

## *The Effect of Underlying Diseases on Kidney Transplant Survival Rate*

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### **Abstract**

**Background and Objective:** Identifying factors affecting kidney transplant survival in patients with end-stage renal disease is essential to improve transplant survival and improve the kidney transplant process. This study aimed to determine the effect of underlying diseases on kidney transplant survival rates in transplant recipients from living donors at Farhangian Hospital.

**Methods:** This cross-sectional and retrospective study was conducted on 700 patients who underwent kidney transplantation in Farihectan Hospital between April 2020 and September 2023. Sampling was based on a census, and researcher-made demographic information questionnaires and inpatient files of transplant patients were used to collect data. Kaplan-Meier, Cox regression, and log-rank tests were utilized to estimate survival rates and identify the impact of underlying diseases on transplant survival using SPSS version 23. The significance level of the tests was considered smaller than 0.05.

**Findings:** The Kaplan-Meier method estimated the 1-year, 2-year, 3-year, and 4-year transplant survival rates at 94.71%, 86.4%, 81.1%, and 77.0%, respectively. The Cox regression model demonstrated that recipient age ( $P < 0.05$ ), donor age ( $P < 0.05$ ), and the presence of diabetes and hypertension as underlying diseases ( $P < 0.001$ ) significantly affected kidney transplant survival rates.

**Conclusion:** The transplant survival rate in Farhikhtegan Hospital was higher than in the past years and in some of the country's major transplant centers. Therefore, it seems necessary to pay attention

to other factors affecting graft survival rates in addition to the present ones.

**Keywords:** Transplant survival- Kidney transplant - Graft rejection - Underlying disease.

### **Introduction**

Kidney transplantation is the most cost-effective and preferred strategy for managing patients with end-stage renal disease (ESRD), which is considered one of this century's most successful transplant procedures and a significant advancement in treating renal failure (1). Over recent years, substantial progress has been made in dialysis and kidney transplantation, and current knowledge strongly supports the finding that kidney transplantation markedly improves quality of life and significantly reduces complications and mortality associated with ESRD (2). In the past decade, survival rates for kidney transplant recipients have improved due to advancements in immunosuppressive therapies, surgical techniques, and follow-up protocols. Additionally, the number of transplants from living donors has also increased. According to the European dataset, the global 5-year survival rate is approximately 92% for deceased-donor transplants and 95% for living-donor transplants. Regarding graft survival, these rates are estimated at around 81% and 87%, respectively (3). Identifying factors affecting transplant survival is essential to further extending kidney graft longevity.

A kidney transplant recipient's prognosis can be affected by several variables, including but not limited to donor and recipient age, donor type (living or deceased), recipient comorbidities (e.g., hypertension, diabetes,

hepatitis B infection, cardiovascular diseases), race, HLA mismatch, dialysis duration, postoperative complications, polyomavirus infection, immunologic rejection, socioeconomic status, and several others. Some of these details, such as gender and age, is possible to be determined before the kidney transplant procedure. According to studies, previous kidney transplants may affect the graft's survival rate. However, Meier-Kriesche et al. reported that whether the transplant was the first or a repeat did not have an independent or significant impact on kidney transplant survival (4). Results regarding transplant survival and transplant patients have varied across studies. In a 2022 study, Mohammad Rahimi and colleagues indicated that survival rates differed between male and female patients (5). In contrast, a 2021 study by Sevim et al. reported that recipient gender did not correlate with transplant survival (6). In a 2019 study, Behnani et al. identified diabetes as a significant predictor of survival rates in kidney transplant recipients, emphasizing that this factor should be considered to improve transplant longevity (7). Ying et al. highlighted in a 2020 study that reductions in early and late post-transplant mortality over the past 40 years represent a significant achievement (8). Similarly, Alenazi et al. (2019) reported that graft survival was unaffected by the gender of the donor or recipient, as well as the presence of diabetes or hypertension in recipients (9). This body of research highlights the complex interplay of factors influencing kidney transplant outcomes, underscoring the need for individualized assessments and tailored management strategies to optimize patient and graft survival.

Based on the resources, the most common comorbidities among the patient population include diabetes, high blood pressure, cardiovascular diseases, infections, tumors, and autoimmune diseases (10). Pre-transplant diabetes mellitus (DM) in kidney recipients has been associated with a higher risk of cardiovascular diseases, increased mortality rates, and shorter allograft survival. Some studies have indicated that the death rate and

graft rejection in transplant recipients with diabetes are almost two to three times higher than in healthy recipients (11). In kidney transplant recipients, cardiovascular syndrome, characterized by diastolic dysfunction due to venous congestion along with chronic pulmonary hypertension, left ventricular hypertrophy, and heart failure, contributes to reduced kidney transplant survival (10). More explanation about the complications of cardiovascular diseases in kidney transplant recipients compared to the general population with a high prevalence of coronary artery disease and left ventricular hypertrophy has been provided (12). Given the significance of these factors, the present study was conducted at Farhangian Hospital to determine the impact of comorbidities on kidney transplant survival rates among transplant patients with living and deceased donors.

### **Materials and Methods**

This cross-sectional study utilized retrospective data and included all adult kidney transplant patients (aged over 18) who received transplants from living or deceased donors between 2020 and 2023 at Farhangian Hospital. The related data were gathered from the registered data in the patient's clinical records at the hospital. Sampling was conducted through a census approach, resulting in 700 samples being included in the study. Inclusion criteria comprised the completeness of medical records, patients over 18, and willingness to respond to phone calls and cooperate with the researcher's questions. Exclusion criteria included records with erroneous data that could not be corrected or cases where the patient passed away in the operating room.

### **Data Collection**

After the proposal approval and obtaining the ethical code written permission and an introduction letter were acquired from the Vice-Chancellor for Research and Technology at the Islamic Azad University, Sari Branch. The principal investigator then visited Farhangian Educational and Research Hospital. To adhere to ethical principles, the

researcher presented the introduction letter to the hospital authorities and explained the study's purpose, subsequently obtaining sampling authorization. Following the sampling protocol, the researcher listed the names, surnames, and contact numbers of individuals who had undergone kidney transplants within the specified period (2020-2023) and had complete medical records. Eligible participants were identified through phone contact, considering the inclusion criteria. After selecting the study participants, data were collected from the patient's medical records and the hospital's Health Information System (HIS) using a custom-designed data collection form. This form recorded details including age, gender of both donor and recipient, history of diabetes, hypertension, hepatitis, autoimmune diseases, transplant survival, and the final health status of the patient. Additional information regarding patients' conditions was obtained via follow-up phone calls by the researcher. The data collection tools included the patient's medical records and a researcher-designed data registration form consisting of two sections. The first section documented demographic information about the kidney transplant recipient and donor, including age, gender, and underlying diseases. The second section was dedicated to specialized factors related to transplant survival.

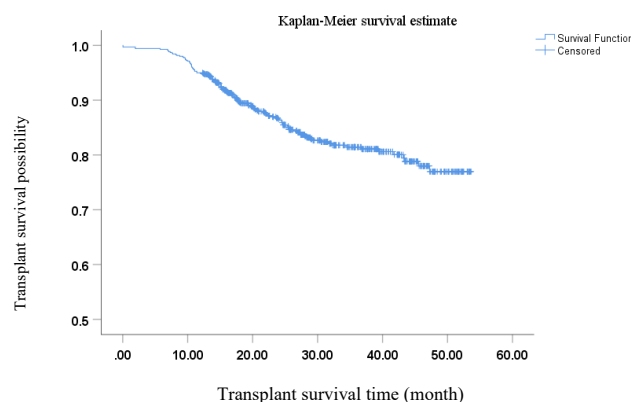
### Data Analysis

After data collection, descriptive statistics were used to describe the data, with central tendency and dispersion indices calculated for quantitative variables and frequency and percentage used for qualitative variables. Data analysis was conducted using SPSS version 27, employing statistical methods including Kaplan-Meier, log-rank test, and Cox regression model. A significance level of 0.05 was set for data analysis.

### Results

A total of 700 donors, including 463 men (66.1%) and 236 women (33.7%), were examined with an average age of  $33.22 \pm 9.74$  years. The most common blood groups among kidney donors were O and A,

accounting for 40.9% and 28.9%, respectively. Of the 700 kidney transplants performed, 529 (75.6%) were from living donors, while 171 (24.4%) were from deceased donors. The kidney transplant recipients included 700 individuals, with 440 men (62.9%) and 260 women (37.1%). The average age of the recipients was  $43.75 \pm 13.04$  years. The most common blood group among recipients was O, comprising 36.9%, while group A accounted for 30%. Among the recipients, 162 (23.1%) had diabetes, 270 (38.6%) had hypertension, 75 (10.7%) had hepatitis, and 57 (8.1%) had autoimmune diseases. Out of the 700 transplants, 178 (21.9%) were conducted in 2019, 194 (23.9%) in 2020, 201 (26.1%) in 2021, and 116 (14.3%) in 2022. Of the transplants reviewed, 583 (71.9%) were successful, with 10 cases (1.2%) experiencing hyperacute rejection, 37 cases (4.6%) acute rejection, and 70 cases (8.6%) chronic rejection. Among the transplant patients, 679 (83.7%) were alive, and 21 (2.6%) had passed away. Of the 700 individuals who underwent kidney transplants, approximately 125 (15.4%) required dialysis post-transplant, while 575 (83.7%) did not require further dialysis. The one-year, two-year, three-year, and four-year kidney graft survival rates are illustrated in Figure 1. The present study's Kaplan-Meier analysis for kidney transplant recipients demonstrated that the one-year, two-year, three-year, and four-year graft survival rates were 94.71%, 86.4%, 81.1%, and 77.0%, respectively.



**Figure 1.** Kidney transplant survival rate curve among transplanted patients examined in a 4-year time frame

As shown in Table 1, there was a statistically significant difference at the level of 1% between the graft survival rates in different groups of transplant recipients and donors ( $P < 0.01$ ). There was no statistically significant difference in the transplant survival rate between male and female transplant recipients and kidney donor gender subgroups ( $P > 0.01$ ).

**Table 1.** Frequency distribution of kidney transplant recipient and donor patients in a 4-year time frame according to age and gender variables and log-rank test results

Parameter	Age (Year)/ Gender	Transplant survival	Standard error	Lower bound	Upper bound	P-value
Transplant Recipient	24-8	47.1	1.6	44.4	50.8	0.07
	44-5	48.8	0.73	46.7	49.0	
	60-5	44.9	1.5	42.2	46.6	
	75-1	43.5	1.5	39.1	46.9	
Transplant Donor	24-8	48.3	1.3	45.2	51.4	0.001
	44-5	46.6	0.35	44.2	47.0	
	60-5	44.7	1.7	41.9	47.5	
	75-1	18.2	0.11	17.2	19.2	
Recipient Gender	Male	46.5	0.61	44.6	47.4	0.79
	Female	46.5	0.74	44.4	48.6	
Donor Gender	Male	47.4	0.14	45.4	48.4	0.03
	Female	45.5	1.9	42.1	47.9	

The results of the univariate Log-Rank test analysis indicated a statistically significant difference at the 1% level ( $P < 0.001$ ) in kidney transplant survival rates between patients with underlying conditions (43.51%) and those without underlying conditions (51.00%). The kidney transplant survival rate was significantly higher in non-diabetic recipients compared to diabetic recipients (Table 2). Similarly, the transplant survival rate was significantly higher in recipients without hypertension than in those with hypertension. On the other hand, there was no statistically significant difference in kidney transplant survival rates between recipients with hepatitis and those without hepatitis ( $P = 0.881$ ). According to Table 2, the univariate Log-Rank test analysis results also showed no statistically significant difference

in kidney transplant survival rates between recipients with autoimmune diseases and those without autoimmune diseases ( $P = 0.305$ ).

**Table 2.** Frequency distribution of kidney transplant recipients from April 2020 to September 2023 based on underlying conditions and Log-Rank test results.

Variable	Subgroup	Transplant Survival (%)	Standard Error	Lower Limit	Upper Limit	P-Value
Diabetes	No	49.17	0.573	48.05	50.29	0.0001
	Yes	38.52	1.51	41.48	51.51	
Hypertension	No	49.20	0.637	47.96	50.45	0.0001
	Yes	42.45	1.12	40.25	44.64	
Hepatitis	No	46.58	0.639	45.32	45.32	0.881
	Yes	45.84	1.81	42.28	48.28	
Autoimmune Diseases	No	46.76	0.626	45.53	47.99	0.305
	Yes	44.67	2.07	40.60	48.75	

## Discussion

The results of the present study indicated that the one-year, two-year, three-year, and four-year kidney transplant survival rates among recipients at the Farhikhtegan Educational Research Hospital were 94.71%, 86.4%, 81.1%, and 77.0%, respectively. In a study by Abedi et al. conducted at Hasheminejad Hospital in Tehran, the estimated one-year, five-year, and eight-year kidney transplant survival rates were approximately 90%, 83%, and 74%, respectively (13). Another study by Ghanai et al. 2012 conducted on transplant patients at Shahid Tajrish Hospital in Tehran calculated the one-year and five-year survival rates at 89% and 82.5%, respectively (14). Comparing the findings of the present study with those of Abedi et al. and Ghanai et al. highlights the improvement in kidney transplant survival rates in Iran. Possible explanations for the improvements in survival rates in these studies and the current study include enhanced experiences in transplant centers and among surgeons, improved surgical techniques, and advancements in prescribed medications throughout different stages of the surgery (15).

The age of both the donor and the recipient is among the crucial factors that may influence kidney transplant survival (16). The present study revealed that kidney transplant survival was significantly higher among recipients aged 18–24 and 25–44 compared to those aged 45–60 and 61–75 years. In line with these findings, Xin et al. demonstrated that kidney transplant survival rates were associated with the recipient's age in patients who underwent transplants at Sichuan



University Hospital (17). Gerbase-DeLima et al. (2020) also reported that lower transplant survival rates in older individuals may be attributed to higher comorbidities and increased susceptibility to infections (18). Explaining the present study's findings, it seems that younger kidney transplant recipients may benefit from stronger immune systems, which contribute to faster recovery and higher survival rates. In contrast to the present study's findings, a study by Hashemian et al. reported no significant association between recipient age and kidney transplant survival (19). Discrepancies between these findings and those of the current study may be due to differences in other demographic variables or the inclusion and exclusion criteria of the studies.

The present study also found that donor age was significantly associated with transplant survival, with a higher survival rate observed in recipients of kidneys from donors younger than 45 years compared to those from donors older than 45 years. This study's increased survival rate for transplants from younger donors may be attributed to structural, functional, and developmental factors that significantly impact kidney transplant survival (20). Consistent with these findings, Gerbase-DeLima et al. (2020) demonstrated that transplants from younger donors tend to have better survival rates, likely due to the higher number of functional nephrons (18). A literature review reveals a lack of consensus among researchers regarding the association between recipient gender and transplant survival. While some studies indicate that men have better kidney transplant outcomes compared to women, others report similar results across genders, and yet others suggest that male gender is an independent prognostic factor for poorer transplant outcomes (21). However, the present study's findings indicated no significant association between recipient gender, transplant survival, or the risk of graft rejection. Contrary to the results of this study, research by Chesnay et al., García et al., and Chen et al. suggested that transplant survival rates are higher in female recipients than in males (22). A possible explanation for these observations and the

inconsistencies with the present study's findings may lie in sociocultural differences between men and women across various countries, which influence health awareness and the likelihood of following healthcare providers' recommendations. In some countries, women may be more attuned to their health status and more inclined to adhere to medical advice, which could positively affect transplant outcomes (23).

An underlying disease significantly impacts transplant and patient survival rates (24). The present study's findings indicated that underlying diseases had a considerable effect on transplant survival. Diabetes is one of the most critical underlying conditions leading to kidney failure, substantially influencing transplant survival. The results demonstrated that transplant survival in diabetic individuals was significantly lower than in non-diabetic patients. These findings align with those of Hashemian et al. (19), who similarly observed that transplant recipients with diabetes had poorer outcomes and lower graft survival rates compared to non-diabetic recipients. Despite extensive research on the pathophysiology and risk factors of diabetes, the exact mechanisms by which this condition affects transplant outcomes remain unclear. Some studies, however, report contrasting results, showing no significant impact of diabetes on kidney transplant survival (25). The discrepancy could be due to the smaller sample sizes in these studies, which may lack the statistical power needed to detect such associations. In explaining the current study's findings, it can be suggested that diabetes, due to complications such as infections and prolonged hospitalization, contributes to reduced transplant survival in diabetic patients compared to non-diabetic individuals.

The results indicated that transplant survival in patients with hypertension was significantly lower than in non-hypertensive individuals. Furthermore, hypertension was identified as a risk factor for transplant rejection. These findings were consistent with previous studies, where Agarwal et al. demonstrated that hypertension in patients significantly decreases kidney transplant

survival compared to non-hypertensive patients (26). Post-transplant hypertension risk factors included those associated with chronic kidney disease, such as renin-angiotensin-aldosterone system activation, sympathetic nervous system activity, and increased extracellular fluid volume, and specific factors related to kidney transplantation, such as calcineurin inhibitors, corticosteroids, transplant renal artery stenosis, and angiotensin II receptor-activating antibodies (27). Additionally, hypertension is a well-established risk factor for post-transplant cardiovascular diseases, including congestive heart failure, ischemic heart disease, and stroke among kidney transplant recipients. Hypertension also an independent risk factor for decreased kidney function and poor graft survival (28). In experimental studies, hypertension in transplant patients accelerates kidney failure progression through increased glomerular capillary hydrostatic pressure and glomerular hyperperfusion (27). Alexandrou et al also demonstrated the adverse effects of hypertension on transplant outcomes (29). All these factors implicitly confirmed the present study's results, highlighting hypertension's negative impact on transplant survival among kidney transplant recipients. Given that hypertension was shown to be a risk factor for transplant rejection in the current study, managing hypertension before transplantation appears to be essential. One of the limitations of the study is that the study population in the present study includes all adult kidney transplant patients (aged over 18 years) from living/cadaveric donors who underwent transplantation at Farhikhtegan Hospital between 2010 and 2013. Therefore, the results may not be generalizable to transplant recipients in other centers or other countries around the world. also The use of self-report instruments in part of the study may have been associated with bias.

#### Conclusion

Based on the results, The present study was conducted to determine the factors affecting the survival rate of kidney transplants in patients transplanted from kidney donors using the Cox model. The results showed the

effect of the factors of donor and recipient age, family relationship between the recipient and donor, duration of dialysis before transplantation, underlying diseases of diabetes and blood pressure, serum creatinine level, postoperative complications, body mass index, receiving a transplant from a living or cadaveric donor, and duration of hospitalization on the survival rate of the transplant. Therefore, it is suggested that special attention be paid to these factors as factors affecting the risk of kidney transplant rejection. Therefore, it is recommended that hospitals pay special attention to these factors as significant risk factors for kidney transplant rejection. Ethical considerations: Before conducting the study, the study objectives were explained to the participants, informed consent was obtained from them, and they were assured that their information would remain confidential. This study was approved by the Ethics Committee of Islamic Azad University, Sari Branch, under the ethics code number (IR.IAU.SARI.REC.1403.084).

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#### Conflict of interest

The authors declare that there is no conflict of interest in this study.

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