ORIGINAL ARTICLE

Comparison of survival outcomes in preemptive versus non-preemptive kidney transplant recipients

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Background: There are conflicting results regarding survival in preemptive versus non-preemptive kidney transplant recipients. The present study aimed to estimate the risk of death in preemptive versus non-preemptive kidney transplant recipients. **Materials and Methods:** In the present retrospective cohort study, all end-stage renal disease (ESRD) patients who underwent kidney transplantation between 1996 and 2021 in referral kidney transplantation centers in Isfahan province were investigated. In total, 499 patients who received dialysis before kidney transplantation (non-preemptive) and 168 patients who received no dialysis before kidney transplantation (preemptive) were included in the final analysis. Data regarding demographic and clinical variables including sex, age, body mass index (BMI), follow-up duration, immunosuppressive regimen change, kidney donor type, underlying causes of ESRD, and comorbidities before and after kidney transplantation were collected. **Results:** The mean age was 55.47 ± 15.53 years in preemptive and 54.87 ± 14.69 years in non-preemptive patients ($P = 0.65$). Mortality rates were 24.44/1000 person-years of follow-up for preemptive and 18.25/1000 person-years of follow-up for non-preemptive patients ($P = 0.013$). In the crude model of Cox regression analysis, preemptive kidney transplant recipients had a significantly higher risk of mortality compared to non-preemptive kidney transplant recipients (hazard ratio [HR] = 1.59; 95% confidence interval [CI]: 1.09–2.33; $P = 0.015$). However, the association attenuated and became insignificant after adjustment for confounders, including age, BMI, immunosuppressive regimen change, kidney donor type, and comorbidities (HR = 1.35; 95% CI: 0.92–1.99; $P = 0.12$). **Conclusion:** The results of the present study indicated that there is no independent association between preemptive kidney transplantation and increased risk of mortality.

Key words: End-stage renal disease, preemptive kidney transplantation, survival

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INTRODUCTION

End-stage renal disease (ESRD), the last stage of chronic kidney disease, has been known as a major public health priority and is associated with poor quality of life, increased healthcare utilization, hospitalization, and mortality.[1,2] Renal replacement therapies are essential for improving survival in ESRD patients. Kidney transplantation has been considered the treatment of choice for ESRD patients since it is associated with further improvements in quality of life and survival compared to dialysis.[3,4] It is believed that preemptive kidney transplantation, defined as transplantation before the initiation of dialysis, is associated with better graft survival and cost-effectiveness.[5,6] However, there is no consensus regarding the effect of preemptive kidney transplantation on patients' mortality risk.

Several previous studies have suggested that preemptive kidney transplantation is associated with a lower risk of death both in cadaver and living transplant

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recipients.[7-9] The results of a study by Meier-Kries *et al*. suggested that longer waiting time on dialysis is associated with higher posttransplantation mortality risk. According to the findings of this study, dialysis treatment for more than 48 months before kidney transplantation increased the mortality risk by 72%.[7] Furthermore, a study of 1849 primary kidney transplant recipients by Papalois *et al*. reported a significantly higher 5-year survival rate in preemptive kidney transplants compared to non-preemptive kidney transplants for both cadaver and living transplants.[8] A reduced risk of death for cadaver and living donor transplants was also reported in another study of 38,836 adult and pediatric preemptive kidney transplant recipients.[9] On the contrary, several other studies did not confirm a significant association between reduced risk of death and preemptive kidney transplantation.[10-13] Due to the poor consensus on the impact of preemptive kidney transplantation on long and short-term patients' survival besides the lack of information on underlying factors, further investigations are crucial to explore whether preemptive kidney transplantation is preferable to other renal replacement therapies. The purpose of the present study was to compare the survival outcomes of preemptive versus non-preemptive kidney transplant recipients in Isfahan province, located in the center of Iran.

METHODS

We retrospectively investigated medical records of adult (>18 years old) ESRD patients who underwent kidney transplantation from 1996 to 2021 in referral kidney transplantation centers (Alzahra and Khorshid hospitals affiliated with Isfahan University of Medical Sciences) in Isfahan province, Iran. The study protocol was approved by the Isfahan University of Medical Sciences, Isfahan, Iran (Ethics Code: IR.MUI.MED.REC.1399.741). Patients with multiple organ transplantation and those with incomplete medical record files or missed follow-up appointments (more than 10%) were excluded from the analysis. We classified patients into preemptive (received no dialysis before kidney transplantation) and non-preemptive (received dialysis before kidney transplantation) groups. Data regarding demographic (age [years] and sex), anthropometric (body mass index [BMI]), and clinical variables were collected by a standard checklist. Patients' clinical data included underlying causes of ESRD, comorbidities before and after kidney transplantation, immunosuppressive regimen change, graft survival, and kidney donor type.

Statistical analysis

Continuous and categorical data were reported as mean ± standard deviation and frequency (percentage), respectively. Continuous and categorical basic demographic and clinical characteristics of participants were compared between preemptive and non-preemptive kidney transplant recipients as well as between died and survived among them using independent samples *t*-test and Chi-squared (or Fisher's exact test when it is appropriate), respectively. We evaluated and compared the survival rate between preemptive and non-preemptive kidney transplant recipients using the Kaplan–Mier survival curve and log-rank test. We also evaluated the incidence rate of death in both groups per 1000 person-year follow-up. Cox proportional hazard ratio (HR) was used to estimate the HR along with 95% condidence interval (CI) for HR of death in preemptive compared to non-preemptive kidney transplant recipients. We fitted Cox regression in crude and adjusted models. In the first model, the crude HR of death in preemptive compared to non-preemptive kidney transplant recipients was estimated, and in the first adjusted model, the confounding effects of age and BMI, the third model further adjusted for immunosuppressive regimen change, and kidney donor type, and finally, we adjusted potential comorbidities before and after kidney transplantation. Proportional HR assumption in Cox regression was evaluated by scaled Schoenfeld residuals and followed by the Chi-squared distributed statistic proposed by Grambsch and Therneau, and it was confirmed in our data.[14,15] All statistical analyses were performed using SPSS version 26 (IBM SPSS Statistics for Windows, Armonk, NY, USA: IBM Corp.) $P < 0.05$ was considered statistically significant.

RESULTS

Of the 743 selected patients, 76 were excluded from the analyses because of noncompliance to follow-up visits ($n = 34$), immigration ($n = 14$), unknown outcomes ($n = 11$), incomplete medical records ($n = 10$), and referring to other therapeutic centers ($n = 7$). In total, 667 kidney transplant recipients were included in the study, of whom 168 patients were preemptive kidney transplant recipients (no dialysis before kidney transplantation), and 499 patients were non-preemptive kidney transplant recipients (receiving hemodialysis or peritoneal dialysis before kidney transplantation).

The basic characteristics of preemptive and nonpreemptive kidney transplant patients are summarized in Table 1. The mean age was 55.47 ± 15.53 years in preemptive and 54.87 ± 14.69 years in non-preemptive patients ($P = 0.65$). The mean follow-up duration was significantly higher in non-preemptive than preemptive kidney transplant kidney patients (11.49 ± 6.28 vs. 8.76 ± 5.13 years, $P < 0.001$). There was also a significant difference between preemptive and non-preemptive kidney transplant recipients regarding kidney donor type ($P = 0.02$), the frequency of

Table 1: The comparison of basic variables between preemptive and nonpreemptive kidney transplant patients

Variable	Preemptive (*n*=168)	Nonpreemptive (*n*=499)	*P*
Sex			
Female	32.7	37.5	0.25
Male	67.3	62.5	
Age (year)	55.47±15.53	54.87±14.69	0.65
BMI (kg/m^2)	24.10±4.22	23.40±4.22	0.06
Follow-up duration	8.76±5.13	11.49±6.28	<0.001
Immunosuppressive regimen change	56.0	64.9	0.04
Donor type			
Cadaveric	33.3	22.6	0.02
Living of relatives	3.0	2.6	
Living of nonrelative	63.7	74.8	
Graft survival	128 (76.2)	355 (71.1)	0.205
ESRD etiology			
Diabetes mellitus	15.2	16.7	0.14
Hypertension	18.6	10.7	
Systemic lupus erythematous	4.0	3.0	
Primary glomerulonephritis	14.0	19.6	
Urinary tract infection	1.0	0.6	
Urological disorders	7.6	8.9	
Rheumatic diseases	0.9	0.0	
Hereditary causes	11.2	16.7	
Unknown causes	26.1	22.0	
Other causes	1.4	1.8	
Comorbidities before kidney transplantation			
Diabetes mellitus	22.6	21.4	0.75
Hypertension	64.3	66.3	0.63
Cerebrovascular diseases	0.6	0.6	0.98
Cardiovascular diseases	3.0	3.0	1.00
Pulmonary diseases	1.8	1.0	0.42
Cancer	1.8	0.8	0.38
Viral infection	3.6	1.0	0.04
Comorbidities after kidney transplantation			
Diabetes mellitus	16.7	14.6	0.52
Hypertension	1.2	3.6	0.11
Cerebrovascular diseases	3.0	2.4	0.78
Cardiovascular diseases	3.0	4.8	0.31
Cancer	14.3	8.6	0.03
Hyperlipidemia	29.2	38.5	0.03
Viral infection	17.9	10.2	0.009

Values in table are mean±SD for continuous variables and percentage for categorical variables, *P* values were obtained from independent samples *t*-test for continuous variables and Chi-square test for categorical ones. ESRD=End-stage renal disease; BMI=Body mass index; SD=Standard deviation

hyperlipidemia after the kidney transplantation ($P = 0.03$), and the prevalence of viral infection before ($P = 0.04$) and after ($P = 0.009$) the kidney transplantation. The frequency of patients with graft survival was not significantly different between the two groups ($P = 0.205$). No significant difference was also observed between the two groups in terms of other variables ($P > 0.05$).

The comparison of survivors and nonsurvivors showed that there was a significant difference between the two groups in mean age (51.76 ± 13.83 vs. 66.95 ± 12.41, $P < 0.001$), and BMI (23.16 ± 3.98 vs. 25.11 ± 4.71, $P < 0.001$). A significant difference was observed between survivors and nonsurvivors in terms of kidney donor type ($P = 0.006$), the frequency of patients with immunosuppressive regimen change ($P = 0.009$), the underlying causes of ESRD ($P < 0.001$), the prevalence of diabetes mellitus ($P < 0.001$), hypertension ($P < 0.001$), and cardiovascular diseases ($P = 0.04$) before the kidney transplantation, and the prevalence of cancer ($P < 0.001$) and hyperlipidemia ($P < 0.001$) after the kidney transplantation [Table 2].

The mean survival rate was 24.91 for non-preemptive and 21.09 for preemptive kidney transplant patients. In addition, mortality rates were 24.44/1000 (95% confidence

Table 2: The comparison of basic variables between survivors and nonsurvivors

Variable	Survivor (*n*=524)	Nonsurvivor (*n*=143)	*P*
Sex			
Female	35.1	29.4	0.19
Male	64.9	70.6	
Age (year)	51.76±13.83	66.95±12.41	<0.001
BMI (kg/m^2)	23.16±3.98	25.11±4.71	<0.001
Follow-up duration	10.98±6.21	10.14±5.76	0.14
Immunosuppressive regimen change	60.1	72.0	0.009
Donor type			
Cadaveric	28.1	15.4	0.006
Living of relatives	2.9	2.1	
Living of nonrelative	69.1	82.5	
ESRD etiology			
Diabetes mellitus	12.2	28.0	<0.001
Hypertension	15.6	20.3	
Systemic lupus erythematous	4.4	1.4	
Primary glomerulonephritis	16.8	10.5	
Urinary tract infection	1.1	0.0	
Urological disorders	8.8	4.9	
Rheumatic diseases	0.6	0.7	
Hereditary causes	13.5	9.1	
Unknown causes	25.6	23.1	
Other causes	1.3	2.1	
Comorbidities before kidney transplantation			
Diabetes mellitus	17.6	37.1	<0.001
Hypertension	61.8	80.4	<0.001
Cerebrovascular diseases	0.4	1.4	0.20
Cardiovascular diseases	2.3	5.8	0.04
Pulmonary diseases	1.3	0.7	1.00
Cancer	1.0	1.4	0.65
Viral infection	1.7	1.4	0.60
Comorbidities after kidney transplantation			
Diabetes mellitus	15.1	15.4	0.93
Hypertension	3.1	2.8	1.00
Cerebrovascular diseases	2.5	2.8	0.77
Cardiovascular diseases	4.0	5.6	0.41
Cancer	7.4	19.6	<0.001
Hyperlipidemia	31.9	51.7	<0.001
Viral infection	11.5	14.7	0.29

Values in table are mean±SD for continuous variables and percentage for categorical variables, *P* values were obtained from independent samples *t*-test for continuous variables and Chi-square test for categorical ones. ESRD=End-stage renal disease; BMI=Body mass index; SD=Standard deviation

interval [CI]: 18.23/1000–33.43/1000) person-years of follow-up for preemptive and 18.25/1000 (95% CI: 15.29/1000–21.94/1000) person-years of follow-up for non-preemptive patients and survival rate for non-preemptive compared to preemptive patients at 5, 10, 15, and 20-year follow-up estimated using the Kaplan–Meier method was 94.8% vs. 94.8 (95% CI: 92.4%–96.5% vs. 89.8%–97.6%), 87.5% vs. 85.1 (95% CI: 86.3%–92.2% vs. 77.1%–90.5%), 75.7% versus 0.58.3 (95% CI: 71.9%–81.4% vs. 45.4%–69.2%), and 57.4% vs. 45.9 (95% CI: 49%–64.8% vs. 40.2%–65.3%), respectively ($P = 0.013$) [Figure 1]. (reply to reviewer 2: This part is presented as Figure 1 and it is not possible to report it in table format as well).

Crude and multivariable-adjusted HRs and 95% CIs for the hazard of mortality in preemptive compared to non-preemptive kidney transplant patients are summarized in Table 3. In the crude model of Cox regression analysis, preemptive kidney transplant recipients had a significantly higher risk of mortality compared to non-preemptive kidney transplant recipients (HR = 1.59; 95% CI: 1.09–2.33; $P = 0.015$). The incremental association was attenuated and became insignificant after adjustment for age and BMI (HR = 1.50; 95% CI: 0.99–2.28; $P = 0.054$), additional adjustment for immunosuppressive regimen changes and donor type (HR = 1.36; 95% CI: 0.93–2.00; $P = 0.11$), and comorbidities (HR = 1.35; 95% CI: 0.92–1.99; $P = 0.12$).

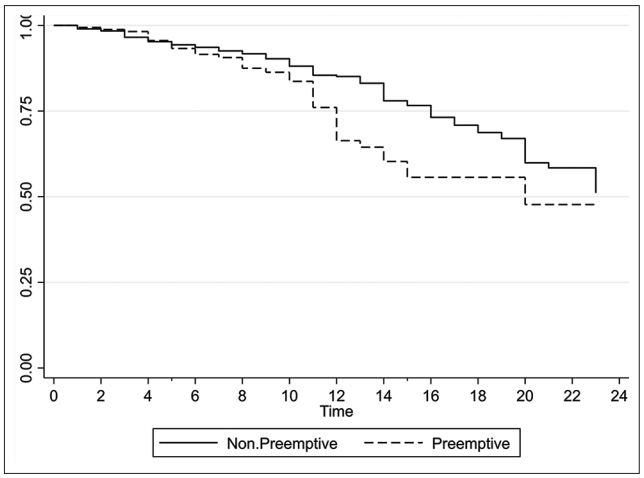

Figure 1: Kaplan–Meier survival curves of preemptive (dash line) and non-preemptive (solid line) kidney transplant patients

Table 3: Crude and multivariable adjusted hazard ratios (95% confidence interval) of the association between mortality and preemptive versus nonpreemptive kidney transplantation

	HR (95% CI)	*P*
Crude model	1.59 (1.09–2.33)	0.015
Model I	1.50 (0.99–2.28)	0.054
Model II	1.36 (0.93–2.00)	0.11
Model III	1.35 (0.92–1.99)	0.12

P<0.05 was considered statistically significant. Crude: Unadjusted, Model 1: Adjusted for age and BMI, Model 2: Model 1 + kidney donor type and immunosuppressive regimen change, Model 3: Model 2 + comorbidities with significant differences between survivors and nonsurvivors before and after the kidney transplantation. CI=Confidence interval; HR=Hazard ratio

DISCUSSION

The present study indicated that the mortality rate was significantly higher in preemptive than non-preemptive kidney transplant patients. The results of the Cox regression analysis indicated that preemptive kidney transplant patients had a 59% higher risk of mortality compared to non-preemptive kidney transplant patients. However, the association is confounded by variables such as age, BMI, kidney donor type, and immunosuppressive regimen change. As far as we know, no previous study has compared the mortality rate between preemptive and non-preemptive kidney transplant patients among Iranian ESRD patients.

Although kidney transplantation has significantly reduced mortality in patients with ESRD,[4,16] survival in these patients can be reduced for various reasons such as preexisting chronic disease, graft function, immunosuppressive regimens, and posttransplantation comorbidities such as cardiovascular disease and cancer.[17,18] It is very important to identify the risk factors of mortality in these patients and establish screening and management strategies in the healthcare systems for high-risk patients. Our results have suggested that in patients with preemptive kidney transplantation, factors such as age, BMI, type of kidney donor, and changes in immunosuppressive regimen can predict the risk of higher mortality in these patients. Therefore, the role of these risk factors in the management of kidney transplant patients should be considered.

The findings of the present study are in contrast with previous studies that have reported the beneficial effect of preemptive kidney transplantation on survival. Preemptive kidney transplantation showed a beneficial influence on survival in a study conducted by Witczak *et al*.; however, the association was confounded by donor type. Such that, the mortality risk in preemptive kidney transplant patients from deceased donors increased significantly.[19] According to the results of a study by Kasiske *et al*., live and cadaveric donor preemptive kidney transplantation were related to 16% and 31% lower risk of mortality, respectively.[9] Recent findings from the French transplant database also indicated that preemptive kidney transplantation is associated with a 40% decreased risk of mortality after adjustment for several covariates.[20] However, several studies did not find any significant differences between preemptive and non-preemptive kidney transplant patients regarding mortality rate.[21-23] Differences in the study population, study design, follow-up duration, and investigated confounders can partly explain the difference observed in the results of these studies. Thus, further large-scale population-based studies considering a comprehensive panel of confounders are warranted to discover the effect of preemptive kidney transplantation on mortality.

The present study has some limitations that should be acknowledged. The retrospective design of the study and relatively small sample size limited the interpretation of our findings. In addition, there are some additional risk factors such as smoking, drug use, laboratory parameters such as albumin, hematocrit, glomerular filtration rate, and duration of ESRD before kidney transplantation that have not been controlled. Nevertheless, to the best of our knowledge, this is the first retrospective cohort study designed to compare mortality between preemptive and non-preemptive kidney transplant patients and related risk factors among the Iranian population.

CONCLUSION

The evidence presented in the present study demonstrated that the mortality risk is significantly higher in preemptive patients than in non-preemptive patients. However, no independent association was found between preemptive kidney transplantation and mortality risk and was confounded by variables such as age, BMI,

immunosuppressive regimen change, and kidney donor type.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Chen SS, Al Mawed S, Unruh M. Health-related quality of life in end-stage renal disease patients: How often should we ask and what do we do with the answer? Blood Purif 2016;41:218-24.
2. Hashmi MF, Benjamin O, Lappin SL. End-stage renal disease. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2018.
3. Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, Jadhav D, *et al*. Systematic review: Kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant 2011;11:2093-109.
4. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, *et al*. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med 1999;341:1725-30.
5. Roake JA, Cahill AP, Gray CM, Gray DW, Morris PJ. Preemptive cadaveric renal transplantation – Clinical outcome. Transplantation 1996;62:1411-6.
6. Mange KC, Joffe MM, Feldman HI. Effect of the use or nonuse of long-term dialysis on the subsequent survival of renal transplants from living donors. N Engl J Med 2001;344:726-31.
7. Meier-Kriesche HU, Port FK, Ojo AO, Rudich SM, Hanson JA, Cibrik DM, *et al*. Effect of waiting time on renal transplant outcome. Kidney Int 2000;58:1311-7.
8. Papalois VE, Moss A, Gillingham KJ, Sutherland DE, Matas AJ, Humar A. Pre-emptive transplants for patients with renal failure: An argument against waiting until dialysis. Transplantation 2000;70:625-31.
9. Kasiske BL, Snyder JJ, Matas AJ, Ellison MD, Gill JS, Kausz AT. Preemptive kidney transplantation: The advantage and the advantaged. J Am Soc Nephrol 2002;13:1358-64.
10. Katz SM, Kerman RH, Golden D, Grevel J, Camel S, Lewis RM, *et al*. Preemptive transplantation – An analysis of benefits and hazards in 85 cases. Transplantation 1991;51:351-5.
11. El-Agroudy AE, Donia AF, Bakr MA, Foda MA, Ghoneim MA. Preemptive living-donor kidney transplantation: Clinical course and outcome. Transplantation 2004;77:1366-70.
12. John AG, Rao M, Jacob CK. Preemptive live-related renal transplantation. Transplantation 1998;66:204-9.
13. Debska-Slizień A, Wołyniec W, Chamienia A, Wojnarowski K, Milecka A, Zadrozny D, *et al*. A single center experience in preemptive kidney transplantation. Transplant Proc 2006;38:49-52.
14. Schoenfeld D. Partial residuals for the proportional hazards regression model. Biometrika 1982;69:239-41.
15. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. Biometrika 1994;81:515-26.
16. Wolfe RA, McCullough KP, Leichtman AB. Predictability of survival models for waiting list and transplant patients: Calculating LYFT. Am J Transplant 2009;9:1523-7.
17. Stoumpos S, Jardine AG, Mark PB. Cardiovascular morbidity and mortality after kidney transplantation. Transpl Int 2015;28:10-21.
18. Au E, Wong G, Chapman JR. Cancer in kidney transplant recipients. Nat Rev Nephrol 2018;14:508-20.
19. Witczak BJ, Leivestad T, Line PD, Holdaas H, Reisaeter AV, Jenssen TG, *et al*. Experience from an active preemptive kidney transplantation program – 809 cases revisited. Transplantation 2009;88:672-7.
20. Prezelin-Reydit M, Combe C, Harambat J, Jacquelinet C, Merville P, Couzi L, *et al*. Prolonged dialysis duration is associated with graft failure and mortality after kidney transplantation: Results from the French transplant database. Nephrol Dial Transplant 2019;34:538-45.
21. Pérez-Flores I, Sánchez-Fructuoso A, Calvo N, Marques M, Anaya S, Ridao N, *et al*. Preemptive kidney transplant from deceased donors: An advantage in relation to reduced waiting list. Transplant Proc 2007;39:2123-4.
22. Kessler M, Ladriere M, Giral M, Soulillou JP, Legendre C, Martinez F, *et al*. Does pre-emptive kidney transplantation with a deceased donor improve outcomes? Results from a French transplant network. Transpl Int 2011;24:266-75.
23. Innocenti GR, Wadei HM, Prieto M, Dean PG, Ramos EJ, Textor S, *et al*. Preemptive living donor kidney transplantation: Do the benefits extend to all recipients? Transplantation 2007;83:144-9.