 3-month and 1-year survivors and nonsurvivors was evaluated by receiver-operator characteristic (ROC) curve analysis. Values of $P \leq .05$ were considered statistically significant.

RESULTS

Eighty-six recipients were included; baseline demographics are shown in Table 1. The mean age of living recipients was 48.53 ± 6.64 years, whereas the mean age of the deceased patients was 48.19 ± 7.40 with no statistically significant difference ($P = .83$). The mean age of the donors was 27.88 ± 6.18 years. Recipients were predominantly male (n = 76, 88%); 93% had liver cirrhosis secondary to hepatitis C virus infection.

The 3-month mortality of recipients was 24.42% (n = 21 of 86), whereas the 1-year mortality was 31.4% (n = 27 of 86). Infectious complications such as pneumonia or sepsis were the most common causes of death. Mean preoperative MELD scores of living and deceased recipients were 17.81 and 18.62, respectively, with no statistically significant difference.

Apart from the mean of preoperative UKELD, which showed a statistically significant difference between survivor and nonsurvivor recipients at 1 year ($P = .046$) and was more statistically significant during the early postoperative period ($P = .029$), the mean of other preoperative scores showed no statistically significant difference between living and deceased recipients ($P > .05$) (Table 2).

Table 1. Baseline Demographics of the Study Patients

Characteristic	Value	*P* Value
Number of patients	86	
Male/female	76/10	
Alive	52/7	
Deceased	24/3	
Age, y (mean ± SD)		.92
Recipients		.83
Alive	48.53 ± 6.64	
Deceased	48.19 ± 7.40	
Donor		.20
For living recipients	27.88 ± 6.18	
For deceased recipients	28.96 ± 4.82	
Etiology of cirrhosis virus		
Virus	80 (93%)	
Hepatitis C virus		
Autoimmune hepatitis	1 (1.2%)	
Cholestatic liver disease	2 (2.3%)	
Alcohol	1 (1.2%)	
Cryptogenic	2 (2.3%)	
Indication for liver transplantation		
Recurrent spontaneous bacterial peritonitis	33/86 (38.4%)	
Chronic hepatic encephalopathy	34/86 (39.5%)	
Refractory ascites	57/86 (66.3%)	
Recurrent gastrointestinal bleeding	20/86 (23.3%)	
Hepatocellular carcinoma	24/86 (27.9%)	

Table 2. Mean, Standard Deviation, Median, and Range of All Scores in Alive and Deceased Recipients Early Postoperatively (3 mo) and at 1 y

Preoperative Scores	Mean ± SD	Median	Range	*P* Value
At 3 mo				
MELD				
Alive	17.81 ± 3.38	18	10–25	.085
Deceased	19.40 ± 4.12	20	11–26	
MELDNa				
Alive	21.43 ± 4.15	21.15	11.40–29.70	.072
Deceased	23.88 ± 4.72	24.35	14.60–31.40	
MELD-Na				
Alive	22.34 ± 7.16	20.35	9.90–42	.119
Deceased	26.37 ± 8.97	25.65	11–44.10	
MESO				
Alive	13.34 ± 2.68	13.55	7.20–19.20	.061
Deceased	14.92 ± 3.42	15	8.10–20.30	
UKELD				
Alive	54.64 ± 3.65	54.45	46.00–63.80	.029*
Deceased	57.19 ± 4.39	57.55	49.30–66.10	
At 1 y				
Updated MELD				
Alive	3.89 ± 0.53	3.80	2.60–5.20	.078
Deceased	4.19 ± 0.68	4.20	3.00–5.70	
i-MELD				
Alive	39.02 ± 6.04	39.25	24.30–51.50	.131
Deceased	42.08 ± 6.57	43.15	25.80–51.20	
MELD				
Alive	17.81 ± 3.38	18	10–25	.352
Deceased	18.62 ± 4.19	18.5	11–26	
MELDNa				
Alive	21.43 ± 4.15	21.15	11.40–29.70	.090
Deceased	23.17 ± 4.53	23.10	14.60–31.40	
MELD-Na				
Alive	22.34 ± 7.16	20.35	9.90–42	.096
Deceased	25.37 ± 8.55	24.75	11–44.10	
MESO				
Alive	13.34 ± 2.68	13.55	7.20–19.20	.231
Deceased	14.25 ± 3.37	14.45	8.10–20.30	
UKELD				
Alive	54.64 ± 3.65	54.45	46.00–63.80	.046*
Deceased	56.47 ± 4.22	56.25	49.30–66.10	
Updated MELD				
Alive	3.89 ± 0.53	3.80	2.60–5.20	.185
Deceased	4.08 ± 0.67	4.10	3.00–5.70	
i-MELD				
Alive	39.02 ± 6.04	39.25	24.30–51.50	.132
Deceased	41.20 ± 6.18	40.75	25.80–51.20	
D-MELD				
Alive	486.28 ± 136.27	463	264–780	.117
Deceased	536.42 ± 129.11	528.50	264–800	
D-MELD				
Alive	486.28 ± 136.27	463	264–780	.083
Deceased	559.35 ± 128.04	545.50	264–800	

*Statistically significant.

Using ROC curves and area under the curve (AUC) analysis showed that both preoperative MELD and MELD-Na failed to predict early (3-month) mortality. On the other hand, the performance of all other preoperative score systems in predicting early mortality was poor (AUC < 0.7), but comparison with preoperative MELD revealed that all other scores were better than MELD in predicting early mortality, with D-MELD on the top of the list (AUC = 0.68, $P = .01$), followed closely by UKELD (AUC = 0.67, $P = .025$), then iMELD, MESO, and MELDNa with the same predictive performance (AUC = 0.65; $P < .05$). Updated MELD had the lowest prediction (AUC = 0.640; $P = .04$) (Table 3, Fig 1). The cutoff values for D-MELD and UKELD that could be used to predict early mortality were 485 (70% sensitivity, 60% specificity) and 55.25 (65% sensitivity, 60% specificity), respectively. Furthermore, analysis of AUC showed that all preoperative scores failed to predict 1-year mortality ($P > .05$, AUC 0.55 to 0.62) (Table 4, Fig 2).

DISCUSSION

Prediction of posttransplantation outcome is an important issue. Most studies have concerned outcomes after DDLT rather than LDLT. Evolving data from cadaveric transplantation studies may not be applicable to LDLT. There are many differences between LDLT and DDLT, including the short waiting time, the reduced cold ischemia time, and that the graft is from a healthy donor who is younger, leaner, and lacks other significant comorbidities compared with cadaveric transplant recipients, so posttransplantation outcome may be different [9,10].

Many scoring systems have been suggested to predict the outcome of liver transplantation (LT). All of these scoring systems have been proposed to predict the outcome of DDLT. However, their impact on the outcome in LDLT is still a matter of controversy [9].

This study aimed to assess the performance of preoperative MELD score in predicting early (first 3 months) and 1-year postoperative mortality in LDLT and to compare it with other scores: MELDNa and MELD-Na, UKELD, MESO, updated MELD, D-MELD, and iMELD.

Our results showed that of 86 adult recipients included in the study, 21 were dead within the first 3 months (24.42%) and 27 were dead within the first year posttransplantation (31.4%). There was no statistically significant difference between living and deceased recipients regarding recipient age and sex or donor age.

Table 3. Analysis of Area Under the Curve (AUC) to Predict 3-Month Mortality of MELD and the Other 7 Scores

Score	AUC	*P* Value	95% Confidence Interval
MELD	0.633	.066	0.486–0.787
MELD-Na	0.640	.059	0.491–0.790
MELDNa	0.656	.036*	0.507–0.806
MESO	0.657	.035*	0.507–0.806
UKELD	0.670	.025*	0.519–0.814
Updated MELD	0.646	.049*	0.502–0.791
iMELD	0.659	.033*	0.511–0.806
D-MELD	0.680	.016*	0.552–0.807

*Significant values.

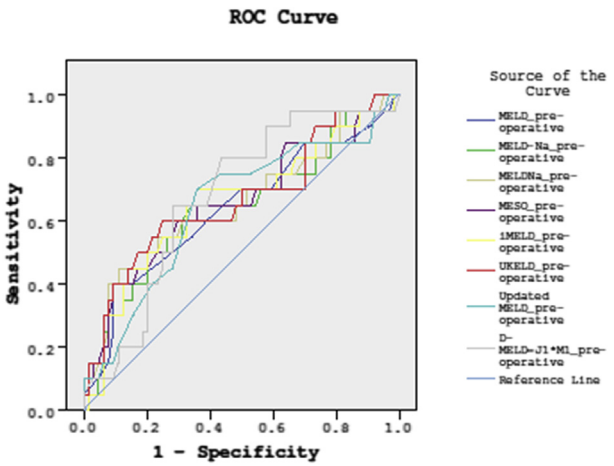

Fig 1. Receiver-operator characteristic curve of different score systems to predict early mortality after living donor liver transplantation.

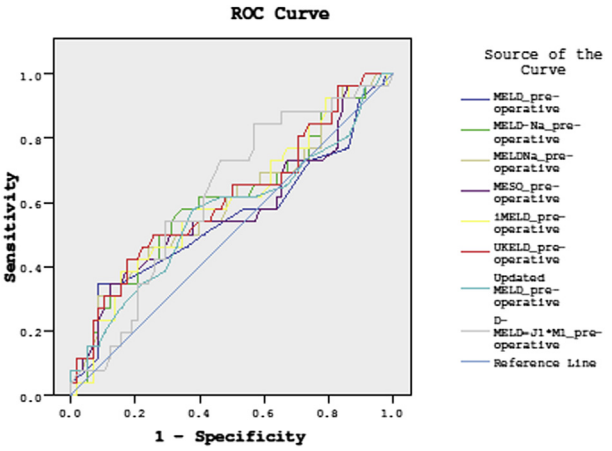

Fig 2. Receiver-operator characteristic curve of different score systems to predict 1-year mortality after living donor liver transplantation.

According to our center's study, apart from preoperative UKELD, which showed a statistically significant difference regarding the mean and the median in the deceased (particularly early postoperative) compared with living recipients (57.19 ± 4.39 vs 54.64 ± 3.65; 57.55 vs 54.45, respectively; $P = .029$), other scores incorporating serum sodium into MELD score using different formulae (MELD-Na, MELDNa, MESO, and iMELD) showed no statistical significance. Also the mean of both D-MELD and updated MELD scores did not show a statistically significant difference. Using the ROC curves and area under the curve to assess the ability of preoperative MELD score in predicting postoperative mortality showed that preoperative MELD failed to predict either early (3 months) or 1-year mortality (AUC = 0.63, $P = .066$; AUC = 0.550, $P = .47$, respectively).

Our results matched those of Cywinski et al. [11], who reported low predictive abilities of both MELD and MELD-Na scores for recipient survival and graft failure after orthotopic live transplantation (OLT), and also with those of Hayashi et al. [12], who found that the pretransplantation MELD score did not predict 1-year posttransplantation survival after LDLT. This is in contrast to the results of Onaca et al. [13], who reported that the MELD score correlated with survival at 2 years after OLT.

Table 4. Analysis of Area Under the Curve (AUC) to Predict 1-Year Mortality of MELD and the Other 7 Scores

Score	AUC	*P* Value	95% Confidence Interval
MELD	0.550	.47	0.405–0.695
MELD-Na	0.602	.14	0.465–0.740
MELDNa	0.601	.14	0.464–0.738
MESO	0.573	.29	0.430–0.715
UKELD	0.613	.10	0.477–0.748
Updated MELD	0.56	.35	0.424–0.705
iMELD	0.601	.14	0.467–0.736
D-MELD	0.623	.07	0.497–0.750

In evaluating other scoring systems in predicting early postoperative mortality, the performance was poor (AUC < 0.7). However, comparison with preoperative MELD revealed that apart from MELD-Na, which showed almost the same results as MELD, all other scores were better than MELD. D-MELD was first (AUC = 0.68, $P = .01$), followed closely by UKELD (AUC = 0.67, $P = .025$), and then iMELD, MESO, and MELDNa with the same predictive performance (AUC = 0.65; $P < .05$). Updated MELD had the lowest prediction (AUC = 0.640; $P = .04$).

It seems logical that D-MELD may give better prediction than MELD alone (AUC = 0.68, $P = .016$ vs AUC = 0.63, $P = .066$; not significant) because it is not only reflecting the severity of liver disease alone but including donor age, which may affect both graft and patient survival. However, according to our results, donor mean age was 27.88 ± 6.18 years vs 28.96 ± 4.82 years, with no statistically significant difference between donors for living and deceased recipients ($P = .20$). On the other hand, incorporating the donor age into the D-MELD score formula showed a statistically significant difference between the groups. A D-MELD cutoff value of 485 had 70% sensitivity and 60% specificity.

Our results were consistent with those of Schrem et al. [14], who found an area under the ROC curve < 0.7 for D-MELD score, concluding that D-MELD failed to predict short-term outcome after liver transplantation with acceptable sensitivity and specificity, but this study was carried out in DDLT. On the other hand, Ikegami et al. [15] reported the D-MELD score as a simple and reliable predictor of early graft survival that assists the matching of donors and recipients in LDLT in adults.

To our knowledge, this is the first study evaluating UKELD to predict postoperative mortality in LDLT rather than organ allocation and prioritization in DDLT. However, it showed poor overall predictive ability of early mortality,

but still better than MELD (AUC 0.67, $P = .025$ vs AUC = 0.63, $P = .066$; not significant), because adding another variable (serum sodium) to original MELD is better than MELD alone. A UKELD cutoff value of 55.25 had 65% sensitivity and 60% specificity, respectively.

Again it seems that incorporating one variable (Na in MELDNa and MESO) or more (age of recipient and Na in iMELD) into MELD may improve its predictive ability of early mortality. Moreover, all of the studied scores (MELD, MELDNa and MELD-Na, UKELD, MESO, updated MELD, iMELD, D-MELD) failed to predict 1-year mortality (AUC 0.550 to 0.613; $P =$ not significant).

Our results are consistent with the results of 15 of 37 studies included in a meta-analysis that showed no statistically significant association between MELD and posttransplantation survival. In the remaining 22, some association was found. Eleven studies also measured predictive ability with c-statistics. Values were below 0.7 in all but two studies, suggesting poor predictive value. Although the majority of studies reported an association between pretransplantation MELD score and posttransplantation survival, they represented a low level of evidence. Therefore, their findings should be interpreted conservatively [16].

CONCLUSIONS

Preoperative MELD score failed to predict both early (3-month) and 1-year mortality in LDLT. Adding one or more variables to MELD score, mainly age of donor (D-MELD), serum Na (UKELD, MELDNa, MESO), and age of recipient plus serum Na (iMELD), may improve the predictive ability of MELD; however, we still need to develop an effective score to predict patient outcomes, especially mortality after LDLT.

REFERENCES

[1] Asrani SK, Kim WR. Organ allocation for chronic liver disease: Model for End-Stage Liver Disease and beyond. Curr Opin Gastroenterol 2010;26:209–13.

[2] Biselli M, Gitto S, Gramenzi A, Di Donato R, Brodosi L, Ravaioli M, et al. Six score systems to evaluate candidates with advanced cirrhosis for orthotopic liver transplant: which is the winner? Liver Transpl 2010;16:964–73.

[3] Luca A, Angermayr B, Bertolini G, Koenig F, Vizzini G, Ploner M, et al. An integrated MELD model including serum sodium and age improves the prediction of early mortality in patients with cirrhosis. Liver Transpl 2007;13:1174–80.

[4] Huo TI, Wang YW, Yang YY, Lin HC, Lee PC, Hou MC, et al. Model for end-stage liver disease score to serum sodium ratio index as a prognostic predictor and its correlation with portal pressure in patients with liver cirrhosis. Liver Int 2007;27:498–506.

[5] Barber KM, Pioli SE, Blackwell JE, Collett D, Neuberger JM, Gimson AE. Development of a UK score for patients with end-stage liver disease. Hepatology 2007;46(Suppl. 1):510A.

[6] Neuberger J, Gimson A, Davies M, Akyol M, O'Grady J, Burroughs A, et al. Selection of patients for liver transplantation and allocation of donated livers in the UK. Gut 2008;57:252–7.

[7] Sharma P, Shaubel DE, Sima CS, Merino RM, Lok AS. Re-weighting the model for end-stage liver disease score components. Gastroenterology 2008;135:1575–81.

[8] Halldorson JB, Bakthavatsalam R, Fix O, Reyes JD, Perkins JD. D-MELD, a simple predictor of post liver transplant mortality for optimization of donor/recipient matching. Am J Transplant 2009;9:318–26.

[9] Chung IS, Park M, Ko JS, Gwak MS, Kim GS, Lee SK. Which score system can best predict recipient outcomes after living donor liver transplantation? Transplant Proc 2012;44:393–5.

[10] Trotter JF, Wachs M, Everson GT, Kam I. Adult-to-adult transplantation of the right hepatic lobe from a living donor. N Engl J Med 2002;346:1074.

[11] Cywinski JB, Mascha EJ, You J, Sessler DI, Kapural L, Argalious M, et al. Pre-transplant MELD and sodium MELD scores are poor predictors of graft failure and mortality after liver transplantation. Hepatol Int 2011;5:841–9.

[12] Hayashi PH, Forman L, Steinberg T, Bak T, Wachs M, Kugelmas M, et al. Model for end stage liver disease score does not predict patient or graft survival in living donor liver transplant recipients. Liver Transpl 2003;9:737–40.

[13] Onaca NN, Levy MF, Sanchez EQ. A correlation between the pretransplantation MELD score and mortality in the first two years after liver transplantation. Liver Transpl 2003;9:117–23.

[14] Schrem H, Reichert B, Frühauf N, Becker T, Lehner F, Kleine M, et al. The Donor-Risk index, ECD score and D-MELD score all fail to predict short-term outcome after liver transplantation with acceptable sensitivity and specificity. Ann Transplant 2012;17:5–13.

[15] Ikegami T, Imai D, Wang H, Yoshizumi T, Yamashita YI, Ninomiya M, et al. D-MELD as a predictor of early graft mortality in adult-to-adult living-donor liver transplantation. Transplantation 2014;97:457–62.

[16] Klein KB, Stafinski TD, Menon D. Predicting survival after liver transplantation based on pre-transplant MELD score: a systematic review of the literature. PLoS One 2013;8:e80661.