The Model for End-Stage Liver Disease (MELD) Predicts Early and Late Outcomes of Cardiovascular Operations in Patients With Liver Cirrhosis

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Background. We aimed to evaluate the severity of cirrhosis as a predictor of early and late outcomes after cardiovascular operations.

Methods. We retrospectively reviewed patients who underwent cardiovascular operations in our institute between October 1999 and April 2009. The severity of liver cirrhosis was assessed using the Child-Pugh classification and the Model for End-stage Liver Disease (MELD) score.

Results. Liver cirrhosis was identified in 32 consecutive patients. Averages of Child-Pugh and MELD scores were 7.2 ± 1.9 and 11.5 ± 5.1, respectively: 14 patients were classified as Child-Pugh class A, 14 as class B, and 4 as class C. The MELD score was less than 10 (category 1) in 10 patients, between 10 and 14.9 (category 2) in 14, and 15 or higher (category 3) in 8. The hospital mortality rate was 16% (5 of 32). Hospital mortality increased significantly as the MELD score category increased: category 1, 0%; category 2, 7%; and category 3, 50% (p = 0.005). There was no significant association between hospital mortality and Child-Pugh classification: class A, 7%; class B, 21%; and class C, 0% (p = 0.60). Overall survival was 72% ± 8% at 5 years and 47% ± 13% at 10 years. The survival rate decreased significantly as the MELD score category increased (p = 0.004). No relationship was found between the Child-Pugh classification and long-term survival.

Conclusions. Our results suggest that the MELD score is useful to predict hospital death and long-term survival after cardiac operations for patients with liver cirrhosis.


Liver cirrhosis is still a challenging problem in patients undergoing cardiovascular operations with cardiopulmonary bypass (CPB). Several studies have assessed clinical outcome in cardiac surgical patients with liver cirrhosis. The surgical risk in cardiac operations in patients with liver cirrhosis has been generally stratified in relation to the Child-Pugh classification [1–5]. However, definitive recommendations and indications for cardiac operations are still unknown because the population of cardiac surgical patients with liver cirrhosis is substantially small.

The Model for End-stage Liver Disease (MELD) score was initially designed to assess short-term mortality in patients who underwent placement of transjugular intrahepatic portosystemic shunts [6]. In contrast to the Child-Pugh score, the MELD score incorporates an evaluation of renal function, which is an established marker of prognosis in cirrhotic patients. The MELD score has been used to stratify patients awaiting liver transplantation [7]. Recent studies demonstrated the usefulness of MELD score to determine the indication of general operations in patients with liver cirrhosis. Several reports [8–10] have documented the relationship between MELD score and early outcome in cardiac operations, but there have not been any publications, to our knowledge, referring to late outcomes after cardiac operations.

In the present study, we have retrospectively evaluated the relationship between the severity of liver cirrhosis and early and late outcomes after cardiac operations in patients with liver cirrhosis.

Patients and Methods
This retrospective cohort study was approved by the Kobe University Graduate School of Medicine Institutional Review Board. The need for patient consent was waived because of the retrospective nature of the study.

Patients
We reviewed the records of all patients with advanced liver cirrhosis who underwent cardiac operations at our institution from October 1999 to April 2009. The diagnosis of liver cirrhosis was established from a liver biopsy specimen or from a combination of clinical findings and radiographic imaging of the liver, including ultrasound, computed tomography, or magnetic resonance imaging showing nodular liver surface, cours ed echogenicity of liver parenchyma, splenomegaly, or ascites. The finding of cirrhotic liver on prior laparoscopy or laparotomy, or the detection of esophageal varices by endoscopy, was

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Severity of Liver Cirrhosis

The Child-Pugh score was calculated according to the degree of ascites (1, absent; 2, slight; 3, moderate), serum total bilirubin (1, < 2.0 mg/dL; 2, 2 to 3 mg/dL; 3, > 3 mg/dL), serum albumin (1, > 3.5 g/dL; 2, 2.8 to 3.5 g/dL; 3, < 2.8 g/dL), the prothrombin time international normalized ratio (1, < 1.8; 2, 1.8 to 2.3; 3, > 2.3), and the degree of encephalopathy (1, none; 2, grade 1 or 2; 3, grade 3 or 4). The grading of severity of cirrhosis was made as follows: class A, 5 to 6; class B, 7 to 9; and class C, 10 to 15 [11].

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The MELD score was calculated according to the original formula proposed by the Mayo Clinic group as 3.8 \log_{10} (bilirubin \text{[mg/dL]}) + 11.2 \times \log_{10} (prothrombin time international normalized ratio) + 9.6 \times \log_{10} (creatinine \text{[mg/dL]}) [6]. The MELD score has been used to stratify patients awaiting liver transplantation. In general, if the MELD score is 10 or higher, patients are evaluated for a liver transplantation [12]. United Network for Organ Sharing used a MELD score exceeding 15 as one of the criteria for prioritization [7]. Patients in this study were stratified by their preoperative MELD scores into three categories: category 1, less than 10, category 2, 10 to 14.9; and category 3, 15 or higher.

Operative Technique and Perioperative Management

Preoperative malnutrition, sodium retention, ascites, or hyperammonemia was treated, if possible. Intraoperatively, 30 mg/kg methylprednisolone was administered into the pump prime. The heparinization protocol for CPB included administration of 200 U/kg with serial monitoring using the celite activator to keep the activated clotting time between 400 and 700 milliseconds. The CPB protocol included avoidance of low-flow CPB (perfusion flow index at 2.4 to 3.2 L/min/m², mean perfusion pressure at 60 to 80 mm Hg), and keeping the on-bypass hematocrit at 25% to 35%. Moderate and severe tricuspid regurgitation was aggressively treated by valve repair or replacement to relieve postoperative liver congestion. A biological valve was the first choice of prosthesis in patients with Child-Pugh class B or C to minimize the effect of anticoagulation on bleeding complications of liver cirrhosis. Dilutional ultrafiltration was performed throughout CPB. Hemodynamic stability (keeping mean blood pressure > 80 mm Hg and cardiac index > 2.5 L/min/m²) and the oxygen supply to the liver (keeping arterial partial oxygen pressure > 120 mm Hg) were maintained during the postoperative period.

Outcome Definitions

Early mortality was defined as death within 30 days after the operation. Postoperative major complications included bleeding requiring reexploration, sepsis, stroke, multisystem disorder, prolonged ventilation for more than 72 hours, myocardial infarction, arrhythmia, and new-onset renal failure.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation. Values with a p of less than 0.05 were considered significant. Comparisons of continuous variables between groups were performed by one-way analysis of variance. Logistic regression analysis was performed to find the predictor of hospital death. Long-term survival was estimated by the Kaplan-Meier method and compared with the log-rank test. Statistical analyses were performed with SPSS 13.1 software (SPSS, Chicago, IL).

Results

Patient and Operative Characteristics

Of 2,079 consecutive patients who underwent cardiovascular operations, 32 (21 men and 11 women) were identified as having liver cirrhosis. Excluded from the study was the Child-Pugh class B patient who was receiving hemodialysis and home oxygenation therapy and did not undergo an operation for asymptomatic aortic stenosis.

Patient and operative characteristics are reported in Tables 1 and 2. The mean patient age was 69.8 ± 9.4 years (range, 45 to 83 years). The underlying etiology of liver cirrhosis was viral hepatitis B in 17 patients, viral hepatitis C in 8, and alcoholic in 7. Five had a history of esophageal variceal hemorrhage. The Child-Pugh score averaged 7.2 ± 1.9 and MELD score averaged 11.5 ± 5.1. The relationship between the Child-Pugh and MELD scores is shown in Figure 1. Types of cardiovascular operations were off-pump coronary artery bypass grafting in 6, valve operations in 19, combined coronary artery bypass grafting and valve operations in 2, and replacement of the thoracic aorta in 6. Emergent operations were required in 7 patients (22%). Of 16 patients who underwent valve replacement, 12 received biological valves and 4 received mechanical valves.

Early Outcomes

Early outcomes are reported in Table 3. Early mortality was 9.4% (3 of 32). Hospital mortality was 15.6% (5 of 32). Cause of early death was multiorgan failure in 2 patients and esophageal variceal bleeding in 1. Two patients who underwent repeat valve operations died of multiorgan failure after persistent hypotension caused by massive perioperative bleeding. One patient, who underwent emergent aortic repair for acute type A aortic dissection without preoperative surveillance of liver disease, died of unexpected massive esophageal variceal bleeding on postoperative day 20. The remaining 2 patients, who experienced sepsis and subsequent multiorgan failure, were not able to achieve postoperative recovery and died of pneumonia at 3 and 6 months after their operation.

One or several major complications occurred in 17 patients (53%). Reexploration for bleeding occurred in 9 (28.1%), sepsis in 7 (21.8%), stroke in 0 (9%), renal failure in 3 (9.4%), multiorgan failure in 5 (15.6%), and prolonged ventilation (> 72 hours) in 10 (31.2%). CPB time exceeded 150 minutes in 14 patients. Longer CPB time had
tendency to increase blood loss, but the difference in blood loss between patients with and without a long CPB time (1,030 ± 458 vs 670 ± 805 mL) was not statistically significant (p = 0.131).

Relationship Between the Severity of Liver Cirrhosis and Early Outcome of Cardiac Operations

Of the 32 patients, 14 were Child-Pugh class A (score < 7), 14 were class B (score = 7–9), and 4 were class C (score > 9). Preoperative and intraoperative variables are listed in Table 1. Patients with a higher Child-Pugh score were more likely to have alcohol-related etiology of liver disease (p = 0.012). Other preoperative risk factors were similar, including age, sex, ejection fraction, and congestive heart failure. The rate of emergency operations increased as the severity of Child-Pugh class increased (p = 0.002).

Patients with Child-Pugh class A, B, and C had hospital mortality of 14%, 21%, and 0%, respectively. The mortality rate and the incidence of postoperative major complications did not increase with increasing the severity of Child-Pugh class (p = 0.06).

Relationship Between MELD Score and Early Outcome

The MELD score was less than 10 (category 1) in 10 patients, between 10 and 14.9 (category 2) in 14, and 15 and higher (category 3) in 8. As reported in Table 1, patients with a higher MELD score were more likely to have chronic kidney disease (p = 0.001) and a higher level of total bilirubin (p = 0.014) and creatinine (p = 0.001). Other preoperative and intraoperative variables were similar across the groups. The incidence of major complications increased in patients with worse MELD scores (p = 0.05). Major complications occurred in 57% of patients with a MELD score of 10 to 14.9 and in 75% of patients with a MELD score of 15 and higher. The incidence of sepsis (p < 0.001), multiorgan failure (p = 0.005), and new-onset renal failure requiring

Table 2. Intraoperative Data

<table>
<thead>
<tr>
<th>Intraoperative Variables</th>
<th>Child-Pugh Score</th>
<th>MELD Score</th>
<th>p Value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of operation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve</td>
<td>&lt;7 (n = 14)</td>
<td>7–9 (n = 14)</td>
<td>≥10 (n = 4)</td>
<td>&lt;10 (n = 10)</td>
</tr>
<tr>
<td>Coronary artery</td>
<td>6 (43)</td>
<td>2 (14)</td>
<td>0</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Aortic</td>
<td>1 (7)</td>
<td>4 (29)</td>
<td>1 (25)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>CPB time, min</td>
<td>185 ± 96</td>
<td>164 ± 75</td>
<td>181 ± 101</td>
<td>113 ± 102</td>
</tr>
<tr>
<td>Emergency</td>
<td>0</td>
<td>4 (29)</td>
<td>3 (75)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>6 (43)</td>
<td>8 (64)</td>
<td>2 (50)</td>
<td>4 (40)</td>
</tr>
</tbody>
</table>

* Continuous data are shown as mean ± standard deviation and categoric data as number (%).

CPB = cardiopulmonary bypass; MELD = Model for End-stage Liver Disease.
dialysis \((p = 0.005)\) significantly increased with increasing MELD score.

**Risk Factors Related to Hospital Death**

Logistic regression analysis showed that a MELD score of 15 or higher \((\text{odds ratio, 17.6; 95\% confidence interval, 1.6 to 193.4; } p = 0.019)\) was a sole predictor of hospital death.

**Long-Term Results**

During a mean follow-up of 5.5 ± 3.7 years (median, 6.7 years; range, 0.1 to 11.9 years), late death was observed in 13 patients at a median of 2.2 years (range, 0.4 to 8.6 years) after their cardiovascular operations. Causes of late death were hepatic failure in 4, esophageal variceal bleeding in 2, sepsis in 2, heart failure in 2, pneumonia in 2, and stroke in 1. Two of 13 late deaths occurred within 1 year postoperatively. Two patients who survived for 30 days died of sepsis, without hospital discharge. Two patients died in other hospitals, one of hepatic failure at 4 months and the other of pneumonia at 10 months. At the latest follow-up, 16 patients were alive. An average of their follow-up was 8.9 ± 1.9 years \((\text{range, 5.2 to 12.1 years})\). All Child-Pugh class C patients died during follow-up. Causes of late deaths in Child-Pugh class C patients were hepatic failure in 1, pneumonia in 1, and esophageal variceal bleeding in 2. The overall survival rate, excluding early deaths, was 86% ± 6% at 1 year, 76% ± 8% at 3 years, 72% ± 8% at 5 years, and 47% ± 13% at 10 years \((\text{Fig 2})\).

The 5-year survival rate \((\text{excluding early deaths})\) was 69% ± 13% in Child-Pugh class A patients, 67% ± 14% in class B, and 73% ± 22% in class C \((\text{log-rank test } p = 0.569, \text{Fig 3A})\). The 5-year survival rate \((\text{including early deaths})\) was 90% ± 10% in patients with a MELD score of less than 10, 69% ± 13% in patients with a MELD score of 10 to 14.9, and 50% ± 20% in patients with a MELD score of 15 or higher. Analysis by log-rank test demonstrated a significant decrease in long-term survival with increasing MELD score \((p = 0.002, \text{Fig 3B})\). Cox proportional hazard analysis identified a MELD score 15 or higher \((\text{hazard ratio, 3.8; 95\% confidence interval, 1.3 to 10.7; } p = 0.012)\) as a significant predictor of survival.

**Comment**

This is a descriptive report of a single-center experience with cardiac operations in 32 patients with liver cirrhosis. We investigated the predictive factors and long-term survival of patients with cirrhosis undergoing cardiac operations. The overall hospital mortality was 16%. The mortality rate was not correlated with the severity of Child-Pugh classification \((\text{class A, 14\%; class B, 21\%; class C, 22\%})\).

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### Table 3. Early Outcome

<table>
<thead>
<tr>
<th>Postoperative Outcome</th>
<th>Child-Pugh Score</th>
<th>MELD Score</th>
<th>(p) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(&lt; 7) ((n = 14))</td>
<td>(7-9) ((n = 14))</td>
<td>(\geq 10) ((n = 4))</td>
</tr>
<tr>
<td>Major complication</td>
<td>5 (36) 8 (64) 4 (100)</td>
<td>0.06</td>
<td>3 (30) 8 (57) 6 (75)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>3 (21) 5 (36) 1 (25)</td>
<td>0.72</td>
<td>2 (20) 4 (29) 3 (38)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1 (7) 5 (36) 1 (25)</td>
<td>0.20</td>
<td>0 1 (7) 6 (75)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 0 0(&gt;0.99)</td>
<td></td>
<td>0 0 0(&gt;0.99)</td>
</tr>
<tr>
<td>Multiorgan disorder</td>
<td>2 (14) 3 (21) 0</td>
<td>0.60</td>
<td>0 1 (7) 4 (50)</td>
</tr>
<tr>
<td>Prolonged ventilation</td>
<td>3 (21) 6 (43) 1 (25)</td>
<td>0.48</td>
<td>1 (10) 5 (36) 4 (50)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 0 0(&gt;0.99)</td>
<td></td>
<td>0 0 0(&gt;0.99)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>0 0 0(&gt;0.99)</td>
<td></td>
<td>0 0 0(&gt;0.99)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1 (7) 2 (14) 0</td>
<td>0.66</td>
<td>0 0 3 (38)</td>
</tr>
<tr>
<td>Early death</td>
<td>1 (7) 2 (14) 0</td>
<td>0.66</td>
<td>0 1 (7) 2 (25)</td>
</tr>
<tr>
<td>Hospital death</td>
<td>2 (14) 3 (21) 0</td>
<td>0.60</td>
<td>0 1 (7) 4 (50)</td>
</tr>
</tbody>
</table>

MELD = Model for End-stage Liver Disease.
C, 0%). We found significant correlation between operative mortality and MELD score. A MELD score of 15 or higher was a sole predictor of early and late outcome after cardiovascular operations in patients with liver cirrhosis.

The life expectancy of liver cirrhosis is an important factor to discuss when a patient with liver cirrhosis presents with an indication for a cardiovascular operation. Survival at the time of the diagnosis of liver cirrhosis was reported to range from 84% to 91% at 5 years and from 68% to 79% at 10 years [13, 14]. A systematic review of 118 studies by D’Amico and colleagues [15] showed survival in patients with liver cirrhosis was 78% at 1 year and 75% at 2 years. In this study, the survival rates among hospital survivors were 81% ± 7% at 3 years and 78% ± 8% at 5 years. These survival rates were similar to the survival rates in patients with liver cirrhosis. If patients with cirrhosis survive the cardiac operation, the prognosis after hospital discharge will be acceptable.

Cirrhotic patients carry a high risk, especially for cardiac operations. The surgical risk in cardiac operations in patients with liver cirrhosis has been generally stratified in relation to the Child-Pugh classification. The published studies are all small, but all have shown increases in postoperative complications and mortality rates [1–5, 16–18]. In the study of 13 patients by Klemperer and associates [1], no deaths were reported in patients with Child-Pugh class A cirrhosis, but mortality was 80% in patients with class B or C cirrhosis. A similar study of 18 patients by Hayashida and associates [3] demonstrated mortality of 0%, 50%, 100% for patients with, respectively, Child-Pugh class A, B, and C cirrhosis. Therefore, Child-Pugh class B or C cirrhosis has been accepted as relative contraindication for elective cardiac operations because of high mortality and morbidity rates. In this series, 3 of 4 Child-Pugh class C patients underwent emergent operations. More recently, however, Lin and associates [4] reported an operative mortality of 0% in 5 patients with class B or C cirrhosis. Filsoufi and associates [5] demonstrated a hospital mortality of 18% in 11 patients with class B cirrhosis. We recently reported improved outcome in cardiac operations in patients with advanced cirrhosis [18].

These improvements in perioperative outcome of cirrhotic patients have been achieved as the result of advances in preoperative imagining, surgical technique, anesthesia, and critical care unit management. However, the most important factor for better outcome in cirrhotic patients is probably based on a careful and accurate patient selection. Today, it has already become difficult to
decide definitive recommendations and indications for cardiovascular operations only by the Child-Pugh classification. The findings of this study suggest that using the MELD score in addition to the Child-Pugh classification will be useful to determine the accurate operative indication in patients with liver cirrhosis. The MELD score was initially designed to assess short-term mortality in patients who underwent placement of transjugular intrahepatic portosystemic shunts [6]. Further analysis of the MELD score demonstrated its usefulness as a clinical tool to assess liver disease severity in general [19, 20]. The advantage of the MELD score is that it is based on multivariate analysis of objective and widely available laboratory tests for serum bilirubin, serum creatinine, and the international normalized ratio of prothrombin time. These biological variables, in contrast to ascites and encephalopathy in the Child-Pugh scoring model, are not influenced by individual judgment. Bilirubin derives from hemolytic factors as well as hepatocellular function and biliary excretion and is correlated to hepatic metabolic capacity tests such as the clearance tests for galactose and for aminopyrine [21]. Hemolysis is known to be a poor prognostic factor in patients with alcohol-related liver disease [6]. Renal dysfunction carries a poor prognosis in patients with chronic liver disease, and several studies have noted the association of elevated creatinine with poor survival in patients with liver cirrhosis [22, 23]. Northup and associates [24] reported that prolonged prothrombin time and elevated creatinine were useful to predict the risk of nontransplant surgical death in cirrhotic patients. The MELD score has been used to stratify patients awaiting liver transplantation [7].

Several clinical series in cardiovascular surgery have assessed the utility of Child-Pugh classification and MELD score. Suman and associates [8] demonstrated that both the Child-Pugh classification and MELD score could predict postoperative hepatic decompensation and death after cardiac operations in 44 cirrhotic patients. Morisaki and associates [9] reported that a MELD score exceeding 13 was significantly associated with hospital morbidity after cardiac operations in 42 cirrhotic patients. Ailawadi and associates [10] reported that a MELD score of 15 or higher predicted death after tricuspid valve operations. However, Filsoufi and associates [5], showed that the Child-Pugh classification had better correlation with early and late outcomes of cardiac operations in 27 patients with liver cirrhosis. We found that the MELD score was a more significant risk factor than the Child-Pugh classification.

Our results indicated that the MELD score of 15 and higher was a reliable predictive value for survival in patients with cirrhosis undergoing cardiac operations. This finding was similar to those in previous studies [9, 10]. In patients with liver cirrhosis who are candidates for cardiac operations, the MELD score may be used to plan management. Postoperative mortality was low enough in patients with a MELD score of less than 15 that the risk of the operation might be judged to be acceptable. In patients with a MELD score of 20 or higher, the risk of death is so high that an elective procedure may be postponed and the patient’s candidacy for liver transplantation should be considered. A cardiac operation combined with liver transplantation could be beneficial [25]. Caution needs to be exercised for patients with MELD scores between 15 and 19, and the MELD score should be adjusted down by optimizing the patient’s condition, if possible.

Tricuspid regurgitation could increase abnormal liver function and hyperbilirubinemia secondary to liver congestion. Henrion and associates [26] analyzed liver biopsy tests in 142 patients with congestive heart failure and demonstrated that hepatocellular necrosis was caused by liver congestion or hypoxia. Lau and associates [27] found a significant correlation between the severity of tricuspid regurgitation and hyperbilirubinemia in patients with congestive heart failure. Thus, tricuspid regurgitation is one of the contributing factors to hepatic damage. Treating tricuspid regurgitation can prevent perioperative congestive hepatic damage and is important, especially in patients with liver cirrhosis. We aggressively treat moderate or severe tricuspid regurgitation.

The present study has several limitations that must be recognized. The study design was retrospective. Although the number of patients was relatively large, the sample size was still small. The types of operations were very mixed, ranging from off-pump coronary artery bypass grafting to valvular and aortic operations. Therefore, analyzing the values for stratified surgical procedures is difficult because of the very small number for each procedure. Another limitation was the possibility that the indication of cardiovascular operations might be determined according to Child-Pugh classification. Higher rate of emergent operations in Child-Pugh class C patients indicated that the bias could be caused among patients stratified according to Child-Pugh class.

In conclusion, in this study we have confirmed the prognostic ability of the MELD score for both hospital death and long-term survival after cardiac operations for patients with liver cirrhosis. We did not find a significant association between Child-Pugh classification and clinical outcome after cardiac operations. Early and late outcomes of cardiac operations were acceptable in patients with a MELD score of less than 15. Our results suggest that the MELD score is useful to predict both hospital death and long-term survival after cardiac operations for the patients with liver cirrhosis. Further investigations with a larger and more homogenous cohort would be needed to provide more definitive evidence.

References


