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Comparative assessment of prognostic value for revised-mayo risk model and child-pugh score in patients with primary sclerosing cholangitis

BILIARY

Erkin Öztaş, Diğdem Özer Etik, Rahşan Olga Metin, İsmail Hakkı Kalkan, Erkan Parlak, Fatih Oğuz Önder, Mehmet Arhan, Nurgül Şaşmaz

Department of Gastroenterology, Yüksek İhtisas Education and Research Hospital, Ankara, Turkey

Original Article

ABSTRACT

Background/Aims: The aim of this study was to compare the utility of the revised Mayo risk model (rMRM) and Child-Pugh scores (CPSs) for predicting the prognosis of disease in patients with primary sclerosing cholangitis (PSC).

Materials and Methods: Patients were divided into 2 groups: Group I (37 patients; alive and not requiring liver transplantation) and Group II (8 patients; deceased or requiring liver transplantation). rMRM suggests the possible survival percentage over a 4-year period. Thus, rMRM scores and CPSs on the first visit were calculated from the data at the time of diagnosis for patients diagnosed with PSC <4 years ago. rMRM scores and CPSs of patients with >4 years of follow-up were calculated using data from the visit 4 years prior to their last follow-up.

Results: Bivariate analyses showed that need for liver transplantation/mortality was correlated with either first visit CPS (r=0.481, p=0.001) or rMRM (r=0.452, p=0.002). Analysis of the area under the curve showed that both models performed similarly in terms of predicting the need for liver transplantation/mortality (rMRM: 0.780; CPS: 0.762; p=0.8). There was a significant difference in Kaplan-Meier survival rates between Group I and Group II for both risk models (rMRM: p<0.001; CPS: p<0.001) when the decisive event was death or need for liver transplantation.

Conclusion: Both rMRM and CPSs are useful in risk assessment of patients with PSC. The ability to predict prognosis is similar for both risk models.

Keywords: Primary sclerosing cholangitis, rMRM, CPS, prognosis prediction

INTRODUCTION

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease. Although the clinical course is variable, progressive obliteration of the intrahepatic and/or extrahepatic bile ducts leads to bile stasis, hepatic fibrosis, cirrhosis, end-stage liver disease, and need for liver transplantation (1-4). The etiology of PSC is undefined; it is most likely a multifactorial disease. There is an increasing body of evidence that immunopathogenetic mechanisms are possibly involved in PSC because of the association with human leukocyte antigen (HLA) complex haplotypes, multiple autoantibodies, and the presence of inflammatory bowel disease (IBD) in >80% of patients. However, PSC lacks the features of a typical autoimmune disease and responds poorly to immunosuppressive therapies (5-10).

Primary sclerosing cholangitis has a variable clinical course and a wide spectrum of disease severity exists, ranging from patients who present with end-stage liver disease requiring liver transplantation within a short time to those who remain asymptomatic for decades. Because of the fluctuating nature of the disease, it is difficult to determine when liver transplantation may be most effective before the onset of debilitating disease (11,12).

There are several prognostic models to estimate survival with PSC and to detect the candidates for and timing of liver transplantation. The revised Mayo risk model (rMRM) and Child-Pugh scores (CPSs) are 2 of the prognostic models that have been used to estimate survival without transplantation among patients with PSC (13).

Address for Correspondence: Erkin Öztaş, Department of Gastroenterology, Yüksek İhtisas Education and Research Hospital, Ankara, Turkey
E-mail: droztaserkin@gmail.com

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The aim of this study was to determine the role of rMRM and CPSs in predicting the clinical outcomes such as the need for transplantation or mortality, endoscopic treatment frequency, or development of a dominant stricture in a Turkish PSC population referred to a tertiary center.

MATERIALS AND METHODS

A retrospective analysis was performed of 56 patients followed-up for PSC at the Department of Gastroenterology, Yuksek İhtisas Hospital, Turkey, between January 1993 and July 2010. Local ethics committee approval was received and written informed consent was obtained from patient who participated in this study. Eleven of these patients were excluded from evaluation because of incomplete data. Data from the remaining 45 patients, including age at diagnosis; gender; duration of disease; frequency of endoscopic intervention for PSC; and presence of IBD, dominant stricture, and small-duct disease was recorded. The diagnosis of PSC was achieved using endoscopic retrograde cholangiopancreatography (ERCP) in 5 (11.1%) patients, magnetic resonance cholangiography (MRCP) in 22 (48.9%) patients, and histological analysis in 10 (22.2%) patients (Table 1).

According to survival, patients were divided into 2 groups. Group I included 37 patients who were alive and did not require liver transplantation, and Group II included the remaining 8 patients in need of liver transplantation or who had deceased.

We computed CPSs using the modification score proposed by Pugh et al. (14) for primary biliary cirrhosis. rMRM scores were computed using the following formula: (0.0295 × age in years) + [0.5373 × Log (bilirubin in milligrams per deciliter)] - (0.8389 × albumin in grams per deciliter) + [0.5380 × Log (aspartate aminotransferase in units per liter)] + [1.2426 × points for variceal bleeding (0; if none, 1; if present)] (13).

Revised Mayo risk model suggests the possible survival percentage over a 4-year period. Thus, rMRM scores and CPSs on the first visit were calculated from the data at the time of diagnosis for patients diagnosed with PSC<4 years ago. rMRM scores and CPSs of patients with >4 years of follow-up were calculated using data from the visit 4 years prior to their last follow-up.

Patients were divided into 3 groups according to CPSs and rMRM scores (CPS:A, B, and C; rMRM: (< 0 low risk group, 0-2 intermediate risk group, >2 high risk group).

Statistical analysis

Statistical analyses were performed using SPSS version 18 (SPSS, Chicago, IL). Descriptive statistics, frequencies, and means and standard deviations were calculated, and Nonparametric variables were compared between the 2 groups using the Mann-Whitney U test. Group characteristics were compared using the chi-square test and Fisher's exact test. Correlation coefficients (r) were used to explore associations between variables: Pearson's r for correlations between interval variables and Spearman's r for correlations including ordinal variables. To directly compare the prognostic abilities of rMRM and CPSs, receiver operating characteristic (ROC) curves were generated and the areas under the curves (AUCs) were compared. Kaplan-Meier survival (KMS) curves were generated according to the CPS and rMRM risk groups. The decisive event was either death or need for liver transplantation.

Table 1. Selected clinical characteristics of the 45 patients with PSC included in the study

Clinical Characteristic	Value
Age * [mean±SD (range)]	35.49±12.48 (16-65)
Females [n (%)]	19 (42%)
Duration of PSC in years [mean±SD (range)]	5.36±4.21 (1-18)
Presence of IBD [n (%)]	28 (66.2%)
Presence of small-duct PSC [n (%)]	3 (6.7%)
Presence of dominant strictures [n (%)]	17 (37.8%)
Frequency of endoscopic intervention [median (range)]	1 (0-7)
rMRM [median (range)]	-0.056 (-2.59 to 3.50)
CPS [median (range)]	5.0 (5-11)
Liver transplantation [n (%)]	5 (11.1%)
Death [n (%)]	3 (6.6%)

*Age at diagnosis (years)
PSC: primary sclerosing cholangitis; IBD: inflammatory bowel disease; rMRM: revised Mayo risk model score on first visit; CPS: Child-Pugh score on first visit

RESULTS

Selected clinical characteristics of the 45 patients with PSC included in the study are listed in Table 1. Liver transplantation was performed in a patient because of recurrent cholangitis episodes, although there was no evidence of advanced stage of liver failure. CPSs, rMRM scores, and frequency of endoscopic intervention were found to be significantly higher in Group II than in Group I. In addition, dominant strictures were more prevalent in Group II than in Group I (75% vs. 25%, p=0.03) (Table 2).

According to rMRM scores, 25% of the patients in Group II were in the high risk group, whereas none of the patients in Group I were in the high risk group (p=0.02). According to CPSs, 25% of the patients in Group II were classified as B or C, whereas all patients in Group I were classified as A (p=0.03) (Table 3).

Bivariate analyses showed that CPSs were significantly correlated with the need for liver transplantation/mortality (r=0.481, p=0.001) and frequency of endoscopic intervention (r=0.306, p=0.04). rMRM scores were also significantly correlated with the need for liver transplantation/mortality (r=0.452, p=0.002) and presence of dominant strictures (r=0.330, p=0.02). Bivariate analyses also showed need for liver transplantation/mor-

Table 2. Comparison of clinical characteristics and PSC predictive risk modalities between Group I and Group II patients

Parameter	Group I	Group II	p value
Age (Years) (mean±SD)	35.5±12	34.8±16	0.6
Females [n (%)]	15 (40.5%)	4 (50.0%)	0.7
Presence of IBD [n (%)]	23 (62.2%)	5 (62.5%)	0.9
Presence of DS [n (%)]	11 (29.7%)	6 (75%)	0.03
Frequency of EI (mean±SD)	0.89±0.936	2.63±2.326	0.03
rMRM (mean±SD)	-0.33±0.924	0.98±1.413	0.01
CPS (mean±SD)	5.14±0.347	6.38±1.996	0.01

SD: standard deviation; IBD: inflammatory bowel disease; DS: dominant stricture; EI: endoscopic intervention; rMRM: revised Mayo risk model score on first visit; CPS: Child-Pugh score on first visit

Table 3. Comparison of Group I and Group II patients according to risk classifications on first visit

	Group I	Group II	p value
rMRM Risk Classification			
Low risk [n (%)]	24 (64.9%)	3 (37.5%)	
Intermediate risk [n (%)]	13 (35.1%)	3 (37.5%)	0.02
High risk [n (%)]	-	2 (25%)	
CPS Classification			
A [n (%)]	37 (100%)	6 (75%)	
B [n (%)]	-	1 (12.5%)	0.03
C [n (%)]	-	1 (12.5%)	

rMRM: revised Mayo risk model score on first visit; CPS: child-pugh score on first visit

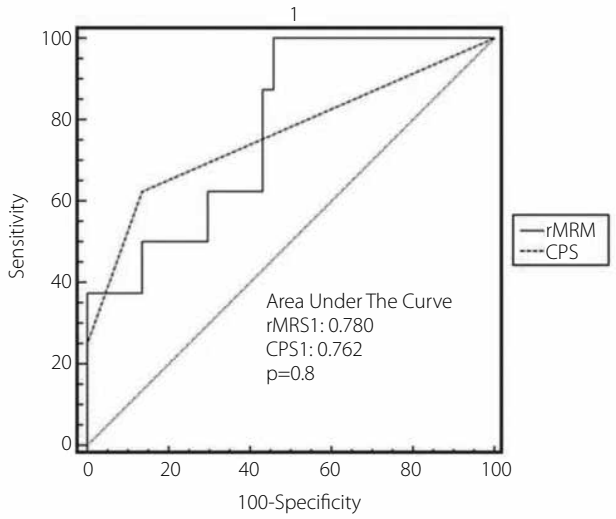

Figure 1. Comparison of rMRM scores and CPSs in terms of predicting the need for liver transplantation/mortality using ROC curves (CPS1: Child-Pugh score on first visit; rMRM1: revised Mayo risk model score on first visit).

tality to be significantly associated with presence of dominant strictures (r=0.357, p=0.01) and frequency of endoscopic intervention (r=0.549, p<0.001). However, there was no correlation between need for liver transplantation/mortality and age (r=-0.20, p=0.89), gender (r=-0.073, p=0.63), or presence of IBD (r=0.003, p=0.98).

In the comparison of rMRM scores and CPSs using ROC curves, need for liver transplantation/mortality was selected for analysis. The 2 models performed similarly in terms of predicting the need for liver transplantation/mortality (rMRM: 0.780; CPS: 0.762; p=0.8) (Figure 1). We developed KMS curves according to the CPS and rMRM risk groups. The decisive event was death or need for liver transplantation. There was a significant difference in survival rates between the groups in both risk models (rMRM: p<0.001; CPS: p<0.001) (Figures 2,3).

DISCUSSION

Primary sclerosing cholangitis is a disease with a variable clinical course without spontaneous resolution. Biliary cirrhosis and its complications, such as portal hypertension and advanced-stage liver failure, occur in a significant proportion of patients owing to obliteration of the biliary tract (11,15). Based on the clinical variables proven to correlate independently with prognosis, predicting survival is of great importance for defining a strategy of therapy and for timing orthotopic liver transplantation. To assist in the selection of and timing for liver transplantation, several investigators have developed prognostic models derived from data of individual patients with PSC to accurately estimate survival (16).

Supporting evidence in the literature defends the use of CPSs and the decision made by the United Network for Organ Sharing (UNOS) to determine CPSs as the major criteria necessary to refer patients for liver transplantation (17). Christensen et al. found that each of the 5 individual variables of CPS (bilirubin, albumin, prothrombin time, ascites, encephalopathy) as well as the Child class had prognostic significance in a heterogeneous group of patients with liver cirrhosis. In another retrospective study, life expectancy of 620 patients with chronic liver disease due to a variety of causes was calculated and compared with an age- and sex-matched normal population. Among patients with cirrhosis, prognosis was dependent upon Child classification (p=0.001) (18,19). In our study, we demonstrated that the need for liver transplantation/mortality (p=0.001) and frequency of endoscopic intervention (p=0.04) at the end of the fourth year correlated with CPSs, suggesting that CPS is a significant prognostic index.

Although CPS is commonly used to assess the severity of liver disease and can be calculated at the patient's bedside, it has some weak points. CPS is based on serum albumin levels, prothrombin time, serum bilirubin levels, ascites, and encephalopathy (14). Because the cut-off points for the quantitative variables (bilirubin levels, albumin levels, and prothrombin time) reduce the prognostic information, the detected cut-off levels may not be optimal. Mortality risks may not be proportional for the 3 categories defined by each variable and the prognostic importance of the 5 variables may not be equal. Assessment of the

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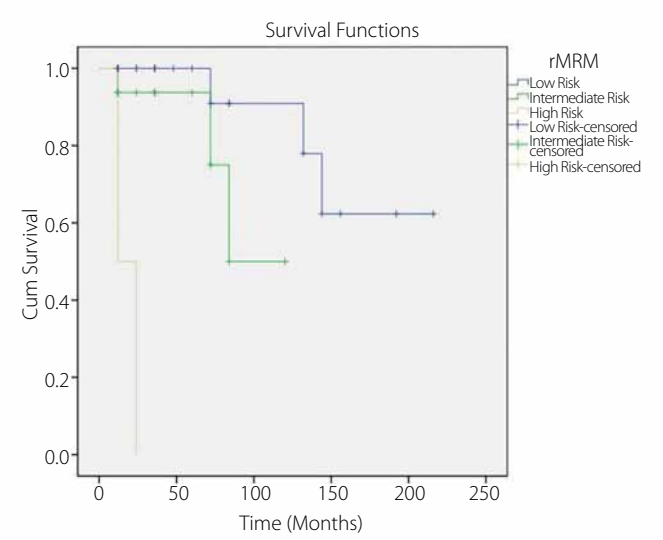

Figure 2. Kaplan-Meier survival curve of patients according to rMRM risk groups (rMRM: revised Mayo risk model).

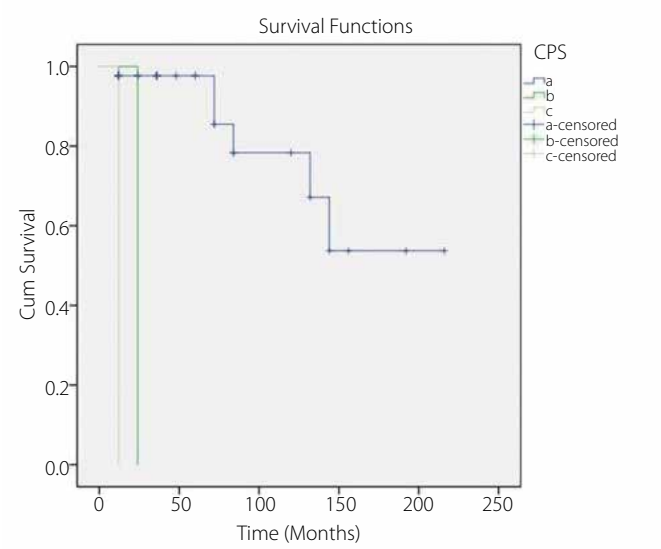

Figure 3. Kaplan-Meier survival curve of patients according to CPS risk groups (CPS: Child-Pugh score).

degree of ascites and encephalopathy may be subject to interpretation. In addition, this model does not include other prognostically important variables such as age, serum creatinine levels, gastroesophageal varices, and variceal bleeding (14,20).

Revised Mayo risk model was developed by Kim et al. on the basis of the course of PSC in 486 patients at 3 referral centers. In contrast to the limitations of CPS, rMRM for PSC has some advantages. First, it appears to be useful in patients with less advanced disease for which the Child-Pugh classification is insensitive. This is because a wide range of disease severities have been used to develop and validate rMRM. Second, MRM uses an interval scale; a uniform impact occurs on the risk of death with a one-unit increment in the risk score. Third, the variables in MRM were selected to minimize the effect of medical interventions. Finally, survival is estimated with relatively narrow confidence intervals by MRM (21).

There is increasing evidence supporting rMRM to be a prognostic index for patients with PSC. Komasiewicz et al. divided patients with PSC according to the calculated rMRM scores: Group A (rMRM <0.56), Group B (0.56≤rMRM≤1.56), and Group C (rMRM >1.56). The authors found that the mortality risk in patients with rMRM >1.56 was 6.59-fold higher than patients with rMRM <0.56. rMRM >1.56 significantly decreased 5-year survival among patients with PSC. Using multivariate logistic regression, Treeprasertsuk et al. showed that a high rMRM score (≥0.87) was significantly associated with the presence of varices at initial endoscopy (odds ratio=1.9 and 3.9) in patients with PSC (22,23). In support of the prognostic value of rMRM, we found that rMRM scores correlated with the need for liver transplantation/mortality (p=0.02) and presence of dominant strictures (p=0.04) at the end of the fourth year.

In the literature, there are few and controversial results on which model is superior in predicting survival in patients with PSC. Shetty et al. (17) suggested that CPSs are more useful in predicting survival than MRM for patients with PSC, although it should be kept in mind that they used the previous version of the Mayo model in their study. Kim et al. (21) demonstrated that rMRM is more useful in predicting survival than CPSs for patients with PSC.

In our study, the 2 models performed similarly in terms of predicting the need for liver transplantation/mortality when compared using ROC curves (p=0.8). KMS curves revealed that there was a significant difference in survival rates between the groups in both risk models (rMRM: p<0.001; CPS: p<0.001).

Although CPS has been reported to have some limitations when compared with rMRM, it proved useful in our study in risk assessment of patients with PSC. However, the utility of CPS is greatest in patients with decompensated liver cirrhosis, and rMRM is available over a much wider spectrum of severity of PSC (24). In our study, 43/45 (95.6%) patients had Child A liver disease at the beginning, and despite this patient spectrum, there was no difference between predicting the need for liver transplantation/mortality and the frequency of endoscopic intervention. This study showed that rMRM or CPSs have similar abilities in terms of predicting the prognosis of patients with PSC.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: Written informed consent was obtained from patient who participated in this study

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