



**Research Article**

## Outcome of Kidney Transplant Recipients with Graft Failure

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### Abstract

**Background:** Kidney transplantation is the optimal choice for patients with end stage renal disease. However, most kidney grafts will fail at some point during the lifetime of the recipient. This study presents outcome data in patients with failed kidney graft.

**Methods:** Data from 1309 kidney transplant recipients were reviewed. Multivariable cox regression analysis was used to study the predictors of graft and patient outcomes.

**Results:** We identified 85 kidney transplant recipients with graft failure and matched them to 170 patients with functioning graft. Mean age of the participants was 44.9 ( $\pm 15.7$ ) years. Chronic rejection was the most common cause of graft failure (31.7%). Fifty-five patients (64.7%) return to dialysis after graft failure, 13 patients (15.3%) underwent repeat transplantation, and 17 patients (20%) died. A multivariable cox regression analysis showed that increased age was associated with worse patient survival. Graft loss was associated with the diagnosis of diabetes mellitus and hypertension.

**Conclusion:** Patients with kidney graft failure experience significant morbidity and mortality. Strategies to optimize outcomes of such patients are needed with a focus on maximizing opportunities for re-listing and repeat transplantation.

**Keywords:** Graft failure; Kidney transplant recipients; Repeat transplantation

### Introduction

Kidney transplantation has long been the treatment of choice for a significant portion of end stage renal disease (ESRD) patients [1,2] There is a steady increase in the number of patients that are waitlisted for a kidney transplant. [3] Compared with dialysis, kidney transplantation conveys higher survival rates and improved quality of life(QOL), regardless of the status of patient whether on transplantation waiting lists or not [4–7].

Improvement and better understanding in kidney transplantation have translated into better improvements in short-term kidney allograft survival relative to long-term graft survival. Thus, graft loss constitutes a substantial threat to kidney transplant patients [8–12]. The number of patients returning to dialysis after a failed kidney transplant is steadily rising. In fact, noticeable centre-related impact remains evident up till the time of this study, as variable success rates are reported from different countries, which emphasizes the importance of reporting local data all over the globe [13–16].

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Graft failure and return to dialysis is associated with high mortality rates compared to patients with ongoing graft function [8]. Less clear are the outcomes when the graft failure happened in cadaveric versus living transplant as well as the timing of graft failure since transplantation. A better understanding of the outcomes of patients with failed kidney transplant is needed. In this study, we aim to evaluate the outcomes of patient with failed kidney graft in our centre.

## Methods

This is a single-center matched case-control study that included kidney transplant recipients between the period January 1, 2010 and December 31, 2020, at multiorgan transplant centre at King Fahad Specialist Hospital (KFSH-D), Dammam, Saudi Arabia. 1309 patients underwent kidney transplantation during this period. We included adult kidney transplant recipients (above 15 years old). Exclusion criteria were paediatric patients and those with multiorgan transplantation. The follow-up period started by transplantation date and ended with death of the participant or study completion on June 1st, 2022, whichever was earlier. Two controls were recruited for each case and matched based on the age and gender. Study protocol was approved by KFSH-D Institutional review board and participants anonymity was maintained throughout the study.

Statistical analyses were performed using the IBM SPSS Statistics ver. 28. Continuous variables are presented as mean ± standard deviation. Categorical variables are shown as frequencies and percentages. Continuous variables were compared using t-test or Mann Whitney U test, while categorical variables were compared using the Chi-squared or Fisher's exact tests as appropriate. The associations of survival and transplant characteristics were then analysed using univariate analysis with log-rank test and multivariate Cox proportional hazard regression. All reported P-values are two-sided and P-value <0.05 was considered statistically significant.

## Results

During the study period, 85 kidney transplant recipients with graft failure were identified and matched to 170 patients with functioning graft. Mean age of the participants was 44.3 (±15.1) years, and males were more predominant (171 males [67.1%] versus 84 females [32.9%]). Of 255 patients, 93 (36.5%) patients underwent deceased donor renal transplantation (DDRTx) and 162 (63.5%) patients underwent living donor renal transplantation (LRTx). For donor types, 32 (12.5%) cases were from extended criteria donors (ECD), 61 (23.9%) cases were from standard criteria donors (SCD). Diabetes mellitus (DM) was found in 78 patients (30.6%), and hypertension (HTN) was in 169 patients (66.3%). All patients were treated with prednisolone, 239 patients (93.7%) were treated with tacrolimus and 244 patients (95.7%) were treated with Cellcept or myfortic. Two patients received azathioprine and one patient received cyclosporine. (Table

1). No significant differences were detected in age, gender, and medications between both groups. However, DDRTx, diabetes mellitus, and hypertension were significantly higher in the case group.

Considering the primary disease, diabetes mellitus was the most common primary aetiology (62 patients) followed by hypertension in 33 patients and glomerulonephritis in 30 patients. More details are shown in Table 2.

In the whole study, 55 patients died (21.6%); 17 of them were in case-group (20%) and 38 were in control-group (22.4%) with no significant statistical difference (P = 0.748). Figure 1 demonstrates patients' outcomes in the cases group; 55 patients returned to dialysis (64.7%), and 13 patients had re-transplantation (15.3%).

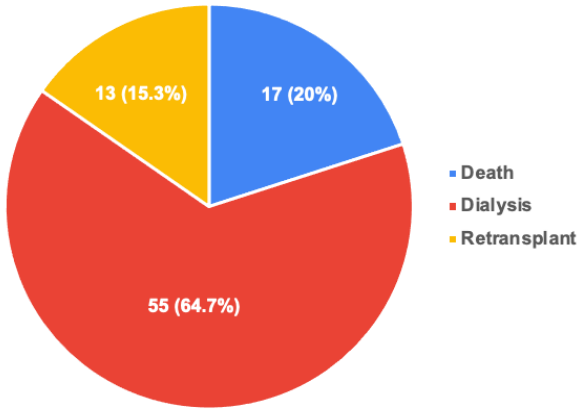
The most common cause of graft loss was chronic rejection encountered in 27 cases (31.7%) followed by acute rejection, and infection with AKI, thrombotic microangiopathy (TMA), in 17.6%, 10.5% and 9.4%; respectively. More details are shown in Table 3.

**Table 1:** Baseline characteristics of study

	Loss cases (n=85)	Controls (n=170)	P value
Age	44.9±15.7	44.1±14.8	0.68
Gender			
Male	57 (67.1%)	114 (67.1%)	1
Female	28 (32.9%)	56 (32.9%)	
Type of Transplant			
DRTx	48 (56.5%)	45 (26.5%)	<0.001
LRTx	37 (43.5%)	125 (73.5%)	
Donor			
ECD	17 (20%)	15 (8.8%)	1*
SCD	31 (36.5%)	30 (17.6%)	
Living	37 (43.5%)	125 (73.5%)	
DM	35 (41.2%)	43 (25.3%)	0.014
HTN	66 (77.6%)	103 (60.6%)	0.008
Prednisone	85 (100%)	170 (100%)	
Tacrolimus	77 (90.6%)	162 (95.3%)	0.173
Cellcept or myfortic	83 (97.6%)	161 (94.7%)	0.345

**Table 2:** Primary disease of ESRD

	Cases	controls
Diabetes	22 (25.9%)	40 (23.5%)
Hypertension	3 (3.5%)	30 (17.6%)
Glomerulonephritis	16 (18.8%)	14 (8.2%)
Urological	8 (9.4%)	7 (4.1%)
Hereditary nephritis	2 (2.4%)	7 (4.1%)
Hemolytic uremic syndrome	1 (1.2%)	0 (0%)
Primary oxaluria	1 (1.2%)	0 (0%)
Unknown	32 (37.6%)	72 (42.4%)



**Figure 1:** Outcome of patients with graft loss.

**Table 3:** Causes of graft loss

N= 85	
Chronic Rejection	27 (31.7%)
Acute Rejection	15 (17.6%)
Infection with AKI	9 (10.5%)
Thrombotic microangiopathy	8 (9.4%)
Disease Recurrence	6 (7%)
Vascular Thrombosis	5 (5.8%)
Chronic allograft dysfunction	4 (4.7%)
Pseudoaneurysm	3 (3.5%)
Polyoma virus (BK) nephropathy	2 (2.3%)
Calcineurin inhibitor Toxicity	2 (2.3%)
De-novo glomerulonephritis	1 (1.1%)
Others	1 (1.1%)

Mean time to graft loss graft was 10.1 years and 1-year, 5-year and 10-year graft survival rates were 88.35%, 74.33% and 65.63% respectively (Figure 2). LRTx had higher graft survival rate than DRTx with significant statistical difference ( $P < 0.001$ ). For LRTx, 1-year and 5-year survival rate was 95.38% and 83.69%; while for DRTx was 75.69% and 57.23%, respectively. (Figure 3)

To examine the association between study variables and graft loss as an outcome, we conducted univariate Cox regression analysis then variables with  $p < 0.2$  were entered in the multivariate analysis model. Diabetes mellitus (HR, 2.185; 95%CI, 1.377 to 3.467;  $P = 0.001$ ), and Hypertension (HR, 3.085; 95% CI, 1.766 to 5.39;  $P < 0.001$ ) were found to be associated with higher risk graft loss whereas LRTx (HR, 0.353; 95% CI, 0.227 to 0.549;  $P < 0.001$ ), and tacrolimus use (HR, 0.327; 95% CI, 0.151 to 0.708;  $P = 0.005$ ) were associated with lower risk for graft loss. Table 4.

Multivariate analysis for survival showed that age (HR, 1.04; 95% CI, 1.021 to 1.059;  $P < 0.001$ ) was associated with worse patient survival (Table 5).

### Discussion

In this study, we report on the outcome of kidney transplant recipients with graft failure. Overall, one and five-year graft survival were 88.35% and 74.33, respectively. One and five-year patients' survival was 95.67%, and 90.74%, respectively. Interestingly, the survival rates of cases (graft loss patients) and controls (patients with functioning grafts) were almost identical over the first 10 years post-transplantation; however, an alteration emerged after 10 years as the patients with functioning grafts had almost 10% percent higher survival



**Figure-2:** Total graft survival (years).

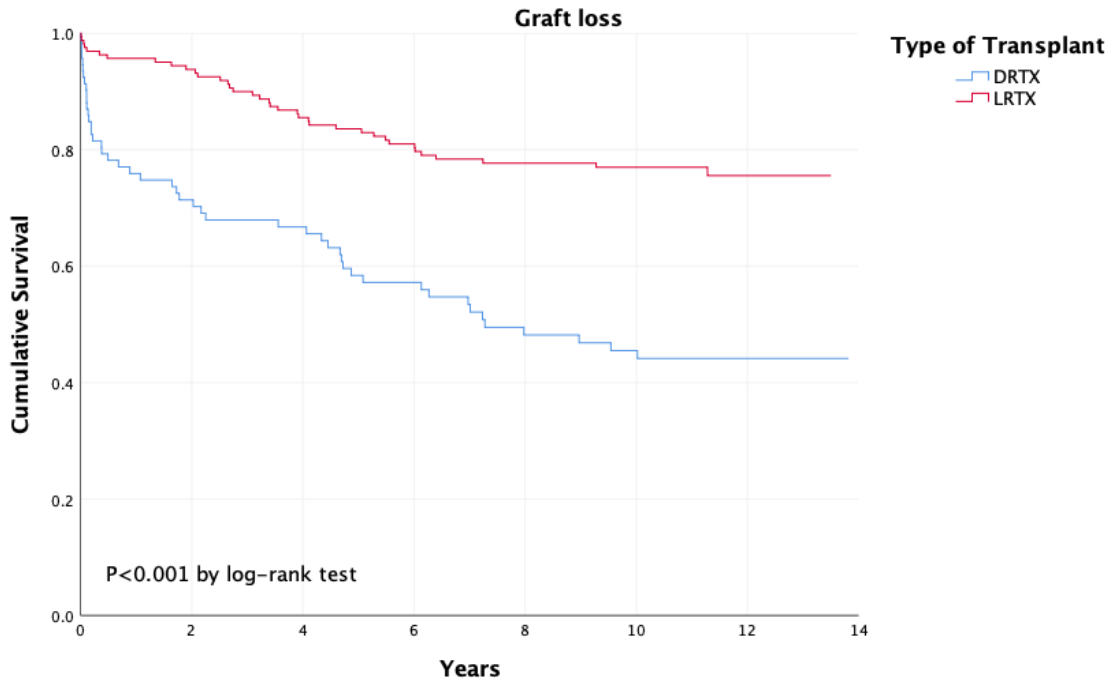


Figure 3: Graft survival according to type of transplant (years).

Table 4: Multivariate analysis of risk factors for graft loss

	HR	95% CI	P value
LRTx	0.353	0.227 to 0.549	<0.001
DM	2.185	1.377 to 3.467	0.001
HTN	3.085	1.766 to 5.39	<0.001
Tacrolimus	0.327	0.151 to 0.708	0.005

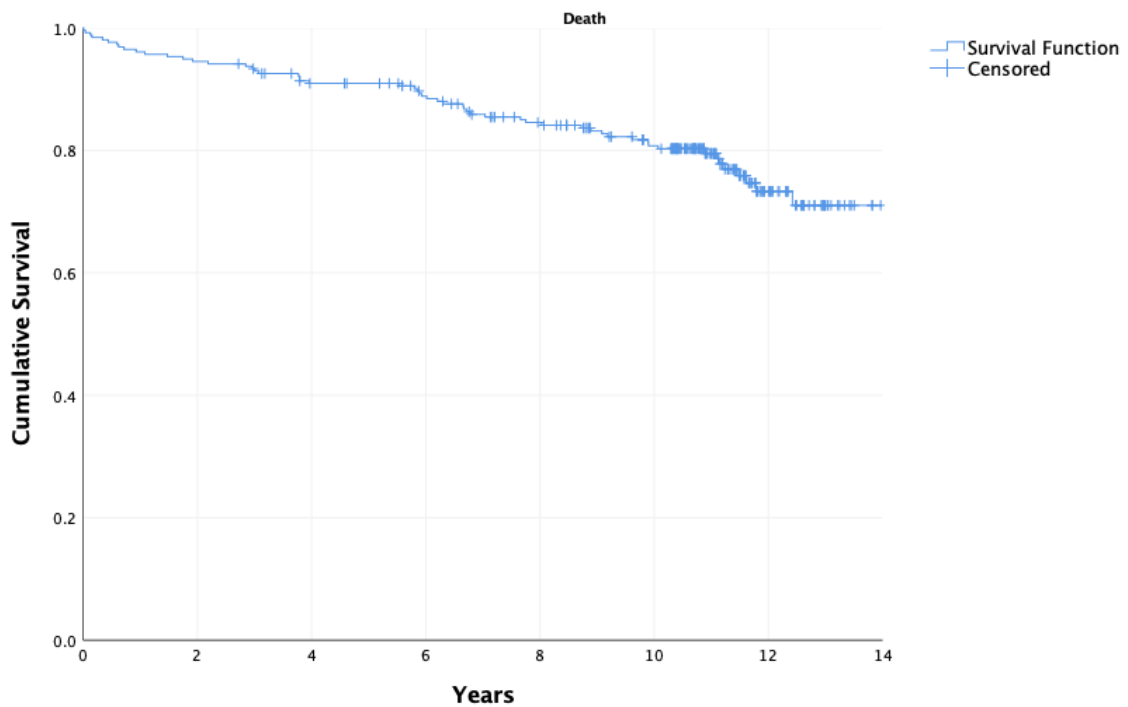


Figure 4: Patients' survival for total study (years).

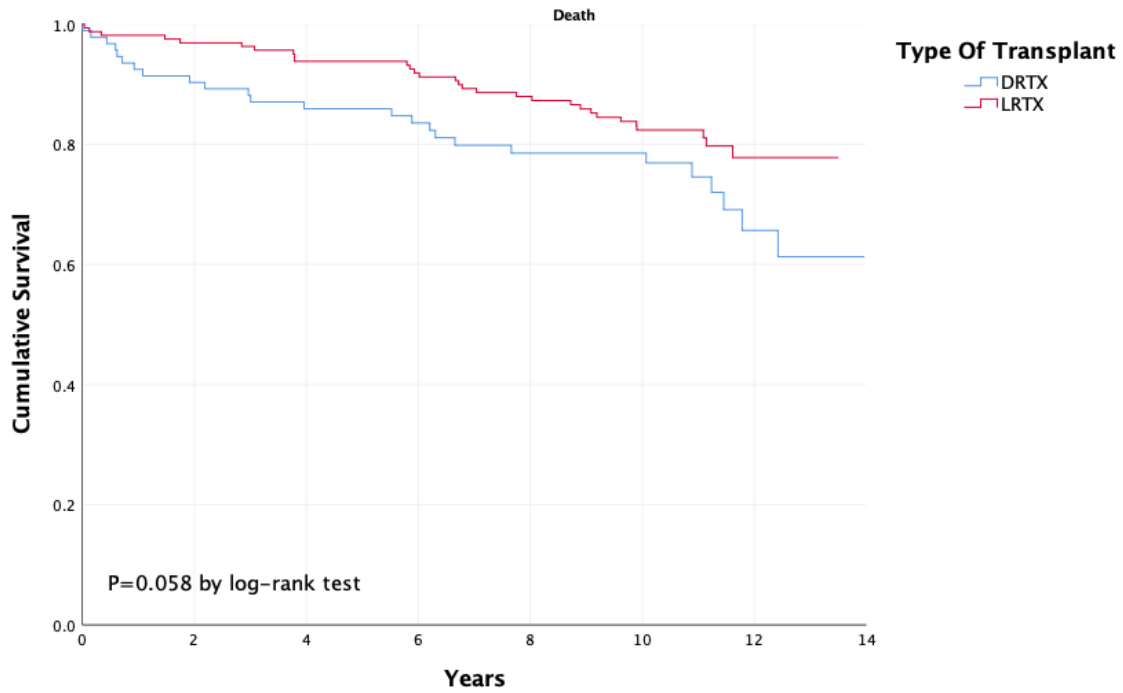


Figure 5: Patients' survival rates according to type of transplant.

Table 5: Multivariate cox regression analysis for mortality

	HR	95% CI	P value
Age	1.04	1.021 to 1.059	<0.001
Female	0.468	0.241 to 0.909	0.025
LRTx	0.592	0.347 to 1.011	0.055

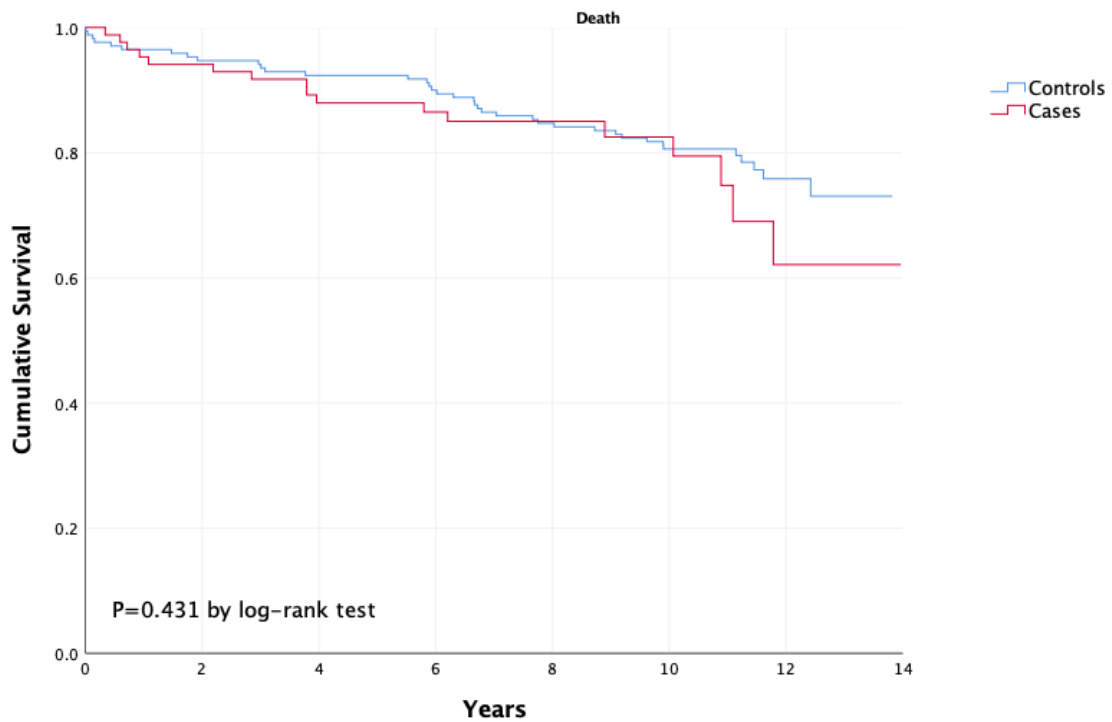


Figure 6: Survival according to graft loss.

rates after 14 years. The survival rates reported in this study are comparable with the survival rates reported by some of the largest studies from USA, Europe, Australia and New Zealand [8][23]. Women had better survival rates than men, a finding that is also supported by other studies [24].

Risk factors for graft failure can be classified into short-term and long-term risk factors; however, there are many interactions between them, and many factors can affect both types; for example, the presence of anti-human leukocyte antigen (HLA) antibodies is associated with increased risk for graft failure both in the short and long term. [20] The type of donor kidney is an important factor, as LRTx is associated with higher graft survival rates post-transplantation. [3,8] LRTx is also associated with higher patients' survival rates post-transplantation; [21,22]. This was confirmed in the current study. Evidence still lacks concerning the association between the function of the graft and patient's survival. The current study compared the survival rates in transplant patient with functioning grafts and those with graft loss. It showed that mean survival of control-group was slightly higher compared with case-group. Noteworthy was that the number of death cases with functioning grafts was much lower than other reported studies. [23,25]. Reason behind that could be related to younger age of the study population. Another notable finding is the insignificant association between hypertension and diabetes mellitus from one side and mortality rate on the other side, a finding that it is contradicted by many other studies and could probably attributed to the limited sample size [26,27].

Patients with failed allografts who return to dialysis are noted to have excess mortality [17]. Repeat transplantation is considered as the transplantation strategy associated with the best outcomes for patients with graft failure. However, there is wide variation among transplant centres and small number of patients with failed graft are placed on waitlist or undergo repeat transplantation [18]. Repeat transplantation in Canada, for example, was 9.9% compared to 15.3% percent in our study [19]. This highlights the needs for clear coordination of care among the transplant centres and nontransplant nephrologist, focusing on optimizing the outcomes of such patients especially relisting or repeat transplantation.

The current study presents important results that might help in understanding the outcome of patients with failed kidney graft. Limitations of this work include its retrospective methodology, small number of patients, and being single centre. Moving forward, transplant healthcare providers should focus on adopting consensus or protocol that help in managing patients with failed kidney grafts and improving their outcomes.

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