

MELD 3.0 is a more accurate predictor of mortality in decompensated cirrhosis than MELD and MELD-Na

Le score MELD 3.0 est meilleur score dans la prédiction de la mortalité au cours de la cirrhose décompensée par rapport au score MELD et MELD NA

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ABSTRACT

Background and aim: Prognostic scores guide organ allocation in cirrhosis. We assessed the performance of MELD, MELD-Na, and MELD 3.0 for predicting mortality in decompensated Tunisian cirrhotic patients

Methods: We conducted a retrospective study including decompensated cirrhosis patients in a Tunisian gastroenterology department.

Results: 152 patients were enrolled (mean age 61 years; viral etiology 65.1%). Mean MELD-Na and MELD 3.0 were 17.7 and 19.4. Mean follow-up: 17.1 months. Decompensation rate: 33.6%; 3-month mortality: 18.4%.

For 3-month mortality, AUROCs were 0.786 (MELD), 0.841 (MELD-Na), and 0.850 (MELD 3.0). MELD 3.0 cut-off of 24 yielded sensitivity 68%, specificity 88% ($p=0.04$ for association with mortality).

Conclusion: MELD 3.0 outperformed MELD and MELD-Na in predicting mortality. A MELD 3.0 score ≥ 24 identifies patients who should be prioritized on the transplant waiting list.

Key words: Cirrhosis-Prognosis-mortality-Liver transplantation

RÉSUMÉ

Objectif : Les scores pronostiques guident l'attribution des greffons dans la cirrhose. Nous avons évalué les performances des scores MELD, MELD-Na et MELD 3.0 pour prédire la mortalité chez des patients tunisiens atteints de cirrhose décompensée.

Méthodes : Nous avons mené une étude rétrospective incluant des patients atteints de cirrhose décompensée dans un service de gastroentérologie tunisien.

Résultats : Cent cinquante-deux patients ont été inclus (âge moyen 61 ans ; étiologie virale 65,1 %). Les valeurs moyennes des scores MELD-Na et MELD 3.0 étaient respectivement de 17,7 et 19,4. Le suivi moyen était de 17,1 mois. Le taux de décompensation était de 33,6 % et la mortalité à 3 mois de 18,4 %.

Pour la mortalité à 3 mois, les AUROC étaient respectivement de 0,786 (MELD), 0,841 (MELD-Na) et 0,850 (MELD 3.0). Le seuil du MELD 3.0 à 24 avait une sensibilité de 68 % et une spécificité de 88 % ($p = 0,04$ pour l'association avec la mortalité).

Conclusion : Le score MELD 3.0 est supérieur aux scores MELD et MELD-Na pour la prédiction de la mortalité. Un score MELD 3.0 ≥ 24 identifie les patients à prioriser sur la liste d'attente de transplantation.

Mots clés: Cirrhose-Pronostic-Mortalité-Transplantation hépatique

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INTRODUCTION

The Model for End-Stage Liver Disease (MELD) has been established as a reliable predictor of short-term survival in patients with end-stage liver disease. It was first introduced in 2002 for prioritization of liver transplant candidates [1]. The current version of the MELD score, commonly referred to as MELD-Na, incorporates serum concentrations of total bilirubin, creatinine, and sodium as well as the international normalized ratio (INR) of prothrombin time. MELD-Na has been used to determine priorities for the allocation of livers for transplant in the United States since 2016 [2]. Recently, in order to further improve the screening ability of the MELD score in liver allocation, Kim and colleagues established a new MELD 3.0 score system with more accurate predictive prognostic ability [3]. Sex and albumin levels were added to this new scoring system. The purpose of this study is to explore MELD 3.0 score for predicting survival in decompensated Tunisian cirrhotic patients.

METHODS

Study population

We conducted an observational, retrospective study involving all patients with decompensated cirrhosis managed in Gastroenterology department of Taher Maamouri hospital during the period from January 2010 to December 2021.

The inclusion criteria were as follows: (1) diagnosis of decompensated liver cirrhosis based on clinical, biochemical, ultrasonographic and/or endoscopic findings and (2) age ≥ 18 years old.

The exclusion criteria were as follows: (1) patients with liver cancer or other active malignancy; (2) congestive heart failure, chronic kidney disease or other significant chronic extrahepatic disease.

Statistical analysis

Statistical calculations were performed using SPSS (Version 26.0). Mortality was assessed using the Kaplan Meier model. The performance of the scores was assessed using the AUROC. P values less than 0.05 were considered statistically significant.

The MELD score was calculated as $6.43 + 9.57 \cdot \log_e \text{creatinine (mg/dL)} + 3.78 \cdot \log_e \text{bilirubin (mg/dL)} + 11.2 \cdot \log_e \text{INR}$.

The MELD-Na score was given by $\text{MELD} + 1.32 \cdot (137 - \text{Na}) - [0.033 \cdot \text{MELD} \cdot (137 - \text{Na})]$. The upper and lower limits of Na are 137 and 125 mmol/L, respectively.

The MELD 3.0 was defined as $1.33 \text{ (if female)} + 4.56 \cdot \log_e \text{(bilirubin)} + 0.82 \cdot (137 - \text{Na}) - 0.24 \cdot (137 - \text{Na}) \cdot \log_e \text{(bilirubin)} + 9.09 \cdot \log_e \text{(INR)} + 11.14 \cdot \log_e \text{(creatinine)} + 1.85 \cdot (3.5 - \text{albumin}) - 1.83 \cdot (3.5 - \text{albumin}) \cdot \log_e \text{(creatinine)} + 6$, which is rounded to the nearest integer. Consistent with prior versions of MELD, bilirubin, INR and creatinine values below 1.0 were set to 1.0. The lower and upper bounds of Na value were the same to MELD-

Na. For serum albumin, lower and upper bounds of 1.5 g/dL and 3.5 g/dL, respectively, were selected.

RESULTS

A total of 152 patients with decompensated cirrhosis managed in our hospital from January 2010 to December 2021 were included. The main causes of chronic liver disease were hepatitis C virus (HCV) infection (cases, 32.2%), hepatitis B virus (HBV) infection (cases, 30.9%), autoimmune liver disease (cases, 10.7%) and alcoholic liver disease (cases, 6.6%).

The median age of patients was 62 years (interquartile range [IQR] 31–71), and 54.6% were men. Ascites and hepatic encephalopathy were present in 90.1% and 14.5%, respectively. The mean MELD score was 15.78. The mean MELD-Na and MELD 3.0 scores were 17.74 ± 6.94 and 19.4 ± 6.53 respectively. The mean Child-Pugh score was 8.56 ± 1.71 with 14 (9.2%), 102 (67.1%), and 36 (23.7%) patients were graded as Child-Pugh A, B, and C, respectively. The overall mortality at 3-month, 6-month and 1-year was 18.4%, 24.3% and 35.5% respectively. The major cause of death was hepatic encephalopathy in this study. Baseline features of the study cohort are summarized in Table 1.

Table 1. Baseline features of the study at inclusion

Characteristic	Value
Age	62
Gender (%)	
Male	54.6
Female	45.3
Etiology of cirrhosis(%)	
HCV	32.2
HBV	30.9
NASH	15.31
Alcoholic	6.6
Cryptogenetic	7.2
Ascites(%)	90.1
Hepatic encephalopathy(%)	14.5
Vrceal bleeding(%)	11.8
Laboratory	
Bilirubin($\mu\text{mol/L}$)	36.5
Albumin (g/L)	26.8
Creatinine($\mu\text{mol/L}$)	96.6
International normalized ratio (INR)	1.7
Sodium (mmol/L)	133.7
MELD score	15.78
MELD-Na score	17.74
MELD 3.0	19.4

The AUROC of the MELD 3.0 score in predicting 3-month, 6-month and 1-year mortality were 0.850 (0.766-0.935), 0.874 (0.807-0.940) and 0.822 (0.750-0.894) respectively, which were superior to the MELD score (0.786 [0.691-0.881]), (0.814 [0.736-0.892]) and (0.801 [0.724-0.787])

and MELD-Na score (0.841 [0.751-0.931]), (0.863 [0.792-0.934]) and (0.821 [0.747-0.895])(Table 2).

Table 2. AUROC of scores for prediction of different survival endpoints

	MELD3.0	MELD	MELD-Na	Child-Pugh
3-month mortality	0.850 (0.766-0.935)	0.786 (0.691-0.881)	0.841 (0.751-0.931)	0.700 (0.580-0.813)
6-month mortality	0.874 (0.807-0.940)	0.814 (0.736-0.892)	0.863 (0.792-0.934)	0.736 (0.640-0.832)
1-year mortality	0.822 (0.750-0.894)	0.801 (0.724-0.787)	0.821 (0.747-0.895)	0.688 (0.595-0.780)

The area under the receiver operating characteristic curve analysis showed that a MELD 3.0 score of 24 best predicted 3-month mortality in cirrhotic patients. There was a significant difference in survival between high-risk (≥ 24) and other patients in our cohort ($P < 0.04$ for log-rank test of Kaplan-Meier's survival curve).

Compared to the MELD-Na, there were more patients up-categorized (18.4%) using the MELD3.0 score than down-categorized (Table 3). Out of the 62 decedents, 48 (77.42%) remained in the same score categories, whereas 14 (22.5%) were correctly reclassified (up-categorized) (Table 4).

Tables 3. Reclassification analysis of patients between MELD-Na and MELD 3.0

N=patients		MELD 3.0				
		6-9	10-19	20-29	30-39	+ 40
MELD-Na	6-9	6	8	0	0	0
	10-19	0	62	16	0	0
	20-29	0	0	48	3	0
	30-39	0	0	0	8	1

Tables 4. Reclassification analysis of deaths between MELD-Na and MELD 3.0

N= deaths		MELD 3.0				
		6-9	10-19	20-29	30-39	+ 40
MELD-Na	6-9	0	2	0	0	0
	10-19	0	11	8	0	0
	20-29	0	0	29	3	0
	30-39	0	0	0	8	1

Out of the 25 female decedents, 14 patients (36%) would be correctly reclassified. In men, the effect was less dramatic yet still positive, with a net gain of 5 decedents (13.5%).

DISCUSSION

Decompensated cirrhosis is associated with a high risk of death. It imposes a substantial health burden on many countries and this burden has increased at the global

level since 1990, partly due to population growth and ageing [4]. Five-year survival varies from 21% to 99% in the different studies [5]. In our study, the overall mortality at 3-month, 6-month and 1-year was 18.4%, 24.3% and 35.5% respectively. The main cause of death, in our study, was hepatic encephalopathy (50%).

To find accurate prognostic scoring system not only could help clinicians to make better decisions but also has a wide significance in the context of organ allocation for decompensated cirrhosis patients. Until now, various scoring systems have been used to predict the mortality of liver decompensated cirrhosis, including the Child-Turcotte-Pugh (CTP), Model for End-stage Liver Disease score (MELD), MELD-Na and MELD3.0. The CTP was first proposed in 1964, and it has been widely used for several decades for the prognostication of patients with cirrhosis [6]. However, CTP is limited in predicting the mortality of patients with decompensated cirrhosis [7]. Compared to CTP, MELD is more objective and clinically useful for defining disease severity.

The first MELD score included three variables: serum bilirubin, serum creatinine, and the INR, which could imply several shortcomings. For example, inter-laboratory variability in the INR and creatinine measurement might contribute to an overall mean variation in calculated MELD of 4.8 points (range 2–11) [8]. A recent study by Godfrey et al [9] suggested that the predictive accuracy of the MELD score has declined over time, attributed to the changing demographics of liver disease, with a C-statistic of 0.80 in 2003 and 0.70 in 2015.

Data show that serum sodium level is an independent predictor of mortality in patients with cirrhosis awaiting transplantation and it provides improved accuracy if added to the MELD score [10]. A systematic review [11] demonstrated that MELD-Na was superior to CTP and MELD for predicting mortality after 12 months, indicating that MELD-Na was a good model to predict long-term mortality in patients with decompensated cirrhosis than CTP and MELD. However, women are at a disadvantage in the current system. It has been reported that women with the same MELD score were significantly less likely to receive a transplant than men [12]. This was associated with an overestimation of glomerular filtration rate (GFR) in serum creatinine, thus underestimating the risk of mortality in women compared to men with the same creatinine [13]. Compared to its predecessors, the MELD3.0 is derived from a recent cohort of liver transplant candidates and characterized by 3 new features: the addition of 2 variables, namely, female sex and serum albumin; a lowered ceiling for serum creatinine from 4.0 mg/dL to 3.0 mg/dL; and the inclusion of 2 interaction terms between albumin and creatinine and between bilirubin and sodium [14]. Kim and al showed that MELD 3.0 had better discrimination of 3 months mortality than MELD-Na (AUROC, 0.869 vs 0.862; $P < 0.01$) [14]. In our cohort, the MELD 3.0 was also significantly superior to the MELD and MELD-Na scores in predicting 3-month survival. The AUROC of the MELD 3.0 score in predicting 90-day mortality was 0.850, that of MELD-Na was 0.841, and that of MELD was 0.786. In our cohort, the MELD 3.0 was also found to be significantly superior to the MELD-Na

score in predicting 6-month and 1-year mortality (AUROC, 0.874 vs 0.863 and 0.822 vs 0.821). Importantly, Kim and al [14] showed that MELD 3.0 correctly reclassified a net of 8.8% of decedents to a higher MELD tier, affording them a meaningfully higher chance of transplantation, particularly in women. In our cohort, out of the 62 decedents, 14 patients (22.5%) were correctly reclassified (up-categorized). Out of the 25 female decedents, a net of 14 patients (36%) would be correctly reclassified. In men, the effect was less dramatic, with a net gain of 5 decedents (13.5%).

Our cohort study includes a vast number of patients. However, our study suffers several limitations related to its retrospective nature, including potential losses in the data records. Another limitation was the albumin serum levels in the blood, since it could be elevated due to the prior administration of albumin, which could modify the MELD 3.0 values.

CONCLUSION

Overall, MELD3.0 shows promising value with the highest AUROC in all assessed scoring systems. MELD 3.0 demonstrated the strongest predictive performance for mortality across multiple time points. Further multicenter studies with larger sample sizes and extended follow-up are warranted to enhance the precision of mortality prediction using these scoring systems in patients with decompensated cirrhosis.

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