Evaluation of the usefulness of sequential organ failure assessment (SOFA) and acute physiology and chronic health evaluation III (APACHE III) scoring systems in outcomes prediction of critically ill cirrhotic patients

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Abstract: Background: The ability to objectively estimate patient risk for mortality or other important outcomes is a new undertaking for clinical research. Empirically based risk assessments for important clinical events have been extremely useful in evaluating new therapies, in monitoring resource utilization, and in improving quality assessment. Attempts at prediction, however, have been much less successful in forecasting individual patient risk or in reducing the uncertainty of daily clinical decision making. Objective risk estimates are particularly important in the high-cost, emotional, and technologically demanding environments of intensive care units (ICUs). Because of the high costs of ICUs, precise quality assurance and utilization management strategies are essential. Knowledge of the risk faced by a patient on the day of ICU admission could provide an empiric basis for quality assurance and utilization activities. Estimates during the course of therapy could be useful in investigating the optimal time for discharge or in deciding how long to continue therapy. **Objective:** The aim of our study was to evaluate the usefulness of sequential organ failure assessment (SOFA) and acute physiology, age, chronic health evaluation III (APACHE III) scoring systems obtained on the first day of intensive care unit (ICU) admission in predicting hospital mortality in critically ill cirrhotic patients. **Methods:** The study enrolled 60 cirrhotic patients consecutively admitted to ICU of TBRI from October 2018 to July2019. Clinical and laboratory variables were analyzed as predicators of survival. Information considered necessary to calculate the SOFA and APACHE III scores on the first day of ICU admission was also gathered. **Results:** The score-matched analytical data showed that the predictive accuracy of SOFA is superior to that of APACHE III in evaluating critically ill patients with cirrhosis. SOFA score has cut of point ≤9, Sensitivity=96.67. Specificity=96.67, PPV=96.7 and NPV =96.7. APACHEIII score has cut of point ≤85, Sensitivity=96.67, Specificity=80, PPV=82.9 and NPV =96.0. **Conclusion:** Our results provide additional evidence that SOFA scores differ significantly in outcome prediction of patients with cirrhosis matched according to APACHE III score. The score-matched analytical data showed that the predictive accuracy of SOFA is superior to that of APACHE III in evaluating critically ill patients with cirrhosis. When considering cost-effectiveness and ease of implementation, the SOFA score is recommended for evaluating long-term prognosis in critically ill patients with cirrhosis.

[Mervat Mohamed Marzouk; Mervat Mohamed Eldmarawy; Sameh Salem Hefny; Rania Mahrous Aly; Ahmed Nasser Abdel Fattah Mahmou. **Evaluation of the usefulness of sequential organ failure assessment (SOFA) and acute physiology and chronic health evaluation III (APACHE III) scoring systems in outcomes prediction of critically ill cirrhotic patients.** *Nat Sci* 2019;17(11):24-30]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 3. doi:10.7537/marsnsj171119.03.

Keywords: Evaluation; sequential organ failure assessment (SOFA); acute physiology and chronic health evaluation III (APACHE III); cirrhotic patient

1. Introduction

Accurate prognostic predictors are crucial for patients admitted to an intensive care unit (ICU). Prognostic scoring systems are useful for clinical management such as predicting a survival rate, making decisions, and facilitating explanation of disease severity by clinical physicians ***(Chung-Ming et al., 2014).***

Several predictive scoring systems have been developed and validated in general intensive care unit populations, to evaluate the severity of illness and prognosis. Although some prognostic models have also been validated in cirrhotics admitted to ICU because there has been renewed interest in critically ill cirrhotics due to increasing use of sophisticated (but more expensive) technology and medical care: e.g. trans jugular intrahepatic Porto systemic shunt placement in uncontrolled gastrointestinal bleeding (GIB) and bio artificial livers in liver failure. In addition, liver transplantation can offer long-term survival. These new therapeutic possibilities require reliable prognostic factors to construct useful therapeutic algorithms for critically ill cirrhotics. Conversely, it is useful to have some basis to assess

when ICU therapy may be futile ***(Cholongitas et al., 2006).***

The APACHE III score, one of the widely used scoring systems, is known for its accuracy in predicting mortality. However, the APACHE III scoring system was initially developed for various diseases and not exclusively for liver-related diseases. By contrast, the SOFA score, another widely used scoring system, is superior to the APACHE III scoring system for assessing specific organ dysfunction including cirrhosis ***(Chung-Ming et al., 2014)***.

This study is going to discuss the different clinical characteristics and Outcomes of cirrhotic patients assessed by SOFA compared with these assessed by APACHE III scores.

Aim of the Work

To determine the accuracy of APACHE III and SOFA scores in outcome prediction for cirrhotic patients.

Patient and Methods

Study Design:

This study was conducted as a prospective randomized study on 60 cirrhotic patients, admitted in the intensive care unit in Theodor Bilharz Research Institute from October 2018 to July 2019. Informed Consent was taken from all subjects.

Study Population:

Patients were enrolled in the study according to the following criteria: All adult cirrhotic patients (aged 18 years or above), of both sexes, who will be admitted to ICU with varying indication e.g. Spontaneous bacterial peritonitis, hepatic encephalopathy and septic shock...etc.

Diagnosis of liver cirrhosis will be done by abdominal ultrasound findings which reveal the presence of liver cirrhosis of any degree in the abdominal ultrasound study.

Patients with the following criteria were excluded from the study: Patients aged less than 18 years old, patients with hepatocellular carcinoma diagnosed by documented previously done histopathological analysis, and patients discharged from the ICU during the first 24 hour.

Sample Size was done using medical program, setting alpha error at 5% and power at 80%. result in previous study ***(Chung-Ming et al., 2014)***, showed that APACHE III has an AUC =0.783 for prediction for mortality in cirrhotic patients compared to an AUC =0.9 for SOFA score, based on this 60 cirrhotic patients will be needed (30 died and 30 lived).

Study Tools:

All patients will be subjected to the following, 24 hours after admission: (1) Thorough history and clinical examination. (2) Liver function tests: serum bilirubin (total and direct) and serum albumin. (3) Complete blood count. (4) Serum urea, creatinine and BUN levels. (5) Arterial blood gas in a sample about 1ml from the radial artery. (6) Serum sodium levels.

(7) Serum Glucose levels. (8) Urine Output (cc/day). (9) Abdominal ultrasonography.

All laboratory investigations will be done through 24 hours of admission to ICU. All laboratory investigations will be done through a 5 ml blood sample taken from a peripheral vein after sterilization of the skin with povidone iodine except arterial blood gas sample which will be done through about 1ml of blood taken from radial artery after sterilization of the skin. APACHE III and SOFA scores will be calculated for each patient on admission. APACHE III and SOFA scores will be compared between deceased and discharged patients.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The comparison between groups regarding qualitative data was done by using ***Chi-square test*** and/or **Fisher exact test** when the expected count in any cell found less than 5. The comparison between two groups regarding quantitative data and parametric distribution was done by using **Independent t-test. Receiver operating characteristic curve (ROC)** was used to assess the best cut off point with its sensitivity, specificity, positive predictive value, negative predictive value and area under curve (AUC) of the studied marker. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

3. Results

Table (1): Demographic data in APACHEIII group

		Alive	**Died**	**Test value**	**P-value**	**Sig.**
		No. = 13	**No. = 17**			
Age	Mean±SD Range	62.69 ± 9.76 49 – 81	67.29 ± 6.60 56 – 77	-1.541•	0.135	NS
Sex	Male Female	9 (69.2%) 4 (30.8%)	6 (35.3%) 11 (64.7%)	3.394*	0.065	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Table (2): Clinical characteristics of APACHEIII-matched group

		Alive	Died	Test value	P-value	Sig.
		No. = 13	No. = 17			
Pulse	Mean ± SD Range	81.46 ± 8.96 65 – 96	87.18 ± 8.44 69 – 98	-1.790•	0.084	NS
MBP	Mean ± SD Range	83.23 ± 10.28 70 – 105	68.32 ± 12.75 36.5 – 90	3.443•	0.002	HS
Temp	Mean ± SD Range	37.27 ± 0.31 37 – 37.8	36.99 ± 3.15 25 – 39	0.320•	0.752	NS
RR	Mean ± SD Range	19.00 ± 3.27 14 – 25	24.71 ± 9.49 18 – 60	-2.068•	0.048	S
UOP	Mean ± SD Range	1784.62 ± 321.06 1300 – 2200	1223.53 ± 360.17 750 – 1850	4.428•	<0.01	HS
ARF	Yes No	4 (30.8%) 9 (69.2%)	15 (88.2%) 2 (11.8%)	10.476*	0.001	HS
GCS Visual	Mean ± SD Range	3.77 ± 0.44 3 – 4	2.71 ± 0.85 2 – 4	4.106•	<0.01	HS
GCS Speech	Mean ± SD Range	4.77 ± 0.44 4 – 5	3.24 ± 0.97 2 – 5	5.286•	<0.01	HS
GCS Motor	Mean ± SD Range	5.77 ± 0.44 5 – 6	4.41 ± 0.87 3 – 6	5.133•	<0.01	HS
Total. GCS	Mean ± SD Range	14.31 ± 1.32 12 – 15	10.35 ± 2.50 7 – 15	5.171•	<0.01	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Table (3): Laboratory parameters of APACHEIII-matched group

		Alive	Died	Test value	P-value	Sig.
		No. = 13	No. = 17			
PaO2	Mean ± SD Range	92.38 ± 27.99 17 – 120	96.29 ± 16.48 60 – 120	-0.479•	0.636	NS
AaDO2	Mean ± SD Range	146.23 ± 18.33 121.4 – 178.9	156.88 ± 19.40 125.2 – 198.9	-1.526•	0.138	NS
Hematocrit%	Mean ± SD Range	31.58 ± 4.85 23.5 – 38.4	29.91 ± 3.53 24 – 37	1.095•	0.283	NS
WBC Count	Mean ± SD Range	14.39 ± 4.88 7.2 – 25	17.38 ± 3.98 9.13 – 22	-1.839•	0.077	NS
S.Creatinine	Mean ± SD Range	1.81 ± 0.57 0.94 – 2.8	2.62 ± 0.69 1.22 – 3.8	-3.408•	0.002	HS
S.BUN	Mean ± SD Range	46.00 ± 20.60 14 – 90	64.94 ± 12.83 28 – 90	-3.095•	0.004	HS
S.Na	Mean ± SD Range	139.69 ± 6.06 125 – 148	139.47 ± 7.95 123 – 154	0.084•	0.934	NS
S.ALBUMIN	Mean ± SD Range	2.52 ± 0.36 1.8 – 2.9	2.14 ± 0.21 1.8 – 2.6	3.545•	0.001	HS
S.Bilirubin	Mean ± SD Range	1.76 ± 0.94 0.9 – 4.5	3.34 ± 1.13 1.3 – 6.4	-4.054•	<0.01	HS
S.Glucose	Mean ± SD Range	127.08 ± 46.76 90 – 215	102.41 ± 30.91 67 – 170	1.738•	0.093	NS
paCO2	Mean ± SD Range	33.54 ± 3.93 25 – 39	27.00 ± 4.72 21 – 38	4.036•	<0.01	HS
pH	Mean ± SD Range	7.38 ± 0.07 7.28 – 7.56	7.35 ± 0.07 7.26 – 7.44	1.154•	0.258	NS
Primary Comorbidity	Cirrhotic	13 (100.0%)	17 (100.0%)	NA	NA	NA

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

*: Chi-square test; •: Independent t-test; ‡: Mann Whitney test

Table (4): Show SOFA score for APACHEIII-matched group

		Alive	Died	Test value•	P-value	Sig.
		No. = 13	No. = 17			
APCHE III Score	Mean ± SD Range	55.69 ± 16.61 43 – 104	95.00 ± 15.86 68 – 113	-6.592	<0.01	HS
SOFA Score	Mean ± SD Range	6.92 ± 1.19 6 – 10	13.38 ± 1.19 10 – 15	-14.725	<0.01	HS

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test

Table (5): ROC Curve interpretation of APACHEIII-matched group

Parameter	AUC	Cut of Point	Sensitivity	Specificity	PPV	NPV
APCHE score	**0.955**	**≤69**	**92.31**	**94.12**	**92.3**	**94.1**
SOFA score	**0.998**	**≤10**	**100.0**	**94.12**	**92.9**	**100.0**

PPV: positive predictive value NPV: negative predictive value

The ROC curve show the SOFA score has higher discrimination ability in the patients with cirrhosis than APACHEIII score (with AUC 0.99) with high sensitivity, PPV and NPV…cut of point≤10.

Table (6): Demographic data of SOFA-matched group

		Alive	Died	Test value	P-value	Sig.
		No. = 17	No. = 13			
Sex	Male Female	9 (52.9%) 8 (47.1%)	10 (76.9%) 3 (23.1%)	1.824*	0.177	NS
Age	Mean ± SD Range	61.94 ± 5.64 54 – 73	63.62 ± 5.92 54 – 73	-0.788•	0.437	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (7): Clinical characteristics of SOFA-matched group

		Alive	Died	Test value	P-value	Sig.
		No. = 17	No. = 13			
MBP	Mean ± SD Range	85.00 ± 5.59 70 – 95	70.00 ± 7.36 60 – 80	6.353•	<0.01	HS
UOP cat.	>500 200 – 500 <200	17 (100.0%) 0 (0.0%) 0 (0.0%)	5 (38.5%) 7 (53.8%) 1 (7.7%)	14.266*	0.001	HS
Total.GCS	Mean ± SD Range	13.71 ± 0.69 12 – 15	7.54 ± 3.15 5 – 13	7.867•	<0.01	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test; •: Independent t-test

Table (8): Laboratory parameters of SOFA-matched group

		Alive	Died	Test value•	P-value	Sig.
		No. = 17	No. = 13			
FIO2	Mean ± SD Range	27.47 ± 7.39 21 – 40	48.85 ± 10.83 35 – 60	-6.427	<0.01	HS
Platelets	Mean ± SD Range	85.94 ± 21.19 41 – 133	74.15 ± 10.17 60 – 92	1.844	0.076	NS
PaO2	Mean ± SD Range	97.53 ± 7.50 90 – 110	109.00 ± 10.75 90 – 120	-3.445	0.002	HS
S.Creatinine	Mean ± SD Range	1.77 ± 0.65 1.02 – 2.8	2.77 ± 0.81 1.8 – 4.5	-3.758	0.001	HS
S.Bilirubin	Mean ± SD Range	2.22 ± 0.57 1.2 – 3.2	3.48 ± 0.81 2.4 – 4.8	-5.007	<0.01	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test

Table (9): Significant of M.V and Vasopressor in outcome prediction

		Alive		Died		Test value*	P-value	Sig.
		No. = 17	%	No. = 13	%			
Mechanical Ventilation	Yes	0	0.0%	11	84.6%	22.713	<0.01	HS
	No	17	100.0%	2	15.4%			
Vasopressor	Yes	3	17.6%	13	100.0%	20.074	<0.01	HS
	No	14	82.4%	0	0.0%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*: Chi-square test

Table (10): Show APACHEIII score for SOFA-matched group

		Alive	Died	Test value•	P-value	Sig.
		No. = 17	No. = 13			
APCHE III Score	Mean ± SD	68.41 ± 10.92	100.15 ± 18.42	-5.894	<0.01	HS
	Range	47 – 85	45 – 115			
SOFA Score	Mean ± SD	6.76 ± 1.79	14.69 ± 2.56	-9.992	<0.01	HS
	Range	4 – 9	8 – 18			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test

Table (11): ROC Curve interpretation of SOFA- matched group

Parameter	AUC	Cut of Point	Sensitivity	Specificity	PPV	NPV
APCHE score	**0.923**	**≤85**	**100.0**	**92.31**	**94.4**	**100.0**
SOFA score	**0.977**	**≤9**	**100.0**	**92.31**	**94.4**	**100.0**

PPV: positive predictive Value, NPV: negative predictive value

The ROC curve show the SOFA score has a higher discrimination ability in the patients with cirrhosis than APACHEIII score (with AUC= 0.97) with high sensitivity, specificity, PPV and NPV….cut of points ≤9.

4. Discussion

Based on our research, this is the study designed to compare the usefulness of different scoring systems for outcome prediction in patients admitted to an ICU with cirrhosis by using a score-matched method.

In our study, 60 patients recruited from the Intensive Care Units of Theodor Belharz Research Institute Hospital and were classified into APACHEIII-matched group (n=30) and SOFA –matched group (n=30). several clinical characteristics and outcomes of critically ill cirrhotic patients with matched APACHE III compared by those matched SOFA scores.

Prediction abilities of the APACHE III and SOFA scoring systems were compared; Table 5, 10, 14 lists the calibration and discrimination of the models.

According to demographic data, APACHEIII and SOFA –matched groups showed no significant differences (p-value >0.05)

According to laboratory parameters in APACHEIII score showed MBP, UOP, GCS, S.Creatinine, S.BUN, S.Albumin and PCO2 have highly impact on outcome (p-value <0.01)

According to laboratory parameters in SOFA score showed MBP, UOP, GCS, FIO2, PaO2, S, Creatinine, S, Bilirubin, Mechanical Ventilation and Vasopressor have highly impact on outcome (p-value <0.01)

In the APACHE III-matched group, the SOFA scoring system demonstrated the highest prediction ability with high specificity, PPV and NPV (AUROC = 0.99) among two systems.

In the SOFA-matched group, the SOFA scoring system was the most accurate predictor among both systems (with AUROC = 0.97)

To determine the selected cut-off points for predicting in-hospital mortality, the sensitivity, specificity, PPV and NPPV were demonstrated in (Table 14).

- SOFA score has **cut of point ≤9, Sensitivity=96.67, Specificity=96.67, PPV=96.7 and NPV =96.7**
- APACHEIII score has **cut of point ≤85, Sensitivity=96.67, Specificity=80, PPV=82.9 and NPV =96.0**

Recent studies have supported the efficacy of the SOFA scoring system for assessing the extent of organ dysfunction and outcome prediction in various groups including critically ill patients with cirrhosis.

Our study was similar to the results found by

- ***Chung-Ming et al. (2014)*** study which show that the predictive accuracy of **SOFA is superior** to that of APACHE III in evaluating critically ill patients with cirrhosis **(AUROC =0.810 ± 0.056 vs 0.624 ± 0.060).**
- ***Chen and Tian (2006)*** show The SOFA and APACHE III models displayed good areas under the receiver–operating characteristic curve (**0.917±0.028 and 0.912±0.029, respectively**). Finally, Both SOFA and APACHE III scores are excellent tools to predict the hospital mortality in critically ill cirrhotic patients. The overall predictive accuracy of SOFA and APACHE III is superior to that of Child–Pugh system. The role of these scoring systems in describing the dynamic aspects of clinical courses and allocating ICU resources needs to be clarified.
- ***Tsai and Chen (2003)*** show the SOFA score demonstrated an excellent discriminative power *(AUROC 0.901),* whereas the performance of Child-Pugh scores is clearly poorer (AUROC 0.748).
- ***Levesque and Hoti (2012)*** show ROC curve analysis demonstrated that **SOFA (0.92)** and SAPS II (0.89) scores calculated within 24h of admission predicted ICU mortality better than the Child-Pugh score (0.79) or MELD scores with (0.79-0.82).
- ***Cholongitas et al. (2006)*** study recommended using of SOFA and APACHE scores in ICU better than new scores e.g. (MELD) in outcome prediction (***SOFA: 0.94 in ROC curve).***

Also in contrast to our study

- ***Knaus and Wagner (1991)*** show that APACHE III score is good indicator for outcome prediction (**AUC = 0.90, p<0.0001**)
- ***Vincent et al. (1996)*** show the assessment of organ dysfunction/failure remains difficult, but the development of the SOFA score represents a valuable approach and most accurate risk estimating morbidity (not mortality) score.

However in a relatively smaller number of studies, like the study performed by ***Deven Juneja et al. (2011)*** show Prognostic scores, especially SOFA and MELD, may guide in deciding which patients may benefit from aggressive management and MV. With area under curve was 0.77 (95% CI, 0.65-0.86) for APACHE II, **0.94 (95% CI, 0.85-0.98) for SOFA**, 0.83 (95% CI, 0.7-0.96) for CP, and **0.93 (95% CI, 0.85-0.98) for MELD (*P*=.096)** in predicting 30-day mortality.

These results of other studies support our study and provide evidence for discriminatory power of SOFA score in prediction of outcome of cirrhotic patients.

Both scoring systems predicted mortality in the patients with cirrhosis. But the SOFA scoring system demonstrated the highest prediction ability.

Although the SOFA score includes a fewer number of items and does not assess age and comorbid conditions, it enhances its simplicity and demonstrates high discriminatory power for predicting outcome of critically ill patients with cirrhosis.

Prognostic scoring models such as APACHE III assume that mortality is affected by physiological disturbances that occur early in the course of illness, whereas organ dysfunction-scoring systems such as SOFA allow determination of organ dysfunction at the time of admission and at regular intervals throughout the stay in an ICU, thus allowing for the assessment of changes in organ function.

Although the SOFA score was originally used to describe morbidity, it was also used in mortality prediction. The accuracy of mortality predictions was higher than other scoring systems all through other studies.

The SOFA score is simpler for assessment than the APACHE III score by clinicians. Meanwhile, the SOFA score allows for sequential measurements and more accurately reflects the dynamic aspects of disease processes and may provide information of higher quality on the mortality risk. Therefore, the SOFA score is a superior and easier-to implement model for predicting mortality in the patients with cirrhosis, with a cut-off value of 9 points.

Despite the encouraging results of the present study, several potential limitations should be considered. **First:** This was a prospective study performed at a single tertiary-care medical Centre (TBRI), which limits generalization of the findings. **Second:** The patient population comprised a high proportion of patients with hepatitis C virus infection. Therefore, this study has limited applicability to patients with hepatitis B virus infection or those with alcohol dependence. **Third:** This study discusses hospital mortality and short term outcome.

By studying a larger number of patients, with different causes of cirrhosis could have increased the power of our study in revealing the accuracy of APACHE III and SOFA score in outcome prediction.

Conclusion

Our results provide additional evidence that SOFA scores differ significantly in outcome prediction of patients with cirrhosis matched according to APACHE III score. The score-matched analytical data showed that the predictive accuracy of SOFA is superior to that of APACHE III in evaluating critically ill patients with cirrhosis. When considering cost-effectiveness and ease of implementation, the SOFA score is recommended for evaluating long-term prognosis in critically ill patients with cirrhosis.

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7/27/2019