VALIDATION OF LACTATE AND THE SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE IN THE PREDICTION OF MORTALITY OF THE CRITICALLY ILL CIRRHOTIC PATIENTS.

Magdy El Serafy [1], Hanan Abd El Hafez *[1], Mohamed Alshafaey [2], Hanan Madany [3], Ismail Anwar [1], Rasha Eletreby [1]

[1]Endemic Medicine Department, Faculty of Medicine, Cairo University, Egypt.

[2]ICU Department, Faculty of Medicine, Cairo University, Egypt.

[3]Chemical Pathology Department, Faculty of Medicine, Cairo University, Egypt.

*Correspondence for Author

Dr. Hanan Abd El Hafez

Endemic Medicine Department, Faculty of Medicine, Cairo University, Egypt.

ABSTRACT

Background and Aim: The aim of this study was to determine the efficacy of SOFA score in comparison with liver specific scoring systems (Child-Turcotte-Pugh (CTP) and Model for End-stage Liver Disease (MELD)) in providing a predictive measure of mortality for critically ill cirrhotic patients. **Methodology**: Forty patients with cirrhosis were admitted to the ICU with varying indications. Informed consents were obtained from the patients' relatives. Patients were assessed clinically, by laboratory and imaging investigations .Different scorning systems such as CTP , MELD and Sequential Organ Failure Assessment (SOFA) scores were calculated on admission, and 48 hours, together with blood lactate level, measured on admission, at 6, 24 and 48 hours. The results were compared between died and surviving patients in a period of six weeks follow up to explore the significant determinants of ICU mortality for cirrhotic patients. **Results:** CTP, MELD and SOFA scores were significantly higher in patients who died than in those who survived. SOFA calculated 48 hours after ICU admission was shown to be the best prognostic model, with AUROC of 0.908. SOFA score predicted mortality of 72% if it exceeded 8. SOFA score tested at 48 h of admission also showed significant progression in survivors compared to non survivors in a decreasing manner. **Conclusions:** In terms of prognostic value, SOFA score is superior to MELD and CTP scores and can be used for prioritization of high risk patients and preservation of ICU resources and its reevaluation after 48 h adds to its prognostic significance.

KEYWORDS: liver cirrhosis, ICU, SOFA score.

INTRODUCTION

Cirrhotic patients admitted to the intensive care unit (ICU) have poor prognosis; with mortality rates ranging from 34 to 69%.[1] Discrimination of cirrhotic patients who will maximally benefit from ICU admission is greatly cost effective given the often limited ICU resources [2]. For this, several prognostic models are being used for comparison and quality assessment in different intensive care units (ICUs)[3]. Two types of such models can be used in cirrhotic patients: general prognostic models, those evaluating severity of illness, namely the Acute Physiology and Chronic Health Evaluation (APACHE) II [4] and Simplified Acute Physiology Score (SAPS) II [5]; and those quantifying organ dysfunction and failure as Sequential Organ Failure Assessment (SOFA) score [6], and disease-specific models as Child–Pugh score and Model for End-Stage Liver Disease (MELD) score.[7]

This study aims at prospective evaluation of the efficacy of the SOFA score in comparison with liver specific scoring system (CTP and MELD) in predicting the outcome of critically ill cirrhotic patients admitted to the ICU for prioritization of high risk patients and preservation of ICU resources.

Patients and methods

This prospective observational cohort study included 40 cirrhotic patients admitted to medical ICU in Kasr Al Aini, Cairo University, Endemic medicine department between February 2013 and December 2013 for intensive monitoring and/or treatment that could not be provided outside of the ICU. eg; (hepatic encephalopathy, spontaneous bacterial peritonitis, gastrointestinal bleeding, hepatorenal syndrome, severe sepsis).

1. Informed consent was obtained from the patients' closest relative and the study protocol was approved by our institute.

2. Patients younger than 17 years or those who needed immediate surgery were excluded.

3. Patients were subjected to the following:

4. Through clinical assessment and history of drug intake.

5. Laboratory investigations including: Liver biochemical profile, complete blood count, INR, renal biochemical profile, arterial blood gases were done on admission and were followed up according to the abnormalities detected.

6. Calculation of MELD [8], Child-Turcotte-Pugh [9] and SOFA [10] scores on admission and after 48 hours.

7. Blood lactate level was measured on admission, at 6, 24, and 48 hours after admission.

8. Abdominal ultrasound examination was done with special comment on parenchyma of liver, whether there are any focal lesions and its size, presence or absence of ascites and portal vein duplex, spleen, and renal condition.

Statistical analysis

1. Statistical analyses were performed using SPSS software for windows, version 21.

2. The ability of the model to discriminate between patients who live and patients who die was tested by the area under the receiver operating characteristic (AUC) curve.

3. Multivariate analysis (logistic regression model) was conducted to explore the significant determinants of ICU mortality for cirrhotic patients.

RESULTS

The present study included forty cirrhotic patients who were admitted to ICU for intensive monitoring and/or treatment; the mean age was (55.7±10.8 years); 60% were men. All of the patients were HCV Ab + ve, except for one patient whose cirrhosis was caused by autoimmune hepatitis. The causes of admission were active upper gastrointestinal bleeding (55%) followed by hepatic encephalopathy (30%), septic shock, respiratory failure and diabetic ketoacidosis (7.5%). The mean and SD of the CTP, MELD, and SOFA scores on admission were 11.5 ± 2.6, 19.9 ± 8.4 and 7.9 ± 4.0 respectively. The mean and SD of the CTP, MELD, and SOFA scores at 48 hours after admission were 10.8± 3.1, 17.2 ± 9.4 and 5.6 ± 4.4 respectively. In a follow up period of six weeks, fifteen patients (37.5%) died in the ICU and 25 patients (62.5%) survived. There was a significant difference between survivors and non-survivors in the occurrence of hepatic encephalopathy and hepatorenal syndrome during the ICU stay with *p* value 0.007 and 0.001 respectively. There was also statistical significant difference among the laboratory parameters such as albumin, prothrombin concentration, urea and sodium in favor of survivors and non survivors with *p* value 0.002, 0,004, 0.01 and 0.001 respectively. Each of the three scores as well as serum blood lactate was significantly higher in non survivors than survivors on admission and after 48 hours. On constructing ROC curve to discriminate predictive value of CTP, MELD and SOFA scores between survivors and non survivors, it showed that it had best results after 48 hours from admission with best sensitivity, specificity, positive and negative predictive value as shown in table 1.

Table 1: Child, MELD and SOFA scores and blood lactate level in prediction of mortality on admission and 48 hours after admission

Test variable	ROC	95% CI	P value	Cut-off point ≥	Sensitivity	Specificity	PPV	NPV
CHILD SCORE 0	0.841	0.711 – 0.971	<0.001	13	80.0%	84.0%	75.0%	87.5%
CHILD SCORE 48	0.907	0.810 – 1.00	<0.001	12	80.0%	88.0%	80.0%	88.0%
MELD SCORE 0	0.813	0.654 – 0.971	0.009	19	86.7%	72.0%	65.0%	90.0%
MELD SCORE 48	0.890	0.776 – 1.00	0.001	17	87.5%	80.0%	58.3%	95.2%
SOFA SCORE 0	0.768	0.565 – 0.970	0.025	8	86.7%	80.0%	72.2%	90.9%
SOFA SCORE 48	0.908	0.769 – 1.00	0.001	7	87.5%	92.0%	77.8%	74.2%
Lactate SCORE 0	0.710	0.509 – 0.911	0.08	2.6	86.7%	60.0%	56.5%	88.2%
Lactate SCORE 48	0.853	0.714 – 0.991	0.003	1.7	75.0%	80.0%	54.5%	90.9%

CI= confidence interval, PPV= positive predictive value, NPV= negative predictive value. P value <0.001 (significant).

As shown in *figure 1,* SOFA score at 48 hours after admission with AUC = 0.908 showed the best discriminative accuracy.
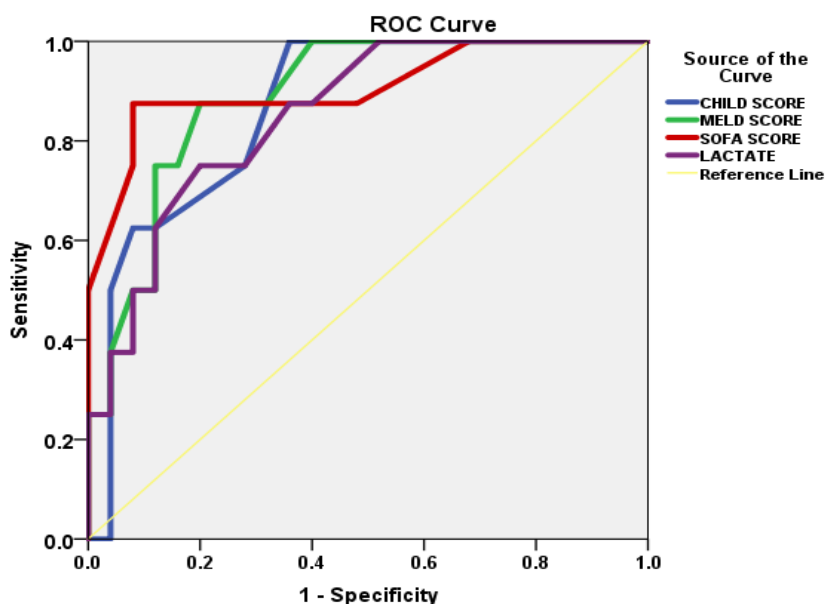

Figure 1: Area under curve (AUC) of CHILD, MELD, SOFA and blood lactate 48 hours after admission.

All scores displayed *p* > 0.1 as regards the degree of correspondence between predicted and observed mortality, confirming that predicted mortality was similar to observed mortality (i.e. good calibration). MELD and CHILD scores with p = 0.795 and 0.737 respectively, achieved the best calibration.

Multivariate Logistic regression for prediction of mortality with SOFA, Child and MELD scores was done. The only significant predictor of mortality was SOFA score while the other two variables did not significantly contribute in mortality. R2 (coefficient of determination) for SOFA score was 0.639, while R2 for Child and MELD scores was only 0.044.

On constructing Progression of each of the scores parameters within survivors & non survivors, it showed that there was a significant difference in progression of values of each of the scores from admission till 48 hours after admission within survivors as shown in (figure 2).
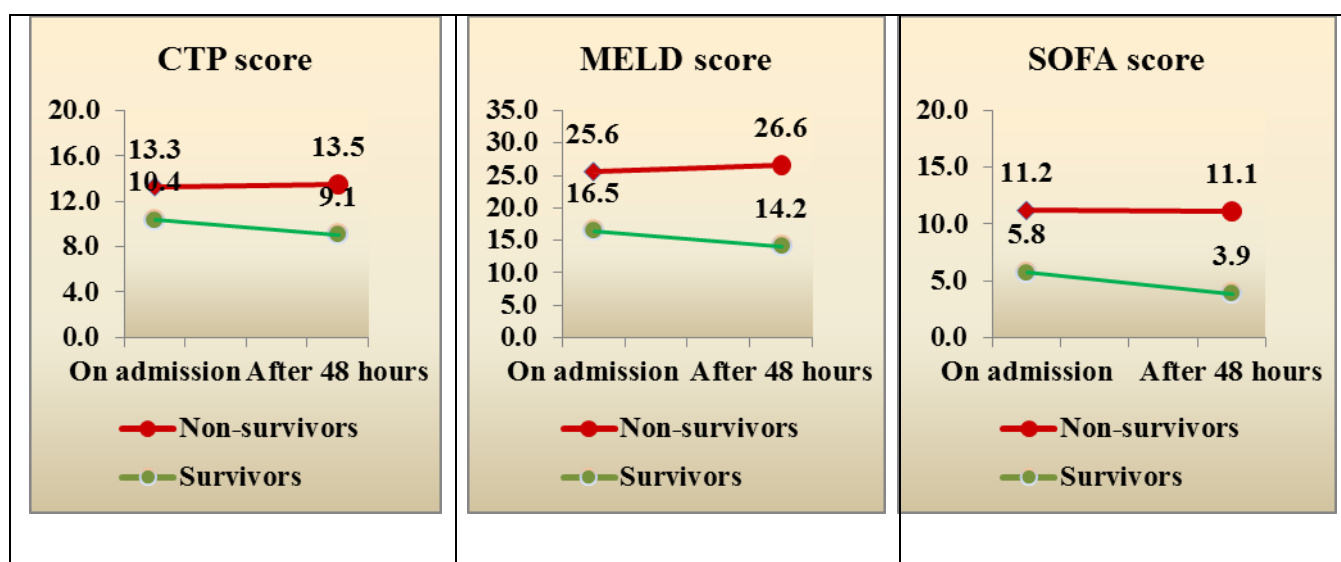

Figure 2: Progression of different scores within survivors & non survivors

DISCUSSION

The present study was conducted to describe the utility of SOFA, MELD and CTP scores in assessing the severity of organ dysfunction and in predicting ICU mortality in cirrhotic patients. In our study, patients with cirrhosis who died during their ICU stay displayed significantly higher values on all prognostic scores at admission when compared to those who survived. SOFA, MELD and CTP scores *p* values were 0.001, 0.001and 0.001 respectively with no statistical difference between them.

Galbois et al, in 2012 [11] pooled organ failure data of cirrhotic patients (SOFA component score >= 3) from four French studies , and showed that the presence of zero, one, two and three or more organ failures correlated with in hospital mortality rates of 14, 34, 66 and 83% respectively [12].In our study, SOFA score of >/=8 on admission showed mortality prediction about 72.2% and after 48 hours SOFA score of >/=7 showed mortality prediction of 77.8%.

SOFA score measured 48 hours after admission had AUC of 0.908 and showed the best discriminative accuracy among other scores .This finding matches with Cholongitas et al., (2008)[13] who reported that the AUROC of the SOFA score increased from 0.81 at the admission to 0.88 at 48 hours.

As regards calibration, SOFA score in our study had *p* value of 0.631 with good calibration but not the best, and the best calibration in our study was to MELD score.

To further elaborate on this point. It is worth noting that how well the model discriminates between individuals who will live and those who will die is termed discrimination, and how close the estimated probabilities of mortality correlate with the observed mortality over the entire range of probabilities is termed calibration. It is rather impossible for any model to have perfect calibration and discrimination at the same time. [14,15]

This does not match with Freire et al. (2011)[15] who found SOFA and MELD scores, with *p* = 0.686 and 0.267, respectively, achieved the best calibration, and this also emphasis the importance of careful evaluation of results concerning prognostication in terms of both calibration and discriminative abilities .

In our study, there was a link between high MELD scores and mortality, with AUC of 0.89 at 48 h. This matches with previous researches as with Cholongitas et al. (2006)[16] who demonstrated that MELD score showed high discrimination, almost the same as SOFA and superior to APACHE II and CTP scores. Similarly, Botta et al. (2003)[17] demonstrated that MELD score was superior to CTP score at predicting one year survival in cirrhotic patients.

As regards calibration, MELD score in our study displayed *p* value of 0.795, and achieved the best calibration among different scores. A meta-analysis on 118 studies showed that higher CTP scores were associated with higher mortality rates [18]**,** which matches with our study that showed a link between a high CTP and mortality in ICU patients with cirrhosis, with AUC of 0.90 at 48 h.

In our study, blood lactate level was significantly higher in non survivors than survivors both on admission, after 6, 24 and 48 hours with no significant differences in blood lactate at different times.

On constructing progression of each parameter within survivors & non survivors, it showed that it had significant difference in progression of value from admission till 48 hours after admission within survivors in CHILD, MELD and SOFA scores. This showed that these parameters are not only good predictors for mortality but also its progression from admission till 48 hours in a decreasing manner is a good indicator for survival, and this magnifies the importance to take several measures of different scores during ICU stay.

CONCLUSION

SOFA score calculated 48 h after ICU admission was shown to be the best prognostic model, among scoring systems studied (CTP and MELD) at predicting prognosis in cirrhotic patients admitted to the ICU, which emphasis the fact that prognosis of acutely ill patients with cirrhosis is influenced not only by the severity of hepatic insufficiency but mainly by the dysfunction of other organ systems and that they often have extra-hepatic organ dysfunction and die of multiple organ failure.

REFERENCES

1. Saliba F1, Ichai P, Levesque E and Samuel D (2013) Cirrhotic patients in the ICU: prognostic markers and outcomeCurr Opin Crit Care,19(2):154-60.

2. Cholongitas E, Agarwal B, Antoniadis N, Burroughs AK. (2012) Patients with cirrhosis admitted to an intensive care unit.J Hepatol; 57.

3. Azoulay E & Sprung CL. (2004) Family-physician interactions in the intensive care unit. Crit Care Med, 32:23-28.

4. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. (1985) APACHE II: a severity of disease classification system. Crit Care Med, 13:818-82.

5. Le Gall JR, Lemeshow S, Saulnier F. (1993) A new simplified acute physiology score (SAPS II) based on a European / North American multicenter study. JAMA, 270:2957-2963.

6. Strand K & Flaatten H. (2008) Severity scoring in the ICU, a review. *Acta Anaesthesiol Scand,* 52:467-478.

7. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, Borg PC. (2000) A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology,* 31:864-871.

8. Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Bensonj T, Edwards E, Therneau TM. (2008) Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med*, 359(10):1018-1026.

9. Child CG & Turcotte JG. (1964) Surgery and portal hypertension. *In: Child CG, 3ed. The Liver and Portal Hypertension,* 24: 453–464.

10. Vincent J, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining, Reinhart CK, Suter P, Thijs LG. (1996) The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med; 22: 707-710.

11. Galbois A, Trompette ML, Das V, Boëlle PY, Carbonell N, Thabut D, Housset C, Ait-Oufella H, Offenstadt G, Maury E. (2012) Improvement in the prognosis of cirrhotic patients admitted to an intensive care unit, a retrospective study.EurJGastroenterol Hepatol, 24; 897- 904.

12. Galbois A, Das V, Carbonell N, Guidet B (2013) Prognostic scores for cirrhotic patients admitted to an intensive care unit:which consequences for liver transplantation? Clin Res Hepatol Gastroenterol, 37:455-466.

13. Cholongitas E, Betrosian A, Senzolo M, Shaw S, Patch D, Manousou P. (2008) Prognostic models in cirrhotics admitted to intensive care units better predict outcome when assessed at 48 h after admission.*J Gastroenterol Hepatol,* 23:1223-1227.

14. Altman D & Royston P. (2000) What do we mean by validating a prognostic model? *Statistics in Medicine,* 19:453–473.

15. Freire P, Romãozinho J, Amaro P, Ferreira M, Sofia C. (2011) Prognostic scores in cirrhotic patients admitted to a gastroenterology intensive care unit.*Rev Esp Enferm Dig,* 103: 177-183.

16. Cholongitas E, senzolo M, Patch D, Show S, Hui C & Burroughs K. (2006) Review article: scoring systems for assessing prognosis in critically ill adult cirrhotics. *Aliment Pharmacol Ther,* 24: 453–464.

17. Botta F, Giannini E, Romagnoli P, Fasoli A, Malfatti F, Chiarbonello B, Testa E, Risso D, Colla G, Testa R. (2003) MELD scoring system is useful for predicting prognosis in patients with liver cirrhosis and is correlated with residual liver function: a European study. *Gut,* 52(1):134–139.

18. Aggarwal A, Ong JP, Younossi ZM, Nelson DR, Hoffman-Hoggl, Arroligo AC. (2001) Predictors of mortality and resource utilization in cirrhotic patients admitted to the medical ICU. *Chest,* 119:1489–1497.