Dialysis Vintage and Outcomes after Kidney Transplantation: A Retrospective Cohort Study

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Abstract

Background and objectives Historically, length of pretransplant dialysis was associated with premature graft loss and mortality after kidney transplantation, but with recent advancements in RRT it is unclear whether this negative association still exists.

Design, setting, participants, &measurements This is a retrospective cohort study evaluating 6979 first kidney allograft recipients from the Austrian Registry transplanted between 1990 and 2013. Duration of pretransplant dialysis treatment was used as categoric predictor classified by tertiles of the distribution of time on dialysis. A separate category for pre-emptive transplantation was added and defined as kidney transplantation without any dialysis preceding the transplant. Outcomes were death-censored graft loss, all-cause mortality, and the composite of both.

Results Median duration of follow-up was 8.2 years, and 1866 graft losses and 2407 deaths occurred during the study period. Pre-emptive transplantation was associated with a lower risk of graft loss (hazard ratio, 0.76; 95% confidence interval, 0.59 to 0.98), but not in subgroup analyses excluding living transplants and transplants performed since 2000. The association between dialysis duration and graft loss did not depend on the year of transplantation (P=0.40) or donor source (P=0.92). Longer waiting time on dialysis was not associated with a higher rate of graft loss, but the rate of death was higher in patients on pretransplant dialysis for >1.5 years (hazard ratio, 1.62; 95% confidence interval, 1.43 to 1.83) compared with pretransplant dialysis for <1.5 years.

Conclusions Our findings support the evidence that pre-emptive transplantation is associated with superior graft survival compared with pretransplant dialysis, although this association was weaker in transplants performed since 2000. However, our analysis shows that length of dialysis was no longer associated with a higher rate of graft loss, although longer waiting times on dialysis were still associated with a higher rate of death.

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Introduction

Kidney transplantation is a cost-effective treatment option for eligible patients with ESRD (1–6). Evidence for prolonged survival for kidney transplant recipients compared with patients on maintenance hemo- or peritoneal dialysis has long been provided (7,8). In addition, duration of pretransplant dialysis itself, *i.e.*, dialysis vintage, has been associated with adverse effects on transplant and patient survival (9).

Large registry analyses using United States Renal Data System data reported that increasing waiting time on dialysis was a significant risk factor for graft loss and mortality after kidney transplantation, suggesting a dose effect of maintenance dialysis duration (10,11). After Mange and colleagues demonstrated superior graft survival in pre-emptive kidney transplant recipients from a living donor compared with kidney transplant recipients who underwent maintenance dialysis before living kidney transplantation, it seemed apparent that length of pretransplant dialysis adversely affects outcomes after kidney transplantation (12). Consequently, pre-emptive kidney transplantation has evolved as the treatment of choice for eligible patients in need of RRT (13,14).

However, more recent data from large renal registries around the globe has shown improved survival on maintenance dialysis despite an aging and potentially sicker ESRD population (15–17). Likewise, transplant outcomes have improved over time with the development of individual immunosuppressive regimens and methods for more precise matching of donors and recipients (18–20). It is therefore questionable whether the earlier observed negative effect of pretransplant dialysis on patient and graft survival still exists. Although studies supporting this concept were published at the turn of the millennium, there is little recent data suggesting that pretransplant dialysis duration no longer adversely affects graft survival (10–12,21).

We therefore aimed to further investigate the association between dialysis treatment duration before kidney transplantation and patient and graft survival using contemporary clinical data of a well maintained national registry. We hypothesized that

dialysis vintage no longer adversely affects transplant outcomes under the current standard of care in RRT.

Materials and Methods

Study Design and Data Sources

We conducted a retrospective cohort study to investigate the association between pretransplant dialysis vintage and kidney transplant outcomes. We additionally included pre-emptive transplant recipients to determine the difference between patients who received no dialysis treatment compared with those who received short-term dialysis before transplantation. All first single-organ kidney allograft recipients transplanted between January 1, 1990 and December 31, 2013 who are represented in the OEsterreichische (Austrian) Dialysis and Transplant Registry (OEDTR; for a detailed description see Supplemental Material) were included in this study, as previously done by our group (22,23). Patients were analyzed from the date of first kidney transplantation until death, graft loss, or end of follow-up on December 31, 2013.

The study was approved by the Ethics Committee of Upper Austria (Studie Nr. K-58–15). The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the "Declaration of Istanbul on Organ Trafficking and Transplant Tourism."

Definition of Exposure, Outcomes, and Covariates

All variables recorded in the OEDTR are annually updated and extracted from the original medical records in which the original data has been assessed at the time of follow-up visit through the responsible physician.

Pretransplant dialysis duration was the exposure of interest and measured in days, starting from the day of the first dialysis treatment until kidney transplantation. We included hemodialysis and peritoneal dialysis patients. Pretransplant dialysis duration was used as categoric predictor classified by tertiles of the distribution of time on dialysis in our study cohort. A separate category was added for pre-emptive transplantation defined as kidney transplantation without pretransplant dialysis. In a secondary analysis, patients were categorized by length of pretransplant dialysis in annual intervals to investigate whether short timeframes on dialysis affect transplant outcomes.

The outcome variables were death-censored graft loss, all-cause mortality, and the composite of both outcomes. Patient survival time was defined as the time from kidney transplantation until death or the end of follow-up, and graft survival time as the time from kidney transplantation until permanent return to dialysis treatment, second transplantation, or end of follow-up, and was censored for death.

Arterial hypertension was defined as the prescription of at least one antihypertensive drug or a systolic BP >140 mmHg or diastolic BP >90 mmHg. We classified patients as having chronic heart disease if they had documented coronary artery disease by angiography or radioisotope methods, or myocardial infarction, instable angina, or chronic heart failure determined by the responsible physician. Presence of diabetes mellitus was determined by the attending physician. Primary renal diagnosis was categorized as either diabetic nephropathy, vascular nephropathy, GN, or other. Kidney donor source was defined as either deceased donor or living donor. Immunosuppressive regimen was classified in either cyclosporine A or tacrolimus-based immunosuppression or other.

Statistical Analyses

Characteristics of patients at transplantation were described by mean and SD, by median and interquartile range, or by frequency and percentage for normally distributed variables, non-normally distributed variables, and categoric variables, respectively. We used either ANOVA or Kruskal–Wallis tests for continuous variables and either Chi-squared tests or Fisher exact tests for comparison of categoric variables between dialysis vintage groups.

Kaplan–Meier plots and logrank tests were used for comparison of mortality, and cumulative incidence rates for comparison of graft loss between dialysis vintage groups (24). The association between dialysis vintage and mortality as well as the composite outcome was further quantified by hazard ratio (HR) estimates and 95% confidence intervals (95% CI) derived from Cox regression models (25). To account for competing risk, we fitted Fine and Gray proportional subdistribution hazard models to compare graft loss between dialysis vintage groups (26). Confounding was addressed with two different approaches to fit multivariable proportional hazards models using all variables with their baseline values at transplantation. In our primary analysis, we selected confounding variables on the basis of clinical judgment ("clinical model") and entered year of transplantation, recipient age, primary renal diagnosis, chronic heart disease, and donor source into the model for graft loss, as well as donor age and immunosuppressive regimen into the model for mortality and the composite outcome.

Additionally, we aimed to obtain more parsimonious adjusted HR estimates to increase the robustness of our finding and used a purposeful selection algorithm ("purposeful model") which has been suggested to improve pure *P* value–based variable selection (27). We adopted a significance level of $P<0.15$ or a change in the log hazard by >15% to include covariates. Confounding variables chosen by the purposeful selection algorithm were transplant year, recipient age, diabetes, chronic heart disease, primary renal diagnosis, and donor source in the analysis of graft loss, and additionally donor age and immunosuppression for the analysis of all-cause mortality and the composite outcome.

To distinguish whether the observed association of pre-emptive transplantation originated from planned living donor transplantation or the absence of pretransplant dialysis, we conducted a subgroup analysis stratified for donor source that excluded living donor transplants. We conducted additional subgroup analyses excluding transplants performed before January 1, 2000 to investigate whether our findings differ in more recent years. The presence of effect modification was evaluated by

Table 1. Baseline characteristics of study participants at transplantation stratified by duration of pretransplant dialysis treatment

Variable	Pre-Emptive Transplant *n*=461	First Tertile *n*=2124	Second Tertile *n*=2119	Third Tertile *n*=2186	Missing Values, *n* (%)	*P* Value
Duration of pretransplant dialysis, yr	0	<1.5	1.5–3.1	>3.1	0	—
Mean recipient age (SD), yr	39 (17)	46 (16)	52 (15)	51 (13)	0	<0.001
Hemodialysis, *n* (%)	—	1817 (86)	1839 (87)	1920 (88)	0	<0.001
Female recipients, *n* (%)	163 (35)	743 (35)	765 (36)	819 (37)	0	0.39
Primary renal diagnosis[a] (*n*, %)					11 (0.2)	<0.001
Diabetic nephropathy	100 (22)	444 (21)	376 (18)	241 (11)		
GN	95 (21)	606 (29)	564 (27)	660 (30)		
Vascular nephropathy	18 (4)	184 (9)	259 (12)	257 (12)		
Other primary renal disease	241 (53)	888 (42)	918 (43)	1028 (47)		
Chronic heart failure, *n* (%)	4 (1)	58 (3)	115 (5)	131 (6)	0	<0.001
Coronary artery disease, *n* (%)	14 (3)	243 (11)	336 (16)	345 (16)	0	0.004
Diabetes mellitus, *n* (%)	41 (9)	365 (17)	389 (18)	287 (13)	0	<0.001
Chronic obstructive pulmonary disease, *n* (%)	4 (2)	63 (4)	106 (7)	98 (7)	2422 (35)	<0.001
Chronic liver disease, *n* (%)	8 (4)	101 (6)	94 (5)	132 (7)	1359 (19)	0.02
Mean donor age (SD), yr	42 (14)	43 (17)	47 (17)	47 (16)	385 (6)	<0.001
Living donor, *n* (%)	257 (56)	401 (19)	80 (4)	30 (1)	0	<0.001
Sum of HLA mismatch (median, IQR)	3.5 (1.6)	2.9 (1.6)	2.9 (1.4)	3.1 (1.2)	2295 (33)	<0.001
Panel reactive antibodies, median (first, third quartile)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	377 (5.5)	0.14
Immunosuppression (*n*, %)					664 (10)	<0.001
Cyclosporine A–based regime	154 (35)	1008 (53)	971 (51)	862 (43)		
Tacrolimus-based regimen	232 (54)	703 (37)	703 (37)	833 (42)		
Other immunosuppressive regimen	49 (11)	187 (10)	226 (12)	299 (15)		

—, not applicable.
[a]Ten percent of the study cohort had ESRD of unknown origin.

determining the significance of the interaction terms between dialysis treatment duration (used as continuous variable) and any other variable in the models.

Because there was <15% missing data in the models, we analyzed complete cases only. Schoenfeld residuals confirmed the validity of proportional hazards assumptions and restricted cubic splines were used to assess the assumption of linearity of continuous variables in all models (Supplemental Material). A P value <0.05 was considered statistically significant and all reported P values are two-sided. We used SAS 9.4 TS 1M2 for Windows (Cary, NC) for all analyses.

Results

Patient Characteristics at Transplantation

We identified 6979 first kidney transplant recipients within the observation period in the OEDTR database, and excluded 89 patients from our analysis because pretransplant dialysis treatment status was unknown (Supplemental Figure 1).

Comparison of baseline characteristics of the study cohort at the time of transplantation stratified by duration of pretransplant dialysis treatment is shown in Table 1. Even though all P values were significant due to the large sample size, the differences between groups were small. Median follow-up time was 8.2 years (first, third quartile, 3.9, 13.7). Of the 6890 patients, 461 received a pre-emptive transplant, 2124 patients underwent pretransplant hemo- or peritoneal dialysis treatment for up to 1.5 years (first tertile), 2119 patients between 1.5 and 3.1 years (second tertile), and 2186 patients for >3.1 years (third tertile). We had 768 (11%) transplants from living donors in our study cohort, of which 257 (4%) were engrafted pre-emptively. Pre-emptive transplant recipients had a median eGFR of 7.9 ml/min per 1.73 m^2 (IQR, 6.2–10.5) before engraftment. Waiting times for a kidney transplant in Austria remained constant throughout the study period (Supplemental Figure 2), with a median waiting time for a deceased donor kidney of 600 days (IQR, 164–1218 days) in 2012.

Death-Censored Graft Loss

In total, 1866 patients in our study cohort lost their graft within the study period. Cumulative incidence for death-censored graft loss at 1, 5, and 10 years was 4.7%, 8.6%, and 12% (Figure 1). The rate of graft loss was significantly lower for pre-emptive transplantation compared with patients who underwent pretransplant dialysis for <1.5 years in the unadjusted analysis (HR, 0.60; 95% CI, 0.47 to 0.75). When confounding was accounted for using the "clinical" and "purposeful" modeling approach, the benefit of pre-emptive transplantation persisted but was less prominent (clinical model HR, 0.76; 95% CI, 0.59 to 0.98; purposeful model HR, 0.71; 95% CI, 0.56 to 0.90; Figures 1 and 2, Supplemental Table 1). But when living donor transplants or transplants before 2000 were excluded, pre-emptive transplantation was no longer associated with a significantly lower graft loss rate compared with dialysis for up to 1.5 years (excluding living transplants: HR, 0.71; 95% CI, 0.50 to 1.01; excluding transplants before

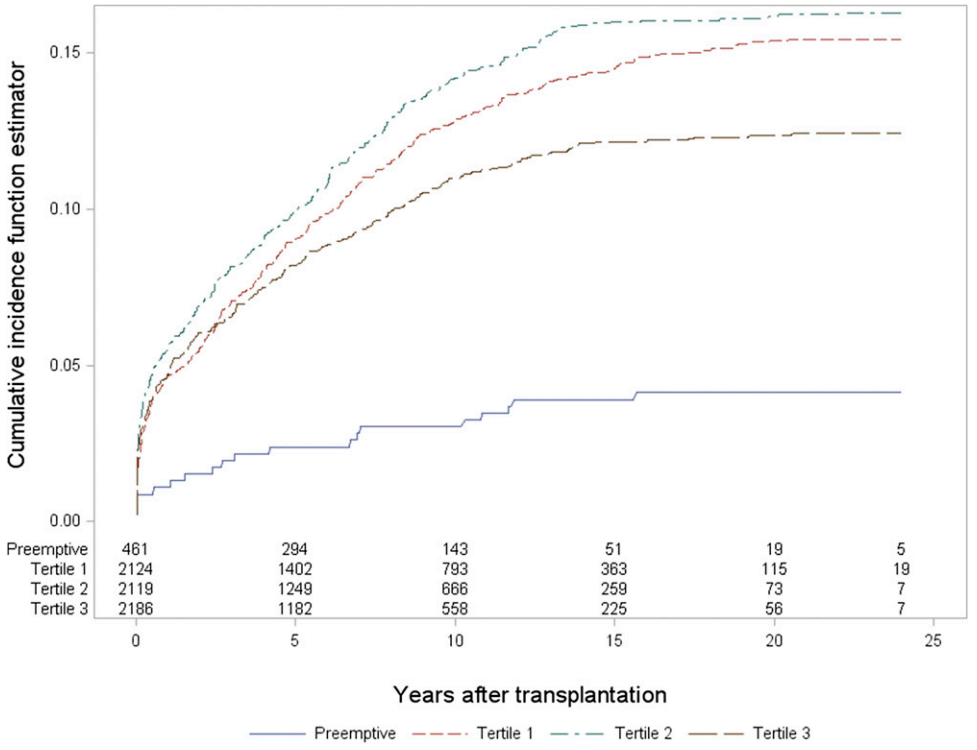

Figure 1. | Cumulative incidence curves for death-censored graft loss stratified by duration of pretransplant dialysis. The number of patients at risk in each stratum at various follow-up times is shown in the bottom panel.

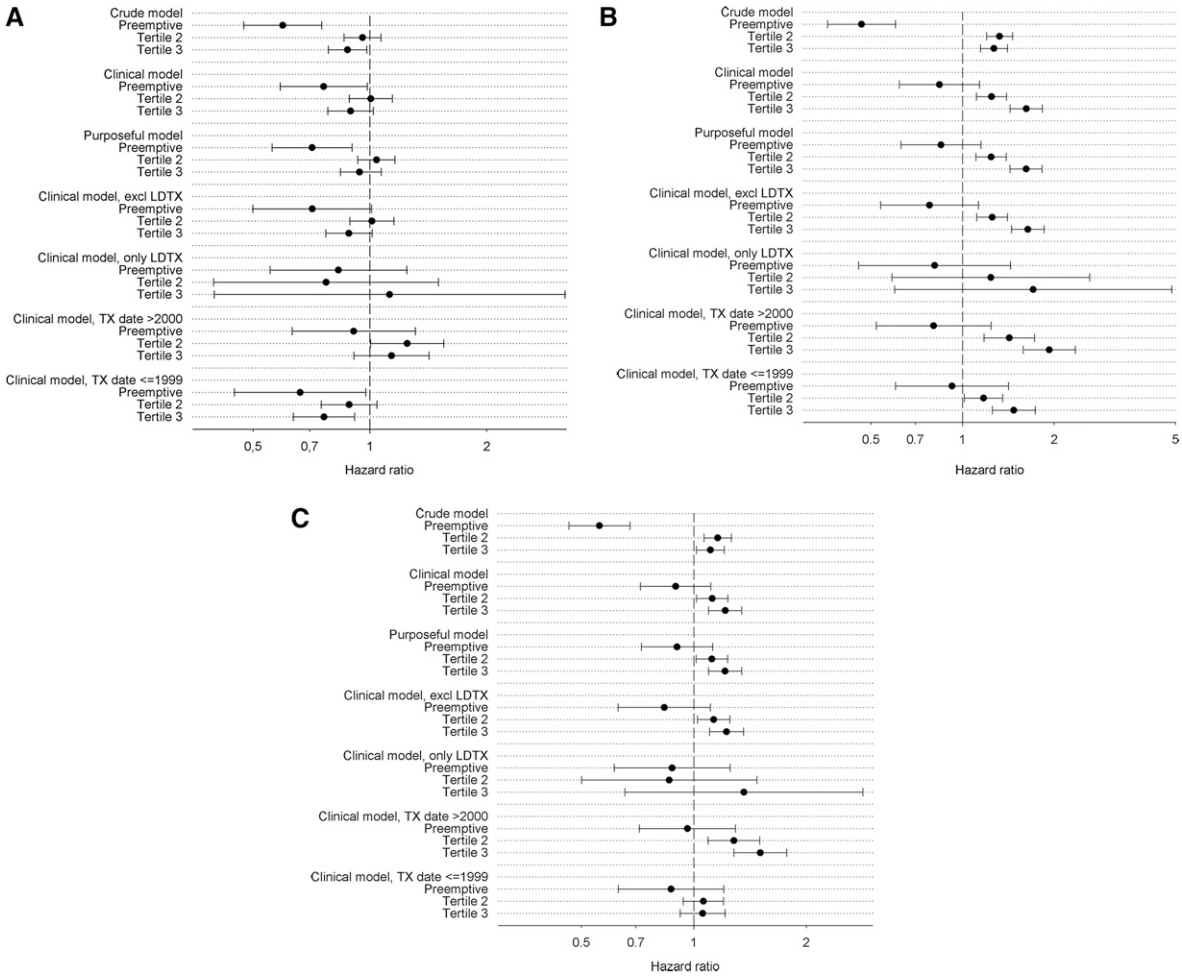

Figure 2. | Forest plot of Fine and Gray models for death-censored graft loss and Cox models for mortality and the composite outcome of death-censored graft loss and mortality. Crude and adjusted hazard ratio estimates and corresponding 95% confidence intervals associated with duration of pretransplant dialysis are shown for death-censored graft loss in panel (A), mortality in panel (B), and the composite outcome in panel (C). Confounding variables for adjustment in the "clinical model" were selected on the basis of clinical judgment and by purposeful selection algorithm in the "purposeful model." Tertile 1 (pretransplant dialysis for up to 1.5 years) was used as reference group in all models. LDTX, living donor transplants; TX, transplant.

2000: HR, 0.91; 95% CI, 0.63 to 1.31; Table 2). There was no difference in graft loss between longer durations of pretransplant dialysis (second and third tertile) compared with patients in the first tertile with shorter dialysis before engraftment. The association of pretransplant dialysis duration on graft loss was not modified by year of transplantation (P=0.40) or donor source (P=0.92) or any other covariate.

All-Cause Mortality and Composite Outcome

Two-thousand-four-hundred-and-seven patients died within the study period of 24 years, 769 due to cardiovascular causes, 629 as a result of infections, and 1009 resulting from other causes (Supplemental Table 2). One-, 5-, and 10-year patient survival rates in the study cohort were 94%, 84%, and 69%, respectively. In the crude analysis, preemptive transplantation was associated with significantly lower mortality (HR, 0.47; 95% CI, 0.36 to 0.60) compared with pretransplant dialysis for up to 1.5 years, whereas pretransplant dialysis treatment for >1.5 years was associated with significantly higher mortality compared with pretransplant dialysis treatment for up to 1.5 years (second tertile: HR, 1.32; 95% CI, 1.20 to 1.46; third tertile: HR, 1.27; 95% CI, 1.15 to 1.40; Figures 2 and 3, Supplemental Table 3). After accounting for confounding, the rate of death remained significantly higher for patients in both tertiles undergoing pretransplant dialysis for >1.5 years compared with pretransplant dialysis duration up to 1.5 years (clinical model: second tertile: HR, 1.24; 95% CI, 1.11 to 1.39; third tertile: HR, 1.62; 95% CI, 1.43 to 1.83). This adverse association of longer pretransplant dialysis persisted in subgroup analyses that excluded living donor transplants and transplants performed before 2000 (Figure 2, Table 2). However, the difference in mortality between pre-emptive transplantation and pretransplant dialysis for up to 1.5 years lost significance in all models (clinical model: HR, 0.84; 95% CI, 0.62 to 1.14).

Table 2. Summary of subgroup analyses for death-censored graft loss and all-cause mortality

Subgroup	Hazard Ratio (95% CI)					
	Complete Study Cohort		Excluding Living Kidney Transplants		Excluding Transplants before 2000	
Death-censored graft loss[a]						
Tertile 1 (reference)	*n*=1896	1	*n*=1514	1	*n*=1047	1
Pre-emptive transplant	*n*=430	0.76 (0.59 to 0.98)	*n*=183	0.71 (0.50 to 1.01)	*n*=345	0.91 (0.63 to 1.31)
Tertile 2	*n*=1898	1.00 (0.88 to 1.14)	*n*=1819	1.01 (0.89 to 1.15)	*n*=1220	1.25 (1.00 to 1.55)
Tertile 3	*n*=1994	0.89 (0.78 to 1.02)	*n*=1967	0.88 (0.77 to 1.01)	*n*=1458	1.14 (0.91 to 1.42)
All-cause mortality[b]						
Tertile 1 (reference)	*n*=1814	1	*n*=1462	1	*n*=990	1
Pre-emptive transplant	*n*=406	0.84 (0.62 to 1.14)	*n*=176	0.78 (0.54 to 1.13)	*n*=324	0.80 (0.52 to 1.24)
Tertile 2	*n*=1815	1.24 (1.11 to 1.39)	*n*=1739	1.25 (1.11 to 1.40)	*n*=1158	1.42 (1.18 to 1.72)
Tertile 3	*n*=1871	1.62 (1.43 to 1.83)	*n*=1848	1.64 (1.45 to 1.85)	*n*=1355	1.93 (1.58 to 2.39)

95% CI, 95% confidence interval.
[a]Adjusted for year of transplantation, recipient age, primary renal diagnosis, chronic heart disease, and donor source.
[b]Adjusted for year of transplantation, recipient age, primary renal diagnosis, chronic heart disease, donor source, donor age, and immunosuppressive regimen.

Analyzing pretransplant dialysis in annual intervals showed a significantly higher mortality in all intervals compared with dialysis vintage of up to 1 year and no difference between pre-emptive transplantation and pretransplant dialysis for up to 1 year (Supplemental Table 6). We found a significant interaction between pretransplant dialysis duration and recipient age (P=0.002), whereas the association of dialysis duration and mortality was not modified by all other covariates.

Results for the composite outcome showed no significant difference between pre-emptive transplantation and dialysis for up to 1.5 years after multivariate adjustment, but both upper tertiles with dialysis for >1.5 years (tertile 2 and 3) were significantly associated with a higher rate of graft loss or mortality compared with tertile 1 (clinical model: second tertile: HR, 1.14; 95% CI, 1.04 to 1.26; third tertile: HR, 1.31; 95% CI, 1.18 to 1.45), which persisted in both subgroup analyses excluding living donor transplants and transplants performed before 2000 (Figure 2, Supplemental Table 4).

Discussion

Our study found that pre-emptive transplantation was associated with a lower rate of graft loss compared with pretransplant dialysis, but also suggests that the potential beneficial effect of pre-emptive transplantation was reduced in more recent years. However, prolonged waiting times on dialysis for >1 year were associated with higher mortality as well as a higher rate of the composite outcome after transplantation.

Previous studies have consistently shown that pre-emptive transplantation is associated with improved transplant outcomes and our study further strengthens this observation, which is important as randomized trials to prove efficacy of pre-emptive transplantation compared with dialysis before transplantation are not feasible (10,12). Our results contribute to the evidence supporting recent recommendations to enhance pre-emptive transplantation programs (14). Our findings are also consistent with earlier reports of higher mortality in patients with a history of longer dialysis treatment duration (10,11). Notably, subgroup analyses indicate that the beneficial effect on graft loss associated with pre-emptive transplantation was reduced in more recent years, potentially due to better immunosuppressive regimens that are available nowadays. However, our results also suggest that if patients receive pretransplant dialysis, then graft loss is no longer affected by duration of dialysis treatment preceding the transplant. In agreement with another recently conducted registry analysis from Finland, these findings mitigate earlier observed negative effects of pretransplant dialysis on graft survival (21).

We believe this shift toward less influence of dialysis vintage on transplant outcomes reflects achievements in both delivering dialysis and caring for kidney transplant recipients that have changed the standard of care throughout the past two decades. More importantly, the widespread use of erythropoietin stimulating agents and iron therapy has substantially reduced the need for blood transfusions, which resources for sensitization to

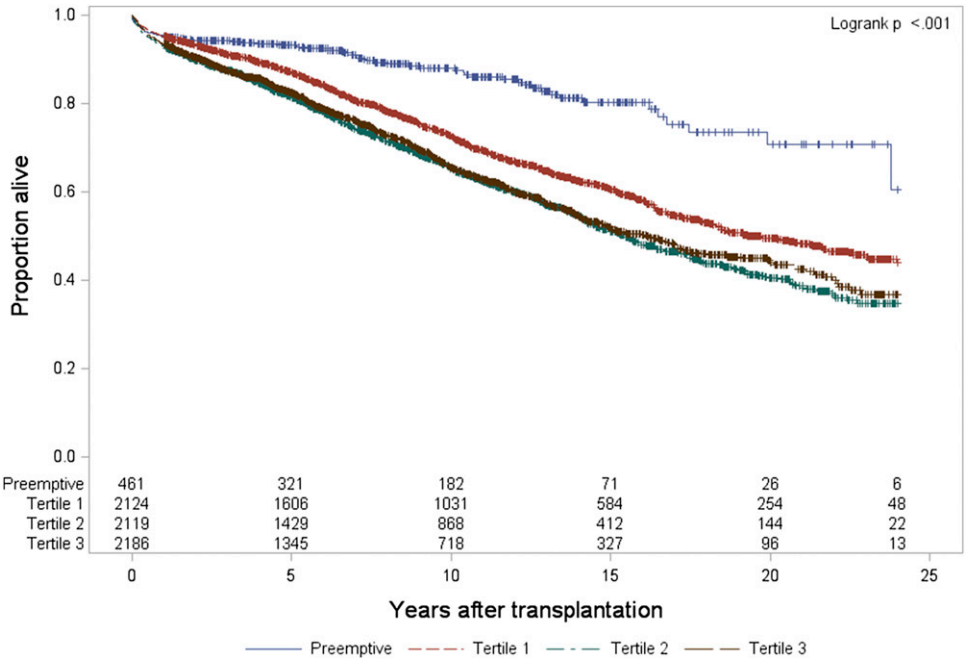

Figure 3. | **Kaplan-Meier curves of all-cause mortality stratified by duration of pretransplant dialysis.** The number of patients at risk in each stratum at various follow-up times is shown in the bottom panel.

HLA antibodies in patients awaiting a transplant (28,29). In addition to this reduction in HLA antibody formation, techniques to detect and characterize HLA antibodies before transplantation facilitated more precise matching of donor-recipient pairs (30,31). Also, paired kidney exchange programs have been implemented in recent years to increase the pool of suitable living donors (32). At the same time, protocols have been developed for effective antibody reduction to minimize the risk of rejection in sensitized patients otherwise facing long waiting times for a suitable donor (33). Poor transplant outcomes in patients with a history of long-term dialysis vintage might have been driven by these sensitized, high-risk transplant candidates in earlier studies. Last but not least, modern immunosuppression paved the way for more effective and less toxic levels, thus ameliorating graft injury (34,35). Although we acknowledge that the magnitude of each individual factor would unlikely have been large enough to offset the potential adverse effect of dialysis on graft survival, it is sensible to argue that the combination of all advancements has compensated previously reported adverse effects of pretransplant dialysis of any length. The fact that a more recent year of transplantation was significantly protective in our observational study appears to mirror improvements over time, which have also been observed by others (10). In addition to the aforementioned biologic explanations, differences in health care systems, access to care, and the delivery of RRTs between Europe and the United States have been discussed to explain variations in transplant outcomes (21,36). Extended time from ESRD until waitlisting was previously associated with graft loss and found to be determined by socioeconomic status (37). Contrary to these findings in the United States, confounding by socioeconomic status is negligible in Austria due to universal health insurance coverage and a more homogenous distribution of income compared with the United States (38).

Some limitations need to be considered when interpreting our results. Despite contemporary statistical modeling approaches with multivariate adjustment to reduce bias and rigorous methods to test underlying assumptions, our findings might still be affected by residual confounding; as is true for any observational analysis, unmeasured confounders cannot be taken into account (39). The study cohort is representative for a Central European, primarily white population, and thus our findings might not be generalizable to populations in other regions of the world or with different ethnic backgrounds (40). Furthermore, waitlisting criteria and the transplantation procedure, including the immunosuppressive regimen, vary across countries.

However, our study features a number of strengths, in particular the high quality of our national registry, almost complete follow-up, and mandatory annual data collection. These contemporary data update the association between dialysis vintage and transplant outcomes with a large sample size that facilitated further comprehensive analysis of dialysis duration in annual intervals. Unlike others, we had a sufficiently large sample size of preemptive transplants to include in the analyses as separate category and strictly classified pre-emptive kidney transplant recipients in a distinct category in all our models to clearly differentiate associations of pre-emptive transplantation from short term dialysis (11,21). We found that pre-emptive transplantation was associated with lower death-censored graft loss compared with pretransplant

dialysis, but did not observe this benefit in transplants performed since 2000. However, prolonged pretransplant dialysis was still associated with higher mortality and a higher rate of the composite of mortality and graft loss. On the basis of these findings, policy makers should consider the avoidance of extended dialysis duration before transplantation by giving additional waitlist priority to patients on long-term pretransplant dialysis.

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Disclosures

None.

References

1. Haller M, Gutjahr G, Kramar R, Harnoncourt F, Oberbauer R: Cost-effectiveness analysis of renal replacement therapy in Austria. *Nephrol Dial Transplant* 26: 2988–2995, 2011
2. Woodroffe R, Yao GL, Meads C, Bayliss S, Ready A, Raftery J, Taylor RS: Clinical and cost-effectiveness of newer immunosuppressive regimens in renal transplantation: A systematic review and modelling study. *Health Technol Assess* 9: 1–179, 2005
3. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, Held PJ, Port FK: Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 341: 1725–1730, 1999
4. Wong G, Howard K, Chapman JR, Chadban S, Cross N, Tong A, Webster AC, Craig JC: Comparative survival and economic benefits of deceased donor kidney transplantation and dialysis in people with varying ages and co-morbidities. *PLoS One* 7: e29591, 2012
5. Rabbat CG, Thorpe KE, Russell JD, Churchill DN: Comparison of mortality risk for dialysis patients and cadaveric first renal transplant recipients in Ontario, Canada. *J Am Soc Nephrol* 11: 917–922, 2000
6. Merion RM, Ashby VB, Wolfe RA, Distant DA, Hulbert-Shearon TE, Metzger RA, Ojo AO, Port FK: Deceased-donor characteristics and the survival benefit of kidney transplantation. *JAMA* 294: 2726–2733, 2005
7. Vollmer WM, Wahl PW, Blagg CR: Survival with dialysis and transplantation in patients with end-stage renal disease. *N Engl J Med* 308: 1553–1558, 1983
8. Schnuelle P, Lorenz D, Trede M, Van Der Woude FJ: Impact of renal cadaveric transplantation on survival in end-stage renal failure: Evidence for reduced mortality risk compared with hemodialysis during long-term follow-up. *J Am Soc Nephrol* 9: 2135–2141, 1998
9. Cosio FG, Alamir A, Yim S, Pesavento TE, Falkenhain ME, Henry ML, Elkhammas EA, Davies EA, Bumgardner GL, Ferguson RM: Patient survival after renal transplantation: I. The impact of dialysis pre-transplant. *Kidney Int* 53: 767–772, 1998
10. Meier-Kriesche HU, Port FK, Ojo AO, Rudich SM, Hanson JA, Cibrik DM, Leichtman AB, Kaplan B: Effect of waiting time on renal transplant outcome. *Kidney Int* 58: 1311–1317, 2000
11. Meier-Kriesche HU, Kaplan B: Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: A paired donor kidney analysis. *Transplantation* 74: 1377–1381, 2002
12. 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* 344: 726–731, 2001
13. Abecassis M, Bartlett ST, Collins AJ, Davis CL, Delmonico FL, Friedewald JJ, Hays R, Howard A, Jones E, Leichtman AB, Merion RM, Metzger RA, Pradel F, Schweitzer EJ, Velez RL, Gaston RS: Kidney transplantation as primary therapy for end-stage renal disease: A National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQITM) conference. *Clin J Am Soc Nephrol* 3: 471–480, 2008
14. Abramowicz D, Hazzan M, Maggiore U, Peruzzi L, Cochat P, Oberbauer R, Haller M, Van Biesen W; Descartes Working Group and the European Renal Best Practice (ERBP) Advisory Board: Does pre-emptive transplantation versus post start of dialysis transplantation with a kidney from a living donor improve outcomes after transplantation? A systematic literature review and position statement by the Descartes working group and ERBP. *Nephrol Dial Transplant* 31: 691–697, 2015
15. ERA-EDTA Registry, AMC, Department of Medical Informatics, Amsterdam, The Netherlands: ERA-EDTA Registry Annual Report 2012. 2014
16. U.S. Renal Data System: *USRDS 2013 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States.* Bethesda, MD, NIoH, National Institute of Diabetes and Digestive and Kidney Diseases, 2013
17. ANZDATA Registry: 38th Report, Chapter 3: Mortality in End Stage Kidney Disease. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2016. Available at: http://www.anzdata.org.au. Accessed November 17, 2015
18. Halloran PF: Immunosuppressive drugs for kidney transplantation. *N Engl J Med* 351: 2715–2729, 2004
19. Stallone G, Schena A, Infante B, Di Paolo S, Loverre A, Maggio G, Ranieri E, Gesualdo L, Schena FP, Grandaliano G: Sirolimus for Kaposi's sarcoma in renal-transplant recipients. *N Engl J Med* 352: 1317–1323, 2005
20. Masson P, Henderson L, Chapman JR, Craig JC, Webster AC: Belatacept for kidney transplant recipients. *Cochrane Database Syst Rev* 11: CD010699, 2014
21. Helantera I, Salmela K, Kyllonen L, Koskinen P, Gronhagen-Riska C, Finne P: Pretransplant dialysis duration and risk of death after kidney transplantation in the current era. *Transplantation* 98: 458–464, 2014
22. Heinze G, Mitterbauer C, Regele H, Kramar R, Winkelmayer WC, Curhan GC, Oberbauer R: Angiotensin-converting enzyme inhibitor or angiotensin II type 1 receptor antagonist therapy is associated with prolonged patient and graft survival after renal transplantation. *J Am Soc Nephrol* 17: 889–899, 2006
23. Heinze G, Kainz A, Hörl WH, Oberbauer R: Mortality in renal transplant recipients given erythropoietins to increase haemoglobin concentration: Cohort study. *BMJ* 339: b4018, 2009
24. Kaplan EL, Meier P: Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 53: 457–481, 1958
25. Cox D: Regression models and life-tables. *J R Stat Soc Series B Stat Methodol* 34: 187–220, 1972
26. Fine JP, Gray RJ: A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc* 94: 496–509, 1999
27. Bursac Z, Gauss CH, Williams DK, Hosmer DW: Purposeful selection of variables in logistic regression. *Source Code Biol Med* 3: 17, 2008
28. Yabu JM, Anderson MW, Kim D, Bradbury BD, Lou CD, Petersen J, Rossert J, Chertow GM, Tyan DB: Sensitization from transfusion in patients awaiting primary kidney transplant. *Nephrol Dial Transplant* 28: 2908–2918, 2013
29. Scornik JC, Meier-Kriesche HU: Blood transfusions in organ transplant patients: Mechanisms of sensitization and implications for prevention. *Am J Transplant* 11: 1785–1791, 2011
30. Heidt S, Witvliet MD, Haasnoot GW, Claas FH: The 25th anniversary of the Eurotransplant acceptable mismatch program for highly sensitized patients. *Transpl Immunol* 33: 51–57, 2015
31. Konvalinka A, Tinckam K: Utility of HLA antibody testing in kidney transplantation. *J Am Soc Nephrol* 26: 1489–1502, 2015

32. Organ Procurement and Transplantation Network (OPTN): Available at http://optn.transplant.hrsa.gov/learn/professional-education/kidney-allocation-system/. Accessed November 17, 2015
33. Marfo K, Lu A, Ling M, Akalin E: Desensitization protocols and their outcome. *Clin J Am Soc Nephrol* 6: 922–936, 2011
34. Chinen J, Buckley RH: Transplantation immunology: Solid organ and bone marrow. *J Allergy Clin Immunol* 125: S324–S335, 2010
35. Webster AC, Ruster LP, McGee R, Matheson SL, Higgins GY, Willis NS, Chapman JR, Craig JC: Interleukin 2 receptor antagonists for kidney transplant recipients. *Cochrane Database Syst Rev* 1:CD003897, 2010
36. Ojo AO, Morales JM, González-Molina M, Steffick DE, Luan FL, Merion RM, Ojo T, Moreso F, Arias M, Campistol JM, Hernandez D, Serón D; Scientific Registry of Transplant Recipients and; Spanish Chronic Allograft Study Group: Comparison of the long-term outcomes of kidney transplantation: USA versus Spain. *Nephrol Dial Transplant* 28: 213–220, 2013
37. Schold JD, Sehgal AR, Srinivas TR, Poggio ED, Navaneethan SD, Kaplan B: Marked variation of the association of ESRD duration before and after wait listing on kidney transplant outcomes. *Am J Transplant* 10: 2008–2016, 2010
38. World Bank: *World Development Indicators 2015.* Washington, DC, World Bank, 2015
39. Heinze G, Oberbauer R: Does size matter? *Nephrol Dial Transplant* 22: 2725–2726, 2007
40. Keith DS: Preemptive deceased donor kidney transplant not associated with patient survival benefit in minority kidney transplant recipients. *Clin Transplant* 26: 82–86, 2012

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