Comparison of the prognosis value of CTP - crea, traditional CTP, MELD in cirrhotic patients with acute variceal bleeding

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Abstract

Background: Variceal bleeding is a severe complicaton of portal hypertension due to cirrhosis with high rate of motality. The aims of this study was to compare the accuracy of CTP - crea (creatinine-modified Child Turcotte Pugh score) with traditional CTP and MELD score for predicting in rebleeding and mortality within first five days and 6-week in cirrhotic patients with acute variceal bleeding. **Methods:** Prospective study in 118 cirrhotic patients presenting with acute variceal bleeding were hospitalized and diagnosed by upper GI endoscopy submited to calculate CTP-, CTP - crea I/II- and MELD- score. Exclusion criteria were patients with chronic kidney diseases, hepatocellular carcinoma, severe primary cardiopulmonary failure. **Results:** The mean age of patients was 53.39 ± 11.97 years, male accounted for 91.0%. The patients with bleeding from esophageal varices were accounted for 82.2% and from gastric varices for 17.8% of which GOV2, IGV1, GOV1 were 11.9%, 3.4%, 2.5%, respectively. Acute kidney injury (AKI) was presented in 16.7% of patients. The prognostic value of these scores in early rebleeding (first five days) were: CTP - crea I (AUC: 0.788) > CTP - crea II (AUC: 0.771) > MELD (AUC: 0.754) > CTP (AUC: 0.671), in early mortality were: CTP crea I (AUC: 0.860) > CTP - crea II (AUC: 0.859) > MELD (AUC: 0.849) > CTP (AUC: 0.775). For the 6-week rebleeding, only the CTP - crea I score has prognostic value with AUC = 0.67 ($p < 0.05$), while the 6-week mortality, the prognostic value of CTP - crea I was the best score (AUC: 0.818) > CTP - crea II (AUC: 0.804) > MELD (AUC: 0.772) > CTP (AUC: 0.745). **Conclusions:** The CTP - creatinine scores improved the traditional CTP score and was better than the MELD score in predicting the rebleeding and mortality outcomes in patients with acute variceal bleeding. It is possible to routinely apply this score in clinical practice to stratify and predict the outcomes in variceal bleeding cirrhotic patients in Vietnam.

Key words: *variceal bleeding, CTP, Creatinine.*

1. BACKGROUND

Bleeding from varices is one of the most feared complications of portal hypertension and a significant factor in the death of cirrhotic patients with mortality rates following an episode of variceal bleeding were up to 50% after one year and half of them occurred within 6 weeks [1], [2]. Baveno consensus recommend the 6-week mortality associated with variceal bleeding should use as a predictor outcome of the cirrhotic patients in all study program for these patients [3, 4]. Child-Turcotte-Pugh (CTP) and the Model for End-stage Liver Disease (MELD) scores have traditionally been used to stratify and assess prognosis in cirrhotic patients after variceal bleeding. However, these classification systems have limitations in its application when the serum creatinine level has recently seen as an important predictor of survival in patients with liver cirrhosis was not included in the CTP classification [5] and MELD has been shown to be superior to the CTP score as an index of liver disease severity in patients awaiting liver transplantation and TIPS [6, 7] but not in patients with acute variceal bleeding [8].

Many recent studies have tried to give an answer to the question which prognostic score has better features in prediction of episodes of acute variceal bleeding, one of them was the creatinine-modified Child Turcotte Pugh score (CTP-crea) taking into account serum creatinine levels. The first analysis of CTP-crea score was performed by Angemayr et al [6] and then several recent studies quite clearly confirm that CTP-crea score contributed to improvement of the CTP score in assessment of survival [9-11].

In Vietnam, there have been many studies on the role of CTP and MELD scores in the prognosis of cirrhotic patients with acute variceal bleeding [12-15], but the validity of the CTP-crea score was not yet applied and compared with other score in clinical practice. The aim of this study was to compare validity of CTP-crea I and II scores with traditional CTP and MELD scores in assessment of five-day- and 6-week- mortality and rebleeding after acute variceal bleeding in patients with decompensated cirrhosis.

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2. MATERIALS AND METHODS

2.1. Patients

In this descriptive case series study we studied 118 consecutive cirrhotic patients with acute variceal bleeding, who were admitted to Hue University of Medicine and Pharmacy Hospital and Hue Central Hospital from April 2019 to August 2021.

2.2. Methods

The diagnosis of cirrhosis was based on clinical, laboratory and acute variceal bleeding was diagnosed by upper GI endoscopy. Patients with hepatocellular carcinoma, severe primary cardiopulmonary failure or intrinsic kidney disease were excluded.

According to our routine clinical practice, detailed medical history, complete physical examination, and a serie of laboratory tests were performed in all patients on the day of admission to calculate CTP, MELD, CTP - crea I and CTP - crea II scores.

- CTP scores: CTP-A score includes numerical value from 5 - 6 points, CTP-B from 7 - 9 points, CTP-C from 10 - 15 points.

Child Turcotte Pugh score

Parameter	1 point	2 points	3 points
Total bilirubin (mg/dL)	< 2	2 - 3	> 3
Serum albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
PT/INR	< 1.7	1.71 - 2.30	> 2.30
Ascites	No ascites	Medium	Medium to large
Hepatic encephalopathy	Stage 0	Stage I-II	Stage III-IV

- CTP-crea I score (5 - 19 points) was calculated by adding the points determined by serum creatinine level. With no added points were patients whose serum creatinine level was less than 1.3 mg/dL, and 4 points were added to numerical value of CTP score in patients whose serum creatinine level was higher than 1.3 mg/dL;

- CTP-crea II score (5 - 19 points) includes three categories as follows: 0 points are added to patients whose serum creatinine level does not exceed 1.3 mg/dL; 2 points are added to patients whose serum creatinine level is between 1.3 - 1,8 mg/dL; 4 points are added to patients whose serum creatinine level exceeds 1.8 mg/dL.

- MELD = {9.57 × ln [creatinine(mg/dL)] + 3.78 × ln [bilirubin(mg/dL)] + 11.2 × ln (INR) + 6.43};

Criteria of rebleeding within the first 5 days and 6 weeks according to Baveno V; criteria of acute kidney injury (AKI) according to International Club of Ascites.

2.3. Statistical Methods

The accuracy of the different score systems for predicting outcomes which include in death and rebleeding in first 5 days and in 6 weeks was evaluated through the urea under the receiver operating characteristic (ROC) curve. The accuracy of the different models as predictors were evaluated by the concordance (c)-statistics (equivalent to the area under the ROC curve). All data analyses were conducted using SPSS version 22.0. A two-tailed $p < 0.05$ was considered statistically significant.

3. RESULTS

In this case series study which included 118 variceal bleeding cirrhotic patients of which 107 (90.7%) were male. Mean age of the patients was 53.39 ± 11.97 year. Bleeding occurred most often in alcoholic liver cirrhosis (65.2%) and traditional CTP class in grade B and C were accounted for 80.5% of patients. Acute kidney injury (AKI) was presented in 16.7% of patients.

The patients with bleeding from esophageal varices were accounted for 82.2% and from gastric varices for 17.8% of which GOV2, IGV1, GOV1 were 11.9%, 3.4%, 2.5%, respectively.

The rate of early -rebleeding and -mortality (in the first 5 days) were 11.9% (14/118) and 6.8% (8/118), respectively. The rate of rebleeding and mortality in 6-week were 11.8% (13/110) and 7.3% (8/110), respectively.

3.1. Values of prognostic scores for early rebleeding and mortality (in first 5 days):

Table 1. Values of prognostic scores for early rebleeding

Scores	AUC	95% CI	Cutoff	Sensitivity (%)	Specificity (%)	p
CTP	0.671	0.522-0.821	10.5	50.0	81.7	< 0.05
CTP - crea I	0.788	0.661-0.916	10.5	71.4	80.8	< 0.05
CTP - crea II	0.771	0.642-0.901	10.5	64.3	80.8	< 0.05
MELD	0.754	0.609-0.898	16.5	71.4	74.0	< 0.05

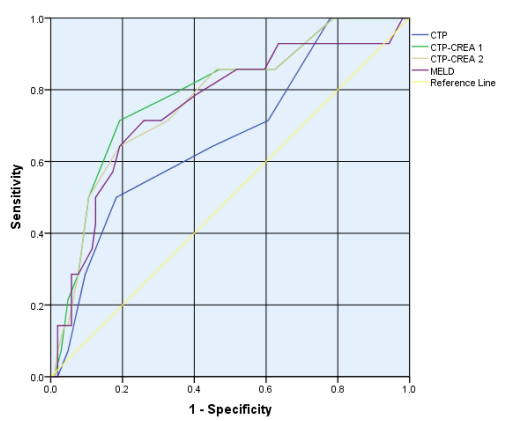

Figure 1. ROC curves of CTP, CTP-crea I, CTP-crea II and MELD score for early rebleeding

The prognostic value of early rebleeding (within the first 5 days) with the highest AUC of the CTP - crea I score, followed by CTP - crea II, MELD, CTP were 0.788, 0.771, 0.754, 0.671, respectively. When comparing each pair, the CTP - crea I score has significantly better prognostic value than CTP score (p = 0.048). The CTP - crea I score with a cutoff of 10.5 has a predictive value for early rebleeding with a sensitivity of 71.4% and a specificity of 80.8%; CTP - crea II with a cutoff of 10.5 has a predictive value for early rebleeding with a sensitivity of 64.3% and a specificity of 80.8%.

Table 2. Values of prognostic scores for early mortality

Scores	AUC	95% CI	Cutoff	Sensitivity (%)	Specificity (%)	p
CTP	0.775	0.607-0.943	10.5	75.0	81.8	< 0.05
CTP – crea I	0.860	0.700-1.000	10.5	87.5	79.1	< 0.05
CTP – crea II	0.859	0.700-1.000	10.5	87.5	80.0	< 0.05
MELD	0.849	0.708-0.989	17.5	87.5	80.0	< 0.05

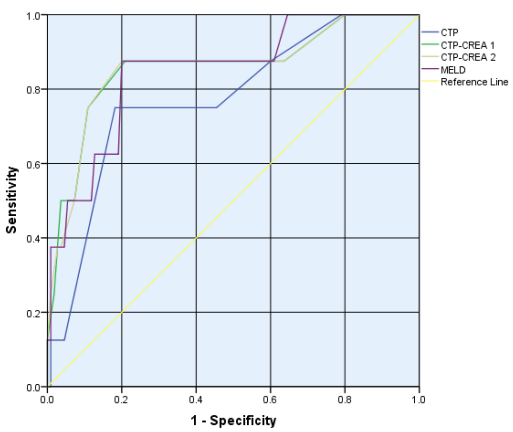

Figure 2. ROC curves of CTP, CTP-crea I, CTP-crea II and MELD score for early mortality

The prognostic value of early mortality with the highest AUC of the CTP - crea I score, followed by CTP - crea II, MELD, and traditional CTP were 0.860, 0.859, 0.849, 0.775, respectively. The CTP - crea I score with a cutoff of 10.5 has a predictive value of early mortality with a sensitivity of 87.5% and a specificity of 79.1%; CTP - crea II with a cutoff of 10.5 has a predictive value of early mortality with a sensitivity of 87.5% and a specificity of 80.0%.

3.2. Values of prognostic scores for 6-week rebleeding and mortality outcomes:

Table 3. Values of prognostic scores for 6-week rebleeding

Scores	AUC	95% CI	Cutoff	Sensitivity (%)	Specificity (%)	p
CTP	0.586	0.431-0.741	7.5	76.9	42.3	> 0.05
CTP - crea I	0.672	0.517-0.827	7.5	92.3	40.2	< 0.05
CTP - crea II	0.655	0.503-0.808	7.5	92.3	40.2	> 0.05
MELD	0.646	0.491-0.801	12.5	84.6	42.3	> 0.05

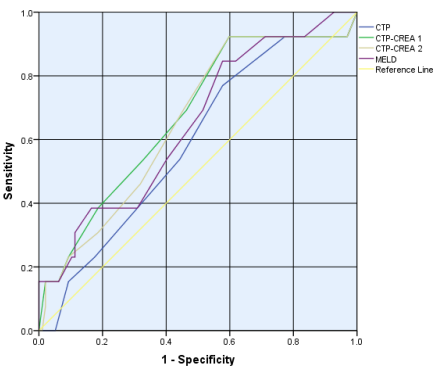

Figure 3. ROC curves of CTP, CTP-crea I, CTP-crea II and MELD score for 6-week rebleeding

When analyzing the area under the ROC curve, only the CTP - crea I score was statistically significant in the prognosis of 6-week rebleeding (AUC = 0.672) with a cut-off of 7.5 has a predictive value of 6-week rebleeding with a sensitivity of 92.3% and a specificity of 40.2%.

Table 4. Values of prognostic scores for 6-week mortality

Scores	AUC	95% CI	Cutoff	Sensitivity (%)	Specificity (%)	p
CTP	0.745	0.621-0.869	9.5	68.8	71.6	< 0.05
CTP - crea I	0.818	0.706-0.931	10.5	68.8	81.4	< 0.05
CTP - crea II	0.804	0.689-0.920	11.5	56.3	91.2	< 0.05
MELD	0.772	0.635-0.909	17.5	68.8	82.4	< 0.05

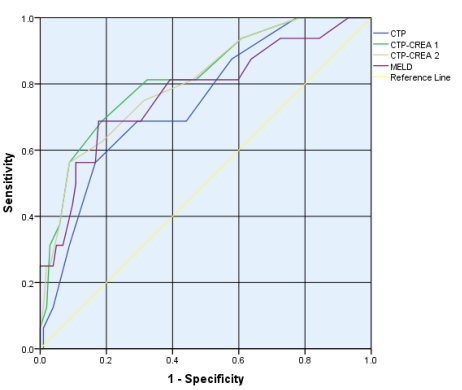

Figure 4. ROC curves of CTP, CTP-crea I, CTP-crea II and MELD score for 6-week mortality

The prognostic value of 6-week mortality with the highest AUC of the CTP - crea I score, followed by CTP - crea II, MELD, CTP were 0.818, 0.804, 0.772, 0.745, respectively. The CTP - crea I score with a cut-off of 10.5 has a predictive value of 6-week mortality with a sensitivity of 68.8% and a specificity of 81.4%; CTP - crea II with a cut-off of 11.5 has a predictive value of 6-week mortality with a sensitivity of 56.3% and a specificity of 91.2%.

4. DISCUSSION

This study was conducted at two tertiary hospitals in the Central region, Vietnam, which included 118 variceal bleeding cirrhotic patients of which 107 (90.7%) were male, mean age of the patients was 53.39 ± 11.97 year. Our result is consistant with previous studies in Vietnam [13-15] with the main cause of cirrhosis being alcohol accounted for 65.2%. The majority of cirrhotic patients belong to CTP class B or C (80.5%), this finding was reasonable because acute variceal bleeding often occur in patients with decompensated cirrhosis. There were 16.7% patients with AKI complications, this rate was lower than the study results of Kim JH et al with 28.0% [5]. In this study, patients with bleeding from esophageal varices were accounted for 82.2% and from gastric varices for 17.8%. This result is consistent with many studies in the world, esophageal variceal bleeding accounts for more than 80%, bleeding from ruptured gastric varices is less common, but often more severe and higher mortality rate [7], [16, 17].

4.1. Values of prognostic scores for early rebleeding and mortality (in first 5 days):

When analyzing the area under the ROC curve (Figure 1), all four scores above were valuable in predicting early rebleeding in variceal bleeding patients. In the details, CTP - crea I score has the highest predictive value with an AUC of 0.788, followed by CTP - crea II (0.771), MELD (0.754) and the lowest traditional CTP score with AUC: 0.671. This result showed that, adding creatinine to the traditional CTP score increases the predictive value of early bleeding outcomes in variceal bleeding cirrhotic patients.

For the early mortality outcome, analysis of the area under the ROC curve (Figure 2) showed that the CTP - crea I, CTP - crea II and MELD scores had good value in predicting this outcome with AUC were 0.860, 0.859 and 0.849, respectively. Meanwhile, the CTP score has the lowest prognostic value with AUC was 0.775. The CTP - crea scores significantly improved the predictive value of early mortality compared to traditional CTP score and better than the MELD score. The study of Hassanien M et al showed that the CTP - crea II score has the highest value in predicting mortality during hospital stay in hepatitis virus cirrhotic patients with acute variceal bleeding with AUC was 0.826 [9]. The results of other studies also show that rebleeding in the first 5 days plays an important outcome not only in predicting early mortality but also in predicting in 6-week mortality after admission [18].

4.2. Values of prognostic scores for 6-week rebleeding and mortality outcomes:

According to the Baveno consensus, 6-week mortality is recommended as the endpoint in the evaluation of the efficacy of treatment of an acute acute bleeding episode [3, 4]. Our study showed that, only the mean value of the CTP - crea I score has a statistically significant difference between the group of rebleeding and non-rebleeding within 6-week after the patients were admitted to the hospital. Analyzing the area under the ROC curve, the CTP - crea I score was significant in predicting this outcome with an AUC of 0.672, with a cut-off of 7.5 has a predictive value of 6-week rebleeding with sensitivity and specificity of 92.3% and 40.2%, respectively.

For the 6-week mortality outcome, when analyzing the area under the ROC curve (Figure 4), it was found that the CTP - crea I score had the best value in predicting this outcome in patients with acute variceal bleeding with AUC of 0.818, followed by CTP - crea II (AUC: 0.804), MELD (AUC: 0.772), the lowest traditional CTP with AUC of 0.745. The study by Conejo et al showed that the 6-week mortality predictive value of creatinine-modified CTP scores was improved compared with traditional CTP (AUC of 0.78 vs 0.75) [19]. In addition, another study performed on 126 hospitalized patients with end-stage cirrhosis showed that variceal bleeding patients with CTP - crea I score > 10.5 had an increased risk of the one month mortality higher than 3.1 times compared with patients without bleeding and CTP - crea II > 11.5, this risk was 3.7 times higher [18]. The cut-off values in this study are also similar to our study.

5. CONCLUSION

From the results of our study, it showed that the CTP - creatinine scores improved the traditional CTP score and was better than the MELD score in predicting the early and 6-week - rebleeding and -mortality outcomes in patients with acute variceal bleeding. Thereby, it is possible to routinely apply this score in clinical practice to stratify and predict outcomes in variceal bleeding cirrhotic patients in Vietnam.

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