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PROGNOSTIC EVALUATION OF CHRONIC LIVER DISEASE PATIENTS WITH VARIOUS SCORING SYSTEMS

Showkat Ahmad Malik[1], Abdul Qayoom Rather[2], Peerzadi Shabeena[3], Waseem Raja[4]

[1]Medical Officer, Health and Medical Education Department, Jammu and Kashmir, Srinagar, India; [2]Senior Resident, Department of Medicine, Government Medical College, Srinagar, India; [3]Senior Resident, Department of Medicine, Government Medical College, Srinagar, India; [4]Senior Resident, Department of Medicine, Government Medical College, Srinagar, India.

ABSTRACT

Background: Prognostic evaluation of patients with chronic liver diseases is an important topic, often challenging the clinician. The number of patients on waiting lists for orthostatic liver transplantation (OLT) is becoming increasingly higher compared with the number of available donor livers. Correct timing of orthostatic liver transplantation can reduce the mortality of patients on waiting lists and improve post-transplantation survival.

Objective: To evaluate the short and medium term survival prognosis of chronic liver disease patients by means of various scoring systems.

Material and Methods: Our study was a hospital based retrospective study in which 93 chronic liver disease patients of either sex, age > 18 years and of any etiology were included. Medical records of these patients were retrospectively reviewed. Child-pugh, MELD, MELA-Na and updated forms of MELD and MELD-Na were calculated from data. Predictive value of survival at 3 months and 1 year were compared between scores through AUROC (Area under receiver operating characteristics and p value of < 0.05 was considered significant.

Results: 23 patients died including 4 who lost follow up, but all where belonging to Child Pugh class C and so considered dead. At both levels of assessment the scores of patient who died where significantly higher than those who survived, but there was no statistically significant difference in prediction of survival between various scores at both times as shown by their AUROC.

Conclusion: All these scoring systems are useful for predicting survival of chronic liver disease patients and so more studies are warranted to investigate the superiority of one model over others..

Key Words: Child Pugh, MELD, MELD-Na, Updated MELD-Na, AUROC

INTRODUCTION

The prevalence of chronic liver disease patients is increasing in the world, because of hepatitis B, C, alcoholic and non-alcoholic fatty liver disease (NAFLD), so are the patients on waiting list for orthostatic liver transplantation (OLT). Correct timing and selection for OLT can reduce the mortality and improve post-transplantation survival.[1,2]

Over the years many clinical and biochemical parameters have been suggested in order to accurately predict the prognosis of cirrhotic patients and correctly access their short and medium term survival. Child Pugh score is still considered the cornerstone in the prognostic evaluation of cirrhotic patients although it has some drawbacks, such as subjectivity of some clinical parameters and limited discriminatory ability.[2] In 1999 United Network for Organ Sharing (UNOS) formulated the model for end stage liver disease (MELD) as an objective assessment tool.[3] The present study aims to evaluate the prognostic accuracy of the Child Pugh, MELD, MELD-Na and updated forms of MELD and MELD-Na.

MATERIAL AND METHODS

Our study was a retro-prospective hospital based study, conducted in SMHS hospital Srinagar (J&K) – a tertiary care

Corresponding Author:
Dr. Abdul Qayoom, Senior Resident, Department of Medicine, Government Medical College, Srinagar, India.
Cell: +91-9018703732; E-mail: drqayoomrather@yahoo.com

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teaching hospital. 93 patients of chronic liver disease patients of either gender, age ≥ 18 years and of any etiology were included who visited the hospital from October 2009 to October 2010. The diagnosis of cirrhosis is confirmed on clinical, radiological and or biopsy (wherever feasible), detailed medical history, complete physical examination and laboratory tests (i.e. CBC, prothrombin time and INR, serum urea/creatinine, electrolytes, liver function tests) were performed in all patients at the time of registration and at 3 months and 1 year. Encephalopathy graded according to Zakim and Boyer (1996) classification[4]. Ascites diagnosed clinically and its degree evaluated by ultrasonic examination. Based on collected data various scores for each patients were calculated.

Various scores in each patients were calculated according to following equations:

MELD = 3.78 [Ln.Sr.Bil.(mg/dl)+11.2 [Ln.INR] + 9.57 [Ln.Sr.Creat.] + 6.43.

MELD-NA = MELD-Na – [0.025 x MELD x (140 – Na) + 140

Updated MELD = 9.39 [Ln.Sr.Bil.mg/dl] + 16.58 [Ln.INR] + 12.66 [Ln.Sr.Creat] + 6.43

Updated MELD-Na = Updated MELD-Na – [0.025xupdated MELD] x [140-Na] + 140

Child Pugh scoring was calculated from following patient parameters.

Serum Bilirubin (mg/dl), Sr. Albumin (g/dl), PT/INR, Presence or absence of Ascites or presence or absence of hepatic encephalopathy. Each patients was then allotted a Child class according to his or her score. Class A (5-6); Class B (7-9) and Class C (10-15) scores.

RESULTS AND OUTCOME

A total of 93 patients were enrolled, 56 were males (60.21%) and 37 were females (39.78%). 15 were belonging to Child Pugh class A, 45 Child Pugh class B, and 33 were belonging to Child Pugh class C. Most common etiology was cryptogenic (48 (51.6%) out of 93) followed by hepatitis B (26 (27.95%) out of 93), hepatitis C (10 (10.73%) out of 93), autoimmune 6 (6.45) out of 93) and least were mixed HBV and HCVG related (3.22%).

Table 1: Demographic, Clinical and Biochemical Parameters of the studied patients at the time of registration

Age (Years)		**58.36+7.86**
Sex	Males	56 (60.22%)
	Females	37 (39.78%)
Etiology	Cryptogenic	48 (51.61%)
	HBV	26 (27.95%)
	HCV	10 (10.73%)
	Autoimmune	6 (6.45%)
	HBV/HCV	3 (3.22%)
Serum Biochemistry	Bilirubin (mg/dl)	2.28+1.36
	Creatinine (mg/dl)	1.38+0.96
	PT/INR	1.51+0.35
	Albumin (g/dl)	3.43+0.70
	Serum Sodium (mEq/l)	136.85+2.20
Scores at the time of Registration	Child Pugh	8.58+2.15
	MELD	15.88+5.0
	MELD-Na	18.31+5.0
	Updated MELD	22.95+8.0
	Updated MELD-Na	24.96+7.0

PT = Prothrombin time; INR = International Normalized Ratio; MELD = Model for End Stage Liver Disease.
Data are expressed as a number (%) or mean + SD.

23 patients died including 4 who lost follow up, but all where belonging to Child Pugh class C and so considered dead. At both levels of assessment the scores of patient who died where significantly higher than those who survived, but there was no statistically significant difference in prediction of survival between various scores at both times as shown by their AUROC.

Table 2: Comparison of Clinical, Biochemical Parameters and Various Scores Between Patients who were alive and those who died at 3 months

Characteristics		Alive (n=86)	Died (n=7)	P-value
Median Age		55	60	< 0.05
Serum Biochemistry	Bilirubin (mg/dl)	1.9	2.57	< 0.01
	PT/INR	1.52	1.90	< 0.01
	Albumin (g/dl)	3.6	2.40	< 0.01
	Sr.Creatinine (mg/dl)	1.0	1.2	0.416
	Sr. Sodium (mEq/l)	136	130	< 0.01
Scores at the time of registration	Child Pugh	9	12	< 0.01
	MELD	16	20	< 0.01
	MELD-Na	18	22	< 0.01
	Updated MELD	23	28	< 0.01
	Updated MELD-NA	24	30	< 0.01

PT = Prothrombin time; INR = International Normalized Ratio;
MELD = Model for End Stage Liver Disease, NA = Serum sodium
Data are expressed as a number (%) or mean ± SD.

Table 3: Comparison of Clinical, Biochemical Parameters and Various Scores Between Patients who were alive and those who died at 1 Year

Characteristics		Alive (n=86)	Died (n=7)	P-value
Median Age		58	60	NS
Serum Biochemistry	Bilirubin (mg/dl)	1.895	2.51	< 0.01
	PT/INR	1.28	1.70	< 0.05
	Albumin (g/dl)	3.70	2.8	< 0.01
	Sr.Creatinine (mg/dl)	1.0	1.2	0.416
	Sr. Sodium (mEq/l)	136	132	< 0.01
Scores at the time of registration	Child Pugh	9	11	< 0.01
	MELD	14	19	< 0.01
	MELD-Na	16	22	< 0.01
	Updated MELD	20	28	< 0.01
	Updated MELD-NA	21	29	< 0.01

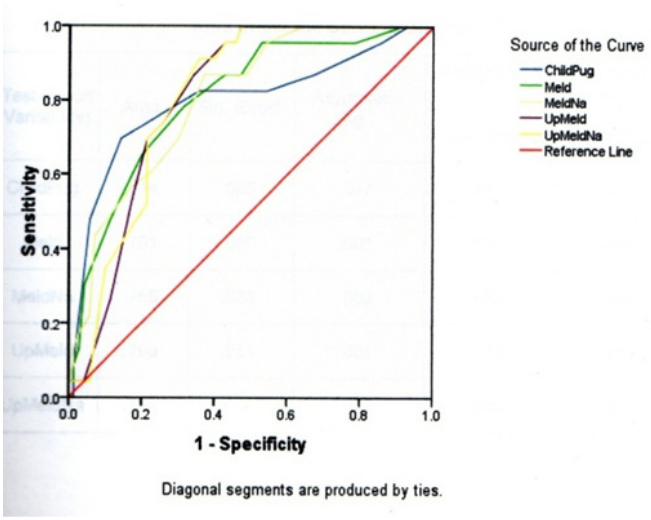
PT = Prothrombin time; INR = International Normalized Ratio; MELD = Model for End Stage Liver Disease, NA = Serum sodium
Data are expressed as a number (%) or mean + SD.

Comparison of Prognostic Accuracy Between Various Scores

To compare the accuracy of various scores as predictors of survival at 3 months and one year. The area under the operating characteristics curve (AUROC) was calculated. 23 patients died over study period of one year, 7 at 3 months and total of 23 at one year including those 4 who lost follow up. The AUROC of Child Pugh MELD, MELD-Na, updated MELD and updated MELD-Na were 0.799, 0.805, 0.806, 0.809 and 0.810 at 3 months and 0.714, 0.791, 0.765, 0.790 and 0.793 at one year.

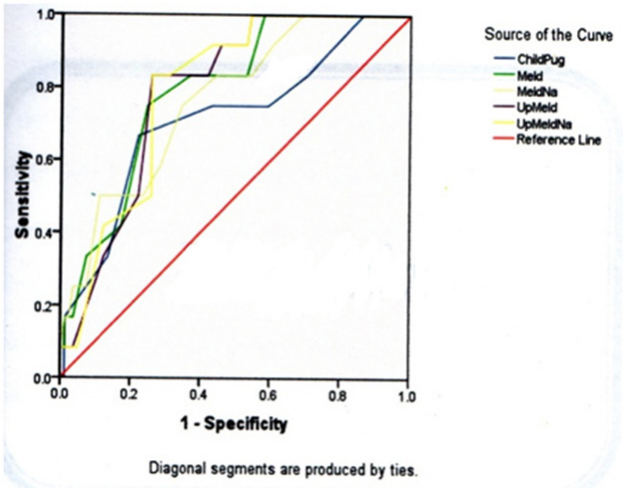
Area Under the Curved at 3 months					
Test Result Variables (s)	Area	Standard Error	Asymptotic Significance	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Child Pugh	0.799	0.061	0.000	0.680	0.918
MELD	0.805	0.051	0.000	0.705	0.905
MELD-Na	0.806	0.047	0.000	0.713	0.899
Updated MELD	0.809	0.044	0.000	0.723	0.895
Updated MELD-Na	0.810	0.044	0.000	0.724	0.895

AUROC (Area Under Receiver Operater Characteristic Curve) at 3 months



Area Under the Curved at one year					
Test Result Variables (s)	Area	Standard Error	Asymptotic Significance	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Child Pugh	0.714	0.085	0.017	0.547	0.881
MELD	0.791	0.060	0.001	0.673	0.909
MELD-Na	0.765	0.068	0.003	0.632	0.898
Updated MELD	0.790	0.054	0.001	0.683	0.896
Updated MELD-Na	0.793	0.054	0.001	0.688	0.898

AUROC (Area Under Receiver Operater Characteristic Curve) at 1 year



DISCUSSION

The enhanced efficacy of liver transplantation as a treatment for end stage liver disease has led to a progressive discrepancy between supply and demand for donor livers. As a result, the proportion of patients dying while on the wait list has steadily increased[5] in an attempt to reduce wait list mortality, a new allocation policy replacing the CTP with MELD has been adopted since 2002. Indeed, by allowing available grafts to the sick patients, the MELD system has led to a decrease in wait list mortality,[6] without impairing the transplant outcome.[7] Nevertheless the MELD system does not take into account important prognostic factors. In particular, the role of hyponatremia as an independent predictor of mortality has been convincingly demonstrated[8] and some studies assessed the prognostic value of a new scores derived from integration of sodium in the MELD score.[9,10] The applicability of sodium based MELD scoring systems in organ allocation has some limitation due to inter-laboratory variability and the potential variability of serum sodium concentration after simple therapeutic maneuvers such as administration of diuretics or intravenous hypotonic fluids or plasma volume expanders. Despite these caveats, Na based MELD scoring system represent a major advance in the prognostic assessment of patients with cirrhosis.[11]

To date only two studies[12,13] with an adequate sample size have evaluated the impact of modified MELD score on wait list mortality, and both reported that the incorporation of Na into the MELD score may enhance prognostic accuracy. One study elaborated the MELD-Na formula on the data from the huge register of U.S. organ procurement and transplantation network[14] and other proposed the UKELD score which is currently used to prioritize patients on the liver transplantation wait list in the United Kingdom.[12] Recently based on the observation that Na inversely correlated with severity of cirrhosis, another score derived from the ratio between MELD and sodium concentration (MESO) has been proposed, but it was tested and validated in patients not listed for liver transplantation.[15,16] Other MELD based models have also been devised that incorporate Na concentration and add either age[10] or presence of ascites.[17] However the addition of ascites in a MELD based score enhanced its prognostic ability only in patients with low standard MELD[17], and its applicability to the entire spectrum of listed patients needs further assessment.

To the best of our knowledge, only two studies have compared the performance of different scores. However one study suffered from a small size, whereas the other enrolled patients who were rather old for liver transplantation and mostly had HBV related cirrhosis.[18]

Our study compared all the latest prognostic scores predicting short term and medium term survival prognosis of chronic liver disease patients, that includes Child-Pugh, MELD, MELD-Na, updated MELD and updated MELD-Na.[19] The mean MELD at registration was 15.88±5, the minimal value from the survival benefit at one year has been demonstrated.[20] The etiology of cirrhosis did not modify the actual survival rate of listed patients, which then allowed an assessment of the prognostic ability of scores not influenced by the etiology of liver disease. Finally, the issue of assessing the test performances in the entire spectrum of disease severity within our patients was specifically addressed.

Our discrimination analysis showed that all scores namely Child-Pugh, MELD, MELD-Na, updated MELD and updated MELD-Na predicted survival or chronic liver disease patients to same degree. The AUROC of Child Pugh, MELD, MELD-Na, updated MELD and updated MELD-Na were comparable, indicating good prognostic accuracy, so our study is in agreement with the studies of Jeong Han Kim et al (2009)[19] and Laurence S et al (2009)[21]. Sharma et al (2009)[14] recently tried to improve MELD performance by modifying the three coefficients of the formula, using data from scientific registry of transplant recipients for all listed adult candidates in the United States. However in our study updated MELD and standard MELD had comparable predictive value at 3 and 12 months. In their study such variant results could likely be explained by differences among enrolled patients.

Having found that 3 months and 12 months AUROC of Child Pugh, MELD, updated MELD and updated MELD-Na were not significantly different, so any one of these scores can be used for prognostic assessment and allocation of liver transplant in chronic liver disease patients.

CONCLUSION

All these scoring systems were useful for predicting survival rate of chronic liver disease patients. MELD has been accepted useful mainly for predicting short term prognosis of 3 months. Our results showed that it could be also useful for long term period upto 12 months. But it is difficult to conclude that updated MELD or updated MELD-Na are superior to pre-existing prognostic tools such as MELD, MELD-Na or Child-Pugh scores. So more studies are warranted to investigate superiority of one prognostic model over the other.

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