# Long-Term Outcome of Kidney Retransplantation in Comparison With First Transplantation: A Propensity Score Matching Analysis

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ABSTRACT

Background. Advances in renal transplantation have improved graft survival. However, many patients experience graft failure due to chronic renal allograft nephropathy. Although renal retransplantation is increasingly performed, its outcome is controversial. The aim of this study was to evaluate outcomes of renal retransplantation compared with those of first renal transplantation.

Methods. From March 1969 to August 2018, there were 3000 cases of renal transplantation performed at Seoul St. Mary's Hospital, Korea. Because the number of third renal transplantation was too small, only first and second renal transplantation groups were compared using propensity score matching. Outcomes of the third renal transplantation were then added. Graft survival rates were determined using Kaplan-Meier survival curves and assessed for significance using log-rank test.

Results. Five- and 10-year patient-graft survival rates for the first renal transplantation were 82.6% and 72.8%, respectively. Those for the second renal transplantation were 78.4% and 73.9%, respectively ($P = .588$). Five- and 10-year patient survival rates were 91.2% and 85.1%, respectively, for the first renal transplantation. These were 87.8% and 85.5%, respectively, for the second renal transplantation ($P = .684$). Five- and 10-year death-censored graft survival rates were 88.8% and 80.6%, respectively, for the first renal transplantation. These were 84.6% and 80.5%, respectively, for the second renal transplantation ($P = .564$).

Conclusions. This study showed that graft survival of second renal transplantation was not significantly different from that of first renal transplantation. Therefore, renal retransplantation might be a reasonable option for patients who lost the first renal graft.

RENAL transplantation is the best treatment option for patients suffering from end-stage renal disease [1]. Advances in renal transplantation have improved graft survival. However, many patients experience graft failure due to chronic renal allograft nephropathy [2]. Patients who have failed the first renal transplantation should receive either dialysis or renal retransplantation as a renal replacement therapy [3]. Renal retransplantation provides a better chance for long-term survival and quality of life in patients with allograft loss compared to lifelong dialysis [4]. The number of patients waiting for renal retransplantation is steadily growing [5]. Although renal retransplantation is increasingly performed, its outcome is controversial [6]. Some studies have demonstrated that survival rates of renal retransplantation are lower than those of first renal transplantation [7,8] whereas others have reported that survival rates of renal retransplantation are similar to those of first renal transplantation [9,10]. The aim of this study was to evaluate outcomes of renal retransplantation compared with those of the first renal transplantation. Prognostic factors of patient-graft survival were also examined.

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0041-1345/19
https://doi.org/10.1016/j.transproceed.2019.03.070

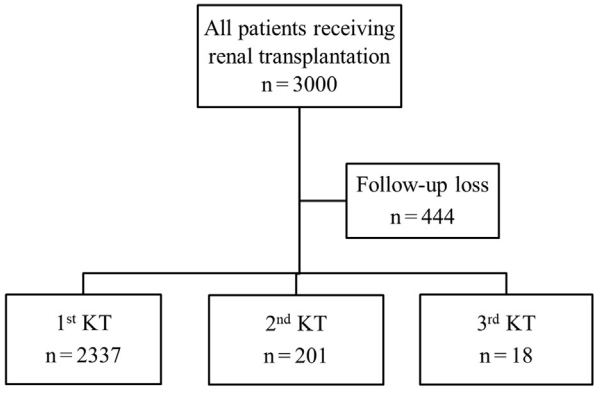


**Fig 1.** Distribution of patient receiving renal transplantation. KT, kidney transplantation.

## METHODS

From March 1969 to August 2018, 3000 cases of renal transplantation were performed at Seoul St. Mary's Hospital, Korea. Except for follow-up loss, there were 2337 cases of first renal transplantation, 201 cases of second renal transplantation, and 18 cases of third renal transplantation. Consequently, 2556 patients were retrospectively analyzed (Fig 1). Because the number of third renal transplantation was too small, only first and second renal transplantation groups were compared using propensity score matching. Outcomes of the third renal transplantation were then added. The Institutional Review Board of Catholic University College of Medicine approved this study (No. KC19RESI0041).

Clinical characteristics, such as age, sex, body mass index, type of donor, immunosuppressive regimen, hypertension, diabetes mellitus, HLA mismatch, and total ischemia time were evaluated. Patient-graft survival was defined based on the time from transplantation to the first event between return to dialysis and patient death with a functional graft. Patient survival was defined based on the time from transplantation to patient death with a functional graft by censoring return to dialysis. Death-censored graft survival was defined based on the time from transplantation to return to dialysis by censoring death with a functional graft [11]. Main immunosuppressants were divided into 3 groups: azathioprine, cyclosporine, and tacrolimus.

### Statistical Analysis

Continuous variables are presented as mean ± SD. Categorical variables are presented as percentages. Analysis was performed with Student $t$ test for continuous variables and $\chi^2$ test for categorical variables. Propensity score was generated by binary logistic regression. Patients with similar propensity scores were selected from the first and second renal transplantation groups (1:1 matching) to reduce the bias in patient distribution. Propensity score was a conditional probability of being part of a group according to a set of measured covariates, including donor age, recipient age, deceased donor, and main immunosuppressant. Comparative analyses were performed for the propensity score-matched group as well as the total population. Graft survival rates were determined using Kaplan-Meier survival curves and assessed for significance using log-rank test. Multivariate analysis was performed using the Cox proportional hazard model. Continuous variables were dichotomized at their median values for statistical analysis. Values of $P < .05$ were considered statistically significant. Statistical analyses were performed using SPSS Statistics version 23.0 (IBM, Armonk, New York, United States).

## RESULTS

### Clinical Characteristics

Characteristics of patients with first and second renal transplantation are summarized in Table 1. After propensity score matching, almost all variables were comparable between both groups except that the first transplantation group had higher recipient body mass index ($P < .001$).

**Table 1. Clinical Characteristics of Patients With First and Second Renal Transplantation (n = 2538)**

| Factor | Before Propensity Score Matching | | | After Propensity Score Matching | | |
|---|---|---|---|---|---|---|
| | First (n = 2337) | Second (n = 201) | *P* Value | First (n = 201) | Second (n = 201) | *P* Value |
| Mean patient age (y) ± SD | 42.3 ± 12.2 | 45.3 ± 10.0 | .001* | 44.8 ± 12.1 | 45.3 ± 10.0 | .663 |
| Mean donor age (y) ± SD | 41.6 ± 12.9 | 40.1 ± 13.1 | .110 | 39.8 ± 13.2 | 40.1 ± 13.1 | .850 |
| Male patient, n (%) | 1416 (60.6) | 127 (63.2) | .470 | 106 (52.7) | 127 (63.2) | .068 |
| Male donor, n (%) | 1275 (54.6) | 111 (55.2) | .855 | 109 (54.2) | 111 (55.2) | .617 |
| Mean patient BMI (kg/m$^2$) ± SD | 22.45 ± 3.56 | 21.33 ± 2.76 | <.001* | 22.63 ± 3.69 | 21.33 ± 2.76 | <.001* |
| Mean donor BMI (kg/m$^2$) ± SD | 23.44 ± 3.32 | 23.19 ± 3.25 | .357 | 23.34 ± 3.32 | 23.19 ± 3.25 | .687 |
| Type of donor | | | .059 | | | 1.000 |
| Living, n (%) | 1800 (77.0) | 143 (71.1) | | 143 (71.1) | 143 (71.1) | |
| Deceased, n (%) | 537 (23.0) | 58 (28.9) | | 58 (28.9) | 58 (28.9) | |
| Main immunosuppressant | | | <.001* | | | .926 |
| Azathioprine, n (%) | 135 (5.8) | 4 (2.0) | | 3 (1.5) | 4 (2.0) | |
| Cyclosporine, n (%) | 888 (38.0) | 44 (21.9) | | 45 (22.4) | 44 (21.9) | |
| Tacrolimus, n (%) | 1314 (56.2) | 153 (76.1) | | 153 (76.1) | 153 (76.1) | |
| Hypertension, n (%) | 1796 (78.1) | 153 (76.1) | .873 | 156 (78.4) | 153 (76.1) | .861 |
| Diabetes, n (%) | 504 (21.9) | 40 (20.3) | .672 | 44 (22.1) | 40 (20.3) | .660 |
| Mean HLA mismatch ± SD | 3.3 ± 1.5 | 3.3 ± 1.4 | .911 | 3.3 ± 1.5 | 3.3 ± 1.4 | .705 |
| Mean total ischemia time (min) ± SD | 98.5 ± 89.6 | 99.1 ± 85.2 | .812 | 97.4 ± 90.0 | 99.1 ± 85.2 | .854 |

Abbreviation: BMI, body mass index.
*$P < .05$ is statistically significant.

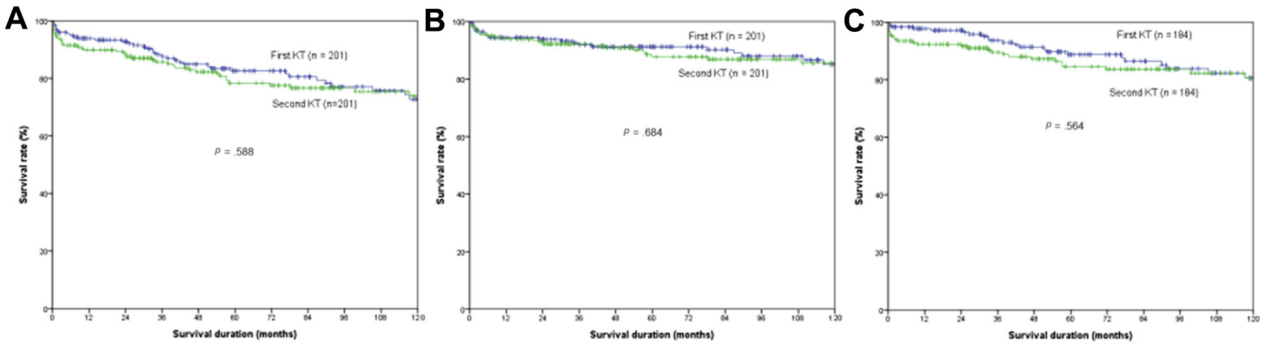


**Fig 2.** Kaplan-Meier survival curve demonstrating **(A)** patient-graft survival; **(B)** patient survival; and **(C)** death-censored graft survival comparing first and second renal transplantation cases (n = 402). KT, kidney transplantation.

### Survival Comparison

The mean duration of the second renal transplantation from the first one was 162.9 months. Median follow-up duration was 75.2 months for the first renal transplantation group and 84.5 months for the second renal transplantation group.

Five- and 10-year patient-graft survival rates for the first renal transplantation were 82.6% and 72.8%, respectively. Those for the second renal transplantation were 78.4% and 73.9%, respectively ($P = .588$). Five- and 10-year patient survival rates were 91.2% and 85.1%, respectively, for the first renal transplantation. These were 87.8% and 85.5%, respectively, for the second renal transplantation ($P = .684$). Five- and 10-year death-censored graft survival rates were 88.8% and 80.6%, respectively, for the first renal transplantation. These were 84.6% and 80.5%, respectively, for the second renal transplantation ($P = .564$) (Fig 2).

### Outcomes of Third Renal Transplantation

The median follow-up duration for the third renal transplantation was 79.5 months. The 5-year patient-graft survival rate for the third renal transplantation was 73.7% (Fig 3). Patient-graft survival rate for the third renal transplantation was lower than that for the first or the second renal transplantation. However, such a difference was not statistically significant ($P = .091$).

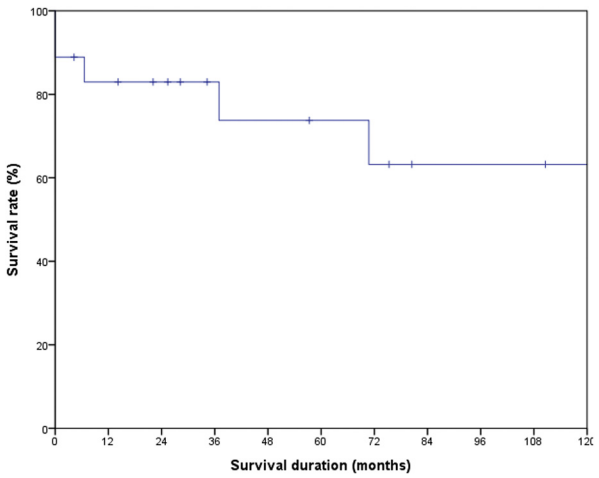


**Fig 3.** Kaplan-Meier survival curve for patient-graft survival after third renal transplantation (n = 18). KT, kidney transplantation.

### Prognostic Factors of Patient-Graft Survival

Prognostic factors of patient-graft survival analyzed for all 2556 patients are shown in Table 2. Older recipient age (≥55 years) (hazard ratio [HR] = 1.440; 95% confidence interval [CI], 1.156–1.793; $P = .001$), older donor age (≥55 years) (HR = 1.681; 95% CI, 1.411–2.003; $P < .001$), male recipient (HR = 1.320; 95% CI, 1.136–1.534; $P < .001$), and immunosuppressant (HR = 2.118; 95% CI, 1.774–2.528; $P < .001$) were independent prognostic factors for patient-graft survival. Retransplantation was not a prognostic factor for patient-graft survival ($P = .715$).

## DISCUSSION

Although renal transplant survival has significantly improved over the years, the risk of graft loss after transplantation has remained unchanged over time primarily attributed to the development of chronic allograft injury [12]. Renal allograft survival is still limited with an estimated half-life of 9 years for primary deceased donor renal graft [13]. A number of patients with renal graft failure are relisted for renal retransplantation. However, renal retransplantation accounts for a small fraction of overall renal transplantation [14].

It is well established that retransplantation has better patient survival than a return to dialysis [15]. In addition, return to dialysis due to renal graft failure results in a poor quality of life [16]. Patients who have failed renal transplantation have high mortality and morbidity compared to patients on dialysis. Renal retransplantation is their best treatment option [17]. However, based on an overview of the literature, the prognosis of renal retransplantation compared to first renal transplantation remains unclear [18]. As renal retransplantation increases, it is important to evaluate the outcome of renal retransplantation.

Previous studies comparing renal retransplantation with first renal transplantation have limitations due to several confounding factors that might affect patient-graft survival.

**Table 2. Univariate and Multivariate Analysis of Patient-Graft Survival of Studied Population (n = 2556)**

| Factor | Univariate Analysis | | | Multivariate Analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | *P* Value | HR | 95% CI | *P* Value |
| Old patient age (≥55 y) | 1.301 | 1.048–1.616 | .017* | 1.440 | 1.156–1.793 | .001* |
| Old donor age (≥55 y) | 1.652 | 1.388–1.967 | <.001* | 1.681 | 1.411–2.003 | <.001* |
| Male patient | 1.390 | 1.197–1.615 | <.001* | 1.320 | 1.136–1.534 | <.001* |
| Female donor | 1.190 | 1.034–1.370 | .015* | 1.203 | 0.946–1.864 | .087 |
| Patient BMI (≥30 kg/m$^2$) | 1.646 | 0.946–2.864 | .078 | | | |
| Donor BMI (≥30 kg/m$^2$) | 0.966 | 0.497–1.879 | .919 | | | |
| Deceased donor | 0.933 | 0.774–1.124 | .464 | | | |
| Main immunosuppressant (azathioprine, cyclosporine) | 1.968 | 1.655–2.339 | <.001* | 2.118 | 1.774–2.528 | <.001* |
| Hypertension | 0.853 | 0.534–1.363 | .507 | | | |
| Diabetes | 1.140 | 0.699–1.857 | .600 | | | |
| HLA mismatch (≥4) | 1.055 | 0.896–1.241 | .521 | | | |
| Total ischemia time (≥59 min) | 1.165 | 0.736–1.842 | .515 | | | |
| Retransplantation | 1.055 | 0.791–1.406 | .715 | | | |

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.
*$P < .05$ is statistically significant.

In the present study, we used propensity score matching analysis for an accurate comparison between the first and second renal transplantation by taking possible confounding factors into account.

The main factor that has a positive influence on graft survival has been found to be the development of immunosuppressant treatments [19]. The present study also revealed that immunosuppressants were the strongest predictor of patient-graft survival in multivariate analysis (HR = 2.118; 95% CI, 1.774–2.528; $P < .001$). Many studies have shown that the survival of renal retransplantation does not significantly differ from the first transplantation after using new immunosuppressive regimens [20,21]. Patients with renal retransplant are commonly HLA-sensitized because of their exposure to previous allograft [22]. They have high rates of acute rejection as reported in previous studies [23,24]. In the present study, there was no significant difference in HLA mismatch between the 2 groups. Further studies are needed to understand immune and non-immune mechanisms that affect graft survivals in renal retransplantation.

Regarding factors that could influence patient-graft survival, our data showed that patient age, donor age, male sex, and immunosuppressant used significantly influenced patient-graft survival. However, retransplantation had no effect on the patient-graft survival. In addition, there were no significant differences in patient-graft survival rates, patient survival rate, or death-censored graft survival rate between the first and second renal transplantation. Therefore, renal retransplantation is a feasible option that should be assessed in patients with renal graft failure.

This study has several limitations. A major limitation of this study was that this was a retrospective study. Although we performed propensity score matching analysis, our results might still be affected by unmeasured confounders. In addition, only survival rates were presented here. Data such as acute rejection, delayed graft function, or perioperative complications were not examined.

## CONCLUSIONS

It is important to study the survival of renal retransplantation because the waiting-list of renal transplantation is increasing. This study showed that graft survival of renal retransplantation was not significantly different from that of first renal transplantation. Renal retransplantation might be a reasonable option for patients who have lost the first renal graft. Therefore, renal retransplantation can be encouraged.

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