Predicting Mortality Across a Broad Spectrum of Liver Disease—An Assessment of Model for End-Stage Liver Disease (MELD), Child–Turcotte–Pugh (CTP), and Creatinine-Modified CTP Scores

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***Background/Aims*: The role of model for end-stage liver disease (MELD) among Indian patients with cirrhosis is uncertain. We studied and compared MELD with Child–Turcotte–Pugh (CTP) and creatinine-modified-CTP (CrCTP) scores for predicting 1-, 3-, and 6-months mortality. *Methods*: One-hundred and two patients with cirrhosis were studied. The CrCTP was calculated by adding creatinine score of 0, 2 and 4 with creatinine levels of ≤1.2 mg/dL, 1.3–1.8 mg/dL and ≥1.9 mg/dL, respectively to CTP score. Survival curves were plotted and receiver operating characteristics (ROC) curves were used to compare the scores. Predictors of mortality were analyzed using Cox proportional hazards model. *Results*: Scores of CTP, CrCTP, and MELD have excellent diagnostic accuracy for predicting mortality (c-statistics >0.85). The MELD was superior to CTP for predicting 3-months [c-statistic and 95% confidence interval, 0.967 (0.911–0.992) vs 0.884 (0.806–0.939)] and 6-months [0.977 (0.925–0.996) vs 0.908 (0.835–0.956)] mortality ($P=0.05$), while CrCTP [0.958 (0.899–0.988)] was better than CTP for predicting 3-months mortality ($P=0.02$). Serum creatinine (hazard ratio 4.43, $P<0.0001$) is a strong independent predictor of mortality. *Conclusion*: The MELD accurately predicts mortality in cirrhosis and is better than CTP for predicting the short-term and intermediate-term mortality. Adding serum creatinine to CTP though significantly improves its diagnostic accuracy for short-term mortality; however, it remains lower than MELD alone. (J Clin Exp Hepatol 2011;1:161–168)**

Cirrhosis

Prognosis in cirrhotic patients has had a resurgence of interest because of liver transplantation and new therapies for complications of end-stage cirrhosis. On February 27, 2002, the system of organ allocation for liver transplantation in the United States changed to a 'sickest first' approach, with priority based on model for end-stage liver disease (MELD).[1,2] The MELD score, originally developed to predict 3-months survival in cirrhotic patients undergoing transjugular intrahepatic portosystemic shunt (TIPSS),[3,4] has been shown to be a valid, independent predictor of short-term as well as long-term survival for both outpatients and hospitalized patients with cirrhosis due to a broad spectrum of liver disease across the USA and Europe.[5–7] Although MELD score has shown to be better than Child–Turcotte–Pugh (CTP) score in predicting mortality among cirrhotic patients,[7–11] not all studies obtained the same positive results,[12–14] and the MELD score did not show higher accuracy as compared with the CTP[5] or to other prognostic scores[15–17] in other subsets of cirrhotic patients. Nevertheless, MELD is particularly attractive as a basis for organ allocation because its components—serum creatinine, bilirubin and international normalized ratio (INR)—are objective measurements not readily subject to bias or manipulation.[18] The advantage of MELD over CTP system relies on the use of objective parameters, generalizability of the score across different centers, lack of ceiling effect of the variables used in the score, and the inclusion of serum creatinine value in the score.[18,19] Indeed, serum creatinine level proved to be an

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Abbreviations: ALT: alanine aminotransferase; Anti-HCV: antibody against hepatitis C virus; AST: aspartate aminotransferase; AUC: area under the curve; BCS: Budd–Chiari syndrome; CI: confidence interval; CrCTP: creatinine-modified Child–Turcotte–Pugh score; CTP: Child–Turcotte–Pugh score; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HCV: hepatitis C virus; HR: hazard ratio; INR: international normalized ratio; MELD: model for end-stage liver disease; NPV: negative-predictive value; PPV: positive-predictive value; PT: prothrombin time; ROC: receiver operating characteristic; SBP: spontaneous bacterial peritonitis; SD: standard deviation; SE: standard error; TIPSS: transjugular intrahepatic porto-systemic shunt
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independent predictor of survival in cirrhotic patients during the natural course of the disease as well as during acute complications.[12,20–22] It was shown that the addition of serum creatinine to original CTP score (creatinine-modified [crCTP]) improved its diagnostic accuracy in predicting the short-term mortality, but MELD score was shown to have a prognostic yield that was better than CTP or crCTP scores.[8]

There are little data on the role of MELD in assessing prognosis in Indian patients with cirrhosis.[13] This study prospectively examined the cohort of cirrhotic patients and compared the predictive abilities of MELD, CTP, and CrCTP scores for 1-, 3-, and 6-months mortality.

PATIENTS AND METHODS

We performed a prospective study on 107 consecutive patients attending the Liver Clinic and the inpatients admitted in the Department of Hepatology, Postgraduate Institute of Medical Education and Research, a tertiary level healthcare center at Chandigarh, India, with the diagnosis of cirrhosis of liver based on clinical, biochemical, ultrasound, and/or endoscopic findings.[23,24] The Ethics Committee of the Institute approved the study. Etiology work-up of cirrhosis including alcohol, chronic hepatitis B and C, nonalcoholic steatohepatitis, and cryptogenic was performed as described in our previous study.[23,24]

These patients were enrolled into the study after obtaining an informed consent. Three patients with hepatocellular carcinoma and two with acute liver failure were excluded from the study. Thus, 102 consecutive patients with cirrhosis were analyzed in the final cohort.

Patients were investigated for liver functions [serum bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum alkaline phosphates, total protein, albumin, prothrombin time, (INR)], renal functions (serum creatinine and urea), serum electrolytes (sodium and potassium), and for other appropriate laboratory data (hemoglobin, platelet count, etc.). Complications of liver disease such as hepatic encephalopathy, ascites, and variceal bleed were also recorded. Diagnosis of encephalopathy was made using the criteria of West Haven,[25] after excluding head trauma, drug intoxication, and concurrent metabolic or endocrine disorders and graded from grades 1–4. The presence of ascites was detected clinically or by ultrasonography and graded from mild through moderate to severe.

Spontaneous bacterial peritonitis was diagnosed in patients with ascitic fluid neutrophil count >250/mL and/or positive ascitic fluid culture.[26] In the initial visit itself MELD, CTP, and CrCTP scores were calculated. The MELD score was calculated using website calculator (http://www.mayoclinic.org/meld/mayomodel6.html) and CrCTP was calculated as follows: a creatinine score of 0, 2, and 4 was assigned to patients with serum creatinine values of ≤1.2 mg/dL, 1.3–1.8 mg/dL, and ≥1.9 mg/dL, respectively.[9] The CrCTP was then calculated by adding each patient's creatinine score to their CTP score. Survival was calculated from the date of first clinical contact. Mortality data were obtained from hospital records or by telephonic communication.

Statistical Analysis

Kaplan–Meier estimates of survival were obtained for CrCTP and MELD categories with log-rank tests used to compare the survival by different category. Cox proportional hazards model was used to evaluate the impact of the above scores as a continuous scale. A multivariable Cox proportional hazards regression model was constructed to identify the independent predictors of mortality. Hazard ratio with 95% confidence intervals (CI) was reported. Receiver operating characteristics (ROC) curves were plotted and the area under curve (AUC) was used to measure the accuracy and compare the performance of CTP, CrCTP, and MELD scores in predicting 1-, 3-, and 6-months mortality for entire cohorts. The concordance c-statistic (equivalent of AUC) was used to evaluate the performance.[27] The c-statistic may vary from 0 to 1, with 1 indicating perfect discrimination and 0.5 indicating what is expected by chance alone. Any c-value of >0.7 is considered as a useful diagnostic test with value >0.8 indicating a good diagnostic test. For this analysis, death within 1, 3, or 6 months, respectively, was recorded as an event. The c-statistic was applied for 1 month, 3 months, and 6 months survival for these variables. Comparison of the areas under the ROC curves was done by utilizing the standard errors estimated using the method of Hanley and McNeil.[28]

RESULTS

Table 1 shows the baseline demographic profile and clinical characteristics. Mean age of the patients was 47.8 years and males constituted 87.3%. Alcohol was the most common etiology of cirrhosis constituting 44.1% of all patients (Table 1). Cryptogenic cirrhosis was the next common cause (21.6%), while hepatitis C virus (HCV) and hepatitis B virus (HBV) accounted for 17.6% and 13.7%, respectively. Ascites was the single-most common cause of presentation (69.6%) and 25.5% of patients had a variceal bleed. All of the patients with alcohol-related cirrhosis were males, whereas females constituted 22.8% among nonalcoholic group. A total of 11 (10.8%) and 24 (23.5%) patients developed spontaneous bacterial peritonitis and hepatic encephalopathy, respectively. There was no significant difference in the demographic profile and clinical characteristics between patients with alcohol-related cirrhosis and those without this etiology (Table 1).

Twenty-seven (26.5%) patients died during follow-up period of 6 months with 13 (12.7%) deaths during the first month and 21 (20.6%) deaths during a 3-months period. Fifteen (33.3%) patients with alcohol-related cirrhosis,

Table 1 Baseline demographics and clinical characteristics of the enrolled patients.

Variables	Total patients enrolled (n=102)	Patients with alcohol-related cirrhosis (n=45)	Patients with non-alcoholic cirrhosis (n=57)
		Mean (95% CI) or %	Mean (95% CI) or %
Age (yr)	47.8 (45.5–50.1)	47.4 (44.5–50.2)	48.2 (44.7–51.7)
Gender			
Male	89 (87.3%)	45 (100%)	44 (77.2%)
Etiology			
Alcohol-related cirrhosis	45 (44.1%)		
HBV	14 (13.7%)		14 (24.6%)
HCV	18 (17.6%)		18 (31.6%)
BCS	3 (2.9%)		3 (5.3%)
Cryptogenic	22 (21.6%)		22 (38.6%)
Ascites	71 (69.6%)	35 (77.8%)	36 (63.2%)
SBP	11 (10.8%)	6 (13.3%)	5 (8.8%)
Hepatic encephalopathy	24 (23.5%)	14 (31.1%)	10 (17.5%)
Variceal bleed	26 (25.5%)	14 (31.1%)	12 (21.1%)
AST (IU/L)	36.9 (32.8–41.2)	31.3 (26.1–36.4)	41.5 (35.2–47.7)
ALT (IU/L)	29.9 (25.5–34.2)	23.5 (18.6–28.4)	34.9 (28.3–41.5)
Albumin (mg/dL)	3.08 (2.9–3.2)	3 (2.8–3.2)	3.1 (2.9–3.3)
Bilirubin (mg/dL)	2.89 (2.2–3.6)	3 (2.2–3.9)	2.8 (1.6–3.9)
PT prolonged (sec)	7.9 (6.6–9.2)	9 (7.2–10.9)	7 (5.1–8.8)
INR	1.8 (1.7–2)	2 (1.8–2.2)	1.7 (1.5–1.9)
Creatinine (mg/dL)	1.36 (1.2–1.5)	1.5 (1.2–1.7)	1.2 (1–1.5)
Sodium (mEq/L)	136.0 (135.1–137)	135.4 (134–136.9)	136.5 (135.3–137.7)
MELD	17.7 (16.1–19.4)	19.8 (17.4–22.1)	16.1 (13.8–18.4)
CTP	9.5 (9–10)	10.2 (9.5–10.9)	8.9 (8.2–9.6)
CrCTP	10.5 (9.8–11.1)	11.4 (10.4–12.4)	9.7 (8.8–10.6)

Data are presented as mean (95% CI) or %.
CI: confidence interval; HBV: hepatitis B virus; HCV: hepatitis C virus; BCS: Budd–Chiari syndrome; SBP: spontaneous bacterial peritonitis; AST: aspartate aminotransferase; ALT: alanine aminotransferase; PT: prothrombin time; INR: international normalized ratio; MELD: model for end-stage liver disease; CTP: Child–Turcotte–Pugh; CrCTP: creatinine-modified CTP.

4 (28.6%) patients with HBV-related cirrhosis, 2 (11.1%) patients with HCV-related cirrhosis, 5 (22.7%) patients with cryptogenic cirrhosis, and 1 (33.3%) patient with Budd–Chiari syndrome (BCS) died during the 6-months follow-up. All the patients with MELD score above 30 and CrCTP score above 16 died while 86.7% of patients with CTP score of 13 and above had died at 6 months.

Analysis by Cox Hazards Model

Univariate analysis of clinical variables and the severity scores for predicting 1-, 3-, and 6-months mortality using Cox proportional hazards model are shown in Tables 2 and 3. This model showed the association of CTP, CrCTP, and MELD with mortality throughout the follow-up. To choose a small set of variables that can independently predict the survival, multivariate Cox proportional hazards model was applied using the variables from univariate analysis that had shown to be significantly (P<0.05) associated with mortality (Table 4). Using this model, serum creatinine was found to be a strong independent predictor of mortality throughout the follow-up. Multivariate analysis of different scores showed that MELD and CrCTP were strong independent predictors of mortality at 3 and 6 months. However, CrCTP was shown to be the only significant, independent predictor of 1-months mortality (Table 5).

Analysis of Receiver Operating Characteristics Curves

To further assess the prognostic utilities of different scores, ROC curves were plotted and c-statistics was calculated using AUC. The ROC curves for CTP, MELD, and CrCTP and their comparisons for predicting mortality at 1-, 3-, and 6-months for all the patients with cirrhosis are shown in Figure 1. The c-statistics for all the scores was >0.85 indicating excellent predictive accuracy. The AUC of MELD was better than the AUC of CTP in predicting 3 months [c-statistics 0.967 (95% CI 0.911–0.992) vs 0.884 (95% CI 0.806–0.939); P=0.05] and 6 months [c-statistics 0.977 (95% CI 0.925–0.996) vs 0.908 (95% CI 0.835–0.956); P=0.05] mortality, while CrCTP score [c-statistics 0.958

Table 2 Univariate analysis of variables.

Variables	1-month		3-months		6-months	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age	1.02 (0.97–1.07)	0.456	1.01 (0.98–1.05)	0.492	1.0 (0.97–1.04)	0.689
Gender	1.3 (0.29–5.89)	0.729	1.19 (0.35–4.06)	0.776	0.89 (0.27–2.94)	0.844
Etiology	0.34 (0.1–0.01)	0.07	0.67 (0.29–1.58)	0.365	0.59 (0.27–1.26)	0.171
SBP	9.97 (3.33–29.83)	<0.0001	6.88 (2.75–17.18)	<0.0001	6.28 (2.73–14.47)	<0.0001
HE	6.26 (2.04–19.17)	0.001	5.81 (2.44–13.84)	<0.0001	4.29 (2.01–9.16)	0.001
Variceal bleed	1.32 (0.41–4.28)	0.645	0.93 (0.34–2.54)	0.889	0.84 (0.34–2.08)	0.709
Albumin	0.42 (0.18–0.99)	0.047	0.43 (0.21–0.85)	0.015	0.48 (0.26–0.88)	0.019
Bilirubin	1.19 (1.1–1.28)	<0.0001	1.18 (1.11–1.26)	<0.0001	1.2 (1.13 –1.27)	<0.0001
INR	2.01 (1.43–2.83)	<0.0001	2.19 (1.68–2.86)	<0.0001	2.37 (1.85–3.04)	<0.0001
Creatinine	4.17 (2.59–6.72)	<0.0001	5.14 (3.17–8.33)	<0.0001	4.76 (3.06–7.41)	<0.0001
Sodium	0.98 (0.87–1.1)	0.721	0.97 (0.88–1.06)	0.496	0.98 (0.9–1.07)	0.697

HR: hazard ratio; CI: confidence interval; HE: hepatic encephalopathy; SBP: spontaneous bacterial peritonitis; INR: international normalized ratio.
Gender-risk of death, males compared with females; etiology-risk of mortality, alcoholic-related cirrhosis compared with nonalcoholic cirrhosis; SBP, HE and variceal bleed, risk of mortality associated with the presence of these complications compared with their absence; bilirubin, INR and creatinine—applied as a continuous scale and hazard ratio is shown as risk of mortality associated with each unit increase in these variables; albumin and sodium—applied as continuous scale and hazard ratio is shown as risk of mortality associated with each unit decrease in these variables.

Table 3 Univariate analysis of the different scores.

Scores	1-month		3-months		6-months	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
MELD	1.17 (1.11–1.24)	<0.0001	1.21 (1.15–1.27)	<0.0001	1.23 (1.17–1.29)	<0.0001
CTP	1.77 (1.37–2.27)	<0.0001	1.72 (1.42–2.08)	<0.0001	1.73 (1.47–2.04)	<0.0001
CrCTP	1.78 (1.42–2.25)	<0.0001	1.96 (1.58–2.43)	<0.0001	1.88 (1.57–2.25)	<0.0001

HR: hazard ratio; CI: confidence interval; MELD: model for end-stage liver disease—applied as continuous score; CTP: Child–Turcotte–Pugh score (range 5–15); CrCTP: creatinine-modified CTP (range 5–19).
Hazard ratio is shown as risk of mortality associated with each unit increase in the score.

Table 4 Multivariate analysis of variables (model 1) and scores (model 2).

Model	1-month		3-months		6-months	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Model 1						
SBP	1.18 (0.23–6.14)	0.845	0.79 (0.19–3.23)	0.738	0.97 (0.28–3.38)	0.956
HE	3.44 (0.68–17.27)	0.134	2.4 (0.7–8.21)	0.163	1.73 (0.61–4.88)	0.301
Albumin	1.18 (0.39–3.58)	0.771	1.25 (0.51–3.05)	0.62	1.41 (0.68–2.93)	0.351
Bilirubin	1.08 (0.93–1.25)	0.319	1.05 (0.94–1.17)	0.379	1.05 (0.95–1.16)	0.299
INR	1.53 (0.72–3.23)	0.266	2.11 (1.21–3.7)	0.009	2.53 (1.56–4.11)	<0.0001
Creatinine	3.12 (1.55–6.3)	0.001	4.68 (2.36 –9.28)	<0.0001	4.43 (2.32–8.47)	<0.0001
Model 2						
MELD	1.06 (0.97–1.16)	0.22	1.09 (1.01–1.18)	0.02	1.14 (1.06–1.22)	<0.0001
CTP	0.97 (0.59–1.59)	0.91	0.85 (0.58–1.23)	0.39	0.99 (0.72–1.34)	0.93
CrCTP	1.57 (1.0–2.48)	0.05	1.78 (1.23–2.57)	0.002	1.48 (1.09–2.02)	0.01

HR: hazard ratio; CI: confidence interval; SBP: spontaneous bacterial peritonitis; HE: hepatic encephalopathy; INR: international normalized ratio; MELD: model for end-stage liver disease—applied as continuous score; CTP: Child–Turcotte–Pugh score (range 5–15); CrCTP: creatinine-modified CTP (range 5–19).
Hazard ratio is shown as risk of mortality associated with each unit increase in the score; SBP and HE, risk of mortality associated with the presence of these complications compared with their absence; bilirubin, INR and creatinine—applied as a continuous scale and hazard ratio is shown as risk of mortality associated with each unit increase in these variables; albumin—applied as continuous scale and hazard ratio is shown as risk of mortality associated with each unit decrease in these variables.

Table 5 Comparisons of model for end-stage liver disease and creatinine-modified Child–Turcotte–Pugh score with Child–Turcotte–Pugh score in predicting 1-, 3-, and 6-months mortality among alcohol-related and nonalcoholic cirrhosis.

	MELD	CrCTP	CTP
1-month mortality			
Non-alcoholic	0.910 (0.804–0.969; *P=0.62)	0.939 (0.842–0.984; †P=0.12)	0.851 (0.732–0.932)
Alcohol-related	0.944 (0.832–0.990; *P=0.29)	0.920 (0.799–0.979; †P=0.32)	0.875 (0.742–0.954)
3-months mortality			
Non-alcoholic	0.980 (0.901–0.997; *P=0.15)	0.969 (0.885–0.996; †P=0.11)	0.896 (0.786–0.961)
Alcohol-related	0.955 (0.847–0.993; *P=0.18)	0.940 (0.826–0.988; †P=0.14)	0.874 (0.741–0.954)
6-months mortality			
Non-alcoholic	0.972 (0.890–0.996; *P=0.22)	0.963 (0.876–0.994; †P=0.18)	0.911 (0.805–0.970)
Alcohol-related	0.993 (0.908–1.000; *P=0.08)	0.916 (0.793–0.977; †P=0.77)	0.904 (0.779–0.971)

MELD: model for end-stage liver disease; CrCTP: creatinine-modified Child–Turcotte–Pugh score; CTP: Child–Turcotte–Pugh score; c-statistics (95% confidence interval) are reported.
*P value between MELD and CTP.
†P value between CrCTP and CTP.

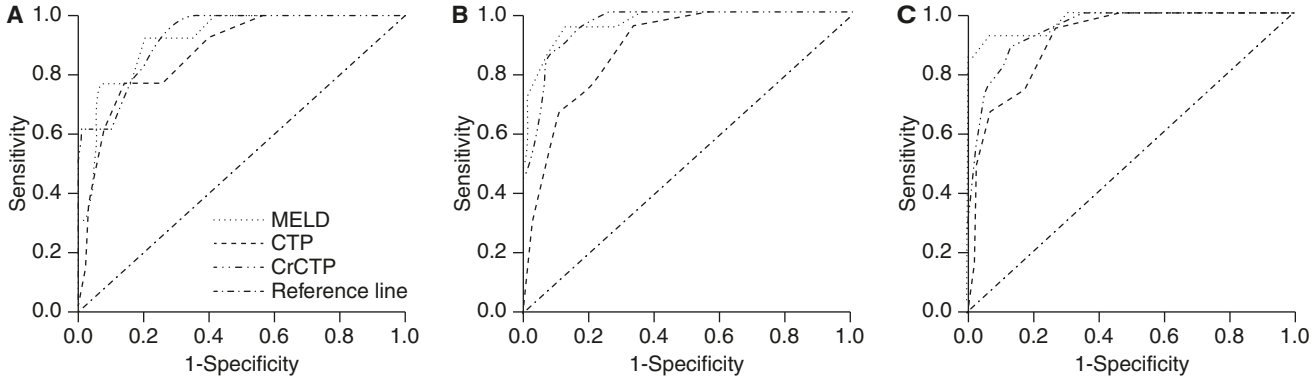

Figure 1 Receiver operating characteristics curves for MELD, CTP, and CrCTP scores with reference line showing the comparison of different score AUCs in predicting 1-month (A), 3-months (B), and 6-months (C) mortality. (A) C-statistics of CTP 0.875 (95% CI 0.794–0.932), CrCTP 0.925 (95% CI 0.856–0.968), and MELD 0.920 (95% CI 0.849–0.964) in predicting 1-month mortality; *P* value—CrCTP vs CTP=0.16, MELD vs CTP=0.44, and CrCTP vs MELD=0.9. (B) C-statistics of CTP 0.884 (95% CI 0.806–0.939), CrCTP 0.958 (95% CI 0.899–0.988), and MELD 0.967 (95% CI 0.911–0.992) in predicting 3-months mortality; *P* value—CrCTP vs CTP=0.02, MELD vs CTP=0.05, and CrCTP vs MELD=0.73. (C) C-statistics of CTP 0.908 (95% CI 0.835–0.956), CrCTP 0.946 (95% CI 0.883–0.981), and MELD 0.977 (95% CI 0.925–0.996) in predicting 6-months mortality; *P* value—CrCTP vs CTP=0.15, MELD vs CTP=0.05, and CrCTP vs MELD=0.22.
AUC: area under curve; MELD: model for end-stage liver disease; CTP: Child–Turcotte–Pugh; CrCTP: creatinine-modified CTP.

(95% CI 0.899–0.988)] showed better predictive accuracy than CTP score at 3 months (P=0.02). A cut-off point in the ROC curve of MELD was chosen to give the best sensitivity and specificity. A MELD score >20 had a sensitivity and specificity of 92.3% and 79.8% at 1-months mortality, 95.2% and 87.6% at 3 months and 92.6% and 93.3% at 6 months, respectively. The ROC curves were further plotted to compare these scores between alcoholic and nonalcoholic cohorts.

Survival Analysis Using Kaplan–Meier Curves

Patients were grouped into different categories according to their CrCTP and MELD scores and analyzed using Kaplan–Meier survival curves. Kaplan–Meier survival curves for various categories in predicting mortality are shown in Figures 2 and 3. Higher scores were associated with decreased survival; in pairwise comparisons using log-rank test, all categories were significantly different from each other. Patients with cirrhosis and renal failure (serum creatinine levels above 1.5 mg/dL) were shown to have higher mortality than patients without renal failure (P<0.0001) (Figure 4).

DISCUSSION

Our study being a prospective study utilizing large cohort of Indian patients with broad spectrum of cirrhosis demonstrated that MELD has excellent diagnostic accuracy in predicting very short (1 month), short (3 months), and intermediate-term (6 months) mortality with a good sensitivity and specificity. Demonstration of the validity of MELD in predicting the short-term survival among patients with cirrhosis of liver expands and broadens the

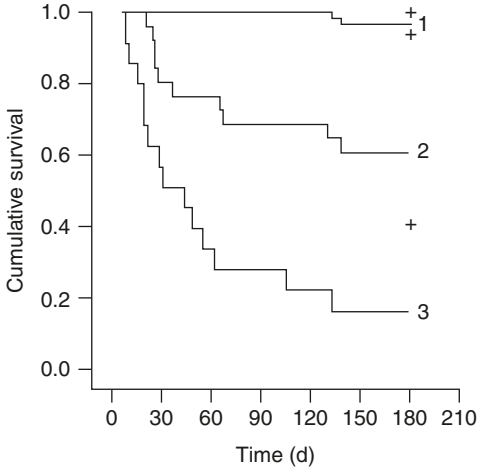

Figure 2 Kaplan–Meier survival curves for creatinine-modified Child–Turcotte–Pugh score (CrCTP), predicting increased mortality with higher CrCTP categories. Categories: 1=CrCTP≤10, 2=CrCTP 11–14, 3=CrCTP≥15. Pairwise comparisons: 1 vs 2, $P<0.0001$; 1 vs 3, $P<0.0001$; 2 vs 3, $P<0.0001$.

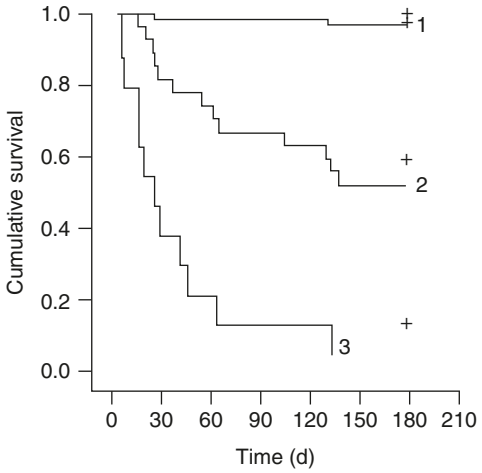

Figure 3 Kaplan–Meier survival curves for model for end-stage liver disease (MELD), predicting increased mortality with higher MELD categories. Categories: 1=MELD≤18, 2=MELD 19–28, 3=MELD≥29. Pairwise comparisons: 1 vs 2, $P<0.0001$; 1 vs 3, $P<0.0001$; 2 vs 3, $P<0.0001$.

utility of MELD for the objective assessment of patients with cirrhosis of liver. All the variables used in the MELD score were also strongly associated with mortality. The discriminant ability of MELD was demonstrated when the score was grouped into different categories and showed that each MELD category was significantly different from other. Since its introduction, MELD has been studied extensively to evaluate its predictive accuracy in chronic liver disease. One such study has shown MELD to be a useful tool in predicting 3 months and 1-year mortality among both outpatients and inpatients with cirrhosis.[6] The same study also showed that MELD had a weaker predictive ability for long-term mortality. We have demonstrated that

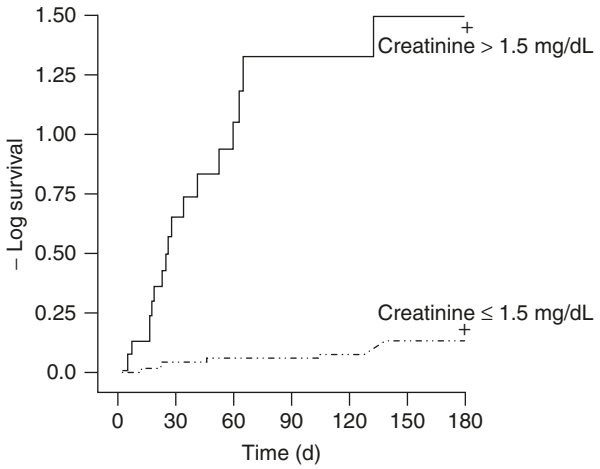

Figure 4 Mortality differs by renal failure in patients with cirrhosis. Kaplan–Meier analysis shows patients with cirrhosis and renal failure had significantly higher mortality than those with cirrhosis but no renal failure ($P<0.0001$) throughout the follow-up.

MELD score can significantly predict mortality with an excellent diagnostic accuracy which was shown by the c-statistics (0.920, 0.967, and 0.977 for 1-, 3-, and 6-months mortality, respectively). This accuracy was much better than the previous findings in other retrospectively evaluated cohorts of patients with decompensated cirrhosis.[5,9] A cut-off MELD score of >20 was shown to have very high NPV (98.6%, 98.6%, and 97.2%) and sensitivity (92.3%, 95.2%, and 92.6%), indicating that it is a very good predictor of 1-, 3-, and 6-months survival.[5]

We have shown that MELD is significantly superior to CTP for predicting 3- and 6-months mortality. Previous studies have demonstrated MELD and CTP to be equivalent in predicting the short- and intermediate-term mortality in patients with cirrhosis and those undergoing TIPS while others have shown MELD to have superior predictive accuracy for 12- and 24-months survival.[3–9,29] In this study, we have not only shown that MELD as a disease severity index is superior to CTP for both short-term and intermediate-term, but also demonstrated excellent diagnostic accuracy of MELD in predicting 1-, 3-, and 6-months mortality (c-statistics 0.920, 0.967, and 0.977, respectively). One reason for the superior predictive ability of MELD compared with CTP is the inclusion of serum creatinine. Previous studies have shown serum creatinine to be strongly associated with mortality in patients with liver cirrhosis of varied etiology with or without complications of liver disease.[12,19–21] Indeed, in our study, serum creatinine levels were shown to be a strong independent predictor of mortality throughout the follow-up period. Patients of cirrhosis with creatinine level above 1.5 mg/dL separated the patients who are at increased risk of death.

In theory including an independent predictor of survival to any score should increase the diagnostic accuracy of that score. By including serum creatinine to the original

CTP, we analyzed whether it could increase its predictive accuracy. On comparison using ROC curves, we found that CrCTP was better than CTP in predicting 3-months mortality with excellent diagnostic accuracy throughout the follow-up period. The discriminant ability of the CrCTP was also evident when the score was separated into different categories and analyzed using the Kaplan–Meier survival curves. In the past, studies which have analyzed the inclusion of serum creatinine to CTP have also demonstrated similar predictive advantages.[8,9] However, the prognostic accuracy (c-statistics 0.925, 0.958, and 0.946 for 1-, 3-, and 6-months mortality) obtained from our study was better than that from the previous studies. The level of serum creatinine was found to be a prognostic marker even in patients with good liver synthetic function and normal renal function. It has been shown in the past that in patients who achieved therapeutic benefit from TIPS, serum creatinine levels were found to be an independent predictor of death.[12] Hence, by adding this strong predictor of survival to CTP, we have demonstrated its excellent diagnostic accuracy and superiority over CTP for predicting very short-, short-, and intermediate-term mortality in cirrhotic patients.

The other advantage of CrCTP over CTP score would be the better discriminative ability than CTP, i.e., creatinine-modified CTP score provides broader range (range 5–19) than that of CTP (range 5–15). This broader scale could discriminate the severity of liver disease better than the much narrower scale of traditional CTP. This strong predictive accuracy of creatinine-modified CTP which is better than CTP combined with its ease of application at the bedside without the need for sophisticated calculation may justify its wider use in day-to-day clinical practice. Thus, CrCTP which takes into account most of the complications of cirrhosis including ascites, hepatic encephalopathy (unlike MELD), and renal dysfunction (unlike CTP) can be used as a prognostic index which can accurately reflect the severity of the underlying liver disease. This accuracy could challenge the predictive power of MELD as disease severity index in cirrhotic patients. However, though addition of serum creatinine to CTP could better the accuracy of CTP, our study did not show better accuracy for CrCTP than that provided by MELD and supports the observations reported earlier.[8] This shows that the superior diagnostic result of MELD is not only related to the presence of serum creatinine but also to the absence of subjective criteria and the consistency of the use of objective laboratory parameters. One such parameter included in the MELD score is INR which has shown to be the predictor of mortality in cirrhosis.[30] In our study, INR along with serum creatinine was a strong independent predictor of 3- and 6-months mortality. Moreover, the dynamic nature of MELD score, which is expressed within a continuous scale of 34 points, improves the discriminatory ability and thus accurately predicts the severity of cirrhosis without producing a ceiling effect unlike CTP. In our study, we have demonstrated that the occurrence of complications related to portal hypertension like variceal bleed does not predict mortality in these patients either at short-term or intermediate-term. The MELD in previous studies has also shown to predict the mortality independent of the occurrence of complications of portal hypertension like variceal bleed.[5,31] Hepatic encephalopathy and spontaneous bacterial peritonitis are the major complications of cirrhosis and past studies on MELD have shown no correlation between MELD and the occurrence of these complications in terms of outcome prediction.[32]

CONCLUSION

We have validated MELD as an excellent prognostic marker for very short-, short-, and intermediate-term mortality among patients with cirrhosis due to varied etiology. Prognostic accuracy of MELD is better than CTP in predicting short- and intermediate-term mortality and the inclusion of serum creatinine to CTP improves its predictive accuracy which justifies its wider use in day-to-day clinical practice. Finally, MELD score has maintained excellent diagnostic accuracy in both alcoholic and nonalcoholic groups of patients with cirrhosis of liver.

CONFLICTS OF INTEREST

All authors have none to declare.

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