10.1515/chilat-2017-0002

ORIGINAL ARTICLE

Results of Deceased Donor Kidney Transplantation in Young Recipients after Age-matched and Mismatched (Old-to-young) Transplantation

Janis Jushinskis*,, Vadims Suhorukovs*,**, Aleksandrs Malcevs*,**, Ieva Ziedina*,**, Rafails Rozentals*,****
* Laboratory of transplantology, Riga Stradins University, Riga, Latvia;
** Latvian Transplantation Center, P.Stradins clinical university hospital, Riga, Latvia

Summary
Introduction. During the previous years the number of organ transplantations from elderly donors increased, and lack of young donors leads to necessity to allocate organs from elderly into young recipients.
Aim of the Study. Was to analyse results of "old-to-young" allocation.
Material and methods. This retrospective study analysed results of all consecutive deceased donor kidney transplantations (DDKT) performed in one transplant centre during the period from 01.01.2004 till 31.12.2007. Patients were selected based on availability of 5-year follow-up and age < 50 years (158 DDKT). Patients were divided into 2 groups according to donor age: age-mismatched group (donor age was > 55 years and at the same time > 15 years older than recipient; n=8, male/female=2/6, age 39,4 + 4,8 years, donor age 59,4 + 2,4 years), and age-matched group (n=150, male/female=88/62, age 36,0 + 11,0 years, donor age 37,3 + 12,0 years). Groups were compared for clinical and demographical features and posttransplant outcomes (delayed graft function, s-creatinin levels at discharge and after 5 years, acute rejection rate, graft and patient 5-year survival).
Results. Comparison of demographical and clinical features revealed only relatively higher BMI in elderly donors (p=0.081) and higher frequency of age-mismatched allocation into female recipients (p=0.066). Early and late post-transplant outcomes showed no significant difference between groups, with similar 5-year graft and patient survival (p=NS for all compared factors).
Conclusion. Results showed good kidney allograft function even in cases of age-mismatched allocation, which is significant opportunity in current situation with increasing age of deceased donors.
Key words: kidney transplantation, elderly donors, young recipients, posttransplant outcomes

INTRODUCTION

Kidney transplantation (KT) remains the best way to help patients with end-stage chronic kidney disease, offering better quality of life, clinical outcomes and survival, as also economic efficiency. At the same time, it is associated with universal organ shortage causing the necessity to expand donation criteria both from living and deceased donors (DD) (1). Development in transplantation medicine and immunosuppression ensures good patient and graft survival even from expanded criteria donors, and nowadays age is no longer a limiting factor for donation, however careful approach to elderly donors is recommended (2). In most of cases of such donation cases, the final say about the possibility to use these organs belongs to the surgeons who perform organ procurement and can visually assess the approximal level of sclerosis and the quality of organ perfusion by conservation solutions. In doubtful circumstances a more precise evaluation can be made through the histological assessment of biospies taken from procured organs (3).

Kidney transplantation from older DD is usually limited to recipients within the similar age group or in the predefined range $\pm$ 15-20 years from donor age (1). This gives a great opportunity for elderly recipients to receive kidney graft, whereas younger recipients remain wait-listed for longer period, which is associated with poorer outcomes (4).

In our transplantation centre kidney transplantation from expanded criteria donors started more than a decade ago, and there is clear tendency to increase the use of such donors. In several cases, depending on the decision of the procurement team, organs from those donors were also allocated into recipients younger for more than 15 years than those donors.

THE AIM OF THE STUDY

Was to analyse results of such "age-mismatched" kidney transplantations.

MATERIAL AND METHODS

This retrospective study included all consecutive kidney transplantations from deceased donors into recipients younger than 50 years performed in a single transplantation centre during the period since January 1st, 2004 till December 31st, 2007. Exclusion criteria were: unavailability of 5-year follow-up, panel reactive antibody (PRA) titre >10%, third and following KT with intraabdominal surgical approach. After selection procedure study included 158 DD kidney graft recipients (male/female = 90/68, mean age 36.2 $\pm$ 10.8 years) from 94 DD (male/female = 65/29, mean age 38.8$\pm$13.2 years), recipient and donor demographical and clinical features are shown in Table 1. Donor organ procurement utilized in-situ preservation by HTK solution. Donor kidney "zero" biopsies were performed by "Tru-Cut"

method before or immediately after the initiation of organ perfusion. Organ allocation was performed based on ABO identity and cross-match. Allocation of "age-mismatched" donor kidneys in each case was performed based on information about the quality of procured kidneys provided by the procurement team (no signs of severe sclerosis, good quality of perfusion, normal donor kidney anatomy, and normal values of serum creatinine (s-crea) in donors on admission to the hospital) and recipient's informed consent. In 4 cases donor age was between 55 and 59 years with a combination of factors according to expanded criteria donation, and in 4 cases donors were older than 60 years.

All recipients received induction immunosuppression by monoclonal (basilixumab or daclizumab) or polyclonal (ATG) antibodies with a 5-day steroid pulse, and maintenance by per oral steroids, mycophenolate mofetil and cyclosporine A as guided by the blood level.

All cases were divided into two groups according to discrepancy between donor and recipient age: "age-matched" group, where donor's age was not higher than 55 years and not higher than 15 years above recipient's age and "age-mismatched" group, where recipients received kidney grafts from donors older than 55 years and older than 15 years compared to recipient's age. "Age –matched" group included 150 recipients (male/female=88/62, recipient's mean age 36,0 $\pm$ 11,0 years, donor's mean age 37,3 $\pm$ 12,0 years). "Age-mismatched" group included 8 recipients (male/female=2/6, recipient mean age 39,4 $\pm$ 4,8 years, donor mean age 59,4 $\pm$ 2,4 years, mean age difference 21.0 $\pm$ 3.0 (17 – 26) years).

Results of donor kidney "zero" biopsies were available in 63 of the "age-matched" group and in all of the "age-mismatched" group. The groups were compared for demographical and clinical features and posttransplant outcomes (delayed graft function (DGF, defined as a need for at least one dialysis during the first posttransplant week), biopsy proved acute rejection (AR) rate, s-crea level at discharge from hospital and at the end of 5-year follow-up (for functioning grafts), and 5-year graft and patient survival).

Statistical analysis of groups was performed by one-way ANOVA, χ^2 and Kaplan-Meier survival tests (SPSS 17.0, SPSS Inc.).

RESULTS

"Age-mismatched" kidney allocation was performed in 8 cases during the 4-year period and consisted only 5% of all KT in patients younger than 50 years.

Comparison of demographical and clinical factors of study groups revealed only relatively higher body mass index of donors (p = .081) and higher frequency of female recipients (p = .066) in "age-mismatched" group. Mean cold ischemia time was shorter in 'age-mismatched" group (14.8 $\pm$ 3.9 vs. 16.6 $\pm$ 4.8 in "age-matched" recipients), however statistical significance was not achieved (p = .296).

Other factors, including donor "zero-biopsy" results, intraoperative vascular reconstructions of kidney grafts and number of allocations of female donor kidneys into male recipients were similar in both groups (p = NS).

Results of post-transplant outcomes showed similar rates of DGF, the similar graft function at the time of discharge and after 5 years for functioning grafts and relatively higher AR rate of AR in "age-mismatched" group (62.5 vs 41.3% in "age-matched" group). Graft losses were observed in 1 case (12.5%) in "age-mismatched" group and in 47 cases (31.1%) in "age-matched" group, and patient deaths were observed in 2 and in 23 cases (25 and 15.3%), respectively, however also these differences did not show statistical significance either (Table 2).

The 5-year death-censored graft survival rate as well as patient survival was similar in both groups (Log Rank (Mantel-Cox) = 0.729 (p = .393), and 0.634 (p = .426), respectively) (Figure 1).

DISCUSSION

Organ shortage leads to expansion of donation criteria, and nowadays KT from expanded criteria and elderly DD is a widely-used practice approved also by guidelines (2). Reported outcomes of such transplantations are generally poorer than those from standard criteria donors, however, there is little surprise in that because the risk of poorer initial condition of the graft increases with age and co-morbidities of donor (5–7). At the same time this condition is much more dependent of various lifestyle factors of kidney donors, and sometimes this initial conditions of kidneys from older donors is much better than such from younger donors with a number of negative factors (8). Of course, pretransplant donor kidney biopsy results can give very valueable information for assessment of kidneys from older donors (3, 9).

It is also very important is to define and avoid recipient and transplantation factors that may negatively impact outcomes. Avoidance of factors, associated with DGF may significantly improve results of kidney transplantation from senior donors (10). Reduction of CIT and allocation to recipients without circulating donor-specific antibodies (DSA) may also improve results (11).

Allocation of older donor kidneys into younger recipients is not a standard procedure, but, regarding the fact of a negative impact of time spent on dialysis on a patient and graft survival, the possibility to transplant young recipients becomes very important. In our study we discovered only 8 cases of such allocation from older donors into younger recipients during the 4-year period, and in all cases this decision was based on the information obtained from the procurement team about the good quality of retrieved donor kidneys. 5-year outcomes showed acceptable results with good function at 5 years and only one lost graft during this period (in two cases of patient deaths there were normally functioning grafts). However, analysis of results shgould take into consideration the fact, that "age-mismatched" group had relatively low number of patients.

CONCLUSIONS

In conclusion, the results showed good kidney allograft function even in cases of "age-mismatched" allocation

(old donor into young recipient), which is a significant opportunity in the current situation with an increasing age of deceased donors. Of course, there is a need to continue studies in this field with a higher number of observations and longer follow-up period to ensure a safe use of this approach to allocation.

Conflict of interest: None

REFERENCES

1. Maggiore U, Oberbauer R, Pascual J, Viklicky O, Dudley C, Budde K, Sorensen SS, Hazzan M, Klinger M, Abramowicz D. Strategies to increase the donor pool and access to kidney transplantattion: an international perspective // Nephrol Dial Transplant, 2015; 30(2):217-22
2. European Directorate for the Quality of Medicine and HealthCare (EDQM), Council of Europe. Assessment of donors // In: Guide to the quality and safety of organs for transplantation. 5th edition: Council of Europe; 2013; 49-82
3. Remuzzi G, Cravedi P, Perna A, Dimitrov BD, Turturro M, Locatelli G, Rigotti P, Baldan N, Beatini M, Valente U, Scalamogna M, Ruggenenti P. Long-term outcome of renal transplantation from older donors // N Engl J Med 2006; 354: 343-352
4. Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis // Transplantation 2002; 74(10): 1377-81
5. Veroux M1, Grosso G, Corona D, Mistretta A, Giaquinta A, Giuffrida G, Sinagra N, Veroux P. Age is an important predictor of kidney transplantation outcome // Nephrol Dial Transplant 2012; 27(4): 1663-71
6. Oppenheimer F, Aljama P, Asensio Peinado C, Bustamante Bustamante J, Crespo Albiach JF, Guirado Perich L. The impact of donor age on the results of renal transplantation // Nephrol Dial Transplant. 2004; 19 (3): iii11-5
7. Dempster NJ, Ceresa CDL, Aitken E, Kingsmore D. Outcomes following renal transplantation in older people: a retrospective cohort study // BMS Geriatrics, 2013; 13: 79
8. De Rosa P, Muscogiuri G, Sarno G. Expanded Criteria Donors // in Kidney Transplantation: The Role of Older Donors in a Setting of Older Recipients. ISRN Transplantation; 2013, Article ID 301025, 8 pages. http://dx.doi.org/10.5402/2013/301025
9. Pierobon ES, Sandrini S, De Fazio N, Rossini G, Fontana I, Boschiero L, Gropuzzo M, Gotti E, Donati D, Minetti E, Gandolfo MT, Brunello A, Libetta C, Secchi A, Chiaramonte S, Rigotti P. Optimizing utilization of kidneys from deceased donors over 60 years: five-year outcomes after implementation of a combined clinical and histological allocation algorithm // Transplant Int 2013; 26(8): 833-41
10. Cohen B, Smits JM, Haase B, Persijn G, Vanrenterghem Y, Frei U. Expanding the donor pool to increase renal transplantation // Nephrol Dial Transplant, 2005; 20: 34-41
11. Aubert O, Kamar N, Vernerey D, Viglietti D, Martinez F, Duong-Van-Huyen JP, Eladari D, Empana JP, Rabant M, Verine J, Rostaing L, Congy N, Guilbeau-Frugier C, Mourad G, Garrigue V, Morelon E, Giral M, Kessler M, Ladrière M, Delahousse M, Glotz D, Legendre C, Jouven X, Lefaucheur C, Loupy A. Long term outcomes of transplantation using kidneys from expanded criteria donors: prospective, population based cohort study // BMJ 2015;351:h3557

Address:
Janis Jushinskis
Riga Stradini University,
Laboratory of Transplantology.
Pauls Stradins Clinical University Hospital,
13 pilsonu street, Riga, LV-1002, Latvia.
e-mail: Janis.Jusinskis@rsu.lv

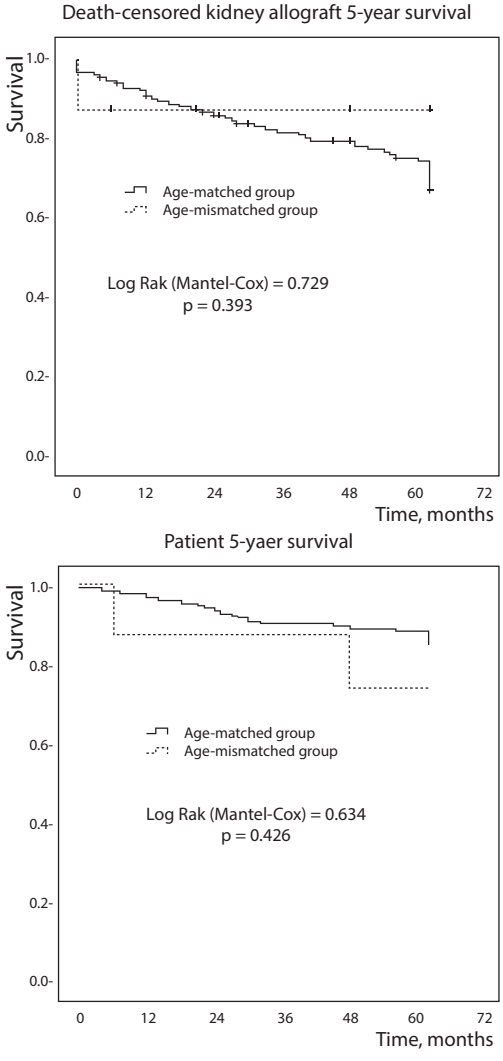

Fig. 1. Graft and patient 5-year survival in age-matched and mismatched groups (Kaplan-Meier estimate)

Table 1. Demographical and clinical features of study population

Factor	Number
Donors (n)	94
Mean age (y)	38.8±13.2
Gender, male/female (n)	65 / 29 (69% / 31%)
Brain death, traumatic/nontraumatic (n)	54 / 40 (57% / 43%)
Body mass index (kg/m^2)	25.2±3.9
Asystole/hypotension (n)	38 (40%)
Recipients (n)	158
Mean age (y)	36,2±10,8
Gender, male/female (n)	90 / 68 (57% / 43%)
Weight (kg)	69.5±18.2
Dialysis type, HD/PD (n)	147 / 11 (93% / 7%)
Diagnoses	
Chronic glomerulonephritis (n)	67 (42%)
Diabetes mellitus (n)	23 (15%)
Polycystic kidney disease (n)	16 (10%)
Chronic interstitial nephritis (n)	14 (9%)
Hypertensive nephropathy (n)	10 (6%)
Reflux nephropathy (n)	9 (6%)
Obstructive nephropathy (n)	8 (5%)
Lupus nephritis (n)	6 (4%)
Other (n)	5 (3%)

Table 2. Comparison of study groups

	Age-mismatched group, n = 8	Age-matched group, n = 150	*p*
Donors			
Age (y)	59.4 ± 2.4	37.3 ± 12.0	< .001
Gender, male /female (n)	6 / 2	105 / 45	.558
BMI (kg/m^2)	27.4 ± 2.7	25.0 ± 3.9	.081
Stay in ICU (d)	2.5 ± 0.9	2.9 ± 2.5	.608
Brain death, nontraumatic (n)	5 (63%)	86 (57%)	.538
Asystole/hypotension (n)	6 (75%)	93 (62%)	.369
«0» biopsy results:			
Interstitial sclerosis (%)	3.6 ± 5.4	2.7 ± 5.4	.616
Glomerular sclerosis (%)	2.8 ± 2.8	0.9 ± 4.4	.245
Laboratory data:			
Creatinine (mkmol/l)	112 ± 68	112 ± 40	.949
Urea (mmol/l)	6.2 ± 4.1	6.6 ± 3.4	.717
Recipients			
Age (y)	39.4 ± 4.8	36.0 ± 11.0	.395
Gender, male /female (n)	2 / 6	88 / 62	.066
Weight (kg)	68.3 ± 14.1	69.6 ± 18.4	.840
Peritoneal dialysis (n)	0	11 (7.3%)	.554
Transplantation			
Cold ischemia time (h)	14.8 ± 3.9	16.6 ± 4.8	.296
Female donor / male recipient (n)	1 (12.5%)	29 (19.3%)	.530
Graft vascular reconstructions (n)	3 (37.5%)	76 (50.7%)	.345
Post-transplant outcomes			
Delayed graft function (n)	1 (12.5%)	24 (16%)	.630
Acute rejections (n)	5 (62.5%)	62 (41.3%)	.207
S-Crea at discharge (mkmol/l)	125 ± 31	130 ± 73	.875
S-Crea at 5 years (mkmol/l)	156 ± 42	153 ± 59	.901
Graft losses, death-censored (n)	1 (12.5%)	47 (31.3%)	.241
Patient deaths (n)	2 (25%)	23 (15.3%)	.370