

# One-Year Follow-up of the Changes in Renal Function After Liver Transplantation in Patients Without Chronic Kidney Disease

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## ABSTRACT

**Background.** Impaired renal function is a strong risk factor for morbidity and mortality after liver transplantation (LT). There is clearly a progressive deterioration in renal function after LT. The greatest loss of renal function occurs within the 1st year after LT. Several factors, including calcineurin inhibitors, are associated with decreased renal function. The aims of the present study were to identify changes in renal function before and after LT and to determine the risk factors related to decreased renal function after LT.

**Methods.** We reviewed medical records of 106 LT recipients without moderate to severe chronic kidney disease (estimated glomerular filtration rate [eGFR]  $\geq 60$  mL/min/1.73 m<sup>2</sup>). We investigated eGFR changes from before to 1 year after LT with the use of propensity score matching. Statistical significance of differences between clinical parameters and 1-year eGFR changes was assessed with the use of univariate and multivariate analyses.

**Results.** Mean age was  $49.5 \pm 10.9$  years, and 66% of the patients were male. Mean differences in 1-year eGFR and serum creatinine were  $-32.0 \pm 29.2$  mL/min/1.73 m<sup>2</sup> and  $0.3 \pm 0.3$  mg/dL, respectively. Variables significantly associated with renal dysfunction 1 year after LT were old age, low pre-LT eGFR, low post-LT hemoglobin, and perioperative acute kidney injury. Multivariate analysis showed that pre-LT renal function was an independent risk factor for decreased renal function after LT. However, there was no significant correlation between 1-year eGFR change and serum tacrolimus level.

**Conclusions.** Renal function significantly decreased the 1st year after LT, and baseline renal function was an independent risk factor for worsening renal function in LT recipients.

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**I**MPAIRED renal function after liver transplantation (LT) increases morbidity and mortality of LT recipients [1–6]. Renal impairment, defined as an estimated glomerular filtration rate (eGFR)  $< 60$  mL/min/1.73 m<sup>2</sup>, occurs in 20%–70% of LT long-term survivors [1,7]. Five percent of patients per year develop end-stage renal disease (ESRD) requiring renal replacement therapy [8]. Because the number of patients undergoing LT has been increasing steadily, appropriate management of impaired renal function is considered to be very important. Risk factors for decreased renal function include hepatitis C, age, female sex, diabetes mellitus (DM), hypertension, preexisting proteinuria, a reduced eGFR before or 6–12 months after LT, and

calcineurin inhibitor (tacrolimus) [9]. It is well known that decreased renal function is common within the 1st year after LT and is related to long-term renal function [5].

However, studies of impaired renal function after LT in patients without moderate to severe chronic kidney disease (CKD) before LT are rare. Risk factors for decreased renal function after LT are also obscure. The aims of the present

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study were to investigate changes in renal function from before to 1 year after LT and to determine risk factors associated with decreased renal function in LT recipients.

## METHODS

In this retrospective single-center study, we reviewed medical records of patients who had undergone LT at Daegu Catholic University Medical Center from January 2012 to December 2013. During this study period, 136 patients underwent LT. Among them, 106 patients without moderate to severe CKD were included in this study. All registered patients were followed for >1 year. Renal function was evaluated with the use of eGFR calculated by means of the Modification of Diet in Renal Disease equation. We excluded patients diagnosed with CKD stage III-V (eGFR <60 mL/min/1.73 m<sup>2</sup>) before LT and those who were lost to follow-up or died within 1 year after LT. Calcineurin inhibitor (tacrolimus)-based immunosuppressive therapy was given to all patients.

We calculated the change in eGFR from before to 1 year after LT. Patients were divided into 2 groups based on their eGFR 1 year after LT to analyze clinical parameters associated with decreased renal function. Patients with GFR ≥60 mL/min/1.73 m<sup>2</sup> were assigned to group 1, and the remaining patients to group 2. We defined moderate to severe CKD as eGFR <60 mL/min/1.73 m<sup>2</sup>.

## Statistical Analysis

Demographic and clinical characteristics of the 2 groups were summarized with the use of descriptive statistics. Quantitative variables were expressed as mean (SD), and qualitative variables were expressed as *n* (%). Propensity score matching (PSM) with the use of age, sex, and DM as confounding matching variables was used to address the statistically significant difference in age and DM between the 2 groups. In the PSM method, logit was used for calipers, the caliper size was 0.145, the matching ratio was 2:1, and the seed number was 34567. Selected variables that were statistically significant in univariate analysis were included as covariates in multivariate analysis using binary multiple logistic regression. The odds ratio (OR), 95% confidence interval of the OR, and *P* value as determined by means of binary multiple logistic regression are presented. A 2-sided *P* value of <.05 was considered to be statistically significant. IBM SPSS v 19.0 was used for all statistical analyses.

## RESULTS

### Characteristics of the Study Population

The average age was 49.5 ± 10.9 years, and the male-to-female ratio was 1.9:1. Livers were transplanted from living donors in 83% of patients. Hepatitis B virus cirrhosis (58.5%) was the most common reason for undergoing LT, and 36.8% of the patients had been diagnosed with liver cancer. Patients with DM (13.2%) and hypertension (8.5%) were included in this study. Perioperative acute kidney injury (AKI) was observed in 43.4% of patients.

### Changes in Renal Function After Liver Transplantation: One-Year Follow-Up

Before LT, mean creatinine was 0.81 ± 0.24 mg/dL and mean eGFR 106.1 ± 27.7 mL/min/1.73 m<sup>2</sup>. One year after LT, mean creatinine was 1.11 ± 0.29 mg/dL and mean

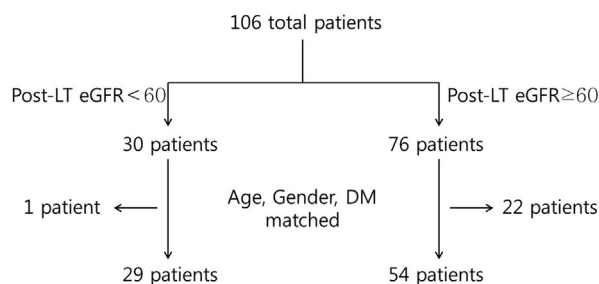
eGFR 74.1 ± 22.6 mL/min/1.73 m<sup>2</sup>. Thus, mean creatinine increased by 0.31 ± 0.34 mg/dL and mean eGFR decreased by 32.1 ± 29.2 mL/min/1.73 m<sup>2</sup>. There were 76 patients in group 1 and 30 in group 2. There were no statistically significant differences in confounding variables between groups after PSM. The number of propensity score-matched patients was 73, with 54 patients in group 1 and 29 in group 2 (Fig 1). Changes in creatinine in groups 1 and 2 were 0.19 ± 0.30 mg/dL and 0.58 ± 0.25 mg/dL, respectively, and the percentages of patients with GFR <90 mL/min/1.73 m<sup>2</sup> before LT in groups 1 and 2 were 19.7% and 50.0%, respectively (Table 1). After PSM, changes in creatinine levels in groups 1 and 2 were 0.18 ± 0.31 mg/dL and 0.58 ± 0.25 mg/dL before and after LT, respectively, and the percentages of patients with GFR <90 mL/min/1.73 m<sup>2</sup> before LT in groups 1 and 2 were 22.2% and 48.2%, respectively (Table 2).

### Risk Factors for Decreased Renal Function After Liver Transplantation

Mean age of patients in group 2 (54.7 ± 9.4 years) was greater than in group 1 (47.4 ± 10.9 years). Both before and after matching, in group 2, perioperative AKI was more common and hemoglobin level 1 year after LT was lower than in group 1. As well as, low pre-LT GFR and rapid GFR loss were significantly more common in group 2 than in group 1 patients. There were significant differences in age, perioperative AKI, hemoglobin, and pre-LT GFR between the 2 groups. There was no significant correlation between decreased renal function and calcineurin inhibitor (tacrolimus) levels in serum (Tables 1 and 2). Multivariate analysis revealed that renal function before LT was an independent risk factor for decreased renal function after LT (Table 3).

## DISCUSSION

LT has been the criterion standard of treatment for patients with end-stage liver disease since the 1st human LT was performed in 1963. More than 6,000 patients received LT in the United States in 2012 [10]. The total number of LTs performed to date is roughly twice the number that had



**Fig 1.** Flow chart of changes in patient number after propensity score matching. Abbreviations: Post-LT eGFR, estimated glomerular filtration rate 1 year after liver transplantation; DM, diabetes mellitus.

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