1415

Cadaveric renal transplantation using kidneys from donors greater than 60 years old

Vivas CA, O'Donovan RM, Jordan ML, Hickey DP, Hrebinko R, Shapiro R, Starzl TE, Hakala TR. Cadaveric renal transplantation using kidneys from donors greater than 60 years old.
Clin Transplantation 1992: 6: 77–80.

Abstract: Transplantation of kidneys from donors over the age of 60 yr is controversial. However, as the demand for cadaveric kidneys far exceeds the supply, exploration of the usefulness of kidneys outside the currently accepted donor pool is necessary. Between January 1987 and July 1989, 31 (5.5%) of the 558 cadaveric renal transplants performed at the University of Pittsburgh utilized organs from donors older than 60 yr. Median recipient age was 41 yr (range 24–71 yr); 4 recipients were diabetic and 6 had panel-reactive antibody levels greater than 20% at the time of transplant. All recipients were treated with cyclosporine, prednisone and azathioprine. The 1-yr allograft survival was 65% which was less than but not statistically different from the graft survival of 80% in a retrospective selected control group who received grafts from younger donors aged 11 to 50 yr. However, the 1-yr graft survival of older donor kidneys with cold ischemia time greater than 48 hours was 38%, which was significantly poorer than the 78% 1-yr graft survival seen with cold ischemia times less than 48 h ($p=0.04$ Breslow). The mean serum creatinine was significantly higher in the older donor kidneys at 1, 3, and 12 months post-transplant than in the control kidneys even when kidneys with greater than 48 h of cold ischemia time were excluded. In summary, transplantation of cadaver kidneys from donors older than 60 yr results in acceptable graft survival rates. These kidneys are more susceptible to cold ischemic injury and function with a higher serum creatinine than kidneys from younger donors. Expansion of the donor pool by the use of older donor kidneys in selected recipients could have an impact on alleviating the chronic national cadaver kidney shortage.

Carlos A. Vivas, Richard M. O'Donovan*, Mark L. Jordan, David P. Hickey, Ronald Hrebinko, Ron Shapiro, Thomas E. Starzl and Thomas R. Hakala**

Division of Urologic Surgery/Renal Transplantation Department of Surgery, University of Pittsburgh, Presbyterian University Hospital, Pittsburgh, PA, *School of Medicine, Tulane University, New Orleans, LA, U.S.A. and **Department of Urology, Beaumont Hospital, Dublin, Ireland.

Key words: transplantation – donors – elderly

Mark L. Jordan, M.D., 4414 Presbyterian University Hospital, 230 Lothrop Street, Pittsburgh, PA 15213, U.S.A.

Accepted for publication 17 July 1991

Introduction

In 1989 more than 100 000 patients with end-stage renal disease were on dialysis. More than 16 000 of these were awaiting renal transplantation, yet only 8886 were transplanted (1). Expansion of the donor pool could be achieved by using kidneys from older donors. However, these kidneys may yield inferior results (2). We report a retrospective study of our experience over a 2–1/2-yr period with donors older than 60 yr in an attempt to evaluate their potential utility.

Material and methods

Between 1 January 1987 and 31 July 1989, 558 renal transplants were performed at the University of Pittsburgh. Thirty-one (6%) of the kidneys were recovered from donors older than 60 yr. The median donor age was 62 yr (range 60 to 67 yr). There were 21 (68%) female and 10 (33%) male donors. The cause of death was intracranial bleeding in 21 donors (68%), trauma in 8 (26%) and cardiac arrest in 2 (6%). The median cold ischemia time (CIT) was 42 h (range 20 to 60 h). The median donor serum creatinine was 1.1 (0.6 to 1.9 mg%). Twenty-four (77%) of the recipients were male and 7 (29%) were female. Median recipient age was 41 yr (range 24 to 71), 4 patients (13%) were diabetic and 6 patients (19%) had a panel-reactive antibody (PRA) level greater than 20% at the time of transplantation. All patients received cyclosporine, azathioprine and prednisone for immunosuppression. Rejection episodes were treated with high-dose steroids and 8 patients received OKT3 for steroid-resistant rejections.

Follow-up period ranged from 9 to 41 months (median 19 months). A retrospective recipient control group matched for PRA, incidence of diabetes, date of transplant, and immunosuppressive proto-

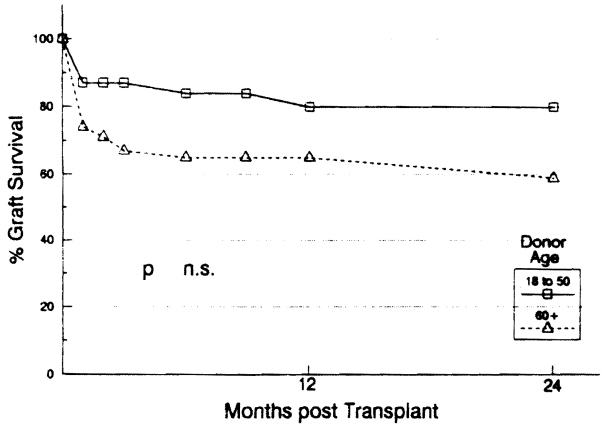

Fig. 1. Survival of renal allografts from donors >60 yr compared to those from donors aged 18 to 50 yr.

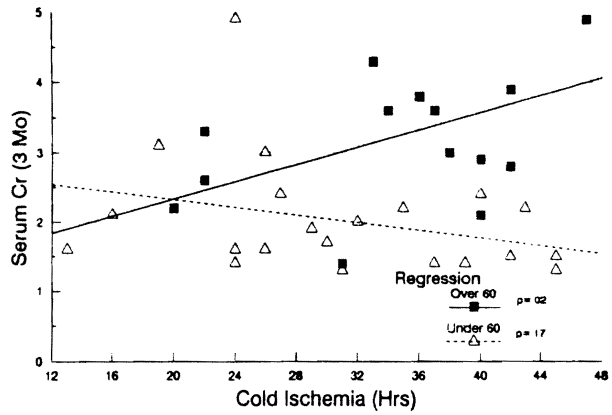

Fig. 3. Regression analysis of the influence of CIT on the SCR at 12 months in recipients of older and younger kidneys.

col who received kidneys from donors aged 18-50 yr (Group 2) was compared to recipients of kidneys from donors older than 60 yr (Group 1). Table 1 illustrates the demographics of these two patient groups. Actuarial survival and statistical analysis were performed using BMDP software.

Results

Patient survival

Overall 1-yr patient survival in recipients of older (>60 yr) donor kidneys was 87%. Two of the 4 deaths were due to sepsis, 1 following cecal perforation and the other following allograft nephrectomy for accelerated rejection. A 3rd patient died of a myocardial infarction 2 wk post-transplant. The 4th patient died of massive lower G.I. bleeding due to granulomatous enterocolitis, 6 months post-transplant.

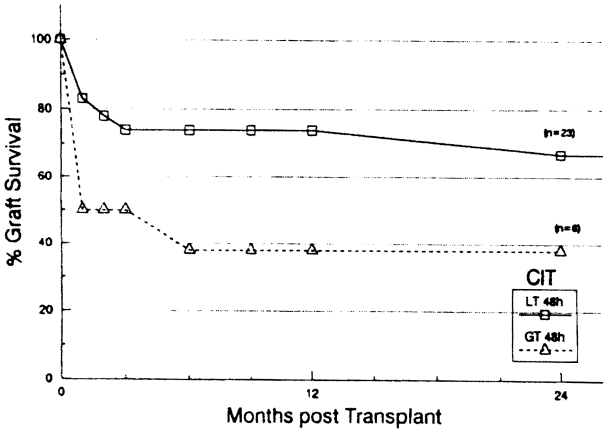

Fig. 2. The effect of CIT on survival of renal allografts from donors >60 yr. LT = less than; GT = greater than. p = 0.04.

Allograft survival

The 1-yr allograft survival in recipients of kidneys from donors older than 60 yr was 65%. This was not statistically different from the 80% survival seen in recipients of kidneys from younger donors (Fig. 1). Allograft survival in kidneys from older donors with a CIT greater than 48 h (n = 8) was significantly decreased compared to that with CIT less than 48 h (76% versus 38%), p = 0.04 (Breslow) (Fig. 2).

Cause of renal allograft failure

Thirteen (42%) allografts failed during the follow-up period. Causes of allograft failure were rejection (n = 8), primary nonfunction (n = 4) and renal vein thrombosis (n = 1).

Allograft function

As shown in Table 2, the delayed graft function rate was 55% in the older donor group (Group 1) compared to 35% in the younger donor group (Group 2) (p < 0.01). The mean serum creatinine (SCR) was significantly higher at 1, 3, and 12 months in Group 1 than in Group 2 (Table 2). Regression analysis indicated that there was a sig-

Table 1. Older vs younger donors: demographics of recipients

Recipient	Group 1 (Donors aged 60 yr)	Group 2 (Donors Aged 18–50 yr)
No. of Patients	31	31
Median Age	41 yr (24–71)	43 yr (28–72)
Male/Female	24/7	21/10
Diabetics	4 (13%)	6 (19%)
PRA >20%	7 (23%)	11 (35%)

Table 2. Older vs younger donors: Comparison of allograft function excluding donor organs with CIT > 48 h

	Group 1 (Donors aged > 60 yr)	Group 2 (Donors aged 18–50 yr)	p*
ATN	55%	35%	< 0.01
Serum Cr (mg/dl)			
1 Month	4.2	3.0	0.03
3 Month	3.4	2.0	< 0.01
12 Month	3.3	1.7	< 0.01

* Mann-Whitney rank sums test.

nificant relationship between the CIT and SCR in the recipients of older donor kidneys. This trend was not evident in patients who received kidneys from younger donors (Fig. 3). Ten recipients of older donor kidneys had SCR greater than 3.0 mg/dl at 1 yr. Nine (90%) of these are still functioning at a median follow-up of 17 months (range 13–41 months), and 6 have lower SCR's at last follow-up compared to their SCR's at 1 yr. Recipients of older donor kidneys had similar 12-h trough HPLC CSA levels to those of younger donor kidneys (Table 3). There was no deliberate attempt to alter cyclosporine doses or levels in recipients of older donor kidneys compared to recipients of younger donor kidneys.

Discussion

In a SEOPF study of 6152 cadaveric kidneys recovered between 1977 and 1982, 1264 (20%) were discarded (3). Older donor age and death from cerebrovascular accidents (CVA) were among the more frequent reasons cited for non-utilization of kidneys. Kidneys from females older than 30 yr and kidneys from CVA donors have poorer graft survival rates than kidneys recovered from young male trauma victims (2). Female and CVA donors each comprised 68% of the older donors reported here.

Kidney function declines with age. Renal mass may be reduced by up to 27% by the 8th decade (4) and is accompanied by a decline in glomerular filtration rate. In one study, inulin clearance decreased from 122.8 to 65.3 ml/min 1.73 m^2 between the ages of 20 and 90 (5), a decline of 46%. Over the age of 30, GFR decreases by 0.8 ml/minute/yr (6) but, owing to decreased muscle mass, this GFR reduction is not reflected in serum creatinine (SCR), which retains the same value as in young adulthood. Calculation of creatinine clearance by use of the Gault-Cockroft (7) formula might be more appropriate in the pretransplant assessment of older donor kidneys. Virtually all functions are altered; afferent and efferent arteriolar resistance is increased, contributing to a decrease in renal blood flow and increased filtration fraction. Renal cortical blood flow is particularly decreased. Other functions such as autoregulation, sodium retention, urinary concentrating ability and capacity to excrete an acid load are also reduced (4). Histologically, senescent glomeruli are found in greater numbers. Kaplan et al. (8) in an autopsy study of 122 patients older than 60 yr, found that up to 15% of the glomeruli were sclerotic. In our series, pretransplant biopsy was performed in 11 (36%) renal allografts. In 7 kidneys sclerosis involved 5% of glomeruli, and in 4 kidneys sclerosis involved 5–12% of glomeruli. The biopsy findings did not have predictive value as far as allograft outcome was concerned.

Table 3 Cyclosporine levels-older vs younger donors

	Mean Cyclosporine levels (12 hour trough HPLC ± S.D.)		
Time post-transplant	Donor Age > 60	Donor Age < 60	p
1 week	228±101	302±178	0.28
1 month	329±140	342±160	0.89
3 months	220±134	246±165	0.65
6 months	214±171	173±59	0.48

With decreased renal blood flow, lower GFR and impaired autoregulatory capacity older kidneys may be more sensitive to ischemia and toxic insults. Takemoto and Terasaki (9) reported that kidneys from donors older than 65 yr had a 23% poorer graft survival than kidneys from 16-yr-old donors. They also showed that the lower survival was more noticeable after 1985, thus implicating cyclosporine in this trend. All our patients received cyclosporine. Kidneys from older donors may also be more sensitive to the effects of cold ischemia. Our 1-yr allograft survival was 38% for kidneys with CIT of 48 h or higher compared to 76% for those with CIT less than 48 h ($p < 0.04$). Four (50%) of the kidneys with a CIT greater than 48 h never functioned. If kidneys with a CIT greater than 48 h are excluded from this analysis the 76% 1-yr graft survival compares favorably with the graft survival in the recipients of the younger donor kidneys. The major graft loss was in the group of kidneys with prolonged cold ischemia. Fig. 1 illustrates that such graft loss occurs early and that the survival curve parallels that of the younger kidneys after the 1st month.

Renal function in surviving grafts from the older donor has not been addressed in the literature. Even excluding donor kidneys with CIT greater than 48 h, the renal function is poorer than in kidneys from donors between 18–50 yr. The mean

SCR in recipients of the older kidneys was 4.2, 3.4, and 3.3 mg/dl at 1, 3, and 12 months post-transplant. This was significantly inferior to the function in the younger donor group in whom SCR's were 3.0, 2.0, and 1.7 mg/dl ($p=0.03$, <0.01, and <0.01 Mann-Whitney Rank Sums). Eventual renal function was significantly correlated with CIT in these older kidneys but this was not the case in the younger donor group. Ten of the 17 recipients of older donor kidneys functioning at 1 yr had SCR's greater than 3.0 mg/dl. Only 1 of these kidneys has subsequently failed. Of the 9 still functioning (follow-up ranging from 13–41 months), 6 have better renal function at most recent follow-up compared to SCR at 1 yr. Therefore, while these kidneys function with a higher SCR than kidneys from younger donors this does not preclude long-term graft survival.

In conclusion, kidneys from donors over 60 yr of age function with a higher SCR at 1, 3, and 12 months than kidneys from younger donors. They are probably better used in older recipients who will make less metabolic demands on the kidney. Low PRA recipients should be selected as the reduced functional reserve of these kidneys may impair recovery from injury. They appear to be more sensitive to cold ischemia and probably should not be used with a CIT greater than 48 h. Selective use of these donors can provide dialysis-free life, increase the donor pool, and make available younger kidneys for patients expected to make greater physiological demands on their graft.

References

1. UNOS Transplantation Statistics, 1989.
2. Cecka SM, Cook DJ. Optimal Use of Cadaver Donor Kidneys. Transplantation Proceedings 1989: 21: 1417.
3. Lucas BA, Vaughn WK, Spees EK, Sanfilippo F. Identification of Donor Factors Predisposing to High Discard Rates of Cadaver Kidneys and Increased Graft Loss Within One Year Post Transplantation. SEOPF 1977–1982. Transplantation 1987: 43: 253.
4. Levin M, Rowe J. Aging and the Kidney. In: Schrier and Gottscholt, eds. Diseases of the Kidney: Boston: Little, Brown, 2657–2679, 1988.
5. Davies DF, Shock N. Age Changes in Glomerular Filtration Rate, Effective Renal Plasma Flow, and Tubular Excretory Capacity in Adult Males. J Clinic Invest 1950: 29: 496–507.
6. Kasiske BL. The Influence of Donor Age on Renal Function in Transplant Recipients. Am J Kidney Dis 1988: 11: 248.
7. Cockroft D, Gault M. Prediction of creatinine clearance from serum creatinine. Nephron 1975: 16: 31.
8. Kaplan C, Pasternak B, Shak H, Gallo G. Age Related Incidence of Sclerotic Glomeruli in Human Kidneys. American Journal of Pathology 1987: 80: 227.
9. Takemoto S, Terasaki PI. Donor and Recipient Age. In: Tereasaki PI, ed. Clinical Transplant 1988. Los Angeles: UCLA Tissue Typing Lab, 1988, 345.