



Long-term Outcome of Living Donors Older Than 60 Years

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ABSTRACT

Long-term outcomes of renal transplantation using kidneys from donors >60 years old are generally considered to be poor. This retrospective study included 265 living donor (LD) transplants in adult recipients with a mean follow-up of 13.1 ± 6.1 years (range, 1.3–25.8), all of them under CNI. They were grouped according to the donor age at least ($n = 49$) or less ($n = 216$) than 60 years. Graft and patient survivals were compared using the Kaplan-Meier method and Cox multiple regression.

At 1, 3, and 10 years, postoperatively patient survivals in the group of older LD recipients were 97%, 96%, and 93%, versus 98%, 97% and 92% among the younger LD recipients.

At 1, 3 and 10 years, postoperatively graft survivals uncensored for death were 94%, 92%, and 81% among the older LD recipients versus 93%, 89%, 75% among the control group, respectively, despite a slightly increased creatininemia observed at 10 years among the older LD recipients.

Deaths censored graft survivals were 96%, 96%, and 87% among the older versus 94%, 91% and 78% among the younger LD recipients, respectively.

Therefore, significantly better noncensored death-censored graft survivals, were observed among the recipients of older LD compared with recipients of the younger donor group.

THE EXPANSION of clinical criteria for living donation (LD) is still matter of debate. The use of LD grafts from elderly donors is generally discouraged due to expected poor results.^{1,2} However, the growing number of patients on the waiting list has led transplant surgeons to renew interest in nonoptimal LD to increase the donor pool; among which are elderly LD candidates. In this retrospective study, we examined our experience with 49 kidney transplants in adults from LDs >60 years who were compared for early and long-term outcomes with 216 grafts from younger LDs.

PATIENTS AND METHODS

From May 1969 to December 2008, we performed 2809 renal transplantations. For 351 cases, the graft source (12.5%) was LD. Seeking to standardize the population, we included only LD recipients ≥ 18 years of age and treated with calcineurin inhibitors (CNI), namely, 265 recipients.

All patients had ABO blood group compatibility and negative cross-matches. Preoperative kidney function of LD candidates was evaluated using endogenous creatinine clearance (>60 mL/min/1.73 m²) in association with glomerular filtration rate

(GFR; not <90 /min), which was individually measured by the renogram from the rate of uptake of technetium-99m diethylene triamine penta-acetic acid (^{99m}Tc-DTPA).

Patients with minimal abnormalities upon urine analyses, including isolated asymptomatic microhematuria, or blood pressure a slightly above the normotensive range (130/80 mm Hg) were accepted as candidates for donation. In contrast, proteinuria >150 mg/24 hours, albuminuria >30 /mg/24 h, body mass index >29 kg/m² and elevated fasting blood glucose were considered to be exclusion criteria.

The ages of our living donors significantly increased in the recent periods: namely, in the cyclosporine (CsA)-era (between 1983 and

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1990), the mean donor age was 46.0 ± 9.8 years (range, 22–71), whereas in the last 8 years, it was 51.8 ± 9.5 years (range, 25–77).

A subcostal retroperitoneal minilaparotomy was adopted for the latest 156 LD nephrectomies. In presence of two equivalent kidneys, the right kidney was preferentially removed, as it tends to be smaller and more accessible than the left one, since its position is lower in the abdomen.

The most common arterial anastomosis of the renal artery was end-to-end to the divided internal iliac artery; the external or common iliac artery was employed when the hypogastric artery was unsuitable, in cases of retransplants or for vascular anomalies. Since 1999, we prospectively decided to adopt a more aggressive policy of microsurgical bench reconstruction for kidneys with multiple vessels or for kidneys with one artery that was affected by intrinsic disease.³ The Lich-Gregoire method was the preferred technique of ureteroneocystostomy, due to the need for minimal bladder dissection.

From 1983 to 2001, the therapy consisted of corticosteroids, azathioprine, and CsA: since 2000, we used induction therapy with basiliximab. After 2001, the standard immunosuppressive protocol included CsA (or tacrolimus), mycophenolate mofetil, and corticosteroids.

The living donors were grouped, according to donor age: group I ($n = 49$) aged ≥ 60 years (OLD) included 38 females (77.5%) and 11 males of overall mean age of 63.3 ± 3.9 years (range, 60–77) with 6 (12.2%) unrelated donors, namely, 4 wives, 1 aunt and 1 adoptive father. Ten LDs displayed comorbidities: mild hypertension, proteinuria >150 mg/L, reasonable cardiac abnormalities, BMI > 25 , and GFR <90 mL/min/1.73 m². Two of this group displayed >1 comorbidity. The corresponding recipients were 17 females (34.7%) and 32 males (65.3%) of overall mean age of 39.4 ± 11.3 years (range, 20–73). Eight patients (12.2%) were transplanted as “preemptive” cases and the other 41 (83.8%) subjects had undergone dialysis for a mean of 31.3 ± 37.8 months (range, 1–173). The mean HLA-A, -B, and -DR match was 2.1 ± 0.5 . In 31 cases (63.3%), the right kidney was chosen for transplantation. The 8 (16.3%) major arterial anomalies included (5 kidneys with multiple arteries and 3 with 1 artery affected by severe atherosclerosis or intrinsic diseases. There were 3 major venous anomalies (6.1%) that required technical variations among the OLD group.³ A kidney with a unilateral total duplex collecting system was successfully transplanted in a recipient of this group.

Group II comprised 216 LDs <60 years (YLD) including 153 females (70.8%) and 63 males of overall mean age of 48.3 ± 8.0 years (range, 22–59). There were 37 unrelated donors (17.1%): 26 wives, 10 husbands and 1 cousin. The 80 female (37.0%) and 136 male (63.0%) recipients had a mean age of 34.4 ± 12.1 years (range, 19–66) among whom 27 (12.5%) of them were transplanted as “preemptive” cases and 189 had undergone dialysis for a mean of 24.7 ± 25.6 months (range, 1–156). The mean HLA-A, -B, and -DR match was 2.3 ± 0.6 . There were 25 LDs with comorbidities. The right kidney was chosen for transplant in 71.3% of cases. Major arterial anomalies were present in 50 (23.1%) kidneys: 30 with multiple arteries and 20 with one artery but affected by severe atherosclerosis or intrinsic disease. The 19 (8.8%) major venous anomalies required variations of the standard techniques and/or bench reconstructions.

Two normotensive donors who were asymptomatic displayed aneurysms of the renal artery. In 1 case it was beyond the bifurcation, involving the segmental lower artery with erosion of the vein wall and

near danger of rupture. Both aneurysms were repaired successfully and the grafts are functioning well at 6 and 1 years.

Graft failure was defined as the loss of the transplanted kidney for any reason: that is, death with a functioning graft, retransplantation, or return to dialysis at the end of the study (December 2008). The Kaplan-Meier method was employed to evaluate the actuarial patient and graft survivals, comparing group differences with the log-rank test. A multivariate Cox regression model was used to simultaneously assess the influence of recipient gender, donor gender, recipient age (over or under 45 years), donor age (over or under 60 years), period of LD transplantation (before vs after 2000), as well as years on dialysis. Half-lives were also compared to assess long-term graft survival.

Analyses were performed using the Stata version 11.0 software (StataCorp. 2009. Stata: Release 11. Statistical Software. College Station, Tex).

RESULTS

The mean follow-up of adult LD recipients receiving CNIs was 13.1 ± 6.1 years (range, 1.3–25.8). It was slightly less for the OLD compared with the YLD group: 11.6 ± 5.7 years [range, 1.3–18.1] vs 13.4 ± 6.2 years [range, 1.1–25.7].

No death occurred perioperatively among LDs or LD recipients and there was no need for blood transfusions.

Concerning the recovery of function, the OLD group showed immediate graft function in 47 recipients (96.0%); there was 1 delayed graft function (2.0%) and 1 primary nonfunction (2.0%), the latter probably due to an association of multiple risk factors in a donor of older age: mild hypertension, dyslipidemia, and obesity.

Among the group of YLD recipients, 210 showed immediate graft function (97.3%) 2, delayed graft function (0.9%), and 4, primary nonfunction (1.8%), due to acute rejection and/or vascular thrombosis. No early medical complication was registered among perioperative courses of older donors, except for 2 intraoperative cardiac arrhythmias; in contrast, 3 pulmonary infections, 2 cases of phlebitis, and 1 episode of acute hypothyroidism from contrast medium were observed among the younger donors. No early wound complication was observed in either groups. No late wound complication was observed among the older living donors, whereas 5 wound bulges were observed in the long-term period among the YLD-group: all of them occurred in subjects who practised intensive sports in the pre- and posttransplant periods.

Fewer acute rejection episodes were observed among the OLD group and the serum creatinine values were similar for the 2 groups, except at about 10 posttransplant years, when, despite satisfactory graft survival, the mean creatinemia values were slightly higher among the OLD group.

Within the first postoperative year, only 1 surgical complication (2%), an ureteral fistula, was observed among the OLD versus 8 (3.7%) among the YLD recipients. The latter cases included 3 urologic complications, 2 lymphoceles, 2 bouts of hemorrhage, and 1 intestinal obstruction; all of them were successfully repaired. Within the first postoperative year, 3 (6.1%) group I grafts were lost: 1 due to death from sepsis at 11 months after transplantation associated with hepatic failure in a patient affected by megakaryocytic

glomerulonephritis, a rare disease associated with a poor prognosis, another due to irreversible rejection and 1 due to primary nonfunction, as mentioned. Among group II, 13 (6.0%) grafts were lost within the first postoperative year: 2 deaths were caused by sepsis and Kaposi disease. In addition, there were irreversible rejections and 4 cases of primary nonfunction.⁷

At postoperative years 1, 3, and 10 patient survivals according to the Kaplan-Meier method among Group I were 97%, 96%, and 93%, versus 98%, 97% and 92% in group II. "Crude" graft survival uncensored for death at 1, 3, and 10 years postoperative in group I among OLD recipients were 94%, 92%, and 81%, versus 93%, 89%, and 75% in group II, despite the slight elevation of creatinemia in the later periods among the OLD LD recipients. Graft survivals censored for death were 96%, 96%, and 87% in group I, versus 94%, 91%, and 78% ($P < .05$) in group II at 1, 3, and 10 postoperative years; death with a functioning graft the major cause of failure in both groups.

The half-lives of OLD grafts confirmed the better behavior of this population, resulting significantly longer if compared with those of YLD grafts: 32.6 versus 22.9 years ($P < .001$). The multivariate Cox regression model (Table 1) confirmed a negative impact for recipients over 45 years of age, whereas LD aged >60 years were associated with a decreased risk of graft failure. Transplants performed in recent periods showed a better prognosis. The model also showed the strong negative impact of length of pre-transplant dialysis treatments, namely, a 10% increased graft loss for every year of dialysis.

DISCUSSION

The role of advanced LD age in kidney transplantation remains controversial. Exclusion of older patients from donation has been based on risks of impaired early/long-term recipient outcomes, reduced capacity for compensatory hypertrophy of the remaining kidney, increased risk of the surgical procedure itself, and presumably an higher rate of major complications in the donor.^{1,2} OLD

recipients show a reduced chance of transplantation due to the limited availability of cadaver donor organs. Fewer than 5% of patients >65 years who were on dialysis therapy received transplants, despite the report of Schnuelle et al that these patients showed better patient survival than those remaining on dialysis.^{4,5}

Distinct from the experience of Toma et al,⁶ who observed poorer survival of LD grafts from donors >60 years at 5 years after transplantation, our experience revealed LD grafts from older donors to show superior results compared with kidneys from younger donors. A kidney coming from an even old donor may give an older recipient a chance for long patient and graft survivals with a better quality of life. More intense medical evaluation of older LD candidates and strict psychological support may result in the selection of only healthy, motivated subjects.⁷

In conclusion, our experience confirmed that living donors >60 years old provided excellent kidney function at 10 years after transplantation, when compared with that of patients receiving younger grafts. There were no additional risks for the donors or the recipients, despite the presence of comorbid problems, which theoretically make both of them poor candidates for surgical procedures.

Ex vivo microvascular reconstruction to repair intrinsic renal disease due to atherosclerosis appears to be useful to simplify the anastomosis of multiple arteries, too thereby widening the indications and acceptance criteria for living donors.

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Table 1. Multivariate Cox Regression Analysis of Risk Factors for Failure in LD Recipients

Variable	Characteristic	Hazard Ratio	95% Confidence Interval	P-Value
Recipient gender	(M vs F)	1.27	0.82–1.95	.28
Donor gender	(M vs F)	0.80	0.49–1.28	.35
Recipient age	(45+ vs <45 y)	1.69	1.05–2.72	.03
Donor age	(60+ vs <60 y)	0.54	0.28–1.03	.06
Era of LD-TXs	(2000+ vs <2000)	0.40	0.18–0.89	.025
Years on dialysis		1.10	1.02–1.19	.01