Child-Pugh versus APACHE II Scoring Systems for Prognosis Prediction of Acute Variceal Upper Gasterointestinal Bleeding

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Abstract: Background Accurate risk stratification for patients with acute variceal upper gastrointestinal bleeding would be useful for identifying low-risk patients, who might not require hospitalization and high-risk patients, who require aggressive care in a closely monitored setting. **Objectives:** To evaluate the application of Child-Pugh and APACHE II scoring systems in the prediction of outcome of patients with acute variceal upper gastrointestinal bleeding. **Patients and Methods:** 100 patients were included prospectively. Clinical and laboratory data necessary to both Child-Pugh and APACHE II scores were calculated through 24 hours following admission. During hospitalization patients' outcome was reported. Discrimination was tested using the receiver operating characteristic curves and by comparing areas under the curve. **Results:** 26 patients developed one or more complications, 13 patients developed rebleeding without statistical significant Child-Pugh and APACHE II scores, 3 patients developed renal failure, 21patients had hepatic encephalopathy. All Child A patients survived, only one out of Child B patients died (2.2%) and 9 patients in Child C died (23.7%). Child-Pugh score cut off value for mortality was more than 10, with sensitivity 90%, specificity 77.5%, positive predictive value 31%, negative predictive value 98.6% and accuracy 80.4%. While applying APACHE II score, it was found that the cut off value was more than 15, with sensitivity 70%, specificity 77.8%, positive predictive value 25.9%, negative predictive value 95.9% and accuracy 70.6%. **Conclusions:** APACHE II and Child-Pugh scoring systems are useful for risk stratification of patients with acute variceal bleeding regarding mortality but not for rebleeding. It is preferred to use Child-Pugh score as a more sensitive score as well as more easy to apply to predict mortality.
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Keywords Child-Pugh score; APACHE II score**;** Variceal bleeding; Mortality

1. Introduction

Acute upper gastrointestinal hemorrhage is a life-threatening condition with mortality rate of 5-14% that needs hospitalization and billions of money spent annually for inpatient care of this problem (Alempijevic *et al.,* 2007, van Leerdam, 2008). Most patients are at low risk for further hemorrhage and mortality, but they remain in the hospital for several days with risks of hospital complications. Less common are patients readmitted soon after discharge for rebleeding. Both scenarios represent inefficiency resulting from uncertainty in predicting patient outcome. Accurate risk stratification would be useful for identifying low-risk patients, who might not require hospitalization or who could be safely referred or discharged soon after admission; intermediate-risk patients, who do notneed intensive care; and high-risk patients, who require aggressive care in a closely monitored setting (Imperiale *et al.,* 2007). Numerous prognostic factors have been described to be associated with lethal outcome. It can be classified as clinical, endoscopic or therapeutic risk predictive factors for variceal and non variceal upper gastrointestinal bleeding, such as age of the patient or associated comorbidities (Marmo *et al.,* 2008), time of endoscopy (Ananthakrishnan *et al.,* 2009), stigmata of recent hemorrhage by endoscopy (Imperiale *et al.,* 2007), usage of proton pump inhibitor (Travis *et al.,* 2008) and others (Kalula *et al.,* 2003, Goh *et al.,* 2005, Sarwar *et al.,* 2007, Zaragoza *et al.,* 2008). The Child-Pugh score (CPS) is old empiric method to assess hepatocellular functional reserve in candidates for portosystemic shunting and it has been useful for risk-stratifying groups of patients with cirrhosis (Infante-Rivard *et al.,* 1987,Albers *et al.,* 1989). Acute Physiology, and Chronic Health Evaluation (APACHE) II score was developed by Knaus ***et al*** in 1985 (Knaus *et al.,* 1985). It has been successfully used to risk stratify cirrhotic patients admitted to medical intensive care unit (ICU) (Zauner *et al.,* 1996, Aggarwal *et al.,* 2001).

Objectives

The aim of present study is to evaluate the application of Child-Pugh and APACHE II scoring

systems in the prediction of outcome in patients with acute variceal upper gastrointestinal bleeding.

2. Patients and Methods

Patients

A prospective study was conducted on one hundred patients with acute variceal upper gastrointestinal bleeding proved by upper endoscopy due to liver cirrhosis presented to Nasser institute for research and treatment hospital from December 2009 to December 2010. The study was approved by the medical ethics committee and conducted in accordance with the principles of the declaration of Helsinki. All patients provided written informed consent before enrolment.

Study Design and Procedures

For the purpose of the study, the diagnosis of cirrhosis was based on clinical, laboratory and radiological criteria (Brown *et al.,* 1997, Afessa and Kubilis, 2000). Clinical and laboratory data necessary to both Child-Pugh score (Child and Turcotte, 1964, Pugh *et al.,* 1973) and APACHE II scores (Knaus *et al.,* 1985) were calculated on admission of patients and through 24 hours following admission after the initial attack of haematemesis or melena respectively and both scores were compared as regards their prognostic value as regards the outcome of the studied group of patients. Child-Pugh score employs five clinical measures of liver disease; total bilirubin, serum album, international normalized ratio, ascites and hepatic encephalopathy. Each measure is scored 1-3, with 3 indicating most severe derangement. Chronic liver disease is classified into Child-Pugh class A to C, employing the added score from above; Child A (5-6), Child B (7-9), Child C (10-15).APACHE II score is composed of three parts; physiological measures, age and chronic health status. The APACHE II score is the sum of result of each part. Twelve routine physiological measurements; mean blood pressure, body temperature, heart rate, and respiratory rate, oxygenation (PaO2 or A-aDo2), arterial pH, serum sodium, serum potassium, serum creatinine, haematocrit, white blood cell count and Glasgow coma score, were evaluated during the first 24 hours after admission and the worst measure is used for calculation. Each variable is weighted from 0 to 4, with higher scores denoting an increasing deviation from normal; the sum of these values is added to a mark adjusting for patient age and a mark adjusting for chronic health problems (severe organ insufficiency or immunocompromised patients) to arrive at the APACHE II score. The maximum score is 71. Chronic health status points are considered 5 for all patients because they have chronic liver insufficiency.

Medical treatment started immediately for every patient in the ICU. Upper gastrointestinal (GIT) endoscopy was performed by Olympus Exera II CV-180 videoscope system on the first day of admission or postponed to the second day if the patient is clinically unfit. The oesophagus was examined for evidence of oesophageal varices (OV) with reporting of fibrin clots, red signs and oozing spurters. Grade of varices was assessed according to Westaby *et al.* classification (Westaby *et al.,* 1989). Stomach was examined for evidence of gastric varices and portal hypertensive gastropathy and duodenum was examined for evidence of duodenopathy. Abdominal ultrasound was carried out using real time scanning device Toshiba, just vision 200 (SSA, 320A) with convex probe, 3.5-5 MHz.

The patients included in the study were followed up during the hospitalization period with a maximum of 7 days and the outcome was reported for rebleeding before or after endoscopy, encephalopathy, organ failure either hepatic, renal or pulmonary, surgical intervention, death or improvement and discharge. Renal failure was determined according to RIFLE criteria for acute renal dysfunction (risk, injury, failure, loss, end stage kidney disease) (Bellomo *et al.,*2004).

Statistical Analysis

Statistical analysis was done using the SPSS software package version 17.0. Descriptive statistics were expressed as mean and standard deviation and nominal categorical data were described as number and percentages. Fisher-Exact test was used to assess the differences within Child-Pugh classes A, B, and C. Individual relationship of each score to the prognostic outcome was assessed by t-test. A P value less than 0.05 was considered statistically significant for all above analyses. Discrimination was tested using the receiver operating characteristic (ROC) curves and by comparing areas under the curve (AUCs). For the different scoring systems tested, the sensitivity, specificity, overall correctness of prediction, positive and negative predictive values were calculated, and the cutoff point was determined.

3. Results

One hundred patients with acute variceal upper gastrointestinal bleeding (80 males and 20 females) presented to the emergency department were prospectively enrolled in the study. Eighty six patients presented with hematemsis which was accompanied with melena in sixty of them. The other fourteen patients presented with melena only. Hematemesis was fresh blood (66%), altered blood (18%) or both (2%).The numbers of attacks ranged between 1 to 10 (Table1).

In the present study, 12% of patients were hypertensive, 22% had diabetes mellitus, and 1% was having ischemic heart disease and atrial fibrillation. Infections were found in 7% of studied patients including pneumonia, spontaneous bacterial peritonitis

and cellulitis. Two patients had past history of chronic renal impairment. Regarding malignancy of involved patients, 11% had hepatocellular carcinoma, 2% had bladder carcinoma and 1% had oesophageal carcinoma. 9% of them were having metastatic lesions also.

Inspite of the amount and the number of attacks of hematemesis was more in child A in comparison to other groups, the present results showed that Child C patients ICU stay significantly higher than both Child A and B patients (5.26, 3.35, 3.37 days) respectively . Similarly, the hospital stay was significantly higher in Child C in comparison to Child A and B Patients (6.5, 4.7, 4.8 days) respectively due to rebleeding and development of hepatic encephalopathy. Twenty one patients were presented initially by encephalopathy before admission. Eleven of them had been still encephalopathy at the end of observation period with improvement in the grade of encephalopathy. In addition to 2 liters of crystalloids supplied initially to all patients, packed RBCs provided ranged from 1 to 8 bags (average 3) (Table 1) .

Upper GI endoscopy findings clarified that OV grade one was recorded in 12 patients, OV grade two was found in 24 candidates, OV grade three was detected in 33 cases and OV grade four was noticed in 31patients. Fibrin clot was found in only two cases. The endoscopy showed red signs on OVs of 28 candidates. Only one oozing spurter was detected. The endoscopic management of the varices was by band ligation in 46 cases, injection sclerotherapy in 29 patients while 25 candidates were treated conservatively. Twenty five patients were found to suffer from fundal varices with red signs on seven of them (five out of these seven patients also have red signs on OVs), FV were injected in 23 cases and treated conservatively in two patients. Portal hypertensive gastropathy was detected in 31 cases.

It was found that the improvement occurred in 74 patients, while 26 patients were complicated either by one or multiple complications, 13 patients developed rebleeding without statistical significant Child-Pugh and APACHE II scores and only 3 patients developed renal failure with highly significant values of Child-Pugh and APACHE II scores than patients without renal failure ($p< 0.001$). Urine output of these three cases ranged from 0.3-0.5L/24hours, serum creatinine>3mg/dl at the end of observation period with normal serum creatinine at admission with daily increase of > 0.3 mg/dl. Also it was found that there was a significant increase in the Child-Pugh and APACHE II scores in patients with developed encephalopathy than the patients without encephalopathy ($p< 0.001$). In the present study, all Child A patients survived, only one out of 45 Child B patients died (2.2%) and nine patients in Child C died (23.7%). Two out of the ten patients who died had coincident with renal failure. The first case had nephropathy grade II in ultrasonography and serum creatinine was 3.7 mg/dl at time of admission while the second one had no picture of nephropathy and serum creatinine was 9.7 mg/dl at time of admission. APACHE II and Child-Pugh scores were statistically higher in patients who died (Table 2).

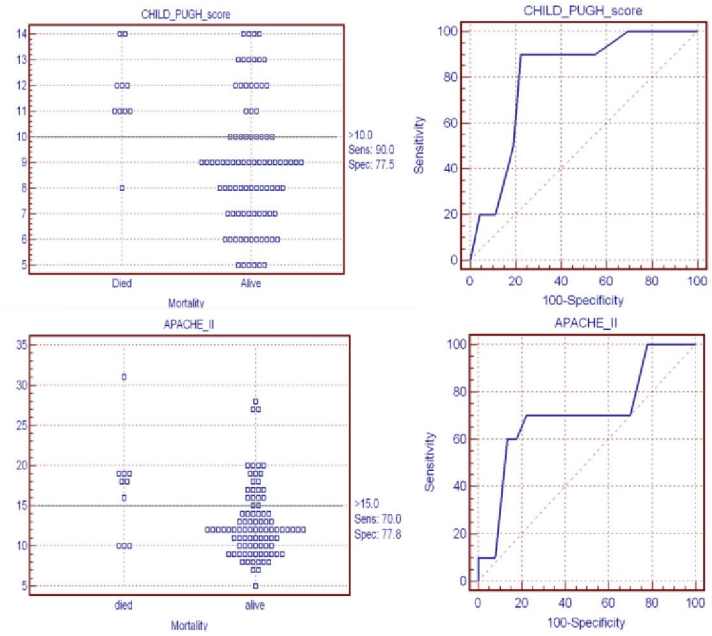

Figure 1 ROC analysis, sensitivity, specificity and accuracy of Child-Pugh and APACHE II in prediction of mortality.

On the other hand, application of Child-Pugh score revealed that the cut off value to determine the mortality was more than 10, with sensitivity 90%, specificity 77.5%, positive predictive value 31%, negative predictive value 98.6% and accuracy 80.4%. While applying APACHE II score, it was found that the cut off value was more than 15, with sensitivity 70%, specificity 77.8%, positive predictive value 25.9%, negative predictive value 95.9% and accuracy 70.6% (Figure 1).

Table 1 Comparison ofdemographic and clinical characteristics of patients in Child-Pugh scoring system [a]

Variable	Class A (N=17)	Class B (N=45)	Class C (N=38)	*P* value
Age	51.118 ± 14.688	54.933 ± 7.478	57.184 ± 9.299	0.104
Attacks of hematemesis	2.647 ± 1.320	2.356 ± 1.897	1.289 ± 1.814	0.008
Amount of Cups of blood (200cc)	2.353 ± 1.835	1.633 ± 0.997	1.303 ± 1.422	0.03
ICU duration of stay (day)	3.353 ± 1.998	3.378 ± 1.642	5.263 ± 2.956	0.001
Hospital duration of stay (day)	4.765 ± 2.412	4.844 ± 2.067	6.579 ± 3.285	0.007

[a] Data are mean ± standard deviation

Table 2 Comparison ofAPACHE II and Child-Pugh scores regarding different outcomes [a]

Variable	No	Yes	*P* value
Rebleeding (N=13)			
Child-Pugh score	9.116 ± 2.471	9.462 ± 2.876	0.647
APACHE II score	13.080 ± 4.452	14.385 ± 6.145	0.352
Renal failure (N=3)			
Child-Pugh score	9.042 ± 2.445	13.000 ± 1.732	0.007
APACHE II score	12.948 ± 4.314	23.000 ± 6.928	0.001
Hepatic Encephalopathy (N=21)			
Child-Pugh score	8.721 ± 2.319	12.077 ± 1.706	0.001
APACHE II score	12.632 ± 4.072	17.385 ± 6.423	0.001
Mortality (N=10)			
Child-Pugh score	8.888 ± 2.447	11.600 ± 1.713	0.001
APACHE II score	12.833 ± 4.322	17.000 ± 6.307	0.007

[a] Data are mean ± standard deviation

4. Discussion

Several scoring systems were evaluated for reliability to detect mortality in variceal bleeding patients such as Child-Pugh score (Lee *et al.,* 2002, ElNibras *et al.,* 2007, Berreta *et al.,* 2008), APACHE score (ElNibras *et al.,*2007), MELD score (Elsayed *et al.,* 2010), Glasgow-Blatchford score (Reed *et al.,* 2014) and Rockall score (Sarwar *et al.,*2007).

Child- Pugh C class was found to be one of the independent hospital mortality predictors in one study with initial endoscopic treatment failure and haemostatic failure in the first 48 hours (Berreta *et al.,* 2008). Also another study conducted on 102 patients with acute variceal bleeding due to both liver cirrhosis and periportal fibrosis. Twenty seven of them had liver cirrhosis and 12 of them died with actual mortality rate of 44.4%. Child-Pugh classification to the patients who died showed that the risk of death in patients with liver cirrhosis seems to correlate better with the Child-Pugh classification than modified APACHE II score with mean predicted mortality (27.3%) which was explained by relative reasonable early stability subsequently followed by decompensation of the liver (ElNibras *et al.,* 2007). Also discrimination power of Child-Pugh score AUC and APACHE III AUC were excellent in another study, while that of APACHE II AUC was acceptable while analyzing ROC curves in predicting short-term, hospital mortality of patients with liver cirrhosis. The Hosmer-Lemeshow statistic revealed adequate goodness-of-fit for Child-Pugh score (P = 0.192), this was not the case for APACHE II and III scores (P = 0.004 and 0.003 respectively) (Chatzicostas *et al.,* 2003).

APACHE system accurately risks stratified critically ill cirrhotic patients (Zimmerman *et al.,*1996) with an overall correct prediction of 70% with good prognostic value (Zauner *et al.,*2000). The overall correctness of prediction values of the APACHE system was 75% while Child-Pugh was 67% in predicting hospital mortality in 282 general ward patients with cirrhosis (Butt et al., 1998). Also in another study APACHE II was more powerful in discriminating the survivors from the nonsurvivors. It showed a better discriminative power (AUROC 0.833 ± 0.039) than Child-Pugh scores (AUROC 0.75 ± 0.05) (P= .024) (Ho *et al.,*2004). Nibras, *et al.,* (ElNibras *et*

al., 2007), found in their studied series that 52% of their patients had a modified APACHE II score of ≥15, out of them 42.6% died. But, in other study the prognostic performances of APACHE II and Child-Pugh scores in 111 cirrhotic patients hospitalized for upper gastrointestinal bleeding did not find significant differences between the two scoring systems (Afessa and Kubilis, 2000).

In the recent study, our results approved the reliability of both Child-Pugh and APACHE II scores in predicting the mortality in patients with acute variceal bleeding but with greater sensitivity, specificity as well as accuracy for Child-Pugh score in comparison to APACHE II score. In our study, mortality was significantly higher in Child C patients reaching 23.7% with longer ICU and hospital stay (mean = 5.2 and 6.5 days respectively) due to development of different complications. This is supported by results from other studies which showed clearly that mortality rate and ICU stay increase with higher Child-Pugh classes (Chatzicostas *et al.,*2003, Siddiqui *et al.,*2005, ElNibras *et al.,*2007). In conclusion, both Child-Pugh and APACHE II scoring systems are useful for risk stratification of patients with acute variceal bleeding regarding mortality but not for rebleeding. It is preferred to use Child-Pugh score as a more sensitive score as well as more easy to apply to predict mortality.

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