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Mortality in Living Kidney Donors With ESRD: A Propensity Score Analysis Using the United States Renal Data System

Amarpali Brar[1], Dimitre G. Stefanov[2], Rahul M. Jindal[3], Moro O. Salifu[1], Madhu Joshi[1], Bair Cadet[1] and Robert Nee[4]

[1]Department of Medicine, Division of Nephrology, SUNY-Downstate Medical Center, Brooklyn, New York, USA; [2]Statistical Design and Analysis, Research Division, SUNY-Downstate Medical Center, Brooklyn, New York, USA; [3]USU-Walter Reed Department of Surgery, Uniformed Services University, Bethesda, Maryland, USA; and [4]Department of Medicine, Division of Nephrology, Walter Reed National Military Medical Center, Bethesda, Maryland, USA

Introduction: In recent years, data have emerged on the outcomes of living kidney donors who develop end-stage renal disease (ESRD). We aimed to evaluate mortality rates in kidney donors who had initiated dialysis compared with a propensity-matched cohort of dialysis patients without previous kidney donation.

Methods: We used the United States Renal Data System (USRDS) and abstracted 274 previous living kidney donors between 1995 and 2009. There were 609,398 individuals on dialysis without kidney donation. We used propensity score matching to identify 258 donors and 258 nondonors. The time-dependent Cox proportional hazards model was used to compare survival between the 2 matched cohorts.

Results: In the propensity score–matched cohort, mortality was lower in donors compared with nondonors (19% vs. 49%; $P < 0.0001$). The time-dependent Cox proportional hazards model demonstrated that donors had significantly lower mortality compared with nondonors 0 to 5 years since start of dialysis (hazard ratio [HR]: 0.17; 95% confidence interval [CI] 0.11–0.27; $P < 0.0001$) and with nondonors 5 to 10 years on dialysis (HR: 0.34; 95% CI: 0.19–0.63; $P < 0.001$). We were unable to estimate the difference between the 2 groups after 10 years on dialysis with any precision (HR: 0.51; 95% CI: 0.18–1.42; $P = 0.20$) due to the small sample size.

Conclusion: We observed a lower mortality rate in living kidney donors with ESRD compared with matched nondonors. This data should guide clinicians in the informed consent process with prospective donors.

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Candidates for living kidney donation in the United States are rigorously screened and have to meet strict medical and psychosocial eligibility criteria before organ donation. Partly because of the current screening evaluation, living kidney donation is generally considered safe. Survival among screened kidney donors appears to be similar or better than those in the general population.[1,2] Furthermore, Segev *et al.*[2] reported that kidney donors were not at higher risk for mortality compared with healthy matched nondonors, after a median of 6.3 years. Nonetheless, kidney donors have an increased relative risk of developing end-stage renal disease (ESRD) compared with healthy matched nondonors, although the magnitude of this risk remains small.[3,4]

Previous living donors who unfortunately progress to ESRD are listed as active status and receive priority on the transplantation waiting list in a timely manner.[5] However, one-half of previous living donors who did not receive preemptive transplantation were on dialysis for ≥332 days before being placed on the list. Potluri *et al.*[6] assessed kidney transplantation outcomes for previous living donors and found that they received higher quality allografts and experienced lower posttransplantation mortality than matched nondonors (HR: 0.19; $P < 0.001$). In an analysis of 99 donors with ESRD who were individually matched to 5 nondonors with ESRD based on demographic and clinical characteristics, Muzaale *et al.*[7] found that donors had lower mortality than matched nondonors (HR 0.7; $P < 0.05$).

Correspondence: Rahul M. Jindal, USU-Walter Reed Department of Surgery, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814, USA. E-mail: jindalr@msn.com

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For the present study, we used a larger sample size based on data from the USRDS to further evaluate mortality among kidney donors who had initiated dialysis compared with a propensity-matched cohort of dialysis patients without previous kidney donation. We used the propensity score method over traditional multivariable regression to provide less biased estimates in a small cohort with fewer outcome events per adjustment covariate.[8,9]

MATERIALS AND METHODS

We used the USRDS to identify living kidney donors who progressed to ESRD from 1995 to 2009, based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis code V59.4. The study cohort was restricted to patients with Medicare as the primary payer upon dialysis initiation. This restriction was necessary to ensure accurate ascertainment of Medicare claims, which might not be reported in patients covered primarily by an insurer other than Medicare. We compared dialysis patients who were previous kidney donors with those who had no history of kidney donation. We excluded patients who were younger than 18 years of age and those on peritoneal dialysis.

We used a propensity score–matched cohort of donors and nondonors to compare all-cause mortality between the 2 groups. We favored a propensity score matching approach more than a regression model adjusting for covariates because of its advantages in bias reduction when large differences in observed covariates exist between groups, without modeling the association between the outcome and the confounders.[8]

Propensity scores were calculated from a logistic regression model, using the following variables: age, sex, race, Hispanic ethnicity, primary cause of ESRD, estimated glomerular filtration rate (eGFR), time when dialysis was initiated since 1995 (start of inception cohort), and comorbid conditions, including hypertension, peripheral vascular disease, diabetes mellitus, chronic obstructive pulmonary disease (COPD), and ischemic heart disease. As indicated by Rosenbaum *et al.*, matching on propensity scores can achieve a balance on the covariates used for creating the scores.[10] Unlike randomization, it does not achieve balance on the covariates not used in the propensity matching, except for the extent that they are correlated with the ones used in the matching. There were several other variables related to mortality that we intended to use, but these were limited by a large number of missing observations. Two such variables were serum albumin and body mass index (BMI).

Donors were matched to nondonors with a 1:1 matching in propensity scores without replacement. As suggested by Rosenbaum *et al.*[10] matching was performed after a transformation of the estimated propensity scores (with the function log [(1 − x)/x]), which resulted in an approximately normal distribution of the transformed scores. The matching was performed with the nearest neighbor method without replacement using a SAS (SAS Institute, Cary, NC) macro developed by Coca-Perraillon.[11]

Survival after dialysis initiation for both donors and nondonors was investigated in the propensity score–matched cohort. The survival curve was estimated using the Kaplan-Meier method, and the log-rank test was used to compare survival between the 2 groups. Proportional hazards assumptions were examined by graphing log (−log [survival function]) versus log (time) for the 2 groups. There were some indications that the assumptions of proportional hazards were not satisfied. Thus, we used a time-dependent Cox proportional hazards model to compare the survival between donors and nondonors. To obtain HRs for each of the 3 time intervals after dialysis initiation (0–5, 5–10, and >10 years), we used time-dependent indicator variables for being a donor, 1 for each time interval. To account for the matching, we used a Cox model with a random effect for the matched pairs (shared frailty model, using a gamma distribution). Baseline variables were compared between donors and nondonors using 2-sample *t* and chi-square tests, as appropriate. As previously described,[8,12] 2-sample *t*-statistic and the standardized percentage difference were used to determine variables with noticeable differences between the groups initially, and to asses if balance was achieved after the matching. The Fine and Gray[13] model was used to compare the cumulative incidence of transplantation in the donors and nondonors groups. This model allowed us to calculate a subdistribution HR for the difference between the groups, considering death as a competing risk of transplantation. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). Statistical significance was defined as a $P < 0.05$.

RESULTS

We identified 274 donors and 609,398 nondonors in our study cohort. Table 1 shows the baseline characteristics of the 2 groups. Nondonors were significantly older at start of dialysis compared with donors (70.5 years vs. 43.9 years; $P < 0.0001$) and were more likely to be female (47.3% vs. 31.8%; $P < 0.0001$). There were significant differences between the 2 groups in terms of the cause of ESRD ($P < 0.0001$). Patients in the nondonor group were more likely to have diabetes mellitus as the primary cause of ESRD compared with donors (45.7% vs. 25.9%). Hypertension as the primary cause