Journal de la Faculté de Médecine d'Oran

Article original

MELD-Na as a prognostic score for cirrhotic patients

Yousra MEGUENNI 1, 2, Zineb TAHIRI 1, 2, Ibtissem KIHEL 1, 2, Mourad NACHI 1, 2, Nazim KORTI 2, 3, Benali ADDAD 1, 2

1 University Hospital Center of Oran, Department of Biochemistry & Molecular Biology.

2 Faculty of Medicine, University of Oran 1, Algeria

3 University Hospital Center of Oran , Department. of Hepato-Gastro-Enterology. ,Faculty of Medicine, University of Oran1, Algeria

Auteur correspondant: mouradnachi1@gmail.com

submitted 18/08/2023 ; accepted 15/11/2023 ; published online 27/12/2023

Citation: MEGUENNI Y, et al. MELD-Na as a prognostic score for cirrhotic patients (2023) J Fac Med Or 7 (2) : 901-906.

DOI : https://doi.org / 10.51782/jfmo.v7i2.204

KEY WORDS
Cirrhosis, MELD, MELD-NA, Prognosis, Biological scores.

Abstract

Background-The high mortality of cirrhosis is a global public health problem. For predicting the outcome of patients with cirrhosis, many prognostic models were proposed.The new Model for End-Stage Liver Disease including serum sodium (MELD-Na) has been proposed as an alternative to the original MELD, to increase the accuracy of the score in predicting short-term mortality. The purpose of this study was to assess the ability of MELD-Na scoring system to predict three-month mortality among cirrhotic patients, and comparing it to the MELD score.

Methods-An observational study was carried out, at the Hepato-Gastro-Enterology Department of the University Hospital Center of Oran. A retrospective review of the medical records of all patients with cirrhosis, between 1st January 2019 and 31st December 2021, was performed. Among 103 patients, 47 were selected after excluding the patients who were lost to follow-up after three months or with missing data. The information collected included demographic data, clinical characteristics and laboratory values of: bilirubin, creatinine, international normalized ratio (INR) of prothrombin and sodium. The MELD-Na and MELD scores were calculated using online calculators, then the ability of the models to predict the risk of mortality at three months was assessed, using the area under the receiver operating characteristic curve (AUC).

Results - : Eight (17%) patients died at three months. The MELD-Na and MELD both had significantly high area under the curve (AUC): MELD-Na: 0.952, 95% confidence interval [CI]: 0.885–1.00, MELD: 0.931, 95% confidence interval [CI]: 0.834–1.000. The MELD-Na score was slightly better than the MELD, with a sensitivity and a specificity of 87.5% and 87.2%, respectively, for a cut-off value = 21.

Conclusion -The MELD-Na score seems to be a good predictor of mortality at three months among patients with cirrhosis.

1. Introduction

Cirrhosis is an important cause of morbidity and mortality worldwide. Predicting the outcome of cirrhosis has been an important issue, and several prognostic scores were developed through the years [1,2].

The first one was the Child-Pugh score that has been widely used to establish the prognosis of cirrhosis for several decades now. Later, the Model for end-stage liver disease (MELD) score was proposed as an alternative to Child-Pugh [3]. It is based on three objective biochemical variables : serum bilirubin, serum creatinine, and the international normalized ratio (INR) of prothrombin time [4,5].

This score is able to accurately predict the risk of short term mortality in end-stage liver disease. In February 2002, The United States implemented a MELD based system for the allocation of liver transplant to reduce waiting list mortality [6,7].

Furthermore, hyponatremia is frequent among cirrhotic patients and is often associated with higher risk of complications and mortality [8].

Therefore, to increase the accuracy in predicting three-month mortality serum sodium was added to the formula and another version of the score, MELD-Na, appeared [9]. MELD-Na has been used, as an alternative to the original MELD, for liver graft allocation since 2016 [10].

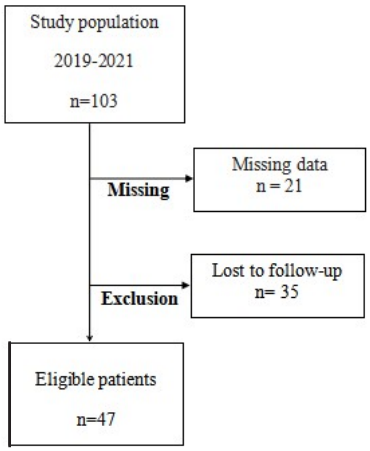
However, no data are available regarding the prognostic utility of these scores for cirrhotic patients in Algeria. Through a descriptive study carried out previously at the Hepato-Gastro-Enterology Department of the University Hospital Center of Oran, it appeared to us that MELD-Na remains unused in current practice [11]. The purpose of this study was to assess the ability of MELD-Na scoring system to predict three-month mortality among cirrhotic patients, and compare it to the MELD score.

2. Methods

An observational study was carried out at the Hepato-Gastro-Enterology Department of the University Hospital Center of Oran. Data were retrospectively gathered from the medical records of 103 patients, between January 1, 2019 and December 31, 2021.

The study included patients with all aetiologies of cirrhosis, aged ≥18 year-old. Thirty-five patients, who were lost to follow-up after three months, and 21 patients with missing data, were excluded. Eventually, a total of 47 patients were eligible for the study.

Figure 1. the flowchart of in- and exclusion for this study



The information collected and analyzed, using Microsoft Office Excel 2007 was: age, sex, aetiology of cirrhosis, Child-Pugh score, total bilirubin, INR, creatinine and sodium levels.

The MELD-Na and MELD scores were calculated using online calculators, at https://www.mdcalc.com, using the following formulas [12,13]:

MELD = 9.57 × ln (Creatinine [mg/dL]) + 3.78 × ln (Bilirubin [mg/dL]) + 11,20 × ln (INR) + 6.43

MELD-Na = MELD score + 1.32 × (137 – Sodium [mmol/L]) – (0.33 × MELD score × 137 – Sodium [mmol/L])

Then, the ability of the models to predict the risk of mortality at three months was assessed, by calculating the area under the receiver operating characteristic (ROC) curve (AUC), using IBM SPSS Statistics Version 22.

The area under the ROC curve of the perfect score tends to 1. A score is considered effective when the area under the ROC curve is between 0.8 and 1 and useful when the area under the ROC curve is ≥ 0.7 [14].

3. Results

Clinical characteristics and demographic data are shown in Table 1. The mean age of the patients was 62 ±12 years (ranging from 18 to 90 years). A total of 51% were females (n=24) and 49% were males (n=23). The main causes of liver diseases were: viral hepatitis C (23%), Non-Alcoholic Steato Hepatitis (NASH) (19%), and autoimmune hepatitis (13%). While for 26% the aetiology of cirrhosis could not be determined. The mean Child Pugh score value was 8 ± 2.The mean creatinine

value was 0.9 ± 0.5 mg/dl, the mean total bilirubin value was 3.7 ± 5.0 mg/dl and the mean INR value was 1.8 ± 0.8. Sodium had an average value of 135.7 ± 5.3 mmol/L (ranging from 126 to147 mmol/L).

The mean MELD value was 15 ± 6, and the mean MELD-Na was 17 ± 7.

Eight (17%) patients died at three months, and 13% had hyponatremia.

Table 1. patient's clinical characteristics and demographic data

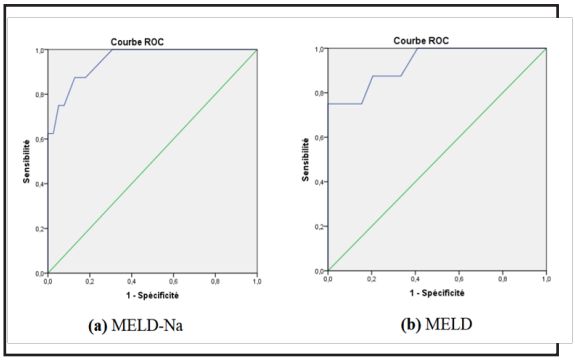
Variable	Value
Sex n (%) Female Male	24 (51%) 23 (49%)
Age (y), mean ± SD	62 ± 12
Score, mean ± SD(rounded to the nearest integer) Child-Pugh MELD MELD-Na	 8 ± 2 15 ± 6 17 ± 7
Cause of liver disease n (%) Undetermined aetiology Hepatitis C NASH Autoimmune hepatitis Alcohol Hepatitis B Other	 12 (26%) 11 (23%) 9 (19%) 6 (13%) 3 (6%) 2 (4%) 4 (9%)
Laboratory value, mean ± SD Total bilirubin level (mg/dL) Creatinine level (mg/dL) International normalized ratio Sodium level (mmol/L)	 3.7 ± 5.0 0.9 ± 0.5 1.8 ± 0.8 135.7 ± 5.3
Three-month mortality n (%) Dead Alive	 8 (17%) 39 (83%)
Hyponatremia n (%)	6 (13%)

The MELD-Na and MELD both had significantly high area under the curve (AUC):0.952, 95% confidence interval [CI]: 0.885-1.000 for MELD-Na and 0.931, 95% confidence interval [CI]: 0.834-1.000 for MELD score **(Table 2 and Figure 2)**.

Table 2. MELD-Na and MELD ROC AUC's for Survival at three months

	MELD-Na ROC AUC	MELD ROC AUC
Value	0.952	0.931
95% CI	0.885–1.000	0.834–1.000

Figure 2. ROC curves of sodium MELD (MELD-Na) (a) and MELD (b) scores



(a) MELD-Na **(b)** MELD

The optimal cut-off value for MELD-Na was 21 (rounded to the nearest integer), for this value, the sensitivity and the specificity was 87.5% and 87.2%, respectively, as shown in table 3.

Table 3. sensitivity and specificity for different MELD-Na values

Cut-off value	Sensitivity	Specificity
7,000	1,000	0,000
40,000	0,000	1,000
8,500	1,000	0,026
9,500	1,000	0,103
36,500	0,125	1,000
10,500	1,000	0,205
33,000	0,250	1,000
11,500	1,000	0,282
12,500	1,000	0,308
30,500	0,375	1,000
14,000	1,000	0,410
15,500	1,000	0,462
16,500	1,000	0,538
24,500	0,625	0,974
27,500	0,625	1,000
21,500	0,750	0,923
17,500	1,000	0,692
18,500	0,875	0,821
22,500	0,750	0,949
19,500	0,875	0,846
20,500	0,875	0,872

Discussion

It is very common for patients with advanced cirrhosis to develop hyponatremia mainly due to hypervolemia. The primary cause is portal hypertension which leads to splanchnic vasodilatation that increases the secretion of antidiuretic hormone. The activation of this compensatory mechanisms causes excessive free water retention and, as a result, dilutional hyponatremia [15,16]. Hyponatremia is considered to be an independent predictor of mortality in cirrhosis. As patients with hyponatremia, have worse outcomes and are more likely to develop serious complications,such as ascites or hepatorenal syndrome[17,18].

MELD-Na combines the prognostic utility of both hyponatremia and MELD to further increase the predictive ability.

Our results showed that both MELD and MELD-Na scores were good predictors of three-month mortality, and the MELD-Na, with an optimal cut-off value of 21, was slightly better than the MELD (AUC: MELD-Na=0.952, 95% CI: 0.885-1.00; MELD=0.931, 95% CI: 0.834-1.000). The AUC of MELD-Na was similar or even higher than observed by other investigators.

In Algeria, Mabizari et al. showed that in-hospital mortality in cirrhotic patients was associated with both MELD score ($p<0.0001$) and MELD-Na score ($p<0.0001$). And although MELD ≥ 18 was found to be a strong predictor of mortality with an OR=4,1, P=0.007, the predictive accuracy of MELD-Na was not assessed in this study [19]. Conforming to a retrospective study conducted by Mouelhi et al. over a 15-year period in Tunisia, the MELD-Na score was significantly predictive of early mortality due to digestive haemorrhage (AUC=0.867, $p<0.001$) with a sensitivity of 70% and a specificity of 82%, for a cut-off value of 19. However, no statistically significant difference was found compared to MELD (AUC=0.838, $p<0.001$) and other scores [20]. In Egypt, El-ghannam found that MELD-Na was superior to the original MELD in predicting mortality (AUC: MELD-Na=0.789±0.03, CI 95%=0.711-0.865; MELD=0.678±0.01, CI95%=0.613-0.682). The cutt-off value was equal to 20.4 [21].

In Another study, published in the journal of Liver Transplantation, by Ruf et al. both MELD and MELD plus serum sodium had excellent c-statistics: 0.894 and 0.908, respectively. Adding serum sodium increased the accuracy of the score to predict mortality with a p value of 0.026. According to this study, even though the increase is only about 1%, it is highly significant considering the relative infrequency of hyponatremia [22]. Indeed, in our data, only 13% of the patients had hyponatremia. Noting that, hyponatremia was defined as sodium level ≤130 mmol/L. This cut-off value was used in previous studies of hyponatremia in cirrhotic patients [23].

Se Yune Kim also verified the usefulness of MELD-Na for predicting short term mortality of cirrhotic patients in Korea. Only MELD-Na was significantly related to three-month mortality (p0.012) and the AUC of MELD-Na was higher, but the difference was not statistically significant (MELD-Na=0.862, MELD=0.845, (p0.05)) [24].

A more significant difference was found by Shahna et al. AUC was 0.801 for MELD-Na and 0.707 for MELD. The cut-off value of MELD-Na was equal to 23.04 and had a sensitivity of 84.5 and specificity of 67.7 [25]. Moreover, a large study, that included patients from all the Eurotransplant region (Austria, Croatia, Hungary, Slovenia), showed that MELD-Na had a high c-index of 0.847 (SE 0.007) and reduced the waiting list mortality by 4.9% [26]. On the other hand, a prospective study in Northern India compared the Child- Pugh, MELD and MELD-Na scores and found different results. The c-statistics was 0.86 ($p < 0.0001$) for the MELD score, and 0.83 ($p < 0.0001$) for the MELD-Na, and the Child- Pugh score was superior to both of them in predicting three-month mortality.

As they mentioned, the clinical presentation and the distribution of causes of liver disease is different across populations and among different regions of the world [27]. This diversity might have contributed to discordant results. Although, as stated above, studies from different countries found similar results. It should be pointed out that, the MELD score values were higher among their patients, with a mean value of 21. As stated by the study of Kim et al. that first validated the usefulness of MELD-Na score in the United States, the effect of sodium concentration is greater in patients with low MELD score [28]. We also noticed that, the optimal MELD-Na cut-off was higher than 32.14. In opposition, Razafindrazoto et al. found that MELD-Na was strongly associated with mortality (OR=1.23; CI95%: 1.12–1.341, p=0.000) compared to MELD score (OR=1.18; CI95%: 1.09 to 1.27, p=0.000) especially when it was ≥32 (OR: 27.5; CI95%: 4.32–174.8; p=0.0004) [29].

Moreover, the MELD Na formula was originally developed for sodium values ranging from 125 to 140 mmol/L. According to Sersté et al.in patients with severe hyponatremia (≤ 125 mmol/L), hyponatremia and Child-Pugh score are better predictors of mortality than MELD Na [30]. In our study sodium values ranged from 126 to147 mmol/L.

Finally, Godfrey et al. recently found that the c-statistic of the MELD score gradually decreased from 0.80 in 2003 to 0.70 in 2015. The same study reported a c-statistic of 0.839 for MELD-Na in 2015[31]. Since the demographic and clinical characteristics of cirrhosis have changed, and therefore, the predictive accuracy of the original MELD score has declined. It is necessary to update the MELD formula by the incorporation of additional objective, quantitative, and reproducible variables such as serum sodium [32,33]. And even thought we must acknowledge that sodium levels can be influenced by several factors such as water balance disorders or the use of diuretics and vaptans, every other component of the score has its own limitations [3,34]. Since 2016, the United Network for Organ Sharing (UNOS) has adopted MELD-Na as a basis for liver graft allocation. As a result, it was shown that 7% of the waiting-list mortality could be avoided using MELD-Na instead of the original MELD score [35].

Conclusion

The MELD-Na score seems to be a good predictor of mortality at three months among patients with cirrhosis. The addition of serum sodium to the MELD score formula increases the predictive accuracy of the score by prioritizing patients with hyponatremia who have a high-risk of morbidity and mortality.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

[1]Ye F, Zhai M, Long J, Gong Y, Ren C, Zhang D, et al. The burden of liver cirrhosis in mortality: Results from the global burden of disease study. Front Public Health 2022;10:909455. https://doi.org/10.3389/fpubh.2022.909455.

[2]Durand F, Valla D. Assessment of the prognosis of cirrhosis: Child-Pugh versus MELD. J Hepatol 2005;42:S100-7. https://doi.org/10.1016/j.jhep.2004.11.015.

[3]Kim HJ, Lee HW. Important predictor of mortality in patients with end-stage liver disease. Clin Mol Hepatol 2013;19:105. https://doi.org/10.3350/cmh.2013.19.2.105.

[4]Barbare JC, Kamath PS, Wiesner RH. MELD, un nouveau score pronostique pour les malades atteints de cirrhose : faut-il tuer Child ? 2002.

[5]Peng Y, Qi X, Guo X. Child-Pugh Versus MELD Score for the Assessment of Prognosis in Liver Cirrhosis: A Systematic Review and Meta-Analysis of Observational Studies. Medicine (Baltimore) 2016;95:e2877. https://doi.org/10.1097/MD.0000000000002877.

[6]Mathurin P. MELD ou Child : faut-il choisir ? La lettre de l'hépato-Gastroentérologue. juin 2006;IX(3):131-2.

[7]Kamath PS, Kim WR. The model for end-stage liver disease (MELD). Hepatology 2007;45:797-805. https://doi.org/10.1002/hep.21563.

[8]Samuel D. MELD-Na as a prognostic score for cirrhotic patients: Hyponatremia and ascites are back in the game. J Hepatol 2009;50:836-8. 1.Speziale, G., et al., Minimally invasive mitral valve surgery: state-of-the-art and our experience. European Heart Journal Supplements, 2015. 17(suppl_A): p. A49-A53.

[9]Ruf A, Dirchwolf M, Freeman RB. From Child-Pugh to MELD score and beyond: Taking a walk down memory lane. Ann Hepatol 2022;27:100535. https://doi.org/10.1016/j.aohep.2021.100535.

[10]Freitas ACTD, Rampim AT, Nunes CP, Coelho JCU. IMPACT OF MELD SODIUM ON LIVER TRANSPLANTATION WAITING LIST. ABCD Arq Bras Cir Dig São Paulo 2019;32:e1460. https://doi.org/10.1590/0102-672020190001e1460.

[11] Rahou H, Seghir IR, Seksaf K, Iles L, Meguenni Y. Etude rétrospective de la cirrhose hépatique au niveau du service d'Hépato-Gastro-Entérologie du CHU d'Oran. Oran : Faculté de médecine Université Oran 1 ; 2022. 94 p.

12]Young S, Rostambeigi N, Golzarian J, Lim N. MELD or Sodium MELD: A Comparison of the Ability of Two Scoring Systems to Predict Outcomes After Transjugular Intrahepatic Portosystemic Shunt Placement. Am J Roentgenol 2020;215:215-22. https://doi.org/10.2214/AJR.19.21726.org/10.1080/00365521.2020.1788139.

[[13]Kim KM, Shim SG, Sinn DH, Song JE, Kim BS, Kim HG. Child-Pugh, MELD, MELD-Na, and ALBI scores: which liver function models best predicts prognosis for HCC patient with ascites? Scand J Gastroenterol 2020;55:951–7. https://doi.org/10.1080/00365521.2020.1788139.

[14]Artru F. Les scores pronostiques en hépatologie : scores génériques de la cirrhose, scores spécifiques de l'hépatite alcoolique et scores pronostiques en réanimation. Hépato Gastro 2015;22:291–302.

[15]Attar B. Approach to Hyponatremia in Cirrhosis. Clin Liver Dis 2019;13:98–101. https://doi.org/10.1002/cld.790.

[16]Alukal JJ, John S, Thuluvath PJ. Hyponatremia in Cirrhosis: An Update. Am J Gastroenterol 2020;115:1775–85. https://doi.org/10.14309/ajg.0000000000000786.

[17]Fisher RA, Heuman DM, Harper AM, Behnke MK, Smith AD, Russo MW, et al. Region 11 MELD Na exception prospective study. Ann Hepatol 2012;11:62–7. https://doi.org/10.1016/S1665-2681(19)31487-5.

[18]Bernardi M, Gitto S, Biselli M. The MELD score in patients awaiting liver transplant: Strengths and weaknesses. J Hepatol 2011;54:1297–306. https://doi.org/10.1016/j.jhep.2010.11.008.

[19]R. Mabizari, N. Debzi, O. Drir, R. Kerbouche, I. Ouled Cheikh, N. Guessab, N. Afredj,D. Hanoun. MELD score and SIRS are predictive factors for in-hospital mortality in cirrhotic patients admitted to CCUH. JOURNAL ALGERIEN DE GASTROENTEROLOGIE.Decembre 2017;13:5-15.

[20]Mouelhi L, Ayadi H, Zaimi Y, Daboussi O, Salem M, Debbech R, et al. scores prédictifs de la mortalité précoce par hémorragie digestive d'origine variqueuse chez le cirrhotique. Tunis Med 2016;94.

[21]EL-Ghannam MT. Performance of Disease-Specific Scoring Models in Intensive Care Patients with Severe Liver Diseases. J Clin Diagn Res 2017. https://doi.org/10.7860/JCDR/2017/24543.9980.

[22]Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. Liver Transpl 2005;11:336–43. https://doi.org/10.1002/lt.20329.

[23]Borroni G, Maggi A, Sangiovanni A, Cazzaniga M, Salerno F. Clinical relevance of hyponatraemia for the hospital outcome of cirrhotic patients. Dig Liver Dis Off J Ital Soc Gastroenterol Ital Assoc Study Liver 2000;32:605–10. https://doi.org/10.1016/s1590-8658(00)80844-0.

[24]Kim SY, Yim HJ, Lee J, Lee BJ, Kim DI, Jung SW, et al. [Comparison of CTP, MELD, and MELD-Na scores for predicting short term mortality in patients with liver cirrhosis]. Korean J Gastroenterol Taehan Sohwagi Hakhoe Chi 2007;50:92–100.

[25]Fathima SS, Gopalakrishnan P, Devadas K, Srijaya S, Prasanth KS, Shanid A, et al. MELD vs MELD Na for Predicting Inhospital Mortality in Decompensated CLD. J Clin Exp Hepatol 2016;6:S36–7. https://doi.org/10.1016/j.jceh.2016.06.074.

[26]Goudsmit BFJ, Putter H, Tushuizen ME, De Boer J, Vogelaar S, Alwayn IPJ, et al. Validation of the Model for End-stage Liver Disease sodium (MELD-Na) score in the Eurotransplant region. Am J Transplant 2021;21:229–40. https://doi.org/10.1111/ajt.16142.

[27]Acharya G, Kaushik RM, Gupta R, Kaushik R. Child-Turcotte-Pugh Score, MELD Score and MELD-Na Score as Predictors of Short-Term Mortality among Patients with End-Stage Liver Disease in Northern India. Inflamm Intest Dis 2020;5:1–10. https://doi.org/10.1159/000503921.

[28]Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. N Engl J Med 2008;359:1018–26. https://doi.org/10.1056/NEJMoa0801209.

[29]Razafindrazoto CI, Randriamifidy NH, Ralaizanaka BM, Andrianoelison JT, Ravelomanantsoa HT, Rakotomaharo M, et al. Factors Associated with in-Hospital Mortality in Malagasy Patients with Acute Decompensation of Liver Cirrhosis: A Retrospective Cohort. Hepatic Med Evid Res 2023;Volume 15:21–6. https://doi.org/10.2147/HMER.S401628.

[30]Sersté T, Gustot T, Rautou P-E, Francoz C, Njimi H, Durand F, et al. Severe hyponatremia is a better predictor of mortality than MELDNa in patients with cirrhosis and refractory ascites. J Hepatol 2012;57:274–80. https://doi.org/10.1016/j.jhep.2012.03.018.

[31]Godfrey EL, Malik TH, Lai JC, Mindikoglu AL, Galván NTN, Cotton RT, et al. The decreasing predictive power of MELD in an era of changing etiology of liver disease. Am J Transplant 2019;19:3299–307. https://doi.org/10.1111/ajt.15559.

[32]Biggins SW, Kim WR, Terrault NA, Saab S, Balan V, Schiano T, et al. Evidence-Based Incorporation of Serum Sodium Concentration Into MELD. Gastroenterology 2006;130:1652–60. https://doi.org/10.1053/j.gastro.2006.02.010.

[33]Kim WR, Mannalithara A, Heimbach JK, Kamath PS, Asrani SK, Biggins SW, et al. MELD 3.0: The Model for End-Stage Liver Disease Updated for the Modern Era. Gastroenterology 2021;161:1887-1895.e4. https://doi.org/10.1053/j.gastro.2021.08.050.

[34]Praharaj DL, Anand AC. Clinical Implications, Evaluation, and Management of Hyponatremia in Cirrhosis. J Clin Exp Hepatol 2022;12:575–94. https://doi.org/10.1016/j.jceh.2021.09.008.

[35] Martin EF, O'Brien C. Update on MELD and organ allocation. Clin Liver Dis 2015;5:105–7. https://doi.org/10.1002/cld.464.