Surgical outcomes after cardiac surgery in liver transplant recipients

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Objective: This was a single-center retrospective study to assess the surgical outcomes and predictors of mortality of liver transplant recipients undergoing cardiac surgery.

Methods: From 2000 to 2010, 61 patients with a functioning liver allograft underwent cardiac surgery. The mean interval between liver transplantation and cardiac surgery was 5.4 ± 4.4 years. Of the 61 patients, 33 (54%) were in Child-Pugh class A and 28 in class B. The preoperative and postoperative data were reviewed.

Results: The overall in-hospital mortality was 6.6%. The survival rate was 82.4% ± 5.1% at 1 year and 50.2% ± 8.2% at 5 years. Cox regression analysis identified preoperative encephalopathy (odds ratio, 5.2; 95% confidence interval, 1.8-15.5; $P = .003$) and pulmonary hypertension (odds ratio, 3.5; 95% confidence interval, 1.3-9.4; $P = .045$) as independent predictors of late mortality. The preoperative Model for End-Stage Liver Disease (MELD) scores of patients who died in-hospital or late postoperatively were significantly greater statistically than the scores of the others (in-hospital death, 23.7 ± 7.8 vs 13.1 ± 4.5, $P < .001$; late death, 15.2 ± 6.1 vs 12.3 ± 4.1, $P = .038$). The Youden index identified an optimal MELD score cutoff value of 13.5 (sensitivity, 56.0%; specificity, 67.6%). Kaplan-Meier survival analysis successfully demonstrated that the survival rate of the MELD score less than 13.5 (MELD <13.5) group was significantly greater than that of the MELD >13.5 group (MELD <13.5 group, 93.8% ± 4.2% at 1 year and 52.4% ± 11.8% at 5 years; MELD >13.5 group, 66.9% ± 9.6% at 1 year and 46.1% ± 11.1% at 5 years; $P = .027$). In contrast, the survival rate when stratified by Child-Pugh class (class A vs B) was not significantly different.

Conclusions: Cardiac surgery in the liver allograft recipients was associated with acceptable surgical outcomes. Preoperative encephalopathy and pulmonary hypertension were independent predictors of late mortality. The cutoff value of 13.5 in the MELD score might be useful for predicting surgical mortality in cardiac surgery. (J Thorac Cardiovasc Surg 2013;145:1072-6)

The survival of liver transplant recipients has been improved by the remarkable advances in surgical technique, pre- and postoperative management, and immunosuppressive protocols,[1] resulting in a potential increase in the number of patients with a history of liver transplantation requiring cardiac surgery. It has been reported that more than 70% of liver allograft recipients experience cardiac events,[2] that cardiac complications after liver transplantation are common, and that these have been the leading cause of death after liver transplantation.[3] Organ allograft recipients require immunosuppressant agents, placing the patients at great risk of peri- and postoperative infection.[4] It has also been assumed that the liver functional reserve in liver transplantation recipients is subnormal,[5] leading to an increased risk of surgical morbidity and mortality. Although this topic is an important entity in clinical practice, only a few of studies are available.

The purpose of the present study was to summarize our experience with surgical management of patients with a history of liver transplantation who were undergoing cardiac surgery and to determine the short- and long-term surgical outcomes and predictors of mortality.

PATIENTS AND METHODS

The quality improvement review committee of the University of Pittsburgh Medical Center approved the present study and waived the need for patient consent. From January 2000 to June 2010, 61 patients with a functioning liver allograft who were undergoing cardiac surgery at the University of Pittsburgh Medical Center were identified, and their data were retrospectively collected from our cardiac surgical database and a review of their medical records. The mean follow-up period was 3.1 ± 2.6 years. The follow-up was completed by telephone interview, and late outcomes were cross-referenced using the Social Security Death Index. The patient demographics are detailed in Table 1. Their mean age was 61.5 ± 8.2 years. Of the 61 patients, 45 (73.8%) were men; 19 patients (31.1%) had chronic renal insufficiency preoperatively, defined as a baseline serum creatinine >2.0 mg/dL, and 13 patients (21.3%) required dialysis. The Child-Pugh class was class A for 33 patients (54%) and class B for 28 patients (46%). No patient in Child-Pugh class C underwent cardiac surgery. All patients were treated and followed up by our liver transplantation team for pre- and postoperative management. Pre- and postoperative

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Abbreviations and Acronyms
AUC = area under the curve
MELD = Model for End-Stage Liver Disease
ROC = receiver operating characteristic

encephalopathy was diagnosed by the liver transplant team using the hepatic encephalopathy grading system.[6] The mean preoperative Model for End-Stage Liver Disease (MELD) score was 13.5 ± 5.2. The mean interval between liver transplantation and cardiac surgery was 5.4 ± 4.4 years. The primary surgical indications included coronary artery disease in 31, valvular disease in 25 (aortic valve in 17, mitral valve in 4, aortic and mitral valves in 3, and tricuspid valve in 1), and other indications in 5. Of the 61 patients, 11 (18%) required emergent surgery. The indications for emergent surgery were unstable acute coronary syndrome in 6, acute endocarditis with acute heart failure in 3, and critical aortic stenosis with progressively deteriorating hemodynamics in 2. Six patients (9.8%) has acute endocarditis diagnosed according to the Duke criteria.[7]

Statistical Analysis

Continuous variables are reported as the mean ± standard deviation and categorical variables as frequencies. Fisher's exact test or the chi-square test was used to evaluate categorical variables on univariate analysis. Student's *t* test or the Mann-Whitney *U* test was used for the continuous variables owing to the distribution of the data. The Kaplan-Meier model was used to calculate the estimates for long-term survival. The logistic regression model and Cox regression model was used to determine the independent predictors of in-hospital mortality and late mortality, respectively. Only variables with $P < .05$ on univariate analysis were retained for the multivariate regression tests. For all analyses, 2-sided tests were used. The sensitivity and specificity of the preoperative MELD score as an indicator of mortality were determined from the cutoff values. Receiver operating characteristic (ROC) curves and the area under the curve (AUC) for the ROC curve were obtained by plotting the sensitivity against the false-positive rate (1 − specificity). The Youden index was used to determine the optimal cutoff values of the MELD score for identification of the surgical risk of mortality (Youden index = sensitivity + specificity − 1). All statistical analyses were performed using SPSS (SPSS, Chicago, Ill).

RESULTS

The surgical procedures are summarized in Table 2. Isolated coronary artery bypass grafting was performed in 31 patients. The off-pump technique was used in 13 (42%) of the isolated coronary artery bypass grafting 31 cases. Single valve replacement or repair was required in 13 cases (21.3%; aortic valve in 9, mitral valve in 3, and tricuspid valve in 1). Double valve surgery (aortic and mitral valves) was performed in 3. Concomitant coronary artery bypass grafting was performed in 8 patients, along with single valve surgery (aortic valve in 6, mitral valve in 1, and aortic root replacement in 1).

The operative data and postoperative complications are listed in Table 3. The mean cardiopulmonary bypass time was 130 ± 64 minutes. Four patients (6.6%) required reoperation for bleeding. Eleven patients (18.0%) experienced prolonged intubation, defined as intubation for longer than 72 hours, and 5 of these patients subsequently required tracheostomy. Seven patients (11.5%) developed acute renal failure, defined as newly occurring postoperative peak serum creatinine >2.0 mg/dL. Four patients (6.6%) newly required dialysis in the postoperative period. Postoperative infection (ie, bacteremia, pneumonia) occurred in 15 patients (24.6%). Postoperative liver complications during the follow-up period developed in 19 patients: 7 developed ascites (5 in the postoperative in-hospital period and 2 after discharge) and 12 developed encephalopathy (8 in the postoperative in-hospital period and 4 after discharge). Additional liver complications occurring after discharge included drug-induced liver dysfunction in 1, bile stricture in 2, graft rejection in 2, and recurrent hepatitis C in 1 patient. The graft rejection was likely because of noncompliance with the immunosuppressant therapy in 1 patient. The second patient required subsequent liver repeat transplantation about 5 months after cardiac surgery for unknown reasons.

The overall in-hospital mortality was 6.6% (4/61). The in-hospital mortality stratified by Child-Pugh class was 6.1% (2/33) and 7.1% (2/28) for class A and B, respectively ($P = 1.00$), Univariate analysis identified preoperative dialysis ($P = .008$), serum creatinine >2.0 mg/dL ($P = .027$), and active endocarditis ($P = .023$) as preoperative predictors and reoperation for bleeding ($P = .01$), prolonged intubation ($P = .005$), new requirement for dialysis ($P = .016$), and new-onset encephalopathy ($P = .043$) as postoperative predictors of in-hospital mortality. No predictor of in-hospital mortality, however, was identified on multivariate analysis. Emergent surgery was not a predictor of in-hospital or late mortality ($P = .14$ and $P = .50$, respectively). The preoperative MELD score was significantly greater for the patients who died in-hospital than for those who survived to discharge (23.7 ± 7.8 vs 13.1 ± 4.5; $P < .001$). The survival rate was 82.4% ± 5.1% at 1 year, 71.8% ± 6.3% at 3 years, and 50.2% ± 8.2% at 5 years after cardiac surgery. Comparing Child-Pugh class A and B, the survival rates were 83.5% ± 6.8% at 1 year and 57.2% ± 10.3% at 5 years for Child-Pugh class A and 81.1% ± 7.6% at 1 year and 39.7% ± 13.2% at 5 years for Child-Pugh class B, respectively, with no significant difference (log-rank test, $P = .603$; Figure 1, *A*). On univariate analysis, the statistically significant factors associated with late mortality were preoperative encephalopathy ($P = .012$), serum creatinine >2.0 mg/dL ($P = .012$), and pulmonary hypertension, defined as pulmonary systolic pressure >60 mm Hg ($P = .016$). The Cox regression analysis revealed preoperative encephalopathy (odds ratio, 5.2; 95% confidence interval 1.8-15.5; $P = .003$) and preoperative pulmonary hypertension (odds ratio, 3.5; 95% confidence interval, 1.3-9.4; $P = .045$) as independent predictors of late mortality. The preoperative MELD score for the late mortality group was significantly greater statistically than in the survivors (15.2 ± 6.1 vs 12.3 ± 4.1; $P = .038$). The Youden index revealed that the optimal