Original Article

Model for End Stage Liver Disease (MELD) and Child-Turcotte-Pugh (CTP) scores: Ability to Predict Mortality and Removal from Liver Transplantation Waiting List due to Poor Medical Conditions

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Abstract

Background: There are many patients awaiting liver transplantation with only few donors providing the organ. The Child-Turcotte-Pugh score (CTP) and the Model for End stage Liver Disease (MELD) are the most common scores for prioritizing patients on waiting lists. In this study, we compared the ability of these scores to predict mortality or removal from the waiting list due to poor medical conditions.

Methods: A total of 257 patients were included in our study and we observed their status in the waiting list over a 9-month period. MELD and CTP of the patients at the time of listing were calculated. We used both ROC-curve and Area Under the Curve (AUC) to calculate the predictive ability of these scores.

Results: During follow up, 22 patients died and 9 patients were removed from the waiting list due to poor medical conditions. Comparing the predictive ability of CTP and MELD, the AUC for CTP was larger than that of MELD (0.75 versus 0.69; *P*-value = 0.065). The best cutoff point for discriminating mortality or removal from the waiting list due to severe deterioration is 8 for CTP and 13.67 for MELD. The sensitivity and specificity was 0.74 and 0.67, respectively for CTP and 0.74 and 0.58, respectively for MELD.

Conclusion: The CTP score can predict mortality or removal from the liver transplantation waiting list better than the MELD over a 9-month period. However, better improved models need to be developed for prioritization of patients in the waiting list.

Keywords: MELD, CTP, liver transplantation, waiting list

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Introduction

Cirrhosis is associated with poor prognosis in patients with liver disease. Decompensated liver disease is followed by even worse prognosis. Liver transplantation is the only cure for cirrhotic patients.[1] The number of patients who need liver transplantation by far exceeds the number of liver donors. Therefore, the number of patients on waiting lists is increasing drastically with time. This highlights the importance of prioritizing patients for liver transplantation. The most common scores used for this purpose are Child-Turcotte-Pugh score (CTP) and the Model for End stage Liver Disease (MELD).

The CTP score was originally utilized to assess the outcome of patients with cirrhosis and portal hypertension.[2] Subsequently, its use was extended for predicting the general prognosis of cirrhotic patients and prioritizing patients for liver transplantation.[3] The CTP score has been criticized for its two subjective components: hepatic encephalopathy and ascites severity. Even the more objective components, such as albumin, may be affected by iatrogenic manipulation with albumin infusion. Also, prothrombin time varies from one laboratory to another, and causes some limitations for comparison.[4] It is also a discontinuous scale and does not include any weighting.[5]

The model for end-stage liver disease was first used to predict mortality of cirrhotic patients who underwent transjugular intrahepatic portosystemic shunts.[6] It has been applied as a new liver organ allocation system for liver transplantation since 2002 in the United States, and since 2006 in Europe.[7,8] MELD consists of 3 objective variables: International Normalized Ratio (INR), serum creatinine and serum bilirubin. These components are objective, available and reproducible. It has also been shown to predict mortality independently of cirrhosis complications and even the liver disease etiology.[8,9] Although many studies have shown that MELD is able to predict mortality in liver transplantation waiting lists better than CTP,[9,10] there are certain reports which fail to indicate any advantage for MELD over CTP.[11,12]

This study aims to address the prognostic ability of the MELD score and the modified CTP score for predicting mortality or removing from the waiting list due to the clinically bad condition in the liver transplantation waiting list.

Material and Methods

Patients

We studied 257 patients with cirrhosis in liver transplantation

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center of Imam Khomeini Hospital, Tehran, Iran, which is one of the two liver transplantation centers in Iran. We began the study in September 2010 and followed the patients up to June 2011. A diagnosis of cirrhosis was made by two physicians, based on clinical, biochemical, ultrasonographic or computed tomography findings and liver biopsy. The patients underwent an elaborate evaluation for the etiology of liver disease. We did not include patients younger than 18, those with a history of previous liver transplantation or transjugular intrahepatic portosystemic shunt placement,orpatients with incomplete biochemical data. The study was approved by the ethics committee of the hospital.

MELD and CTP score

In this study, we used the modified form of MELD score described by Kamath and his team.[8] The formulation is: 3.78 × Ln (bilirubin mg/dL) + 11.2 × Ln (INR) + 9.57 × Ln (creatinine mg/dL) + 6.43. To avoid negative scores, laboratory values less than 1 mg/dL were rounded off to 1, and the maximum allowed measure for creatinine was 4 mg/dLin the MELD score model.

The modified CTP score includes five parameters: serum bilirubin and albumin levels, prothrombin time, and the presence and severity of as cites and encephalopathy.[2] Some more sensitive imaging studies such as ultrasonography, in addition to physical examination, were used to detect ascites. Encephalopathy was considered in case of appearance of signs of occasional forgetfulness, insomnia or distorted sleep pattern.

We used MELD and CTP scores for all patients at the time of listing for numerical analysis.

Statistical methods

Categorical variables were expressed as count with percentage, and continuous variables as mean with standard deviation. The Mann-Whitney test and X^2-test were used for continuous and categorical variables, respectively. In order to assess the validity of MELD and CTP score for prediction of death or withdrawal from the waiting list due to severe deterioration, we used the area under the receiver operating characteristic (ROC) curve. In order to compare the area under the two ROC curves, we used a non-parametric test introduced by DeLong which exploits the properties of the Mann-Whitney statistic.[13] All computations were done using R-package version 2.14.2.[14]

Results

We studied the sickness behavior of 118 women and 139 men over 9 months. The mean age of patients was 40.8 years (range: 18–69). BMI was available for only 149 patients. The mean BMI was 23.95 (range: 15.43–43.28). Among our patients, 34.2% suffered from cryptogenic liver disease and 19.5% from autoimmune hepatitis. Hepatitis B, hepatitis C, primary sclerosing cholangitis, Wilson's disease, primary biliary cirrhosis and alcohol accounted for 18.7%, 14.8%, 8.9%, 2.3%, 1.2%, and 0.4% of the patients, respectively (Table 1). Ascites, hepatic encephalopathy, spontaneous bacterial peritonitis and hepatorenal syndrome were found in 47.1%, 20.2%, 0.8%, and 0.4% of patients, respectively. Other comorbidities not related to liver disease were diabetes (8.95%), hypertension (2.3%), coronary artery disease (0.4%), and ulcerative colitis (2.3%).

The mean waiting time on liver transplantation list was 814.67 days (range 14–3667). At the end of our study, 12 patients were transplanted and 22 patients died. 9 patients were removed from the waiting list due to severe deterioration; one did not require the liver transplantation anymore because of improvement, and another patient voluntarily relinquished waiting (Table 2).

In our univariate analysis, serum albumin and total bilirubin, INR, CTP, MELD, and presence of ascites and encephalopathy were significantly different between those still waiting on the list and those who died or were removed from the waiting list due to poor medical condition (P value < 0.05). Serum creatinine, however, was not significantly different between the two groups (Table 3).

Statistical analysis for prediction of mortality or removal from the waiting list due to severe deterioration, showed AUC of 0.75 for CTP and 0.69 for MELD. Comparing the validity of these scores yielded a P value of 0.065 (Figure 1). The best cutoff for CTP was 8 with 0.74 sensitivity and 0.67 specificity while for MELD, it was 13.67 with 0.74 sensitivity and 0.58 specificity. Nevertheless, 5 patients (16.1%) of those who died or were removed from the waiting list due to poor medical condition had CTP < 8 and MELD < 13.67 (Table 4). The sensitivity and specificity for other cutoffs are listed in Table 5.

Table 1. Baseline characteristics at the onset of the study.

	Mean (SD)	**Range**
Age (year)	40.77 (13.45)	18–69
Body mass index* (kg/m²)	23.95 (4.53)	15.43–43.28
MELD†	14.06 (4.6)	6.43–30.41
CTP‡	7.34 (1.96)	5–13
	Number	**Percentage%**
Female/Male	118/139	45.9/54.1
Etiology		
Cryptogenic	88	34.2
Autoimmune hepatitis	50	19.5
Hepatitis B	48	18.7
Hepatitis C	38	14.8
Primary Sclerosing Cholangitis	23	8.9
Wilson's disease	6	2.3
Primary Biliary Cirrhosis	3	1.2
Alcohol	1	0.4
Comorbidity		
Chronic kidney disease	0	0
Coronary artery disease	1	0.4
Hypertension	6	2.3
Diabetes	23	8.95
Ulcerative colitis	6	2.3
Spontaneous bacterial peritonitis	2	0.8
Hepatorenal syndrome	1	0.4
Ascites	121	47.1
Hepatic encephalopathy	52	20.2

*Body mass index was available for 149 patients. †Model for End stage Liver Disease; ‡Child-Turcotte-Pugh score

Table 2. Events on the waiting list

Patients after 9 months follow up	Number	Percentage%
In the waiting list	212	82.5
Exiting from the waiting list		
Dead	22	8.6
Worse	9	3.5
Transplant	12	4.7
Better medical condition	1	0.4
Quit	1	0.4
Total	**257**	**100**

Table 3. Univariate analysis comparing the group still on waiting list and the group expired or removed from the waiting list due to poor medical condition.

	In list, (*n*=212)	Died or worsen, (*n*=31)	P-value
	Mean ± SD (95% CI), number	Mean ± SD (95% CI), number	
Serum total bilirubin (mg/dL)	2.32 ± 1.92 (2.06, 2.58)	4.52 ± 6.47 (2.15, 6.89)	0.024
Creatinine (mg/dL)	0.88 ± 0.24 (0.85, 0.91)	0.89 ± 0.26 (0.79, 0.98)	0.751
International Normalized Ratio	1.49 ± 0.43 (1.43, 1.55)	1.6 ± 0.47 (1.51, 1.86)	0.012
Albumin (g/dL)	3.71 ± 0.61 (3.63, 3.79)	3.09 ± 0.37 (2.95, 3.22)	< 0.001
Presence of ascites	88	23	0.001
Presence of hepatic encephalopathy	33	13	< 0.001
CTP	7.01 ± 1.79 (6.77, 7.25)	8.68 ± 1.78 (8.03, 9.33)	< 0.001
MELD	13.37 ± 4.2 (12.80, 13.94)	16.26 ± 4.36 (14.66, 17.86)	0.001

Table 4. CTP and MELD of the patients expired or removed from the list due to severe deterioration.

	CTP < 8	CTP ≥ 8
MELD < 13.67	5	3
MELD ≥ 13.67	3	20

Table 5. Sensitivity and specificity for different cutoffs of the MELD and CTP scores.

MELD	Sensitivity	Specificity	CTP	Sensitivity	Specificity
13	0.77	0.50	6	0.93	0.23
13.5	0.74	0.55	7	0.90	0.46
13.6	0.74	0.57	8	0.74	0.67
13.67	0.74	0.58	9	0.61	0.79
13.7	0.70	0.58	10	0.25	0.88
13.8	0.67	0.59	11	0.16	0.95
13.9	0.67	0.60	12	0.06	0.98
14	0.64	0.60	13	0.00	0.99

Discussion

Previous reports from Iran have shown that 51%–56% of Iranian cirrhotic patients were HBsAg positive.[15] Some other studies conducted in Shiraz, southern Iran, showed smaller prevalence rates for hepatitis B etiology on liver transplantation waiting list: 26.5% in Saberifiroozi's study in 2006 and 31.2% in 2009.[16,17] In our liver transplantation waiting list, there is no selection criteria based on the etiology of the patients' chronic liver disease. However, cryptogenic cirrhosis was the top ranking etiology among patients on our waiting list. According to a general judgment, burned-out non-alcoholic steatohepatitis and inactivated past autoimmune hepatitis might be probable causes behind these patients. Due to lack of definite evidence for either non-alcoholic steatohepatitis or atypical forms of autoimmune hepatitis, we could not determine their exact etiology; therefore, we decided to categorize them as "cryptogenic etiology". High incidence of obesity, fatty liver and non-alcoholic hepatitis in most communities as well as potent oral anti-viral agents for hepatitis B virus could explain the higher rank of cryptogenic cirrhosis as the main cause of chronic liver disease on the liver transplantation waiting list. This pattern would be a dominant pattern in most communities in the future.

Patients with cirrhosis should be referred for transplantation when they develop evidence of hepatic dysfunction (CTP ³ 7 and MELD ³ 10) or when they experience their first major complication (ascites, variceal bleeding, or hepatic encephalopathy).[18] In our center, the waiting period for most patients who were transplanted was less than three months; so, most of them received the new liver with lower MELD scores.

We studied the ability of MELD and CTP to predict 9-month mortality or removal from the waiting list due to poor medical condition. It is the nature of decompensated cirrhosis to progress with time. Some of these patients may be removed from the waiting list due to the deterioration of overall clinical condition. There are a few studies which have assessed the ability of CTP and MELD for predicting both mortality and removal from the waiting list due to the deterioration of medical conditions.[19,20]

In our univariate analysis, creatinine was not significantly different between those who survived at the end of our study and those who died or were removed from the waiting list due to bad medical conditions. The reason might be the lack of any chronic kidney disease in the study population and of course, the low prevalence of hepatorenal syndrome among patients on the waiting list.

We used AUC to compare the accuracy of CTP and MELD. It ranges from 0 to 1. Generally, tests are good with AUC > 0.7 and excellent > 0.8, while AUC > 0.9 seldom occurs.[3] In our study, the AUC was 0.75 for CTP and 0.69 for MELD. This indicates that

CTP is superior in predicting mortality or removal from the waiting list due to severe deterioration after 9 months; nevertheless, the *P* value is borderline (0.065). Neither MELD score ≥ 13.67 nor CTP score ≥ 8 could predict the situation of 16.1% of patients who had the prognosis of mortality or removal from the waiting list due to severe deterioration in 9 months.

Some previous studies have shown that MELD performs better than CTP inpredicting mortality on liver transplantation waiting list in 3 months.[9,21,22] A prospective study by Wiesner et al., on 3,437 patients on liver transplantation waiting list in 2003 showed that MELD is significantly superior to CTP for predicting mortality in 3 months (AUC 0.83 versus 0.76). The patients in that study were listed as status 2A and 2B, but not status 3 (which usually refers to patients with lower CTP values).[10] Another study by Heuman et al., on 6,958 patients listed as status 2A, 2B and 3, showed that CTP slightly (but not significantly) outperforms MELD in predicting 3-month mortality (AUC 0.766 versus 0.759).[12] Heuman claimed that Wiesner's conclusion, superiority of the MELD score, is probably the result of a selection bias. Some other studies have failed to confirm the superiority of MELD to CTP.[11,20]

Although our results are in line with Heuman's study, there are differences between the study populations. Cryptogenic disease and alcohol were the most and least common etiologies, respectively, for liver disease on our waiting list. Also, hepatitis B and autoimmune hepatitis were other major etiologies on our waiting list. These are different from the above studies in which the most common etiologies were hepatitis C and alcohol. Moreover, data in those studies were analyzed when transplantation was done based on the time the patients had waited. In our transplantation center, however, MELD and CTP are used for prioritization and this may have caused a selection bias, because patients transplanted were not included in the analysis. Therefore, we expect lower AUC for both CTP and MELD. Despite this bias, CTP and MELD still had AUC above 0.6 which shows that these scores still can be utilized for prioritizing patients on the waiting list.

A similar study by Gotthardt showed that the optimum cutoff to predict mortality or the need for removal from the waiting list due to severe deterioration in one year is 9 for the CTP and 14.4 for the MELD.[20] In our study, the MELD and CTP means and cutoffs were smaller than those in Gotthardt's study. The reason is probably that we included patients some of whom had entered the waiting list before the onset ofour study and had better prognosis. Therefore, it resulted in their survival during the time on list. As the previous studies have shown, lower scores of CTP and MELD are associated with better prognosis.[2,6] Thus, it seems reasonable that CTP and MELD means and cutoffs yielded lower values for our study population.

Our study does not contradict the use of the CTP or the MELD scores for allocating patients in the liver transplantation waiting list in short term and shows that the CTP score outperforms the MELD's in predicting mortality or removal from the waiting list due to bad medical conditions in 9 months. However, our overall perception and conclusion is a need for more valid models of prioritizing patients on liver transplantation waiting lists. We suggest future studies to seek variables that can improve such prioritization algorithms.

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