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PROGNOSTIC PERFORMANCE OF CTP, MELD AND MELD VARIANTS IN PREDICTING 3 , 6 AND 12 MONTH MORTALITY IN A COHORT OF DECOMPENSATED LIVER DISEASE (DCLD)

Gastroenterology

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ABSTRACT

BACKGROUND Decompensated liver disease (DCLD) has high mortality rate and prediction of which is important to prognosticate and to channel high risk patients for Liver transplantation. MELD ,MELD variants and CTP were widely tested for mortality prediction with only few studies comparing them. Aim of the study was to compare the prognostic performance of MELD, CTP and MELD variants in predicting 3 , 6 and 12 month mortality in a cohort of DCLD .

METHODS Retrospective study of 321 DCLD patients were taken up ,MELD ,MELD Na, MEOS , iMELD , UKLED and CTP were calculated on the date of admission. Patient relatives were telephonically contacted regarding date of death and mortality at 3,6 and 12 month were assessed .The prognostic performance of MELD , CTP and MELD variants were calculated using AUROC and cut offs obtained .

RESULTS CTP had maximum AUROC in predicting 3 month mortality (0.767 cut off 11 sensitivity 71% specificity 73.8%) followed by MELD-Na (0.735 cut off 25 sensitivity 65% specificity of 72%). CTP had maximum AUROC in predicting 6 month mortality (0.761 cut off 11 sensitivity 58% specificity 80.5 %) followed by iMELD (0.746 cut off 3.2 sensitivity 72% specificity 73.6%). I-MELD had maximum AUROC in predicting 12 month mortality (0.749 cut off 0.6 sensitivity 74.6% specificity 73%) followed by CTP (0.745 cut off 10 sensitivity 70% specificity 67%)

CONCLUSION CTP is superior to MELD in predicting 3 and 6 month mortalityand I-MELD is the best at 12 month . Since AUROC of all prognostic models were less than 0.8 in predicting mortality better prognostic models are required .

KEYWORDS

Decompensated liver disease (DCLD), MELD ,MELD Na, iMELD , Liver transplantation.

INTRODUCTION

Decompensated liver disease (DCLD) is one of the most common cause of mortality world wide though the etiology varies from place to place .Though many therapies for DCLD had been tried , most of them was not able to provide a curative therapy. Liver transplantation is the only curative therapy for DCLD . Many studies have investigated factors predicting survival in patients with cirrhosis.(1,2)

Many scoring systems were proposed for better allocation of organ for transplantation and to decrease the mortality in transplant waiting list . Among them most important was MELD and MELD variants . MELD was introduced by Malinchoc for TIPSS patients (3). But later it was found to be effective for allocating organs for transplantation candidates based on MELD score(4,5). Patients with decompensated cirrhosis often have refractory ascites and hepato-renal syndrome, which causes hemodynamic changes that may lead to dilutional hyponatremia, increasing the risk of death (6). The role of hyponatremia as a predictor of mortality has been established for patients on liver transplantation waiting list (7-9), leading to several attempts to incorporate serum sodium into the MELD score which is MELD-Na (10,11). Another predictor model of mortality in CLD patients was CTP score which is a subjective score and not a dynamic score like MELD . The Child score, first proposed in 1964 and modified as the Child–Turcotte–Pugh (CTP) score thereafter, has been widely used for over 40 years for prognostication of patients with cirrhosis(12). However, it has some subjective components and does not rate other factors such as renal and pulmonary dysfunction,(13,14) which are common in decompensated cirrhosis

In this study we compare between CTP, MELD and MELD variants like MELD-Na, UKLED, i-MELD and MESO score in a cohort of DCLD in predicting 3,6 and 12 month mortality.

Score	Formula for calculation	Details
MELD	10 × {0.957 x ln (creatinine[mg/dl]) + 0.378 × ln (bilirubin[mg/dl]) + 1.120 x ln (INR) + 0.643}	Score multiplied by 10 and rounded to the nearest integer. Maximum of 40 points. Laboratory values including INR, bilirubin and creatinine values <1.0 are set to 1.0. Creatinine values above 4.0 mg/dl are set to 4.0 mg/dl. Same applies for patients who are under dialysis
MESO Index	[MELD/SNa (mmol/l)] x 10	MELD (as above) laboratory values <1 mg/dl are set to 1.0 mg/dl. Creatinine values above 4.0 mg/dl are set to 4.0 mg/dl. Same applies for patients who are under dialysis. SNa = serum Na+
MELD Na	MELD – Na+ (mmol/l) – [0.025 × (MELD) × (140-Na+ (mmol/l))] + 140	Na+ range of 125–140 mmol/l, lower values and larger values are rounded to the nearest integer in this range. Laboratory values <1.0 are set to 1.0. Creatinine values above 4.0 mg/dl are set to 4.0 mg/dl. Same applies for patients who are under dialysis, rounded to the nearest integer
UKELD	(1.485 × ln (creatinine [μmol/l]) + (3.13 × ln (bilirubin [μmol/l])) + (5.395 x ln (INR)) – (81.565 × ln (Na+ [mmol/l])) + 435	With a creatinine range of 1–400 μmol/l and Na+ range of 112–150 mmol/l. Values outside of these ranges are capped. Bilirubin values below 1.0 μmol/l are set to 1.0 μmol/l, INR values below 1.0 are set to 1.0
iMELD	MELD + [recipient age (years) × 0.3] – [0.7 × Na+ (mmol/l)] + 100	MELD was used as described above

Table 1: MELD and MELD variants compared in our study (15,16,17,18,19)

MATERIALS AND METHODS

It was a retrospective study in a population of DCLD patients with age more than 18 years admitted in department of medical gastroenterology, Trivandrum medical college, from June 2016-January 2019 after excluding patients with hepatocellular carcinoma, extrahepatic malignancy, high DF alcoholic hepatitis .

Data collected from the electronically generated discharge summary and telephonic conversation . Clinical and biochemical parameters were collected on the date of admissions . Patients bystanders were telephonically contacted regarding mortality at 3 ,6 and 12 month from the time of admission and death time from date of admission was assessed . Based on admission variables MELD,CTP and MELD variants were calculated and their predictive powers in 3 , 6 and 12 month mortality was assessed using AUROC curve .

STATISTICALANALYSIS

Continuous variables were compared using Student's t tests and categorical variables were compared using Chi-squared tests or Fisher's tests. The predictive ability for each model was evaluated according to Areas Under Receiver-Operating Characteristics curves (AUROC). Comparisons of AUROCs were performed by MedCalc software version 12.4. The *p* value was considered significant when it was less than 0.05.

RESULTS

321 Patients were taken up for the study ,out of which 62 were females (19.3%) and 259 were males (80.7%) Figure 1

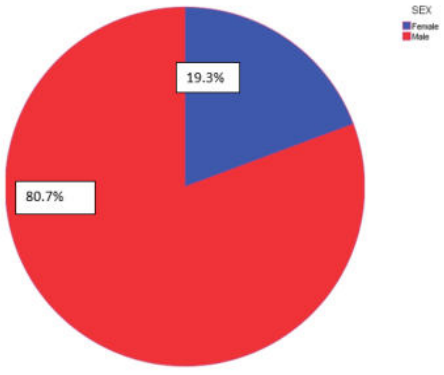


Figure 1 : sex distribution of study population

Among the quantitative study variables analyzed by t test , Hemoglobin, platelet count , albumin , creatinine , bilirubin , sodium level , INR, portal vein diameter , liver span and spleen span were statistically significant in predicting three month mortality(Table 2)

Table 2: Quantitative baseline variables in predicting three month mortality

Variable	P value	Lower	Upper
Hemoglobin	.001	.2616569	1.0561001
Age	.148	-4.424	.667
Total count	.276	-1202.203	4195.680
Platelet count	.045	-2.3285508E3	-26.3672900
Eosinophil count	.545	-29.328	55.459
Albumin	.030	.0121859	.2337954
Creatinine	.000	-.5146837	-.2456901
Bilirubin	.000	-3.3209825	-1.6175222
Sodium	.014	.314	2.770
INR	.000	-.4865465	-.2667245
Portal vein diameter	.002	-1.1167817	-.2645267
LIVER span	.069	-.0278204	.7511848
SPLEEN span	.000	-1.2908248	-.5521658

Among the qualitative variables analyzed by chi square test , Hepatic encephalopathy and Ascites were significant in predicting three month mortality(Table 3)

Table 3: Qualitative variables in predicting three month mortality

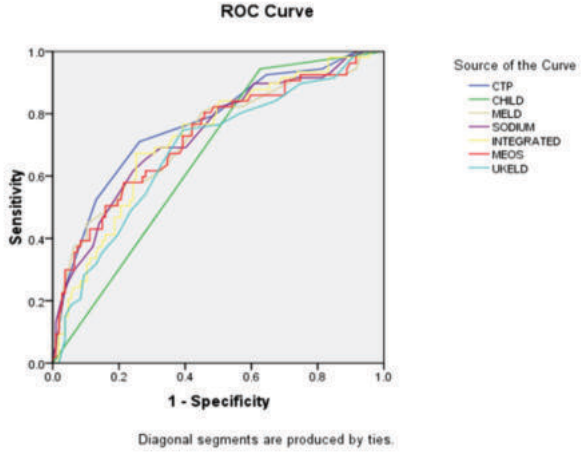
	ASCITES	HE
Chi-Square	3.787[a]	2.391[b]
df	2	3
Asymp. Sig.	.000	.000

AUROC was plotted in comparing CTP, MELD and MELD variants in predicting 3 , 6 and 12 month mortality . In predicting three month mortality the AUROC of CTP was 0.769, Child (As our study was on DCLD only Child B and C was taken) was 0.659 , MELD was 0.727, MELD – Na was 0.735 , I-MELD was 0.723, MESO was 0.727 and UKLED was 0.686 Table 4 and Figure 2

Table 4: AUROC of various predictor model in predicting 3 month mortality

Test Result Variable(s)	Area Under the curve
CTP	.767
CHILD	.659
MELD	.727
MELD-Na	.735
i-MELD	.723
MEOS	.727
UKELD	.686

Figure 2: AUROC of various predictor models for DCLD in predicting 3 month mortality



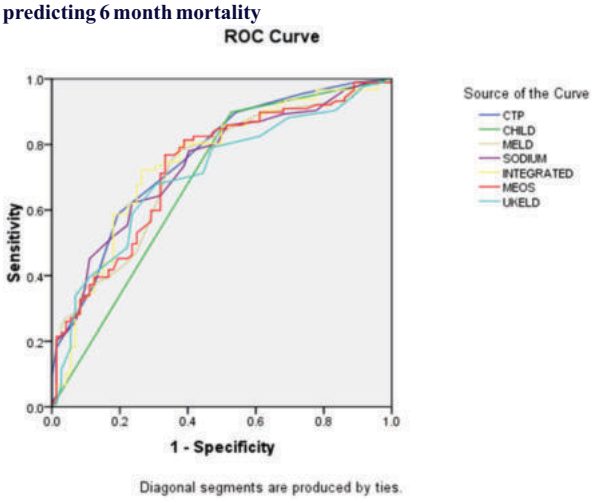
In predicting 6 month mortality , the AUROC of CTP was 0.761, Child was 0.685 , MELD was 0.726, MELD – Na was 0.739 , I-MELD was 0.746, MESO was 0.731 and UKLED was 0.709

Table 5and Figure 3

Table 5- AUROC of various predictor model in predicting 6 month mortality

Test Result Variable(s)	Area under the curve
CTP	.761
CHILD	.685
MELD	.726
MELD-Na	.739
I-MELD	.746
MEOS	.731
UKELD	.709

Figure 3: AUROC of various predictor models for DCLD in predicting 6 month mortality

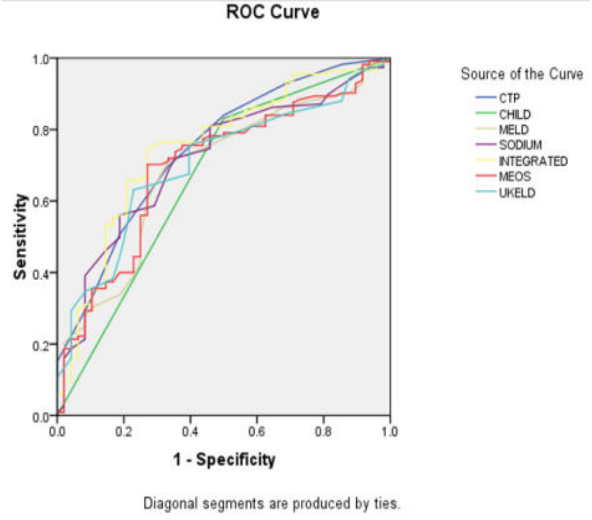


In predicting 12 month mortality , the AUROC of CTP was 0.745, Child was 0.666 (As our study was on DCLD only Child B and C was taken), MELD was 0.686 , MELD – Na was 0.716 , I-MELD was 0.749, MESO was 0.697 and UKLED was 0.705 Table 6 and Figure 4

Table 6: AUROC of various predictor model in predicting 12 month mortality

Test Result Variable(s)	Area under the curve
CTP	.745
CHILD	.666
MELD	.686
MELD-Na	.716
I-MELD	.749
MEOS	.697
UKELD	.705

Figure 4: AUROC of various predictor models for DCLD in predicting 12 month mortality



CTP had maximum AUROC in predicting 3 month mortality (0.767 , cut off of >11 with sensitivity of 71% and specificity of 73.8%,95% Confidence interval 0.717 to 0.813, p <0.0001) followed by MELD-Na (0.735,cut off of >25 with sensitivity of 65% and specificity of 72% , 95% Confidence interval 0.683 to 0.782, p <0.0001).

Figure 5 and 6

Figure 5: AUROC of CTP in predicting 3 month mortality'

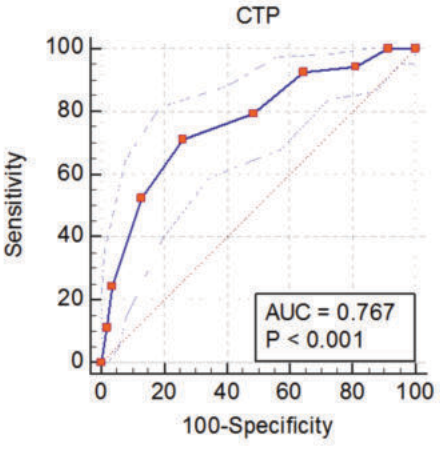
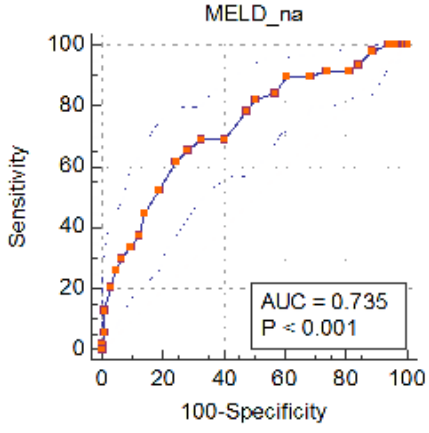


Figure 6: AUROC of MELD-Na in predicting 3 month mortality



CTP had highest AUROC in predicting 6 month mortality (0.761 , cut off of >11 with sensitivity of 58% and specificity of 80.5 %, 95% Confidence interval 0.711 to 0.807, p <0.0001) followed by i-MELD (0.746,cut off of >3.2 with sensitivity of 72% and specificity of 73.6% , 95% Confidence interval 0.695 to 0.793, p <0.0001).

Figure 7 and 8

Figure 7: AUROC of CTP in predicting 6 month mortality

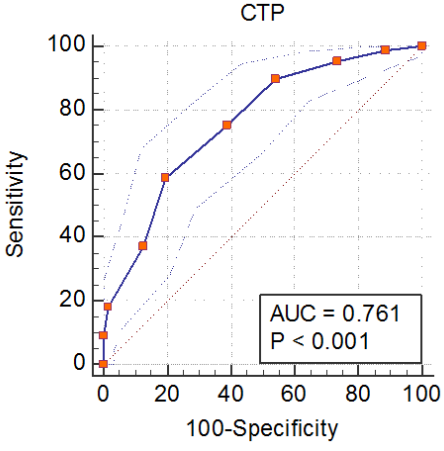
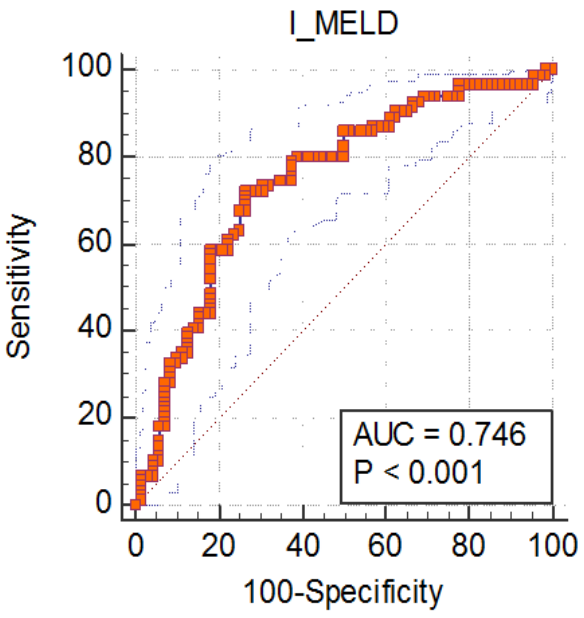


Figure 8: AUROC of i- MELD in predicting 6 month mortality



I-MELD had maximum AUROC in predicting 12 month mortality (0.749 , cut off of >0.6 with sensitivity of 74.6% and specificity of 73%,95% Confidence interval 0.697 to 0.795, p <0.0001) followed by CTP (0.745,cut off of >10 with sensitivity of 70% and specificity of 67%,95% Confidence interval 0.694 to 0.792, p <0.0001) Figure 9 and 10

Figure 9: AUROC of i- MELD in predicting 12 month mortality

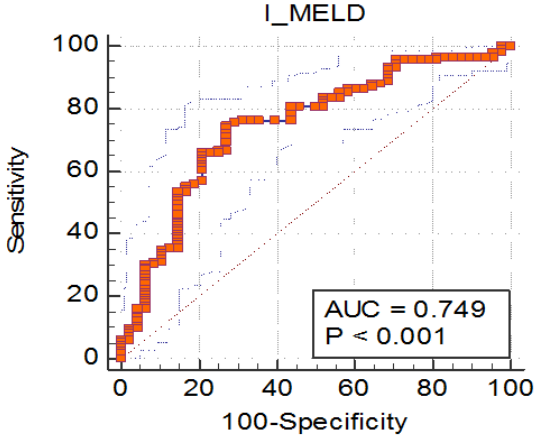
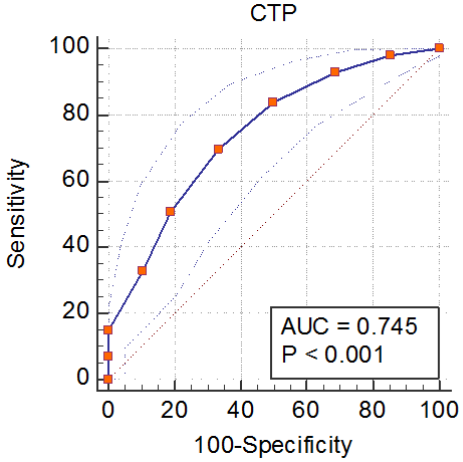


Figure 10: AUROC of CTP in predicting 12 month mortality



DISCUSSION

Accurate prognostic indicators for survival of cirrhotic patients are important, and helpful to guide clinical decision. The MELD score has been used as a tool to evaluate the prognosis of patients with end- stage liver disease and it proved to be useful in assessing 3-month and 1-year survival of patients with liver cirrhosis. However MELD score did not show significantly better prognostic accuracy as compared with the CTP score (20). In our study risk factor analysis showed that presence of ascites and Hepatic encephalopathy were significant in predicting three month mortality . Our study will be first of it's kind comparing all existing models of MELD variants in an Indian population.

In this study CTP had maximum AUROC in predicting 3 month (0.767 , cut off of >11 with sensitivity of 71% and specificity of 73.8%) and 6 month mortality (0.761 , cut off of >11 with sensitivity of 58% and specificity of 80.5 %)which is followed by MELD-Na (0.735,cut off of >25 with sensitivity of 65% and specificity of 72%) and i-MELD (0.746,cut off of >3.2 with sensitivity of 72% and specificity of 73.6%) respectively.

Therefore, despite the criticism that the CTP score is a subjective tool, it is still a very important index to determine the prognosis of cirrhosis patients which is proved by our study.

In our study I-MELD had maximum AUROC in predicting 12 month mortality (0.749 , cut off of >0.6 with sensitivity of 74.6% and specificity of 73%) followed by CTP (0.745,cut off of >10 with sensitivity of 70% and specificity of 67%).

Our results confirmed that the predictive power of the standard MELD can be improved by incorporating sodium into the model, as demonstrated higher AUCs for MELD-Na, MESO index and iMELD in particular for 12 month mortality.

CONCLUSION

- CTP is superior to MELD and comparable to MELD variants in predicting 3 and 6 month mortality
- I-MELD is the best prognostic model in predicting 12month/1year mortality
- AUROC of all prognostic models were less than 0.8 in predicting 3 month , 6 month and 12 month mortality and hence better prognostic models are require for prognostication in Decompenated liver disease patients.

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