

Prognostic Value OF MELD Score IN Acute Variceal Bleeding

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Abstract

Introduction: The Child-Pugh (CP) score has long been used in predicting mortality in acute variceal bleeding. The model of end-stage liver disease (MELD) score was originally determined to predict survival in cirrhotic patients undergoing surgery. It is now used to assign priority for liver transplantation. MELD score is a useful tool to assess prognosis in critically ill cirrhotic patients. There is conflicting results have been found on the comparison between MELD and CP score performance in predicting mortality after variceal bleeding. **The aim of this study** was to determine the prognostic use fullness of MELD score in cirrhotic patients presented with acute variceal bleeding. **Patients and methods:** This prospective study included 200 consecutive patients with liver cirrhosis presented with **first attack** of acute variceal bleeding. After giving appropriate pharmacological and endoscopic therapy, each patient was assigned a Child and MELD score and all patients were followed up for **6 weeks** to assess the outcome (re-bleeding or death). **Results:** Thirty nine patients (19.5%) died through out the follow up period of **6weeks**. Of these deaths, 12(6%) occurred within the first 5 days (in-hospital mortality) and 23 (11.5%) patients had re-bleeding. Patients who died in hospital had significantly higher MELD score as well as Child score compared to the survivors (35.6 ± 4.35 & 12.8 ± 0.9 vs. 13.8 ± 7.9 & 7.4 ± 2.43 respectively $P < 0.01$). Moreover MELD and Child scores were higher among patients who died allover the 6 weeks when compared to those who survived (28.9 ± 6.4 & 8.4 ± 5.3 vs. 10.56 ± 2.5 & 6.6 ± 1.2 respectively $P < 0.001$). MELD score was superior to Child score in prediction of both mortality and re-bleeding after acute variceal bleeding. As MELD score 12 and Child score 6 were associated with re-bleeding (accuracy 90.2% vs. 82% and AUC 0.739 vs. 0.591 respectively), while MELD score 17 and Child score 9 were associated with mortality (accuracy 98% vs. 87% and AUC 0.768 vs. 0.556 respectively). **Conclusion and recommendation:** MELD score allow for early identification of patients with acute variceal bleeding who are at substantially increased risk of re-bleeding or death over the short term. These patients may require care in more specialized units during the bleeding episode, and aggressive follow-up in the immediate post variceal bleed setting. [Researcher 2010;2(4):22-27]. (ISSN: 1553-9865).

Key words: Child score, liver cirrhosis, MELD score, Variceal bleeding.

Introduction:

Upper gastrointestinal variceal bleeding is one of the most serious complications in patients with chronic liver disease and carries a high mortality rate of 20-35%.¹ One of the difficulties with predicting prognosis in patients with cirrhosis following an episode of AVH has been that their outcome is influenced not only by the severity of the bleeding episode itself, but also by the severity of the underlying liver disease.² Several factors have been identified that are associated with mortality risk for an episode of acute variceal haemorrhage (AVH), including active bleeding at initial endoscopy, haematocrit level, amino-transferases levels, hepatic venous pressure gradient (HVPG), presence of portal vein thrombosis, serum bilirubin and albumin levels, hepatic encephalopathy, hepatocellular carcinoma.³ The Child-Pugh (CP) score has long been used in predicting mortality in acute variceal bleeding. The model of end-stage liver disease (MELD) score was originally determined to predict survival in cirrhotic patients undergoing surgery. It is

now used to assign priority for liver transplantation.⁴ MELD score is a useful tool to assess prognosis in critically ill cirrhotic patients. However, its short term prognostic superiority over the traditional CP score has not been definitely confirmed.⁵ There is conflicting results have been found on the comparison between MELD and CP score performance in predicting mortality after variceal bleeding. Some authors reported that MELD performance was not greater than CP score^{2,6,7}, while others showed a better performance of MELD overall.^{8,9} or in identifying those with a higher intrahospital mortality risk.^{10,11}

The aim of this study was to determine the prognostic use fullness of MELD score in cirrhotic patients presented with acute variceal bleeding.

PATIENTS AND METHODS: This prospective study was carried out at the Department of Gastroenterology and Hepatology, Ain Shams university Hospital. 200 consecutive cirrhotic patients presented with **first attack** of melena or haematemesis were included in the study. Patients with gastrointestinal bleeding due to causes

other than esophageal varices, hepatocellular carcinoma, portal vein thrombosis, intrinsic renal disease, heart failure and sepsis were excluded.

All patients underwent complete medical assessment upon presentation to the emergency room including history and physical examination with special emphasis on (blood pressure, pulse, local abdominal examination), laboratory examinations (CBC,AST,ALT, total and direct bilirubin, ALP, total protein, albumin, PT, INR, S cr, BUN, fasting and 2 hour blood glucose), abdominal U/S, feto- protein.

After first aid management, pharmacological therapy was given (octereotide 25ug/h for three days); Upper gastrointestinal endoscopy to identify the source of bleeding was performed to all patients within 24h of presentation, endoscopic injection sclerotherapy was performed if the source of gastrointestinal bleeding was believed to be from esophageal varices that is in the setting of active variceal bleeding defined as visible oozing or spurting of blood from a varix or in the stigmata of recent bleeding or high risk varices were

defined as follows (the presence of an adherent clot or white nipple or red signs on the varices (cherry red spot, red wale sign or haematocystic spots or the presence of varices or blood in the stomach).⁸ All patients were followed up for 6 weeks to assess the outcome (re-bleeding or death).

Re-bleeding was defined according to the Baveno criteria as recurrence of bleeding after the first 24 h and within 5 days of admission for the bleeding episode after initial bleeding control evidenced by new melena or haematemesis requirement of 2 units RBCS in a 24h time period and haemodynamic instability.¹²

Child classification: Each patient was assigned a score and a grade reflecting the severity of liver affection according to the numerical system of Child Turcotte Pugh (CTP). Class A (score 5-6) class B (score 7-9) and class C (score more than 9)¹³ as shown in table (1).

Table (1) Child Turcotte Pugh classification

Parameter	1	2	3
Ascites	Absent	Slight or controlled by diuretics	Moderate despite diuretic
Encephalopathy	None	Grade 1-2	Grade 3-4
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
PT(sec>normal)or INR	<4 <1.7	4-6 1.7-2.3	>6 >2.3

MELD score: Was calculated according to original formula proposed by the mayo clinic group: MELD score = $\{9.57 \times \log_e \text{creatinine (mg/dl)} + 3.78 \times \log_e \text{bilirubin (mg/dl)} + 11.2 \times \log_e \text{INR} + 6.4\}$. we used on-line available worksheet to compute MELD scores (<http://www.mayoclinic.org/gi-rst/mayomode15.html>).

Written informed consent was obtained from all participants.

Statistical analysis: All collected data were expressed as mean \pm SD and analyzed by using SPSS version 13 using the following tests: Student T test, multiple regression analysis, diagnostic validity test and Receiver operating curve (ROC). $P > 0.05$ was considered non significant, $P < 0.05$ was considered significant and $P < 0.01$ was considered highly significant.

Results: 200 patients with liver cirrhosis presented with *first attack* of upper GI bleeding and later found to have variceal source of bleeding on endoscopy were included, they were 146(73%) males and 54(27%) females, their mean age was 53.8 (range 36-71 years). Hepatitis C virus was the most frequent cause of liver cirrhosis (n =164(82%)) followed by hepatitis B virus

(n =26(13%), 8 (4%) patients had both hepatitis B and C, 2(1%) patients had pure bilharzial liver fibrosis, 23 HCV infected patients were co-morbid with bilharziasis. According to the Child Turcotte Pugh classification, 36 patients had class A, 126 patients class B and 38 patients class C. Esophageal varices were the source of bleeding in 168 (84%), while fundal varices were found in 6 (3%) and both esophageal and gastric varices were present in 24(12%) patients and sclerotherapy was done for all patients. Thirty nine patients (19.5%) died through out the follow up period of **6weeks**. Of these deaths, 12(6%) occurred within the first 5 days (in-hospital mortality) and 23 (11.5%) patients had re-bleeding.

The patients were divided into 3 groups:

Group I: One hundred and thirty eight patients survivors without re-bleeding (98(71%) were males & 40 (29%) were females their mean age was 52.13 ± 6.17).

Group II: Twenty three patients survivors with re-bleeding (16(69.6%) were males & 7(30.4%) were females their mean age was 55.30 ± 8.80).

Group III: Thirty nine patients died (in-hospital and overall 6-wk mortality rates were 6% and 19.5% respectively) (32 (82%) were males & seven (18%) were females their mean age was 55.00 ± 7.48).

Child and MELD scores compared to group I and group II (P<0.001) as shown in table 2.

Group III had higher serum Cr, liver enzymes,

Table (2): Comparison between the studied groups as regard laboratory data:

	Group I(138)	Group II(23)	Group III(39)	1vs.2	1vs.3	2vs.3
WBC	9.23 ± 3.36	9.59± 3.25	10.51 ± 3.90	>0.05	>0.05	>0.05
HB	8.8 ± 1.624	8.94 ± 2.17	8.02 ± 1.90	>0.05	>0.05	>0.05
Plat	109.13 ± 39	130.1 ± 79	101.74 ± 59	>0.05	>0.05	>0.05
Cr	0.76±0.27	0.99±0.26	2.38±0.95	>0.05	<0.01	<0.01
AIB	3.27± 0.45	2.65 ± 0.6	2.16 ± 0.55	<0.01	<0.01	<0.01
PT	13.4± 1.7	16.8±3.4	19.8 ± 5.37	<0.01	<0.01	<0.01
I.N.R	1.2 ± 0.28	1.62± 0.37	2.5 ± 0.65	<0.01	<0.01	<0.01
AST	52.9 ± 25.26	65.4 ± 40.5	368.0 ± 688	>0.05	<0.01	<0.01
ALT	46.1 ± 29.2	46± 27.3	177.3 ± 279	>0.05	<0.01	<0.01
Bili	1.06 ± 1.15	2.224 ± 1.6	5.27 ± 6.30	>0.05	<0.01	<0.01
Child	5.90 ± 1.06	7.96 ± 1.22	10.56 ± 2.5	<0.01	<0.01	<0.01
MELD	4.57 ± 5.02	13.3 ± 3.3	28.9 ± 6.4	<0.01	<0.01	<0.01

MELD and Child scores were higher among patients who died in-hospital or within 6 weeks compared to those who survived P < 0.01 as shown in table (3,4).

Table (3): Comparison between survivors and patients died in-hospital as regard Child and MELD scores

Score	Survived (188)	In-hospital death(12)	P
Child	7.4 ± 2.43	12.8 ± 0.9	<0.01
MELD	13.8 ± 7.9	35.6 ± 4.35	<0.01

Table (4): Comparison between survivors and patients died within 6 weeks as regard Child and MELD scores

Score	Survived (161)	Overall death(39)	P
Child	6.6 ± 1.2	10.56 ± 2.5	<0.01
MELD	8.4 ± 5.3	28.9 ± 6.4	<0.01

Table(5): Relationship between MELD score and incidence of death.

MELD score	NO	DEATH	
		NO	%
30-40	14	14	100%
20-29	35	24	68.6%
10-19	57	1	1.8%
0-9	94	0	0

$X^2 = 26.27$ $P < 0.01$ (HS)

The stepwise logistic regression analysis revealed that serum albumin < 2.9 and MELD score > 12 were independent predictors for rebleeding (F ratio (54.4) and P (< 0.001) , while serum bilirubin > 2.9 and MELD score > 17 were independent predictors for mortality (F ratio (143) and P (< 0.001).

The accuracy of MELD score 12 as a predictor of re-bleeding was superior to Child score 6 (accuracy 90.2% vs. 82% and AUC 0.739 vs. 0.591 respectively). Moreover the diagnostic performance of MELD score 17 was higher than Child score 9 in prediction of mortality (accuracy 98% vs. 87% and AUC 0.768 vs. 0.556 respectively).

Table (6): MELD versus Child scores in prediction of re-bleeding:

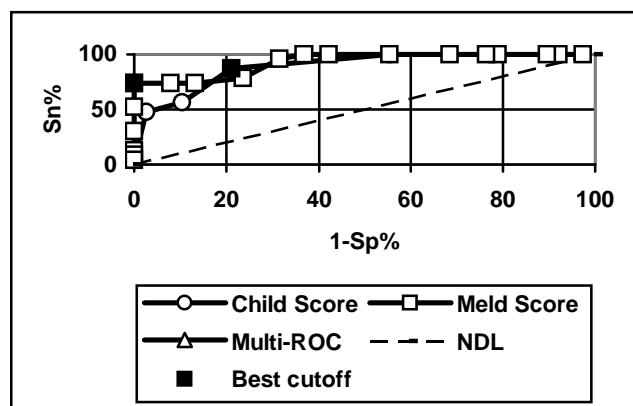
	Cut off	Sensitivity	Specificity	P -	P +	Efficacy
MELD	12	73.9	100.0	86.4	100.0	90.2
Child	6	87.0	78.9	90.9	71.4	82.0

Table (7): MELD versus Child scores in prediction of mortality:

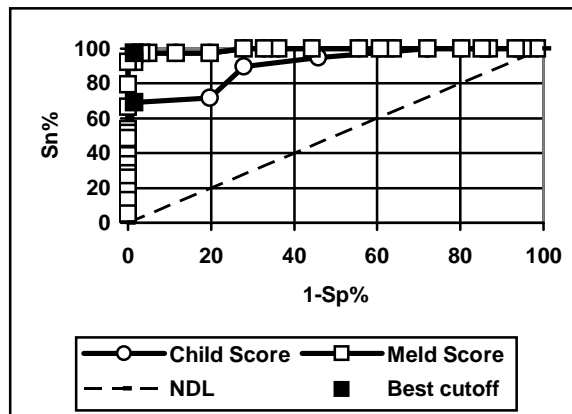
	Cut off	Sensitivity	Specificity	P -	P +	Efficacy
MELD	17	97.4	98.4	98.4	97.4	98.0
Child	9	69.2	98.4	83.3	96.4	78.0

Figure (1): MELD vs. Child scores as a predictor of re-bleeding

Fig. (2): MELD vs. Child scores as a predictor of mortality



AUC child score 0.591, MELD score 0.739



AUC Child score 0.556
MELD score 0.768

Discussion

In this study in-hospital, Six-week mortality rate and re-bleeding rate of first variceal bleeding were 6%, 19.5%, and 11.5% respectively. **Chojkier et al**¹⁴ reported a bleeding-related mortality rate of 35%, whereas **Afessa and Kubilis**¹⁵ found the hospital mortality rate of 21% in bleeding cirrhotic. **Chalasan et al**¹⁶ found in-hospital and 6-wk mortality rate were 14.2% and 17.5%. The variability in the mortality rate may be due to the advances made in the management of variceal bleeding. Prognosis of AVH is influenced by the severity of the bleeding episode as well as the severity of the underlying liver disease.² Moreover the serum creatinine level is an important predictor of survival in patients with liver cirrhosis.⁵ In this study non survivors had higher serum Cr compared to survivors and re-bleeders (2.38±0.95 vs.0.76±0.27 and 0.99±0.26 respectively P<0.001). Non survivors had renal impairment before the occurrence of the bleeding episode, also more severe bleeding may have given rise to acute renal failure due to hemodynamic instability and hypovolemic shock. Serum Cr might be considered as a predictor of mortality this results supported by **Faisal et al**¹⁷ found that serum creatinine independent predictors of mortality in patients with gastro-esophageal variceal

bleeding. We found an increase in the incidence of death in relation to MELD score as the mortality rate was 100% in patients with MELD score 30-40 decreased till reaching 0% with MELD score 0-9. Non survivors either in-hospital or allover the 6weeks had higher MELD and Child scores than survivors P<0.01, these results were supported by **Kamath et al**¹⁸ who found direct relation between MELD score and the mortality rate. This study revealed that MELD score was superior to Child score in prediction of both mortality and re-bleeding after AVH. As MELD score 12 and Child score 6 were associated with re-bleeding (accuracy 90.2% vs. 82% and AUC 0.739 vs. 0.591 respectively), while MELD score 17 and Child score 9 were associated with mortality (accuracy 98% vs. 87% and AUC 0.768 vs. 0.556 respectively) these results were in agreement with **Sempere et al**⁹ who stated that Child score 10 and MELD score 18 were the variables associated with mortality. The accuracy of MELD scores as predictors of 6-week mortality was better than that of Child score (c-statistics: 6 week MELD 0.804, Child 0.762). Moreover these findings were consistent with a previously published on the utility of the MELD score in patients with acute variceal bleeding.^{2,8,9,10,11,19,20}

Furthermore **Amitrano *et al***²¹ evaluated 172 cirrhotics [54 with hepatocellular carcinoma (HCC)] admitted for the first episode of variceal bleeding. Non survivors at 6 weeks and 3 months had significantly higher MELD scores on admission, compared with survivors. However, the area under the ROC curve of MELD and CTP scores were not significantly different for prediction of 6-week (0.80 vs. 0.76, $P = 0.25$) or 3-month (0.79 vs. 0.76, $P = 0.34$) mortality. The cut-off value of 15 points for MELD score had the best sensitivity and specificity to distinguish survivors from non-survivors, particularly, if MELD >15 with advanced HCC, the latter having independent prognostic significance for 3-month survival. However Some authors reported that MELD performance was not greater than CTP score.^{2,6,7,22,23} As **Chalasanani *et al***⁶ compared MELD and CTP scores in 239 consecutive cirrhotics following acute variceal bleeding, MELD was predictive of in-hospital mortality (c-index: 0.82; 95% CI: 0.72-0.92). However, its prognostication was not different than CTP (c-index: 0.85; 95% CI: 0.76-0.94). For 1-year mortality rates, MELD had a c-statistic of 0.75 (95% CI: 0.67-0.82) but it was not different than CTP score (c-statistic: 0.78; 95% CI: 0.70-0.86). Astonishing **Bambha *et al***⁸ reported that Child class was not predictive of mortality, while MELD score 18 and variceal re-bleeding had increased risk of death 6 weeks post-AVH.

The Child score is considered the cornerstone in the prognostic evaluation of cirrhotic patients. It has some drawbacks such as subjectivity of clinical parameters and limited discriminant ability.²⁴ On the other hand the MELD score, although it is more sophisticated, takes into consideration objective parameters (serum creatinine, the international normalized ratio (INR), bilirubin levels) and is computed with statistically derived coefficients on a continuous scale with no upper or lower limits, thus avoiding many drawbacks of the Child score.²⁵

Conclusion and recommendation:

MELD score allow for early identification of patients with AVH who are at substantially increased risk of re bleeding or death over the short term. These patients may require care in more specialized units during the bleeding episode, and aggressive follow-up in the immediate post variceal bleed setting. Such patients would also probably benefit from early referral to a liver transplant centre for consideration of candidacy for transplantation and expedited evaluation.

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