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The advanced age deceased kidney donor: Current outcomes and future opportunities

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The advanced age deceased kidney donor: Current outcomes and future opportunities.

Background. Due to the aging general population, deceased donors ≥55 years will form an increasingly larger proportion of the deceased kidney donor pool.

Methods. Using data from the United States Renal Data System, we determined the change in graft survival between 1996 and 2000 among 32,557 recipients of donors aged <55 years and ≥55 years in univariate and multivariate survival analyses. We identified donor risk factors for graft loss that might influence the decision to accept or reject donors <55 and ≥55 years. The initial glomerular filtration rate established 6 months after transplantation (initial GFR), and the stability of GFR in the first post-transplant year (GFR at 12 months post-transplantation—GFR at six months post-transplantation) were compared between recipients of donors <55 and ≥55 years and the association of these factors with graft survival was determined.

Results. In 2000, one-year graft survival in donors ≥55 years was 86.7%. Between 1996 and 1999 the projected graft half life improved from 11.4 to 14.5 years for recipients of donors <55 years ($P < 0.01$); however, there was no improvement for recipients of donors ≥55 years (8.2 to 9.2 year, $P = 0.46$). Among donor factors studied, only cold ischemic time >24 hours identified recipients of donors ≥55 years at risk for graft loss. Compared to recipients of donors <55 years, recipients of donors ≥55 years established a lower initial GFR (42 vs. 56 mL/min/1.73m^2, $P < 0.0001$), and had less stable GFR in the first post-transplant year (−1.5 vs. −0.6 mL/min/1.73m^2, $P < .0001$). Recipients from donors ≥55 years with initial GFR ≥50 mL/min/1.73m^2 and no drop GFR during the first post-transplant year had graft survival that was superior to that of donors <55 years with either initial GFR <50 mL/min/1.73m^2 or a drop in GFR during the first post-transplant year.

Conclusion. Donors ≥55 years are a valuable resource. Despite improvements in immunosuppression, rejection, and delayed graft function, the projected increase in long-term graft survival among recipients of donors <55 years was not shared among recipients of donors ≥55 years. Recipients of donors ≥55 years had lower initial GFR, and less stable GFR during the first post-transplant year. Limiting cold ischemic time to <24 hours may improve outcomes among recipients of donors ≥55 years. Future studies to maximize initial GFR and minimize early loss of GFR in recipients of donors ≥55 years may lead to improved outcomes from deceased donors ≥55 years.

Key words: kidney transplantatation, cadaveric donor, donor age, graft survival.

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Despite the continued expansion of live donor programs, the demand for kidney transplantation still far exceeds the supply of available organs [1, 2]. As a result, there is increasing need to consider the transplant of organs from deceased donors of advanced age. In 1996, donors aged ≥50 years accounted for 18.2% of all deceased donor kidney transplants performed in the United States compared to only 10.4% in 1988 [3]. In 1998, an estimated 30% of deceased donors in Spain were over 60 years of age [4]. It is likely that deceased donors of advanced age will form an increasingly greater proportion of the eligible donor pool in the future because of aging in the general population and implementation of public safety initiatives to decrease traumatic deaths.

Recipients of advanced age deceased donor kidney transplants have inferior graft survival compared to recipients of younger deceased donor kidney transplants [5, 6]. This has been attributed to a variety of reasons, including reduced nephron mass, senescence, greater susceptibility to ischemic reperfusion injury and, hence, increased incidence of delayed graft function (DGF) and acute rejection [7–9]. In the current era of immunosuppression, the relative importance of traditional barriers to long-term kidney allograft survival, such as acute rejection, has decreased, while there have been relatively few advances in organ procurement and preservation that could impact the survival of organs from deceased donors of advanced age.

The purpose of this study was to reexamine the impact of donor age on long-term graft survival in the current era, and to identify factors that limit the achievement of long-term graft survival from deceased donors of advanced age. The specific aims of this study were: (*1*) to compare the improvement in graft survival during the years

1996 to 2000 between recipients of deceased donor kidneys <55 years and ≥55 years; (*2*) to determine whether donor factors (other than donor age) have a differential association with graft survival in recipients of deceased donor kidneys <55 years and ≥55 years; (*3*) to compare the level of initial allograft function [glomerular filtration rate (GFR) at six months post- transplantation] and stability of allograft function in the first post-transplant year (GFR at 12 months—GFR at six months) between recipients of deceased donor kidneys <55 years and ≥55 years; and (*4*) to compare the association of initial allograft function and stability of allograft function in the first post-transplant year with graft survival in the recipients of deceased donor kidneys <55 years and ≥55 years.

METHODS

Using data from the United States Renal Data System, we studied all adult (>18 years) deceased donor kidney–only transplant recipients in the United States from January 1, 1996 to December 31, 2000. Patients with dual transplants ($N = 338$) were included in the study. Recipients with missing information regarding donor age or extreme donor preprocurement serum creatinine measurements (>3.5 mg/dL or <0.5 mg/dL) were excluded**.** Patients were followed until graft loss (due to death, dialysis, or repeat transplantation) or end of follow-up, December 31, 2000.

Graft failure rates per 100 patient years were determined by donor age. Based on these results, transplant recipients were divided into two groups, those with donors <55 years and ≥55 years. Identical parallel analyses were performed in these two donor age groups. Donor, recipient, and transplant characteristics were described as the mean and standard deviation for continuous variables and frequency for categorical variables, unless otherwise indicated. Transplant characteristics included delayed graft function (DGF), defined by the need for dialysis in the first week following transplantation, and clinical acute rejection (AR), defined by the administration of immunosuppressive medications for the treatment of acute rejection in the first six months following transplantation. Changes in donor, recipient, and transplant characteristics during the study period were determined by transplant year.

The Kaplan-Meier method was used to estimate the graft survival by transplant year. The association of transplant year with long-term graft survival was determined among those patients with graft survival of at least 12 months in parametric multivariate time to event analyses. Recipient age, gender, race, and diabetes as the cause of end-stage renal disease (ESRD), as well as donor race and gender, were chosen a priori to be included in these multivariate models. Additional variables were included based on their association with graft survival in Kaplan-Meier analyses. The final models in recipients of donors <55 years and ≥55 years included the following uniform set of covariates: recipient age, gender, race, cause of ESRD, history of previous kidney transplantation, pretransplant panel reactive antibody level (>20%), degree of HLA mismatch, donor race, donor gender, donor mechanism of death due to cerebrovascular accident (CVA), donor history of hypertension, donor preprocurement serum creatinine >1.5 mg/dL, cold ischemia time (CIT) >24 hours, DGF, AR, use of induction therapy at time of transplantation (interleukin-2 receptor antagonists, polyclonal and monoclonal depleting antibody therapy), and type of maintenance immunosuppression at time of discharge from hospital following transplant surgery (Neoral, Sandimmune, tacrolimus, mycophenolate mofetil, azathioprine, and prednisone). No attempt to impute missing data was made. For patients with missing values for categorical variables, a category of unknown was created, and these patients were included in the multivariate models. Graft half-life was projected assuming both exponential and Weibull distributions for graft failures times [10]. Graphical comparisons of the parametric hazard curves with the empiric hazards were made, and the Weibull distribution was used because it more closely approximated the empiric hazards. Preliminary models did not demonstrate an independent association of donor age with patient survival (date not shown), and therefore, only the results for graft survival (including death as a cause of graft loss) are presented.

To determine whether donor factors had a differential association with graft survival in recipients of deceased donor kidneys <55 years and ≥55 years, the hazard ratios for selected donor factors from parallel Cox regression analyses that included the same donor, recipient, and transplant related factors were compared.

The GFR at six months after transplantation was determined by transplant year using an equation derived from the MDRD study [abstract; Levey et al, *J Am Soc Nephrol* 11:155, 2000]. Among patients with graft survival of at least one year, the stability of graft function in the first transplant year was determined as the change in the estimated GFR between six and 12 months post-transplantation (GFR at 12 months—GFR at six months) (mL/min/1.73m^2). The association of the initial allograft function at six months after transplantation, and the stability of allograft function in the first post-transplant year (drop in GFR between six and 12 months post-transplantation ≥ 0 mL/min/1.73m^2) was then determined in a Kaplan-Meier analysis among patients with graft survival of at least one year in each donor age group. All analyses were performed by SAS statistical software,