



Single-Center Experience Using Marginal Liver Grafts in Korea

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ABSTRACT

Background. Liver transplantation (LT) is an established therapeutic modality for patients with end-stage liver disease. The use of marginal donors has become more common worldwide due to the sharp increase in recipients, with a consequent shortage of suitable organs. We analyzed our single-center experience over the last 8 years in LT to evaluate the outcomes of using so-called “marginal donors.”

Methods. We retrospectively analyzed the database of all LTs performed at our institution from 2009 to 2017. Only patients undergoing deceased-donor LTs were analyzed. Marginal grafts were defined as livers from donors >60 years of age, livers from donors with serum sodium levels >155 mEq, graft steatosis >30%, livers with cold ischemia time \geq 12 hours, livers from donors who were hepatitis B or C virus positive, livers recovered from donation after cardiac death, and livers split between 2 recipients. Patients receiving marginal grafts (marginal group) were compared with patients receiving standard grafts (standard group).

Results. A total of 106 patients underwent deceased-donor LT. There were 55 patients in the standard group and 51 patients in the marginal group. There were no significant differences in terms of age, sex, Model for End-Stage Liver Disease score, underlying liver disease, presence of hepatocellular carcinoma, and hospital stay between the 2 groups. Although the incidence of acute cellular rejection, cytomegalovirus infection, and postoperative complications was similar between the 2 groups, the incidence of early allograft dysfunction was higher in the marginal group. With a median follow-up of 26 months, the 1-, 3-, and 5-year overall and graft (death-censored) survivals in the marginal group were 85.5%, 75%, and 69.2% and 85.9%, 83.6%, and 77.2%, respectively. Patient overall survival and graft survival (death-censored) were significantly lower in the marginal group ($P = .023$ and $P = .048$, respectively). On multivariate analysis, receiving a marginal graft (hazard ratio [HR], 4.862 [95% confidence interval (CI), 1.233–19.171]; $P = .024$) and occurrence of postoperative complications (HR, 4.547 [95% CI, 1.279–16.168]; $P = .019$) were significantly associated with worse patient overall survival. Also, when factors associated with marginal graft were analyzed separately, graft steatosis >30% was independently associated with survival (HR, 5.947 [95% CI, 1.481–23.886]; $P = .012$).

Conclusions. Patients receiving marginal grafts showed lower but acceptable overall survival and graft survival. However, because graft steatosis >30% was independently associated with worse survival, caution must be exercised when using this type of marginal graft by weighing the risk and benefits.

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LIVER TRANSPLANTATION (LT) is an established therapeutic modality for patients with end-stage liver disease. The main limitation of this treatment is the shortage of organ donors [1,2]. In this situation, many strategies have been proposed to increase the liver pool, including split-liver transplantation, living-donor liver transplantation (LDLT), and domino transplantation. Another alternative is to extend the criteria for donor selection, which is the use of so-called “marginal grafts” [2].

Marginal or extended criteria donors are defined as those with a greater risk of initial poor function or graft failure and therefore an increased risk for recipient morbidity and mortality [3]. Although an accepted definition of marginal graft has not been reached by all centers, some circumstances are known to be related to impaired graft function: elderly donors, a high grade of steatosis, non-heart-beating donors, or split grafts. In addition, organs from other marginal donors may not display graft dysfunction but can transmit an infection to the recipient [3,4].

The use of marginal grafts has become more common worldwide due to the sharp increase in recipients, with a consequent shortage of suitable organs [5]. In Asia, the scarcity of deceased donors has resulted in LDLT as a conventional procedure [1]. In the Republic of Korea, the incidence of deceased organ donation has been much lower than in Western countries, but there is a great demand for LT because of the high prevalence of hepatitis B virus infection and hepatocellular carcinoma (HCC); LDLT accounts for almost 80% of all LTs performed [1,6]. The persistent shortage of deceased-donor liver grafts has stimulated the application and development of adult LDLT [6]. However, because not all recipients always have a living donor available, transplant centers have therefore had to widely expand what they deem to be acceptable organs for transplantation to satisfy the demand for donor livers, leading to the increased use of marginal grafts [7]. Because there have been few reports regarding the use of marginal grafts during LT in the Republic of Korea, the present study analyzes our single-center experience over the last 8 years in LT to evaluate the outcomes with these grafts.

PATIENTS AND METHODS

Patients

We retrospectively analyzed the database of all LTs performed at our institution from 2009 to 2017. Only patients undergoing deceased-donor LT were analyzed. Although previous literature has identified variables associated with an increased risk of graft failure loosely termed marginal or extended criteria liver grafts, there is no consensus definition of what constitutes a marginal graft. In our study, marginal grafts were defined as livers from donors aged >60 years, livers from donors with serum sodium levels >155 mEq, graft steatosis >30%, livers with cold ischemic time ≥12 hours, livers from donors who were positive for hepatitis B or C virus, livers from donation after cardiac death, and livers split between 2 recipients (Table 1). Patients receiving marginal grafts (marginal group) were compared with patients receiving standard grafts (standard group). We analyzed the recipient etiology, Model for End-Stage Liver

Table 1. Characteristics of Marginal Liver Grafts Used in the Study Cohort

Characteristic	No. (%)
Graft steatosis >30%	7 (6.6)
Donor age >60 y	17 (16)
Cold ischemia time ≥12 h	2 (1.8)
Donor serum sodium levels >155 mEq	37 (34.9)
Split graft	1 (0.9)
Viral marker positive*	2 (1.8)

*Only positive for hepatitis B surface antigen. There were no grafts positive for hepatitis C virus.

Disease (MELD) score, length of hospitalization, surgical complications, and incidence of early allograft dysfunction (EAD), among other factors. As in other reports, EAD was defined as the presence of at least 1 of the following: serum bilirubin level >10 mg/dL on postoperative day 7, international normalized ratio ≥1.6 on postoperative day 7, and alanine aminotransferase or aspartate aminotransferase levels >2000 IU/mL within the first 7 days [8]. Patient overall survival and death-censored graft survival were compared between the 2 groups. In addition, multivariate analysis was performed to determine factors associated with overall survival.

Operative Procedure and Postoperative Immunosuppression

Deceased donor LT was mainly performed by using the piggy-back technique with cava-cava latero-lateral anastomosis. Patients received immunosuppression consisting of calcineurin inhibitor therapy, mycophenolate mofetil, and steroids, which was quickly tapered within 3 months.

Statistical Analysis

Continuous numerical variables were compared by using the Student *t* test, and incidence variables were compared by using the Fisher exact test. The Kaplan-Meier method was used to calculate and compare survivals according to the log-rank test. The Cox proportional hazards model was used for multivariate analysis of overall survival. *P* values < .05 were considered statistically significant.

RESULTS

Patient Characteristics

A total of 106 patients underwent deceased-donor LT. The most common characteristics of marginal grafts in order of frequency were donor serum sodium levels >155 mEq, donor age >60 years, and graft steatosis >30% (Table 1). Donors positive for viral markers were all positive for hepatitis B surface antigen; there were no hepatitis C virus-positive grafts. The standard group included 55 patients, and the marginal group included 51 patients. There were no significant differences in terms of age, sex, MELD score, underlying liver disease, presence of HCC, or hospital stay between the 2 groups. Hepatitis B was the most common cause for end-stage liver disease and HCC (Table 2). Although the incidence of acute cellular rejection, cytomegalovirus infection, and postoperative complications was similar between the 2 groups, the incidence of EAD was significantly higher in the marginal group.

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