Long-Term Outcome of Renal Transplantation from Older Donors

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ABSTRACT

BACKGROUND

Long-term survival of kidney grafts from older donors is inferior to that of grafts from younger donors. We sought to determine whether selecting older kidneys according to their histologic characteristics before implantation would positively influence long-term outcome.

METHODS

In a prospective cohort study, we assessed outcomes among 62 patients who received one or two histologically evaluated kidneys from donors older than 60 years of age. These outcomes were compared with outcomes among 248 matched recipients of single kidney grafts that had not been histologically evaluated and were either from donors 60 years of age or younger (124 positive-reference recipients who, according to available data, were expected to have an optimal outcome) or from those older than 60 years (124 negative-reference recipients, expected to have a worse outcome). The primary end point was graft survival.

RESULTS

During a median period of 23 months, 4 recipients (6 percent) of histologically evaluated kidneys progressed to dialysis, as compared with 7 positive-reference recipients (6 percent) and 29 negative-reference recipients (23 percent). Graft survival in recipients of histologically evaluated kidneys did not differ significantly from that of grafts in positive-reference recipients but was superior to that of grafts in negative-reference recipients (hazard ratio for graft failure in the negative-reference recipients relative to the recipients of histologically evaluated kidneys, 3.68; 95 percent confidence interval, 1.29 to 10.52; P=0.02). The performance of preimplantation histologic evaluation predicted better survival both in the whole study group (P=0.02) and among recipients of kidneys from older donors (P=0.01).

CONCLUSIONS

The long-term survival of single or dual kidney grafts from donors older than 60 years of age is excellent, provided that the grafts are evaluated histologically before implantation. This approach may help to expand the donor-organ pool for kidney transplantation.

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KIDNEY TRANSPLANTATION TO TREAT end-stage renal disease has evolved rapidly from the first successful transplantations[1] to the current widespread use of grafts from both cadaveric and living donors. Because of the limited supply and increasing demand, many patients needing transplants do not receive them. Of 54,231 patients on waiting lists for kidney transplantation in the United States in 2003, only 12,221 received an allograft, 5754 of them from cadaveric donors.[2] The number of patients on waiting lists for kidney transplantation increases by about 10 percent annually, yet the annual increase in the number of transplantation procedures is only 4 percent.[3] Clearly, a larger supply of organs is needed.

Moreover, better ways of using available allografts are needed. In the United States in 1994, a total of 9531 kidneys were initially accepted by transplantation centers; approximately 7 percent of them, however, were subsequently discarded.[4] In 2003 the number of kidneys that were initially accepted increased to 11,437, but the proportion discarded also increased, to 12 percent.[2] Problems with the quality and size of the kidney or with the age of the donor are the most common reasons for discarding kidneys offered for transplantation.[2] As a consequence, the criteria for accepting kidneys for transplantation have been extended to allow the use of organs that only a few years ago would have been considered unacceptable. Thus, organs from donors older than 55 years of age or from donors with a history of hypertension or diabetes mellitus are being used with increasing frequency.[5] Few data are available, however, about the long-term survival of such "marginal" kidneys, although their survival appears to be considerably shorter than that of ideal kidney allografts.[6,7]

Among kidney allografts, poor long-term outcome may be the consequence of an imbalance between the number of viable nephrons supplied and the metabolic demand of the recipient — a gap that becomes wider when marginal kidneys are transplanted after prolonged cold ischemia.[8,9] Acute rejection episodes and the toxic effects of drugs may further reduce an already low nephron mass.[9] These marginal kidneys, one of which has approximately one third or fewer the number of nephrons present in two normal kidneys, initiate a self-perpetuating process of progressive renal-function deterioration, similar to that observed in animal models in which renal mass is reduced surgically.[10,11] In a study in rats, the concomitant transplantation of two kidneys into one recipient to increase the number of transplanted nephrons prevented renal-function deterioration, a problem that occurred in control animals given a single kidney.[12] These findings highlight the importance of matching the theoretical number of nephrons in the transplant with the metabolic demands of the recipient as a possible way to protect a renal allograft from long-term, progressive loss of function.

In a consensus statement, an international panel of pathologists presented a method of assessing whether kidneys from a donor older than 60 years of age still contain enough viable nephrons to be made available for transplantation and whether single or dual transplantation should be used.[13] This panel suggested a biopsy-based scoring system for kidneys, with scores ranging from a minimum of 0 (indicating the absence of renal lesions) to a maximum of 12 (indicating the presence of marked changes in the renal parenchyma).[13-17] Kidneys with a score of 3 or lower were predicted to contain enough viable nephrons to be used as single transplants. Those with a score of 4, 5, or 6 could be used as dual transplants, on the assumption that the sum of the viable nephrons in the two kidneys approached the number in one ideal kidney. Kidneys with a score of 7 or greater were discarded, since it was assumed that they would deliver an insufficient dose of nephrons, even in a dual transplantation.[13-16] We validated these assumptions in a prospective pilot study that found that six months after transplantation, the recipients of single or dual grafts from older donors that had been selected according to these criteria had serum creatinine levels similar to those of controls who had received single kidneys with ideal characteristics.[13] Furthermore, this strategy did not appear to be associated with an excess risk of surgical complications or acute rejection episodes.

The current study was undertaken to evaluate long-term outcomes among recipients of single or dual grafts from older donors after graft selection according to the histologic criteria described above. Outcomes in this cohort of patients were compared with those in two cohorts of patients who were matched with them according to age, sex, and transplantation period and who had received either a single ideal kidney from a young

donor or a single kidney obtained from a donor older than 60 years of age and allocated without a preimplantation biopsy.

METHODS

STUDY DESIGN

In this prospective, multicenter, matched-cohort study,[18] we evaluated long-term graft survival in a cohort of patients who received single or dual kidney transplants from donors older than 60 years of age after preimplantation histologic evaluation of the donor kidneys. We then compared these outcome data with long-term graft survival in two cohorts of matched recipients of single kidney transplants from donors 60 years of age or younger or older than 60 years of age (positive-reference and negative-reference recipients, who according to available data were expected to have an ideal and a worse outcome, respectively) without a preimplantation biopsy.[14] All the patients provided written informed consent to undergo renal transplantation and participate in this protocol.[19] Patients who were to be recipients of histologically evaluated kidneys also provided consent to participate in the Dual Kidney Transplant Group study and thereby agreed to receive either one or two kidneys, depending on the result of a preimplantation biopsy. The Dual Kidney Transplant Group study was approved by the ethics committee of the Clinical Research Center Aldo e Cele Daccò of the Mario Negri Institute for Pharmacological Research and by the institutional review committees at the participating renal-transplantation centers in Bergamo, Genoa, and Padua (all in Italy).

SELECTION OF PATIENTS

Patients entered the study between August 1997 and September 2002 and were followed until the last enrolled patient had completed one year of follow-up. All donors had established brain death. Donors of histologically evaluated kidneys were older than 60 years, as determined by the transplantation centers in Bergamo, Genoa, and Padua. Kidneys were allocated on the basis of standard Nord Italia Transplant guidelines.[19]

Recipients were older than 50 years of age and were no more than 10 years older or younger than their corresponding donors. All were receiving their first transplants, and all had a panel-reactive antibody titer of less than 50 percent.

For each recipient of a histologically evaluated kidney, two positive-reference recipients and two negative-reference recipients were identified. The recipient of an evaluated kidney and the corresponding reference recipients were matched according to sex, age (within five years), and date of transplantation (within three months).

All patients referred to the centers in Bergamo, Padua, and Genoa were offered the possibility of being on a standard waiting list for a transplant. Those who were older than 50 years were also offered the opportunity to be on an additional list for kidneys from older donors that would be subjected to preimplantation biopsy. If they declined, they were entered on only the standard list and therefore had only the possibility of receiving a single transplant from a donor younger than 60 years. No patients who declined subsequently received older kidneys that were not biopsied, because all kidneys from donors older than 60 years that were referred to the centers in Bergamo, Padua, and Genoa underwent a preimtransplantation histologic evaluation.

HISTOLOGIC EVALUATION

Tissue samples were obtained from the inferior pole of each donor's kidneys with the use of a 16-gauge needle. On average, 40 to 50 glomeruli were obtained per sample. In four kidney biopsies, there were fewer than 25 glomeruli; however, the number of glomeruli obtained from the contralateral kidney of the same donor in these four instances was more than 40. Thus, we judged that, overall, the available material was representative and could be used to calculate the score and allocate the kidney.

Kidneys from which a biopsy specimen was obtained were selected and allocated on the basis of the severity of chronic changes expected to affect the recovery of renal function after transplantation; the severity of changes was quantified by a predefined histologic score.[13-17] Changes in each evaluated component of the kidney tissue (vessels, glomeruli, tubules, and connective tissue) received a score ranging from 0 to 3. Each received a score of 0 if no changes were observed and a score of up to 3 if marked changes were present. The vascular score was 3 when the vessel-wall thickness exceeded the luminal diameter or the lumen was occluded; and the glomerular score was 3 when more than 50 percent of the glomeruli were globally sclerotic. The tubular

score was 3 when more than 50 percent of tubules were atrophic, and the connective-tissue score was 3 when more than 50 percent of the renal parenchyma was replaced by connective tissue. The sum of these scores was defined as the global kidney score, which could range from 0 to 12. Kidneys with a global score ranging from 0 to 3 were considered for use as single transplants and those with a score from 4 to 6 for use as dual transplants; those with a score of 7 or greater were discarded (Fig. 1).

FOLLOW-UP

The demographic characteristics of donors and recipients and their defining clinical data at the time of transplantation were recorded. Data on

the survival of the recipients and their grafts were retrieved from the Nord Italia Transplant database. Additional outcome data on the recipients of histologically evaluated kidneys were retrieved from the Dual Kidney Transplant Group database. Data were used according to the standard regulations of the Nord Italia Transplant network for data registration and use and for the preservation of patients' anonymity and privacy.[19]

STATISTICAL ANALYSIS

The study included all recipients of kidneys evaluated histologically before transplantation and all reference recipients recruited over a five-year period. Characteristics at the time of transplantation were compared with the use of Fisher's exact
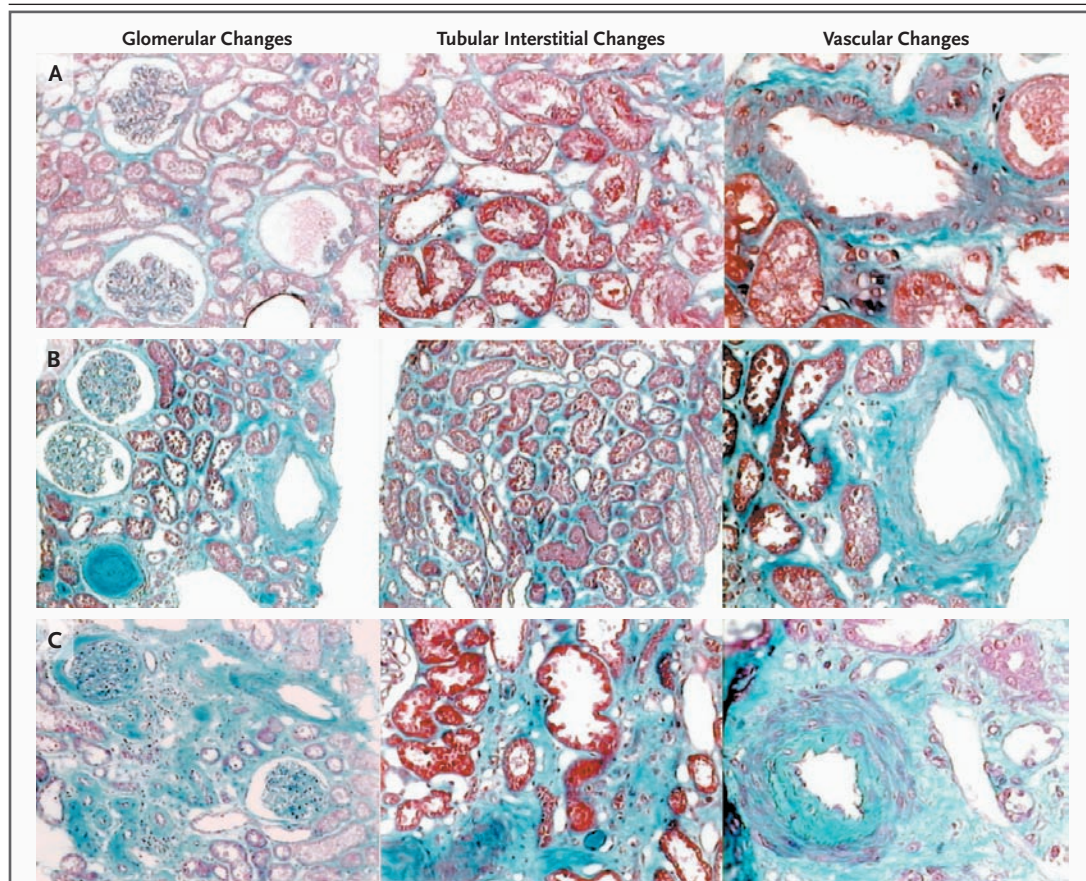

Figure 1. Representative Light Micrographs of Kidney Sections Illustrating the Histologic Scoring Criteria.

Panel A shows three sections of a kidney from a 65-year-old male donor of a single transplant (global score, 2). Panel B shows three sections of a kidney from a 64-year-old male donor of a dual transplant (global score, 5). Panel C shows three sections of a discarded kidney from a 65-year-old man (global score, >7). In each panel, the left section mainly shows glomerular changes, the middle section tubular interstitial changes, and the right section vascular changes.

test, the chi-square test, Wilcoxon's rank-sum test, the Kruskal–Wallis test, or analysis of variance, as appropriate. The primary analysis was a comparison between recipients of histologically evaluated kidneys from older donors and kidneys from older donors that had not undergone histologic evaluation. The primary end point (graft survival) and secondary end points were evaluated with the use of a Cox regression model that included biopsy-guided allocation (yes or no), the donor's creatinine clearance rate, the sex of the donor and of the recipient, the donor–recipient body-weight ratio and body-mass-index ratio, and donor–recipient HLA mismatches.[13] Data from patients who did not reach the primary end point were censored. Rates of event-free survival over time were plotted by the Kaplan–Meier method. In a secondary analysis, data were evaluated with use of the log-rank test. Within the group of recipients of histologically evaluated kidneys, explorative simple and multiple linear regression models were used to identify relationships between the final creatinine clearance rate and the above-listed covariates, the baseline histologic score, the type of transplantation (dual vs. single), and the presence or absence of post-transplantation anuria.

To generate projected estimates of outcomes as long as 10 years after transplantation, we developed theoretical, nonlinear models of the observed cumulative occurrence, calculated every six months, of the need for dialysis or of death with a functioning kidney (the combined outcome) among recipients of histologically evaluated kidneys and negative-reference recipients. Actual and projected outcome rates were expressed as the cumulative number of recipients with the given outcome per 100 transplanted kidneys. For purposes of comparison, the coefficients of the models (intercepts and slopes of curves with 95 percent confidence intervals based on t-distribution values) were also calculated. Statistical analyses were performed with SAS software (version 8) and modeling tools as integrated in Microsoft Excel 2002 (version SP3). All P values were two-sided.

RESULTS

BASELINE CHARACTERISTICS

Sixty-two recipients of one or two kidneys evaluated histologically before transplantation and 248 reference recipients of one kidney that had not been evaluated histologically entered the study (Table 1). Donors whose kidneys were evaluated histologically before implantation and donors to negative-reference recipients (those older than 60 years) were significantly older than donors to positive-reference recipients (those 60 or younger), as expected from the study design. Donors whose kidneys were evaluated histologically before transplantation had lower creatinine-clearance values than donors to positive-reference recipients. Time spent on a waiting list was shorter for recipients of histologically evaluated kidneys than for either positive-reference or negative-reference recipients.

OUTCOMES

All 310 patients were followed for a median of 23 months (interquartile range, 11 to 35) (Table 2). Three-year survival among recipients of kidneys evaluated histologically before transplantation (90 percent) was similar to that among positive-reference recipients (95 percent) and negative-reference recipients (92 percent). Graft survival at three years among recipients of kidneys evaluated histologically before transplantation was similar to that among positive-reference recipients (hazard ratio for graft failure, 0.88; 95 percent confidence interval, 0.26 to 3.00; P=0.83) and was 21 percent greater than that of negative-reference recipients (93 percent vs. 72 percent; hazard ratio for graft failure among negative-reference recipients, 3.68; 95 percent confidence interval, 1.29 to 10.52; P=0.02) (Fig. 2).

At last follow-up, the creatinine clearance rate among recipients of one or two histologically evaluated kidneys was 42.8 ± 21.0 ml per minute per 1.73 m^2. The creatinine clearance rate in this group of recipients was stable and the urinary protein excretion was within the normal range (<500 mg per 24 hours) throughout the study. Major adverse events in this cohort were relatively few (Table 3).

BASELINE PREDICTORS

In the study group as a whole, there were only two significant predictors of graft survival: performance of a histologic evaluation before transplantation (hazard ratio for graft failure, 0.08; 95 percent confidence interval, 0.01 to 0.67; P=0.02) and the age of the donor (hazard ratio, 1.08; 95 percent confidence interval, 1.02 to 1.13; P=0.006).

Table 1. Characteristics of the Donors and Recipients at the Time of Transplantation.*

Group and Characteristic	Donor >60 Yr and Biopsy			No Biopsy		P Value†
	Single Transplant (N=8)	Dual Transplant (N=54)	Overall (N=62)	Donor ≤60 Yr (N=124)	Donor >60 Yr (N=124)	
Donors						
Age (yr)	68±8	69±8	69±8‡	49±9	65±4	<0.001
Male sex (%)	38	51	49	52	47	0.71
Body weight (kg)	71±7	72±12	72±12	69±12	72±11	0.08
Creatinine clearance (ml/min/1.73 m²)	63±6	59±23	60±22§	93±30	78±25	<0.001
Cold-ischemia time (hr)						0.05
Median	18	18	18	15	16	
Interquartile range	16–22	15–20	15–20	12–19	13–19	
Recipients						
Age (yr)	59±3	59±5	59±5	58±5	58±5	0.12
Male sex (%)	25§	67	61	61	61	1.00
Mismatches (no.)						<0.001
Median	5	4	4	3	4	
Interquartile range	4–5	4–5	4–5	2–4	2–4	
Body weight (kg)	60±5	67±11	66±11	69±13	69±12	0.36
Time on a waiting list (mo)						0.09
Median	27	18¶	18¶	26	29	
Interquartile range	17–33	11–32	11–33	8–45	13–45	

* Plus–minus values are means ±SD.
† P values are for the overall comparison among recipients of a kidney from which a biopsy specimen was obtained and evaluated and recipients of a kidney (from either a younger or an older donor) from which a specimen was not obtained.
‡ P<0.05 for the comparison with a kidney from donors 60 years of age or younger whose kidneys were not evaluated with a preimplantation biopsy.
§ P<0.05 for the comparison with a kidney from donors older than 60 years of age whose kidneys were not evaluated with a preimplantation biopsy.
¶ P=0.01 for the comparison with recipients of a kidney from donors older than 60 years of age without a preimplantation biopsy.

Table 2. Duration of Follow-up and Main Outcomes among the Kidney-Transplant Recipients.

Variable	Donor >60 Yr and Biopsy			No Biopsy	
	Single Transplant (N=8)	Dual Transplant (N=54)	Overall (N=62)	Donor ≤60 Yr (N=124)	Donor >60 Yr (N=124)
Follow-up — mo					
Median	13	26	24	23	20
Interquartile range	6–20	14–36	13–36	12–35	9–32
Death — no. (%)	0	3 (6)	3 (5)	5 (4)	10 (8)
Progression to need for dialysis — no. (%)	1 (12)	3 (6)	4 (6)*	7 (6)	29 (23)

* P<0.05 for the comparison with recipients of a kidney from donors older than 60 years of age without a preimplantation biopsy.

Performance of histologic evaluation and a younger donor age predicted longer survival. Among recipients of kidneys from donors older than 60 years, performance of preimplantation kidney biopsy was the only covariate that significantly predicted the outcome (hazard ratio for graft failure, 0.07; 95 percent confidence interval, 0.01 to 0.57; P=0.01). Among recipients of histologically eval-
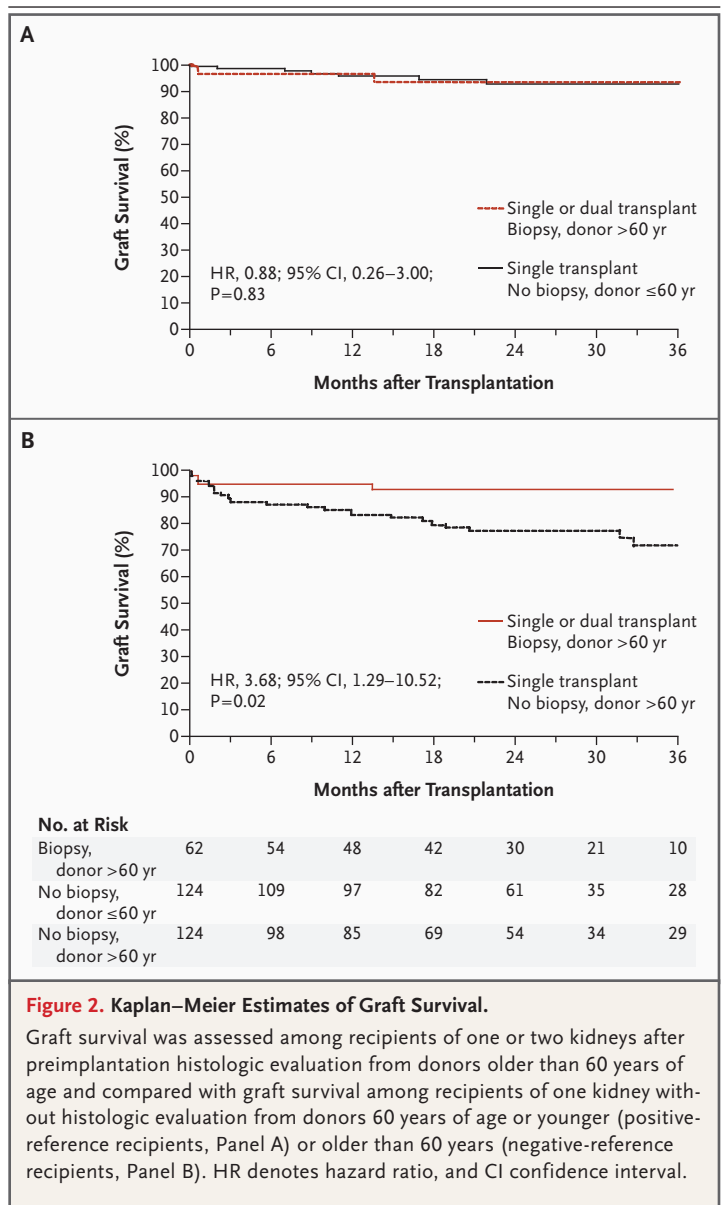
uated kidneys, the donor's age was the only significant predictor of graft survival (hazard ratio, 1.19; 95 percent confidence interval, 1.02 to 1.39; P=0.03) and also of the final creatinine clearance rate.

PROJECTED OUTCOMES

We calculated that for every 100 kidneys obtained from older donors and evaluated histologically, there would be 53 recipients of either one or two kidneys, and that for every 100 kidneys from older donors without histologic evaluation (negative-reference recipients), there would be 100 recipients of a single kidney each. This calculation is modeled on our actual experience: in the study, there were 62 recipients of 116 histologically evaluated kidneys and 124 recipients of 124 kidneys that were not examined in this manner (Table 1). During the observation period, 6 of 100 recipients of kidneys evaluated histologically before transplantation would have died (3 recipients) or had progression to dialysis (3), as compared with 31 of 100 negative-reference recipients (10 and 21 recipients, respectively). The logarithmic models projected a mean excess of 35 negative-reference recipients with progression to death or a need for dialysis over a 10-year period, as compared with recipients of histologically evaluated kidneys ($R^2=0.97$ vs. $R^2=0.96$) (Fig. 3). For every 100 histologically evaluated kidneys from older donors, 9 recipients (95 percent confidence interval, 7 to 10) would, in the projection, die or have progression to dialysis (3 and 6 recipients, respectively) over a 10-year period. In contrast, 44 negative-reference recipients (95 percent confidence interval, 38 to 49), whose grafts were not histologically evaluated before implantation, would be predicted to die or have progression to dialysis (11 and 33 recipients, respectively) during the same period.

DISCUSSION

The current study indicates that the survival of kidney grafts obtained from donors older than 60 years and allocated for single or dual transplantation on the basis of biopsy findings before transplantation was similar to that of single grafts from younger donors and substantially better than that of single grafts from donors older than 60 years when those grafts were selected and allocated on the basis of standard clinical criteria.

Figure 2. Kaplan–Meier Estimates of Graft Survival.

Graft survival was assessed among recipients of one or two kidneys after preimplantation histologic evaluation from donors older than 60 years of age and compared with graft survival among recipients of one kidney without histologic evaluation from donors 60 years of age or younger (positive-reference recipients, Panel A) or older than 60 years (negative-reference recipients, Panel B). HR denotes hazard ratio, and CI confidence interval.

The good long-term outcome of renal grafts allocated on the basis of the histologic score before transplantation appeared to be independent of fulfillment of the criteria for allocation as single or dual transplants. Renal function recovered promptly after transplantation, and creatinine clearance was, on average, about 40 ml per minute three years after transplantation. Moreover, creatinine clearance appeared to be stable throughout the observation period, and urinary protein excretion was consistently within the normal range for up to three years after transplantation. Stable creatinine clearance and normal

Table 3. Adverse Events during Follow-up among Recipients of Histologically Evaluated Kidney Transplants from Donors Older Than 60 Years of Age.

Adverse Event	Single Transplant (N=8)	Dual Transplant (N=54)
Delayed graft function — no. (%)	4 (50)	22 (41)
Discontinuation of dialysis — days		
Median	9	5
Interquartile range	8–21	1–11
Acute allograft rejection — no. (%)	1 (12)	10 (19)
Lymphocele — no. (%)	0	3 (6)
Vascular thrombosis of graft — no. (%)	1 (12)	3 (6)*
Ureteral necrosis — no. (%)	0	1 (2)
Urinary tract infection — no. (%)		
Upper tract	1 (12)	1 (2)
Lower tract	0	6 (11)
Pneumonia — no. (%)		
Mycotic pneumonia	0	2 (4)
Pneumocystis pneumonia	0	0
Sepsis — no. (%)	0	4 (7)
Cytomegalovirus reactivation — no. (%)	1 (12)	3 (6)
Kaposi's sarcoma — no. (%)	0	2 (4)
Other tumors — no. (%)	2 (25)	1 (2)

* In these dual-transplant recipients, one graft failed because of vascular thrombosis but dialysis was not required, since in each of them the second of the two kidneys remained functional.

protein excretion have been reported to be reliable predictors of good long-term allograft outcome.[20]

In each of three recipients of dual grafts from older donors, one graft failed because of vascular thrombosis, but these three recipients were treated without dialysis, since in each of them the second of the two kidneys remained functional. Moreover, no graft was lost because of complications of preimplantation biopsy; the cold-ischemia time (the time elapsed between procurement of the organ and transplantation) was similar among the study cohorts, indicating that evaluation of a preimplantation biopsy specimen is compatible with the routine activities of organ procurement and allocation. Conceivably, the expanded pool of organs resulting from the planned strategy of preimplantation biopsy might explain, at least in part, the shorter waiting-list time among recipients of kidneys that were evaluated histologically before transplantation.

Among several baseline covariates relating to the donors and recipients, the only independent predictor of graft survival and recovery of renal function after transplantation was the donors'

age. Younger age was associated with a better outcome. This finding is consistent with previously reported data from experimental studies[21] and studies in humans,[22-24] indicating that age is a key determinant of graft outcome, and hence confirms that careful matching of donor and recipient according to age is important for kidney grafts allocated according to the results of histologic evaluation.

Long-term survival of grafts allocated on the basis of preimplantation biopsy findings that were from donors older than 60 years of age was about 21 percent better than that of single grafts allocated solely on the basis of routine clinical criteria, irrespective of the creatinine clearance of the kidney to be transplanted at the time of organ procurement. Multivariable analysis indicated that biopsy-guided kidney allocation was the only independent predictor of improved long-term graft survival and that both donors and recipients were very well matched according to other factors potentially affecting graft outcome, such as age, sex, weight, cold-ischemia time, and the number of HLA mismatches. Thus, the current findings provide a strong argument for preimplan-
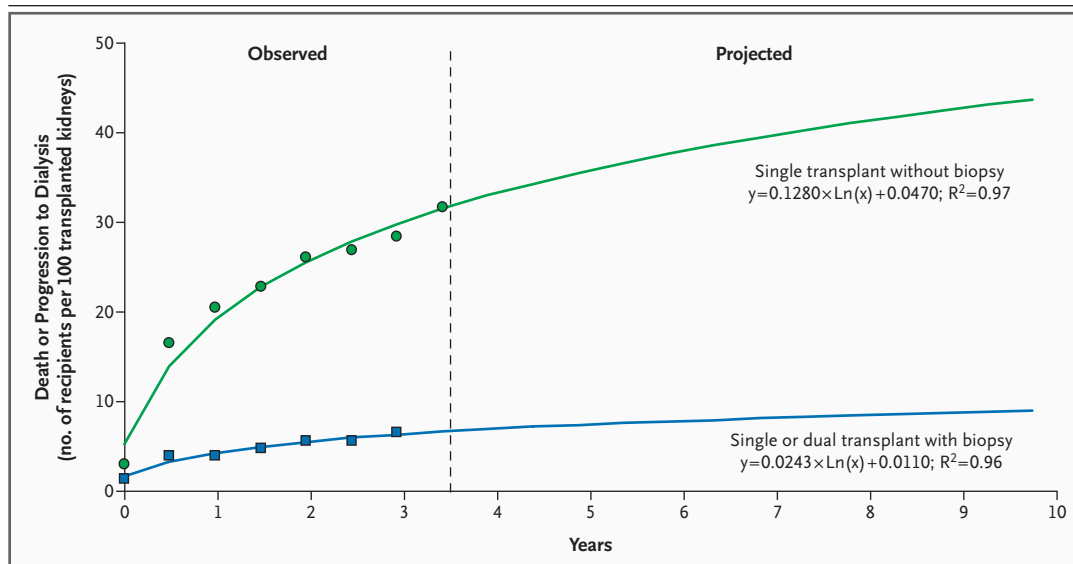
Figure 3. Death or Progression to Dialysis.

The figure shows the number of recipients of kidney transplants from which a biopsy specimen was obtained before implantation (100 single or dual grafts) as compared with the number of recipients of kidneys from which a specimen was not obtained before implantation (100 single grafts) who were projected to die or need long-term dialysis over the 10-year period after transplantation. The symbols show the number of patients who died or had progression to dialysis during the observation period. The curves and corresponding equations (x, time; y, number; Ln(x), natural logarithm of time) describe the number of patients projected to die or to have progression to dialysis within 10 years after transplantation. Over the 10-year period, 3 and 6 recipients of kidneys from which a biopsy specimen was obtained were projected to die or have progression to dialysis, respectively, as compared with 11 and 33 recipients of kidneys from which a specimen was not obtained.

tation biopsy as a strategy to optimize the use of grafts from donors older than 60 years of age.

Biopsy-guided allocation of kidneys from older donors may be a possible strategy for matching nephron dose to the recipient's metabolic demand and thus prolonging graft survival. If successful over time, this strategy might conceivably limit the number of patients who eventually must resume dialysis and who need second transplants. This possibility is important because 20 percent of patients waiting for a kidney from a cadaveric donor are people whose first transplants have failed.[25] Moreover, renal-transplant recipients who resume dialysis have a shorter life expectancy than those who remain independent of dialysis[26] and those who are undergoing dialysis while waiting for their first transplant.[27,28]

When we modeled 10-year outcomes in our patients for every 100 transplanted kidneys from donors older than 60 years, we predicted that only 9 recipients of kidneys evaluated histologically before transplantation would be expected to die or to require long-term dialysis therapy, as compared with 44 of those who received kidneys

that had not been evaluated histologically before transplantation. When we considered patient survival as a single outcome, only 3 recipients of kidneys evaluated histologically before implantation would be predicted to die during the ensuing 10 years, as compared with 11 recipients of kidneys not evaluated in this manner. These predicted outcomes appear to be far better than those of dual transplants reported to the United Network for Organ Sharing (UNOS) registry.[29] Notwithstanding the younger age of the donors in the UNOS registry (60 years on average, as compared with 69 years in our study), only 60 percent of the recipients of dual transplants reported to UNOS had functioning kidneys at three years, as compared with 93 percent in our study. A reasonable explanation for this striking difference is that in the UNOS series, kidneys from older donors were allocated without a preimplantation biopsy.

In conclusion, kidneys from donors older than 60 years of age can provide excellent renal function for up to three years after transplantation, providing that they are allocated as single or dual

transplants according to biopsy findings before transplantation and that kidneys showing more severe, chronic changes on biopsy are discarded. These findings highlight a simple procedure that should permit an expansion of the donor-organ pool for patients older than 50 years of age — a group currently numbering about 60,000 in the United States.[30]

APPENDIX

The participating members of the Dual Kidney Transplant Group and their institutions are as follows: *Investigators:* G. Locatelli, G. Rota, E. Gotti, P. Ondei, P. Cravedi, P. Ruggenenti, and G. Remuzzi (Azienda Ospedaliera, Ospedali Riuniti, Bergamo); M. Beatini, U. Valente, and V. Arcuri (Ospedale San Martino, Genoa); P. Rigotti, N. Baldan, L. Liberati, and M. Costantino (Azienda Ospedaliera Giustinianeo, Università degli Studi, Padua); and M. Scalamogna, G. Rossini, M. Cardillo (Nord Italian Transplant, Ospedale Maggiore Policlinico, Milan); *Database and analysis:* B. Ene-Iordache, M. Turturro, A. Perna, and B.D. Dimitrov (Clinical Research Center for Rare Diseases, Aldo and Cele Daccò, Mario Negri Institute for Pharmacological Research, Bergamo); *Score analysis:* T. Bertani and F. Marchetti (Azienda Ospedaliera, Ospedali Riuniti); J.L. Ravetti (Ospedale San Martino), and A. Parenti (Azienda Ospedaliera Giustinianeo, Università degli Studi).

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