ECRONICON OPEN ACCESS

EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Mini Review

CTP, MELD (Including Na/XI/Delta) and CLIF-SOFA Scoring Systems for Predicting Outcome After Liver Transplantation: Current Mini-Review

Omer Faruk Ozkan*, Ethem Unal, Sema Yuksekdag, Ahmet Topcu and Ozgul Duzgun

Department of General Surgery, Health Sciences University, Umraniye Training and Research Hospital, Istanbul, Turkey

***Corresponding Author:** Omer Faruk Ozkan, Associate Professor of Surgery, Department of General Surgery, Health Sciences University, Umraniye Training and Research Hospital, Istanbul, Turkey.

Received: July 24, 2018; **Published:** August 21, 2018

Abstract

The present study is designed to review the most recent perspective on scoring systems which are used in the prediction of the outcome after liver transplantation. In this review study, a new, recently developed, Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) score was evaluated and compared with older, traditional, but most commonly used Child-Turcotte-Pugh (CTP) and the Model for End-Stage Liver Disease (MELD) scores. Pros and cons of each system are reviewed and discussed, as well.

Keywords: *CTP; MELD; CLIF-SOFA; Liver Transplantation*

The course of cirrhosis is extremely variable due to several factors, including the etiology of cirrhosis, hepatic synthetic reserve and the presence of liver malignancy. As liver transplantation (LT) surgery is the unique procedure to improve the survival and quality of life of patients with end-stage liver disease (ESLD), predicting the outcome becomes the main problem considering the allocation procedure. Many scoring models have been developed in last years to predict the prognosis in cirrhotic patients and to help medical team choose the most appropriate treatment protocol.

The Child-Turcotte-Pugh (CTP) score was first used in 1973 to predict the surgical outcomes of cirrhotic patients with esophageal varices [1]. It has since been modified many times and become a popular instrument worldwide to assess the prognosis in patients with cirrhosis and ESLD. Five factors constitute the total score; three of which showing the synthetic function of the liver (serum bilirubin and albumin, and international normalized ratio, INR) and two of which assessing the clinical assessment (Table 1). The main critic of the CTP score have noted its reliance on clinical assessment (degree of ascites and degree of hepatic encephalopathy), which may result in inconsistency in the measurement of scores [2].

	1 point	2 points	3 points
Total bilirubin	< 2	2 - 3	> 3
Serum albumin (mg/dL)	> 3.5	2.8 - 3.5	< 2.8
INR	< 1.7	1.71 - 2.20	> 2.20
Ascites	None	Mild	Severe
Hepatic encephalopathy	None	Grade I-II	Grade III-IV

Table 1: *Child-Turcotte-Pugh score.*

Explanation of Result: Class A: 5-6 (well-compansated), Class B: 7-9 (significant functional impairment), Class C: 10-15 (decompansated liver function). The prognosis worsens from A to C with worsening decompensation.

The Model for End-Stage Liver Disease (MELD) is a newer system that has been developed to overcome the disadvantages of CTP. Since then, these two systems are often used together to determine LT priority in many transplant centers. MELD uses three objective laboratory parameters (INR, creatinine, and bilirubin) (Table 2) [3,4]. It is calculated as 0.957 ln (creatinine) + 0.378 ln (bilirubin) + 1.120 ln (international normalized ratio, INR)+0.643) × 10.

3-month mortality, %	MELD score
1.9 - 3.7	< 9
6 - 20	10 - 19
19.6 - 45.5	20 - 29
52.6 - 74.5	30 - 39
71 - 100	> 40

Table 2: *The 3-month survival for each MELD score (Creatinine, Bilirubin, INR).*

MELD: Model for End Stage Liver Disease

With the implementation of MELD score, refractory ascites was removed from the list of variables used for assessing the prognosis. However, ascites is known to be associated with the poorest prognosis. Therefore, in refractory ascites; normal creatinine levels and preserved synthesis function could be underscored with MELD system. Moreover, patients with both persistent ascites and low serum sodium levels are going to have a lower MELD score (below 20) and early death can be inevitable [1]. Serum sodium is a simple, readily available, and objective marker of disease severity. During cirrhosis, hyponatremia results from solute-free water retention. A modified score based on serum sodium measurement has been proposed as an alternative to MELD score, and termed as MELD Na [5]. During cirrhosis, hyponatremia results from solute-free water retention. Arterial vasodilation causes the release of antidiuretic hormone (ADH) and dilutional hyponatremia becomes overt in these patients. The activation of this cascade is important in determination of the degree of portal hypertension, and hyponatremia can be used as an indirect marker of portal hypertension. Several other studies have also shown that low serum sodium level in cirrhotic patients is an important predictor of early mortality [6]. In these studies, it was suggested that even a decrease in serum sodium of 1 mEq/L decreases 3-month survival rates [1]. The accuracy of MELD-Na was shown to be slightly superior to that of MELD in candidates for transplantation [1,5,6]. However, the main critic here is the marked changes in serum sodium concentration can result from the treatment with diuretics and intravenous hypotonic solutions.

INR is the variable which has the highest weight in MELD score. Unfortunately, INR is hardly interpretable in patients receiving anticoagulation therapy due to portal vein thrombosis, an underlying prothrombotic state [6]. Most patients with Budd-Chiari syndrome also receive anticoagulation with anti-vitamin K. In this population, INR artificially rises. Using MELD score in this context would result in overestimating disease severity. With the aim of overcoming this difficulty, a modified MELD score termed MELD-XI (for MELD excluding INR) has been designed relying only on bilirubin and creatinine [6,7]. The coefficients ascribed to creatinine and bilirubin have been changed to obtain the optimal linear correlation between MELD and MELD-XI. The validation of MELD-XI score shows that its accuracy for assessing 3-month mortality risk is comparable to that of MELD. Patients with a rapid increase in MELD score over time might be expected to have a worse outcome than those with stable or even decreasing MELD.

Delta MELD (D-MELD) is defined as the difference between current MELD and the lowest MELD measured within 30 days prior to current MELD [6,8]. It was shown to be predictive of early mortality in patients with cirrhosis on univariate analysis. However, D-MELD was no longer predictive of mortality when entered into a multivariate model with current MELD score. These results suggest that current MELD score is the only predictor of mortality regardless of how that score was reached.

MELD evolutions, such as MELD-Na and D-MELD and others (MELD-XI), did not reach acceptable performances [6]. The analysis of donor characteristics is also fundamental to optimise graft-recipient matching and to predict LT outcome. So, donor-risk index (DRI) and extended criteria donor score (ECDS) were proposed. ECDS, DRI and D-MELD, despite providing statistically significant results, had insufficient discriminatory power for short-term graft and patient survival.

Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) score, a modified SOFA score, is a recently developed scoring system and used only for cirrhotic patients. Some authors have designed studies to compare the CLIF-SOFA score with other scoring systems in outcome prediction for LT patients, and showed that CLIF-SOFA score can increase the prediction accuracy of prognosis after transplantation [9,10]. They suggested that CLIF-SOFA score on posttransplant wwk 1 had the best discriminative power in predicting 1-year mortality rate after LT [10]. The score replaces platelet count with INR and replaces Glasgow coma score with different degrees of the hepatic encephalopathy (Table 3). CLIF-SOFA score also considers the usage of terlipressin and dialysis therapy in the grading of other organ/system failures. It also added PaO_2/FiO_2 ratio as an respiration parameter in assessing pulmonary functions.

Organ/System	0	1	2	3	4
Liver (bilirubin, mg/dL)	< 1.2	≥ 1.2 - < 2	≥ 2 - < 6	≥ 6 - 12	≥ 12
Kidney (creatinine, mg/dL)	< 1.2	≥ 1.2 - < 2	≥ 2 - < 6	≥ 6 - 12	≥ 12
Or use of renal replacement therapy					
Cerebral (HE grade)	No HE	I	II	III	IV
Coagulation (INR)	< 1.1	≥ 1.1 - < 1.25	≥ 1.25 - < 1.5	≥ 1.5 - < 2.5	≥ 2.5 or platelet ≤ 20 x 10^9/L
Cardiovascular Hypotension (MAP, mmHg)	≥ 70 mmHg	< 70 mmHg	D ≤ 5/	D > 5/	D > 15/
			Dob/	E ≤ 0.1	E > 0.1
			T	NE ≤ 0.1	NE > 0.1
Respiration PaO_2/FiO_2	> 400	> 300 - ≤ 400	> 200- ≤ 300	> 100 - ≤ 200	≤ 100

Table 3: *CLIF-SOFA score.*

HE: Hepatic Encephalopathy; INR: İnternational Normalized Ratio*; MAP: Mean Arterial Pressure, D: Dopamine; Dob: Dobutamine, T: Terlipressin; E: Epinephrine; NE: Norepinephrine; PaO_2/FiO_2: The Ratio of Arterial Oxygen Partial Pressure to Fractional İnspired Oxygen.*

It has also been shown that both SOFA and CLIF-SOFA scores can be used to assess the overall illness dynamics in serial measurements both before and after LT [10]. Moreover, CLIF-SOFA score also reflects a patient's response to treatment protocols, with a CLIF-SOFA score > 8 on post-transplant day 7 indicating a delayed recovery of multiple organ failure (MOF) from operation. This situation usually results in a higher rate of rejection and poor survival rate.

On the other hand, besides these scores mentioned above (summarized all together in table 4), one should keep in mind that intraoperative anaesthetic management and surgical techniques (duration of the intervention, difficult arterial anastomosis, high blood loss and red blood cell transfusion, intraoperative hemodynamic instability, cold and warm organ ischemia time and ischaemia/reperfusion damage) strongly influence postoperative patient and graft function; and all measures should be taken to get better scores and results.

CTP	MELD/MELD-Na	CLIF-SOFA
Bilirubin	Bilirubin	Bilirrubin
Hepatic encephalopathy	Creatinine	Creatinine
INR	INR	Hepatic encephalopathy
Ascites	Sodium	INR
Albumin		MAP (mmHg)
		PaO_2/FiO_2

Table 4: *Scores of liver failure.*

Conclusion

In conclusion, among additional prognostic scores proposed, MELD is more valuable than the CTP score because it excludes the subjective criterias such as ascites or hepatic encephalopathy. Therefore, MELD has largely replaced the CTP score worldwide for prioritizing donor allocation and early postoperative follow-up. On the other hand, many recent studies have suggested that the short-term prognosis after LT is best predicted by CLIF-SOFA score. The CLIF-SOFA score seems to be superior to the CTP points and MELD score in predicting short-term prognosis. CLIF-SOFA score > 8 on posttransplant day 7 seems to constitute a high risk of acute rejection and worse short-term outcome.

Bibliography

1. Kim HJ and Lee HW. "Important predictor of mortality in patients with end-stage liver disease". *Clinical and Molecular Hepatology* 19.2 (2013): 105-115.

2. Lee H., *et al*. "Comparison of APACHE IV with APACHE II, SAPS 3, MELD, MELD-Na, and CTP scores in predicting mortality after liver transplantation". *Scientific Reports* 7.1 (2017): 10884.

3. Kamath PS and Kim WR. "The model for end-stage liver disease (MELD)". *Hepatology* 45.3 (2007): 797-805.

4. Francoz C., *et al*. "Inaccuracies of creatinine and creatinine-based equations in candidates for liver transplantation with low creatinine: impact on the model for end-stage liver disease score". *Liver Transplantation* 16.10 (2010): 1169-1177.

5. Borroni G., *et al*. "Clinical relevance of hyponatraemia for the hospital outcome of cirrhotic patients". *Digestive and Liver Disease* 32.7 (2000): 605-610.

6. Porcel A., *et al*. "Dilutional hyponatremia in patients with cirrhosis and ascites". *Archives of Internal Medicine* 162.3 (2002): 323-328.

7. Heuman DM., *et al*. "MELD-XI: a rational approach to "sickest first" liver transplantation in cirrhotic patients requiring anticoagulant therapy". *Liver Transplantation* 13.1 (2007): 30-37.

8. Bambha K., *et al*. "Predicting survival among patients listed for liver transplantation: an assessment of serial MELD measurements". *American Journal of Transplantation* 4.11 (2004): 1798-1804.

9. Pan HC., *et al*. "Scoring systems for predicting mortality after liver transplantation". *PLoS One* 9.9 (2014): e107138.

10. Bolondi G., *et al*. "Predictive factors of short term outcome after liver transplantation: nA review". *World Journal of Gastroenterology* 22.26 (2016): 5936-5949.

Volume 5 Issue 9 September 2018