Variation in Dialysis Exposure Prior to Nonpreemptive Living Donor Kidney Transplantation in the United States and Its Association With Allograft Outcomes

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Background: The impact of dialysis exposure before nonpreemptive living donor kidney transplantation on allograft outcomes is uncertain.

Study Design: Retrospective cohort study.

Setting & Participants: Adult first-time recipients of kidney-only living donor transplants in the United States who were recorded within the Scientific Registry of Transplant Recipients for 2000 to 2016.

Factors: Duration of pretransplantation dialysis exposure.

Outcomes: Kidney transplant failure from any cause including death, death-censored transplant failure, and death with allograft function.

Results: Among the 77,607 living donor transplant recipients studied, longer pretransplantation dialysis exposure was independently associated with progressively higher risk for transplant failure from any cause, including death beginning 6 months after transplantation. Compared with patients with 0.1 to 3.0 months of dialysis exposure, the HR for transplant failure from any cause including death increased from 1.16 (95% CI, 1.07-1.31) among patients with 6.1 to 9.0 months of dialysis exposure to 1.60 (95% CI, 1.43-1.79) among patients with more than 60.0 months of dialysis exposure. Pretransplantation dialysis exposure varied markedly among centers; median exposures were 11.0 and 18.9 months for centers in the 10th and 90th percentiles of dialysis exposure, respectively. Centers with the highest proportions of living donor transplantations had the shortest pretransplantation dialysis exposures. In multivariable analysis, patients of black race, with low income, with nonprivate insurance, with less than high school education, and not working for income had longer pretransplantation dialysis exposures. Dialysis exposure in patients with these characteristics also varied 2-fold between transplantation centers.

Limitations: Why longer dialysis exposure is associated with transplant failure could not be determined.

Conclusions: Longer pretransplantation dialysis exposure in nonpreemptive living donor kidney transplantation is associated with increased risk for allograft failure. Pretransplantation dialysis exposure is associated with recipients' sociodemographic and transplantation centers' characteristics. Understanding whether limiting pretransplantation dialysis exposure could improve living donor transplant outcomes will require further study.

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Understanding the association of pretransplantation dialysis exposure with transplant outcomes includes differentiating the benefits of preemptive transplantation from the benefits of limiting pretransplantation dialysis exposure in nonpreemptive recipients and consideration of whether the potential benefits are applicable to both living and deceased donor transplant recipients.

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The association of preemptive transplantation with lower risk for transplant failure was demonstrated for both living and deceased donor transplant recipients in seminal studies based on registry analyses of patients in the United States,[1,2] but recent work has demonstrated that the benefits of preemptive transplantation are not observed in deceased donor transplant recipients outside the United States.[3]

The association of longer pretransplantation dialysis exposure with transplant failure in nonpreemptive patients was first described for deceased donor transplant recipients nearly 20 years ago in the United States.[4] In subsequent national US studies, both deceased and living donor transplant recipients were studied,[5,6] but the association of dialysis exposure with transplant outcomes was not determined separately for living donor transplant recipients or only the univariate association between dialysis exposure and living donor transplant failure was determined.[7] It is notable that the mechanisms underlying the detrimental association of dialysis exposure with transplant failure remain uncertain and may differ between living and deceased donor transplant recipients.[8-10] Recent work has suggested that longer durations of pretransplantation dialysis may identify a subgroup of patients with lower access to transplantation because of medical or socioeconomic factors, and it is these factors, rather than dialysis exposure per se, that lead to inferior transplant outcomes.[11] Living donor transplant recipients typically have better health and higher socioeconomic status than deceased donor transplant recipients, and therefore the impact of dialysis exposure on transplant outcomes may differ from that in deceased donor transplant recipients.

There are a number of reasons why a detailed study of the timing of nonpreemptive transplantation on living donor transplant outcomes is warranted at this time. Recent policy changes to the deceased donor kidney allocation policy in

the United States allow nonpreemptive wait-listed patients to be backdated to their dialysis therapy initiation date.[12,13] Although this change may increase equity in access to deceased donor transplantation, it also may reduce the impetus for early referral of patients who have already initiated dialysis treatment for transplantation, potentially leading to delays in nonpreemptive living donor transplantation. In contemporary practice, increasing demands on living donor programs, including evaluation of older and more complex living donors and transplantation candidates, may lead to delays in the timing of living donor transplantation. Furthermore, the practice of living donation is evolving from one in which donors were mainly highly motivated family members and transplantation centers did little to assist patients without donors to identify potential donors to one in which some transplantation centers directly assist patients to identify potential donors from unrelated individuals.[14,15] Improved understanding of the impact of dialysis exposure on living donor transplant outcomes and factors that contribute to delays in transplantation would inform the importance and design of strategies to ensure timely access to living donor transplantation.

Finally, the current metrics used to evaluate transplantation center performance are based on short-term posttransplantation outcomes and do not include patient access to transplantation.[16] Access to deceased donor transplantation is dependent on deceased organ donation and therefore difficult to include in the evaluation of transplantation center performance. In contrast, the timing of living donor transplantation may be more directly affected by variations in center-level practice.[17] There currently are no standards for the completion of the various processes required to complete a living donor transplantation. Improved understanding of center-level variation in the time to living donor transplantation and the impact of this variation on posttransplantation outcomes may be an important first step to inform the development of such standards.

The purpose of this analysis was to determine the association of the duration of dialysis exposure before nonpreemptive living donor transplantation with transplant failure and identify factors that affect the duration of pretransplantation dialysis exposure, including evaluation of the variation between transplantation centers.

Methods

Patient Protections

This study was performed with the approval of our local hospital research ethics board. Informed consent was waived owing to the use of deidentified registry data.

Data Sources

Data from the Scientific Registry of Transplant Recipients (SRTR) were used for this analysis. The SRTR includes information for deceased donors, wait-list candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight to the activities of the OPTN and SRTR contractors.

Study Population

Adult (aged ≥ 18 years) first kidney-only transplant recipients (ie, excludes combined/simultaneous organ transplant recipients and prior extrarenal organ transplant recipients) captured in the SRTR for January 1, 2000, through November 30, 2016, were studied. Living donor transplant recipients expected to have prolonged pretransplantation dialysis exposures, including recipients of a kidney paired donation transplant (n = 4,944), recipients of an ABO blood group–incompatible transplant (n = 1,048), and HLA antigen–incompatible transplant recipients requiring desensitization (n = 1,099) were excluded to yield a final study population of n = 77,607 patients.

Study Definitions and Calculated Variables

Dialysis exposure before living donor transplantation was calculated as the difference between the date of the first maintenance dialysis treatment and the date of living donor transplantation, with preemptive transplant recipients assigned a value of zero.

Recipient income may affect the duration of pretransplantation dialysis exposure. Median household income for each patient was determined by linking the zip code of residence at the time of transplantation supplied by the SRTR to median household income data recorded at the zip code level in the 2010 US Census, as previously described.[18]

Geographical factors may affect the duration of pretransplantation dialysis exposure. We classified the extent to which the patient's residence location was rural or urban. Rural urban commuting area (RUCA) codes are assigned to each US zip code based on markers of population density, with values ranging from 1.0 (most urban) to 10.6 (most rural). As in previous work, we classified each patient in the current analysis as belonging to 1 of 3 mutually exclusive RUCA groups: metropolitan (RUCA 1.0-3.9, cities with populations > 50,000 and their associated suburban areas), micropolitan (RUCA 4.0-6.0, towns or cities with populations of 10,000-50,000), and rural (RUCA > 6.0, towns with populations < 10,000).[19]

We hypothesized that transplants from older and more medically complex living donors may be associated with the duration of pretransplantation dialysis exposure and used the quintile of living kidney donor profile index to characterize this potential source of variation.[20]

Statistical Analysis

Descriptive Statistics

Characteristics of study patients were described using median and quartiles for continuous variables or frequency and proportion for categorical variables. In addition, we compared the proportion of preemptive living donor transplantation over time using χ^2 test and compared the duration of pretransplantation dialysis exposure over time among nonpreemptive transplant recipients using Kruskal-Wallis test.