Kidney Transplantation in Elderly Recipients: A Single-Center Experience

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ABSTRACT

In this retrospective single-center study we evaluated the outcome after kidney transplant in recipients older than 65 years in terms of patient and graft survival and causes of death.

Patients and Methods. From 1993 to 2016, 109 consecutive first single kidney transplants in recipients older than 65 years were included. Furthermore, 2 age groups have also been identified (group A, 65–70 years old vs group B, 71–76 years old).

Donor and recipient characteristics were analyzed. Other parameters were cold and warm ischemia times, delayed graft function, biopsy-proven acute rejection, and causes of death. Induction immunosuppressive therapy was performed with basiliximab or thymoglobulin. Baseline triple immunosuppression included calcineurin inhibitor, antimetabolite, and steroids.

The results of preimplantation biopsies, which were performed in all expanded criteria donors were analyzed and graded according to Karpinski 2009 classification.

Results. Overall mortality was 39.4%: 23.2% women and 76.8% men. Causes of death were infections in 42%, tumors in 23%, cardiovascular disease in 14%, cerebrovascular disease in 7%, and unknown in 14%. The most common cause of death in men was infections (52%), and the most common cause in women was tumors (55%).

At 1, 3, 5, and 10 years, overall patient survival was 89%, 84%, 72%, and 45%, and overall graft survival was 100%, 97%, 89%, and 84%, respectively. Patient and graft survival were statistically different between group A vs group B ($P = .006$ and $P = .02$, respectively). At univariate analysis significant risk factors for increased mortality were age, delayed graft function, and cold ischemia time. At multivariate analysis, delayed graft function maintained statistical significance.

Conclusions. Kidney transplantation in patients older than 65 years is safe, feasible, and has good graft survival. Mortality is statistically significant in patients older than 71 years, despite a persistent low graft loss.

RECENT reports state the numbers of elderly patients who start dialysis and who are evaluated for kidney transplant (KT) is growing [1] because KT in elderly patients shows a strong superiority over dialysis as therapy for end-stage renal disease [2].

Despite most professional guidelines recommending that advanced age should not be considered a contraindication to transplant per se [3], the main challenge remains to carefully select individuals in whom the benefits of solid organ transplant outweigh potential risks such as deterioration of comorbidities or adverse events associated with immunosuppression in elderly patients [4].

In this retrospective, single-center, cohort study we analyzed a variety of different parameters, such as donor and recipient characteristics, immunosuppression therapy,

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Table 1. Demographic and Clinical Data of Donors and Recipients

Recipients	
Sex, male:female	76:33
Age, mean (SD), y	68 (3)
BMI (SD)	25 (4)
Diabetes mellitus, No. (%)	24 (21)
Hypertension, No. (%)	67 (61)
Arterial vasculopathy, No. (%)	36 (33)
Type of dialysis, No. (%)	
Hemodialysis	99 (91)
Peritoneal dialysis	10 (8)
Years of dialysis (%)	
1–5	16 (15)
6–10	56 (51)
>11	37 (34)
Years of dialysis between activation on waiting list and transplant, mean (SD)	3 (2)
PRA (range)	0 (0–40)
HLA compatibility, No. (%)	
Incompatible	10 (9)
1 locus	39 (36)
2 loci	39 (36)
3 loci	11 (10)
4 loci	9 (8)
5 loci	1 (1)
6 loci	0
Delayed graft function, No. (%)	43 (39)
Acute rejection, No. (%)	14 (13)
Cause of death, No. (%)	
Infection	18 (16)
Cerebrovascular disease	3 (3)
Cardiovascular disease	5 (5)
Tumor	10 (9)
Other	7 (6)
Donors	
Sex, male:female	48:61
Age, mean (SD), y	65 (10)
BMI, mean (SD)	26 (4)
Diabetes mellitus, No. (%)	12 (11)
Hypertension, No. (%)	33 (31)
Arterial vasculopathy, No. (%)	19 (17)
Creatinine serum level, mean (SD), mg/dL	0.92 (0.21)
Cause of death, No. (%)	
Cerebrovascular disease	91 (84)
Trauma	18 (16)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); PRA, panel-reactive antibody.

cold and warm ischemia times, renal score, delayed graft function (DGF), and biopsy-proven acute rejection (BPAR), to evaluate the outcome after transplant in recipients older than 65 years in terms of patient and graft survival and overall causes of death over a 23-year period.

MATERIALS AND METHODS

From 1993 to 2016, 109 consecutive first single kidney transplants (SKTs) in recipients older than 65 years (11.91% of overall KTs performed in the same period) were included. Patients who received dual KT (n = 8) were excluded. All deceased donations were donations after brain death from heart-beating donors. Furthermore, 2 age groups have also been identified (group A, 65–70 years old vs group B, 71–76 years old).

Age, sex, body mass index (BMI), calculated as weight in kilograms divided by height in meters squared, hypertension, diabetes, creatinine, and renal score were considered in donors.

Age, sex, BMI, comorbidities such as hypertension, diabetes, and peripheral vasculopathy, years and type of dialysis, case mix, and immunosuppressive therapy were evaluated in recipients (Table 1). Other study parameters were cold and warm ischemia times, DGF, BPAR, and causes of death.

Induction immunosuppressive therapy was performed with basiliximab or thymoglobulin. Baseline triple immunosuppression included calcineurin inhibitor (either cyclosporine or tacrolimus), antimetabolite (mycophenolate sodium or mycophenolate mofetil), and steroids. In all patients with diagnosis of tumor, calcineurin inhibitors were substituted with everolimus (n = 10).

The results of preimplantation biopsies, which were performed in all expanded criteria donors, were analyzed and graded according to Karpinski 2009 classification; the degrees of tubular atrophy, interstitial fibrosis, glomerulosclerosis, and arterio-arteriolar hyalinosis were classified separately, and the sum of these 4 scores was calculated.

STATISTICAL ANALYSIS

Categorical variables were summarized using frequency tables and analyzed using the χ^2 test. All data are expressed as mean (SD). Patients and allograft survival curves were computed according to the Kaplan-Meier method, and comparison was carried out by long-rank test. A P value $< .05$ was considered significant. Univariate and multivariate Cox regression were used to estimate prognostic factors for increased mortality after the assumption of the proportional hazard was verified.

RESULTS

Donors were 48 men (44%) and 61 women (56%) with a mean age of 65 (SD, 10) years and a mean BMI of 26 (SD, 4). Of 109 recipients, 76 were men and 33 were women, with a mean age of 68 (SD, 3) years and a mean BMI of 25 (SD, 4). Comorbidities such as diabetes, hypertension, and peripheral vasculopathy were present in 17%, 49.5%, and 26.6% of the recipients, respectively.

Hemodialysis was the treatment of choice in 91% of patients, whereas peritoneal dialysis was performed in only 9% of patients. Dialysis was performed in 15%, 51%, and 34% of recipients for a period of 1 to 5, 6 to 10, and >11 years, respectively, prior to transplant. Mean time of dialysis between activation on the waiting list and transplant was 3 (SD, 2) years. Preoperative case mix score defined all the recipients at the elevated risk level.

Regarding transplant parameters, cold ischemia time and warm ischemia time were 1097 (SD, 809) minutes and 45 (SD, 16) minutes, respectively.

DGF and BPAR were evident in 24.7% and 11% of recipients, respectively. Follow-up was 68 (SD, 49) months.

Overall, 39.4% of patients died with an evident men vs women predominance of 76.8% vs 23.2%, respectively;

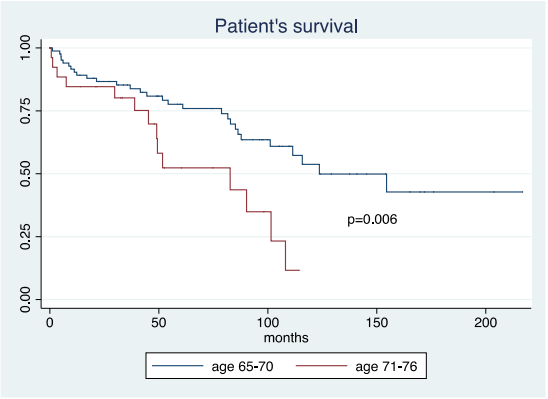

Fig 1. Patient survival.

mortality was equally distributed in the first year, between 2 to 5 years, and between 6 to 10 years (13, 15, and 15 cases, respectively). Causes of death were infections (42%), tumors (23%), cardiovascular disease (14%), cerebrovascular disease (7%), and unknown (14%). The most common cause of death in men was infection (52%), and the most common cause of death in women was tumor (55%). At 1, 3, 5, and 10 years, overall patient survival was 89%, 84%, 72%, and 45%, and overall graft survival was 100%, 97%, 89%, and 84%, respectively.

At univariate analysis, significant risk factors for increased mortality were age (hazard ratio [HR], 1.11; 95% CI, 1.02–1.21; $P = .02$), DGF (HR, 4.08; 95% CI, 1.25–13.27; $P = .02$), and cold ischemia time (HR, 1.00; 95% CI, 1.00–1.01; $P = .005$). At multivariate analysis, DGF (HR, 4.95; 95% CI, 1.28–19.11; $P = .02$) maintained statistical significance.

Patient survival was 90%, 85%, 78%, and 54% in group A and 85%, 80%, 52%, and 12% in group B, with a statistically significant difference ($P = .006$) (Fig 1). Graft survival was also statistically significant between the 2 groups (100%, 100%, 94%, and 87% in group A and 100%, 88%, 74%, and

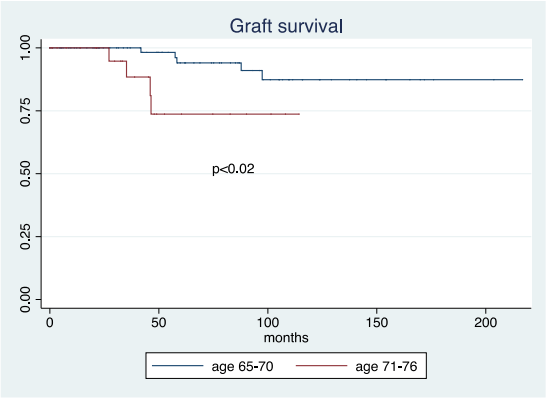

Fig 2. Graft survival.

74% in group B; $P = .02$), without differences in donor characteristics between the 2 groups (Fig 2).

DISCUSSION

In 1999, the analysis of over 46,000 patients on the waiting list for KT provided the convincing evidence of KT superiority over dialysis as therapy for end-stage renal disease [5]. Subsequently, significant improvements were also observed for elderly, diabetic, obese, and cardiopathic patients as well as most of the subjects displaying other major comorbidities [6]. The number of elderly patients requiring replacement therapy has increased worldwide, and this trend is likely to continue [7]. Data from United States Renal Data System registry show that the proportion of KTs in persons older than 65 years increased from 4.2% to 17.2% from 1992 to 2012. Data derived from Eurotransplant confirm the pattern as the proportion of deceased donor recipients in persons older than 65 years increased from 3.6% in 1991 to 19.7% in 2007 [8]. Hellemans et al [9] addressed the important question of whether the assumed benefit of KT over dialysis persists in elderly patients. This is of relevance as survival on dialysis is improving and transplant outcomes in elderly recipients are inferior compared with younger recipients because of a growing number of frail elderly patients receiving kidneys from suboptimal donors.

When needle biopsy was performed, organ allocation was accomplished on the basis of Karpinsky score. Between 2003 and 2006, we applied the policy proposed by Remuzzi et al [10] (score 0–3 to SKT, 4–6 to dual KT, and ≥ 7 discarded); subsequently, score 4 was considered suitable for SKT based on favorable results [11].

In literature there is a substantial amount of evidence that transplant is very effective in patients older than 60 years and provides a quality of life superior to those on dialysis [12]. Elderly patients who remain on dialysis have a death rate 2 times higher than transplant recipients. This lower death rate translates into excellent patient survival after transplant at 93%, 70%, and 46% at 1, 5, and 7 years, respectively. In contrast, survival on dialysis is much lower at 81%, 30%, and 15% at the same intervals [13].

Oniscu et al [14] evidenced 1-year patient survival in the older than 65 years group is comparable with that seen in patients aged 50 to 59 years (77% vs 88%, respectively). Beyond 3 years, the 2 groups have different patient survival (66% vs 81%, respectively). A similar trend is noticed for the graft survival—comparable in the first year, but with a long-term advantage only for younger recipients. Our study reports a 72% and 89% 5-year overall patient and graft survival, respectively. Patient survival decreases significantly at 5 years for the group of patients older than 71 years (52%) without significant concomitant graft loss. The most frequent causes of death in elderly transplant patients are cardiovascular diseases, infections, and malignant neoplasms. It has been observed that older patients who have received a renal transplant have a higher mortality rate

associated with infections than those who are on dialysis and those who are younger [15]. In our study this data was confirmed but only for men, where sepsis is the primary cause of death, with a prevalence in the first year. Tumor remains the main cause of death in women.

CONCLUSIONS

The population of elderly people with chronic renal insufficiency is increasing around the world, and KT is a therapeutic option because elderly patients on the waiting list experience significant survival benefit with KT. Chronological age is not a barrier to transplant, and there is currently no age limit for access to transplant. In our study, KT in elderly selected patients is safe in terms of patient and graft survival. The cutoff age is older than 71 years, when mortality becomes statistically significant and graft loss increases.

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