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Case Report

Comparison of MELD and Child-Pugh Score for the Prediction of Survival in Portal Hypertension Undergoing Transjugular Intrahepatic Portosystemic Shunt

Abstract

Objectives: Recently, the model for End-Stage Liver Disease (MELD) was proposed for the prediction of survival in transjugular intrahepatic portosystemic shunt (TIPS) patients. We therefore compared the prognostic accuracy of the MELD model and the Child-Pugh score, in an unselected cohort of TIPS patients followed long-term.

Methods: A retrospective chart review and statistical analyses were done on 120 patients consecutively admitted for portal hypertension from 2009 to 2013 in the Jinling hospital (Nanjing, China).

Results: The survival rate for all patients was 95.8% at 3 months, 90% at 1 year, and 85.8% at 3 years. Significantly lower survival rates were found in patients with MELD scores of 15 or more in comparison to those with MELD scores of 15 or less ($p < 0.001$). There was no significant difference in survival rate between patients with Child-Pugh classification A and those with Child-Pugh classification B, while the patients with Child-Pugh classification C has a significantly lower survival rate than those with Child-Pugh classification A and B ($p < 0.001$). The discrimination powers of MELD (c statistics: 0.772, 0.680, 0.647 for 3-month, 1-year, and 3-year survival) were not significantly different from the discrimination powers of Child-Pugh score at the same time points (c statistics: 0.795, 0.732, 0.678).

Conclusions: The Child-Pugh classification is only slightly superior to the MELD score for the prediction of long-term survival in TIPS patients. Therefore, the search continues for an entirely new scoring system to further improve prognostic accuracy.

Introduction

The transjugular intrahepatic portosystemic shunt (TIPS) is a portosystemic shunt created using percutaneous endovascular techniques. This procedure was originally used to treat variceal bleeding refractory to medical management in patients with portal hypertension [1,2]. Compared to surgery, TIPS can reduce the mortality rates about these complications. However, some patients may develop progressive liver failure or other serious complications and even die shortly after TIPS procedure [2,3]. Therefore, combined with the relevant clinical data, the real and objective evaluation of liver function after TIPS implantation is particularly important. Prognostic models may help doctors in the clinical decision making and provide patients with a more reliable assessment of their potential outcome which will have a significant influence on the choice of individualized therapy [4,5].

Recently, new models for the prediction of prognosis of patients with liver cirrhosis, such as the MELD score, have emerged and are challenging the position of the Child-Pugh score (CPS), which has been the first-choice prognostic model for decades [5,6]. However, so far no study has demonstrated the MELD score has already completely replaced the Child-Pugh score.

The purpose of this present study was to evaluate the predictive effect of prognostic model on the survival rate of patients after TIPS procedure.

Patients and Methods

The study involved 126 patients consecutively admitted from 2009 to 2013 to research institute of general surgery of Jinling Hospital (Nanjing, China). Six patients were excluded from the analysis (one for hepatic hilar carcinoma, one not

implanted because of transcapsular puncture with peritoneal bleeding, three not implanted for inability to puncture the main branch of the portal vein, one implanted bare stent, one operated splenectomy and azygoportal disconnection). The remaining 120 patients were treated successfully and were thus included in this report. All patients were treated when hemodynamically stable, without active infections, signs of cardiac failure or organic renal diseases.

Data were collected retrospectively through chart review of consecutive patients with the diagnosis of portal hypertension. Baseline demographic, clinical and laboratory characteristics were retrieved from clinical records and are summarized in Table 1. In all cases, porto-systemic venous pressure gradient (PVPG) was measured both before and at the end of the TIPS procedure. MELD and Child-Pugh scores were calculated. Child-Pugh classification A = 5–6 points, Child-Pugh classification B = 7–9 points, and Child-Pugh classification C = 10 or more

Table 1: Demographic, clinical, and biochemical features in patients undergoing TIPS.

Characteristics	Patient Population (n=120)
Age, years	51.21±12.42
Male/female, n	81/39
Cause of liver disease, n (%)	120
Viral	95
Cholestatic	1
Alcoholic	3
Other*	21
Indication for TIPS insertion	
Recurrent variceal bleeding	53
Emergency TIPS in uncontrolled bleeding	33
Refractory ascites	34
Child-Pugh score	8.15±1.77
Child-Pugh classification, n (%)	120
A	23
B	73
C	24
MELD score	9.87±5.18
Hematocrit (HCT), %	26.72±6.56
Hemoglobin (Hb), g/L	85.52±22.83
White blood cell count (WBC), ×10 ⁹ /L	3.89±2.69
Blood platelet count (PLT), ×10 ⁹ /L	69.16±61.03
Prothrombin time (PT), s	16.25±5.36
Activated partial thromboplastin time (APTT), s	42.09±15.45
International normalized ratio (INR)	1.42±0.40
Serum creatinine, μmol/L	76.18±33.61
Urea nitrogen, mmol/L	5.73±3.34
Albumin, g/L	33.26±4.83
Globulin, g/L	23.14±6.20
Glutamate pyruvate transaminase (GPT), U/L	64.33±59.27
Glutamine oxaloacetic transaminase (GOT), U/L	65.78±50.43
Bilirubin, μmol/L	35.81±24.24
Blood ammonia, μmol/L	61.61±38.07
Serum sodium, mmol/L	139.53±5.22
Serum potassium, mmol/L	3.64±0.43
PVPG pre TIPS, cmH ₂ O	38.99±5.09
PVPG post TIPS, cmH ₂ O	21.89±4.36

Mean±SD baseline characteristics at the time of TIPS insertion of the patients enrolled in the study.

Other*: Budd-Chiari syndrome, sclerosing cholangitis and idiopathic liver diseases.

points. The MELD score formula is $9.6 \times \text{Ln}(\text{creatinine mg/dl}) + 3.8 \times \text{Ln}(\text{bilirubin mg/dl}) + 11.2 \times \text{Ln}(\text{INR}) + 6.4 \times (\text{cause of cirrhosis})$ in which the value for cause of cirrhosis was 0 for alcoholic or cholestatic etiology and 1 for viral or other etiology.

Transjugular intrahepatic portosystemic shunt procedure

The procedure was performed by a surgeon with 20 years' experience of TIPS in a dedicated interventional radiology suite under local anesthesia. After puncturing the right internal jugular vein guided by Doppler ultrasound imaging, a 10-French, 41 cm long sheath (Rosch-Uchida TIPS puncture Set; Cook, Bloomington, IN) was placed in the suprahepatic portion of the inferior vena cava. After catheterization of the right hepatic vein, the measure of hepatic venous pressure and the portal pressure were performed. With the use of a hydrophilic guidewire (Radiofocus guidewire; Terumo Europe, Leuven, Belgium), the portal vein was catheterized. The portal pressure was measured while the portography was performed. The dilation of the intrahepatic parenchymal tract was performed using a low-profile balloon with 8 mm diameter. In patients with large varices of the gastric coronary vein, embolization using coils and a gelatin sponge was performed to reduce the risk of re bleeding. Fluency stent grafts (Bard Peripheral Vascular, Tempe, AZ) were deployed. The diameter of the stent graft was 8 mm, and the length was 4 to 6 cm. The Fluency stent graft is an expanded polytetrafluoroethylene (ePTFE)-encapsulated grid-like cylinder made of a biocompatible nickel-titanium alloy. There are four radiopaque tantalum extensions on each end of the Nitinol stent. The Nitinol cylinder is encapsulated with two layers of ePTFE, both considered as a useful test. For prognostic models, a c statistic of 0.9 or greater is seldom seen. Survival curves were computed by means of Kaplan-Meier product-limit estimates and were compared by means of the log-rank test. A P value of less than 0.05 was considered to indicate a statistically significant difference. Statistical analyses were performed with SPSS 15.0 for Windows (SPSS, Chicago, IL).

Results

Clinical outcome

A total of 120 patients underwent a TIPS procedure for prevention of variceal rebleeding and 86 for treatment of refractory variceal hemorrhage. The median follow-up of the 120 patients was 17.9 months (range 0–36). 16 patients died during follow up (13.3%), 5 within three months of TIPS placement, and 1 underwent liver transplantation. 10 stent stenosis occurred, these stenosis were successfully treated in all by angiographic balloon dilatation or re-stenting. 3 patients who occurred late portal thrombosis were treated by catheter-directed thrombolysis. The 3-month, 1-year, and 3-year survival rates were 95.8%, 90%, and 85.8%, respectively.

Baseline demographics

A total of 120 consecutive patients admitted to the liver unit with the clinical diagnosis of portal hypertension. The demographics and clinical characteristics of the patients on the

basis of institution and on an overall basis are given in (Table 1). 34 (28.3%) of the 120 patients underwent TIPS creation to treat ascites, and 53 (44.2%) underwent TIPS creation to treat recurrent variceal bleeding, while 33 (27.5%) for emergency variceal bleeding.

Survival analysis

Kaplan–Meier survival analysis shown in Figures 1,2 compares survival rates based on three classifications of Child–Pugh score and the admission MELD score of <15 and >15. The 3-month survival rates for CPS classifications A, B, and C were 95.5%, 97.3%, and 91.7%, respectively. For classifications A, B, and C, 1-year survival rates were 95.5%, 95.9%, and 66.7%, and 3-year survival rates 95.5%, 94.5%, and 50.0%, respectively (Figure 1). Overall survival did not differ between CPS classifications A and B, whereas survival of patients of classification C was poorer ($p < 0.001$) than that of patients of classification B.

The survival curves based on MELD scores are shown (Figure 2). Survival rates were significantly lower in patients with MELD scores of >15 than in those with MELD scores of <15 ($P < 0.001$). The 3-month survival rates for MELD scores of <15 and >15 were 97.1% and 87.5%, respectively. For the MELD scores of <15 and >15, 1-year survival rates were 94.2% and 62.5%, and 3-year survival rates 93.2% and 37.5%, respectively.

Differences in 3-month and 1-year mortality rates based on patients who underwent elective or emergency TIPS procedure for variceal hemorrhage are given in Table 2.

Due to insufficient sample size, the difference in the mortality based on MELD scores or Child–Pugh classification between elective TIPS and emergency TIPS was not significant ($P > 0.05$). 16 of the 120 patients died during follow up; however, 5 (31.3%) of the 16 patients died within 30 days after TIPS creation in Table 3A,B. the early death rate for this series was 4.17%. The cause of early death was liver failure in 3 patients, renal failure in one, and multiple organ failure in one.

C-Statistics

To further assess prognostic utilities of the two scores, ROC curves were plotted and AUCs were compared. The area under the curves showed a decrease in the predictive value for both scores during follow up. The ROC for 3-month survival is shown (Figure 3, Table 4). The discrimination powers of MELD (c statistics: 0.772, 0.680, 0.647 for 3-month, 1-year, and 3-year survival) were not significantly different from the discrimination powers of CPS at the same time points (c statistics: 0.795, 0.732, 0.678) in Table 5.

Discussion

TIPS has been widely employed to treat patients with severe portal hypertension [2]. Established indications for TIPS in-

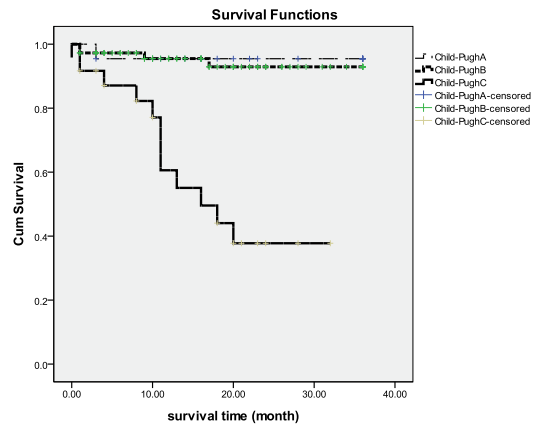


Figure 1: Kaplan-Meier survival curves according to Child-Pugh score classification (A vs B vs C) for 3-year survival.

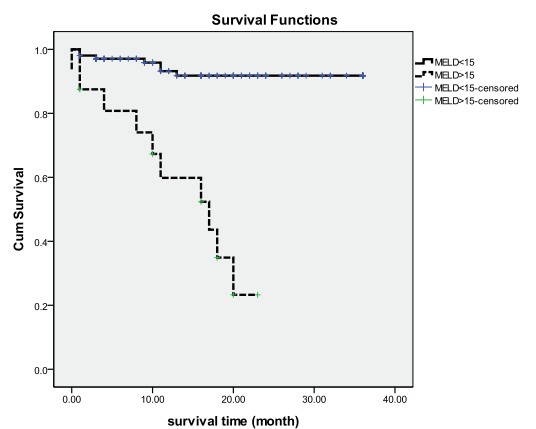


Figure 2: Kaplan-Meier survival curves according to the MELD score for 3-year survival.

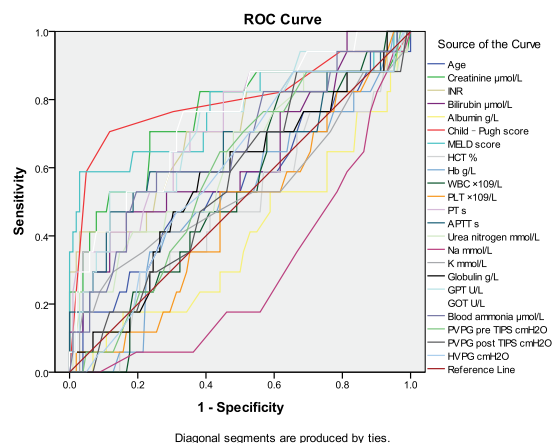


Figure 3: Receiver operating characteristic curve for CPS and MELD for three month survival. The area under the curve (AUC) was 0.795 for CPS and 0.772 for MELD, which was not significantly different.

Table 2: Mortality Based on Patients Who Underwent Elective or Emergency TIPS.

	No. of Patients	Mortality Rate (%)		
		3-month	1-year	3-year
Elective TIPS	53	1.9	7.5	9.4
Emergency TIPS	33	12.5	15.6	18.8

clude active or recurring variceal bleedings, refractory hydrothorax and ascites, Budd–Chiari and veno–occlusive syndrome, hepatopulmonary syndrome, hepatorenal syndrome, and prophylaxis of complications in patients with cirrhosis who need major abdominal surgery. Establishment of prognostic factors is the key towards evaluating the TIPS procedure. The most

widely used prognostic model in patients with cirrhosis is the Child–Pugh score which is developed as a model to predict survival of portacaval shunt [4,7]. A relatively new approach is the MELD score which was initially used as a prognostic indicator for patients undergoing elective TIPS [6,8]. The MELD score was widely employed for patient selection and allocation of or-

Table 3A: 30 Days Mortality Based on MELD Score.

MELD Score		Total N	N of death	N of survival	Survival rate
MELD<15	Elective	49	1	48	98.0%
	Emergency	25	2	23	92.0%
	Overall	74	3	71	95.9%
MELD>15	Elective	4	0	4	100.0%
	Emergency	8	2	6	75.0%
	Overall	12	2	10	83.3%
Overall	Overall	86	5	81	94.2%

Table 3B: 30 Days Mortality Based on Child-Pugh Score.

Child-Pugh Score		Total N	N of death	N of survival	Survival rate
CPS A	Elective	11	1	10	90.9%
	Emergency	6	0	6	100.0%
	Overall	17	1	16	94.1%
CPS B	Elective	34	0	34	100.0%
	Emergency	19	2	17	89.5%
	Overall	53	2	51	96.2%
CPS C	Elective	8	0	8	100.0%
	Emergency	8	2	6	75.0%
	Overall	16	2	14	87.5%
Overall	Overall	86	5	81	94.2%

Table 4: C-Statistics of variables for 3-month survival.

Variable(s)	Area (95% CI)	Std. error	P value
Age	0.552(0.394-0.710)	0.081	0.494
Child–Pugh score	0.795(0.648-0.942)	0.075	0.000**
MELD score	0.772(0.621-0.923)	0.077	0.000**
HCT	0.477(0.327-0.626)	0.076	0.758
Hb	0.504(0.358-0.650)	0.075	0.958
WBC	0.529(0.397-0.660)	0.067	0.704
PLT	0.467(0.325-0.609)	0.072	0.668
PT	0.707(0.559-0.854)	0.075	0.006**
APTT	0.654(0.489-0.819)	0.084	0.042*
INR	0.704(0.548-0.859)	0.079	0.007**
Creatinine	0.751(0.601-0.900)	0.076	0.001**
Urea nitrogen	0.620(0.464-0.775)	0.079	0.114
Albumin	0.392(0.242-0.543)	0.077	0.157
Globulin	0.565(0.418-0.713)	0.075	0.389
GPT	0.720(0.582-0.859)	0.071	0.004**
GOT	0.746(0.619-0.873)	0.065	0.001**
Bilirubin	0.631(0.477-0.786)	0.079	0.084
Blood ammonia	0.661(0.512-0.809)	0.076	0.034*
Na ⁺	0.288(0.168-0.408)	0.061	0.005**
K ⁺	0.528(0.358-0.698)	0.087	0.713
PVPG pre TIPS	0.575(0.437-0.713)	0.070	0.324
PVPG post TIPS	0.555(0.413-0.697)	0.072	0.468
HVPG	0.588(0.450-0.726)	0.070	0.248

HVPG: hepatic venous pressure gradient. *p<0.05, **p<0.01

Table 5: C-Statistics for Prediction of 3-month, 1-year and 3-year Mortality for Child-Pugh and MELD Model.

	3-month survival (95% CI)	1-year survival (95% CI)	3-year survival (95% CI)
MELD	0.772 (0.621-0.923)	0.680 (0.484-0.876)	0.647 (0.417-0.877)
CPS	0.795 (0.648-0.942)	0.732 (0.535-0.930)	0.678 (0.440-0.916)

gans among patients awaiting liver transplantation because of its reproducibility, objectivity [7].

However, despite its theoretical advantages, the MELD score does not include major complications of cirrhosis that traditionally constitute poor prognostic factors, such as bleeding varices, spontaneous bacterial peritonitis (SBP), hypoalbuminemia, refractory ascites, and hepatic encephalopathy. Gomez EV et al prospectively estimated the survival of 172 cirrhotic patients, which concluded a combination of 3 clinical indices (ascites, encephalopathy and bleeding esophageal varices) and 2 biochemical parameters (creatinine and bilirubin), was able to accurately predict short-term (12 wk), intermediate-term (52 wk) and long-term (104 wk) mortality in cirrhotic patients [9]. Several investigators have identified the hepatic vein pressure gradient, serum albumin level, serum sodium level as independent predictors of early mortality of hepatic decompensation in patients. Such as, Hyponatremia may reflect hemodynamic abnormalities in advanced cirrhosis [10]. Addition of serum sodium level to the MELD to create the MELDN a score improved accuracy in predicting or transplant after TIPS [10,11]. Other candidate parameters for incorporation into the MELD score to improve prognostic accuracy are listed as parameters of nutritional status, presence of diabetes mellitus, hypocholesterolemia, indocyanine green clearance (a measure of liver blood flow) [12–15].

In the Child–Pugh scoring system, bilirubin and prothrombin time can accurately reflect the liver function. However, hepatic encephalopathy, ascites and albumin are vulnerable to medical intervention [16]. Moreover, as a result of the “ceiling effect” of the Child–Pugh score, classification C patients cannot be conducted in-depth assessment [17].

Our study demonstrated that increasing laboratory levels of creatinine, INR, PT, APTT, GPT, GOT, hyperammonemia increased significantly the risk of death (p<0.05) (Table 5). Decreasing levels of serum sodium also increased the risk of mortality (p<0.05). Presence of refractory ascites or hypovolemia, or hepatorenal syndrome increased the risk of early death. Although the MELD score has already replaced the Child–Pugh score in some areas, such as liver transplant allocation, so far no multicentric and random study has demonstrated an advantage of the MELD model over the Child–Pugh score with respect to prediction of survival. So Hector Ferral et al. indicated that it would be interesting to evaluate discrimination for mortality with the combination of these two scores in a larger series of patients [18].

TIPS placement changes intravascular blood distribution by shifting trapped prehepatic venous blood volume to central venous blood volume in effect like a side-to-side portocaval shunt and promptly reduces portal pressure. A hemodynamic imbalance with portal and hepatic arterial flows induced by the TIPS creation may worsen liver function. If with a blunted hepatic arterial compensation, patients may have an unfavorable outcome after TIPS, even liver failure [2,19].

A relatively precise estimate of the prognosis of an individual cannot in any way replace careful clinical information of

the individual patient. Unpredictable complications such as stenosis of TIPS, development of malignant tumors, or non-liver related events affect the accuracy of the assessment [4,5,20].

Therefore, in patients undergoing TIPS, a better prognostic model should stratify patients into those with a good prognosis and those with a poor one. Our goal is to apply the model in an attempt to identify those patients in whom the invasive procedure may be potentially harmful. With this information, we should be able to discuss risks and benefits of the procedure with a more objective approach.

Conclusions

At present, to obtain a better prognostic model in the future, we should acquire sufficient amounts of relevant clinical information including follow-up data to a greater extent. Some studies report that gene technology and molecular biology including the influence of certain genotypes will improve the precision of prognostic estimates for individual patients [21]. In conclusion, to build a large-scale information network, pooled analysis of data collected in accordance with uniform standards, it will be the direction of building such predictive models.

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