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Long-Term Outcomes of Kidney Transplantation from Elderly Donors

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Summary
Introduction. During the last years the percentage of elderly organ donors has increased significantly and may impact results of kidney transpalantations (KT).
Aim of the Study. Was to analyse results of kidney transplantation from elderly donors.
Materials and methods. In this study we analysed results of all consecutive KT from deceased donors (DD) performed in a single transplantation center during the period from 01.01.2004 till 31.12.2007, with the following exclusion criteria: unavailability of 5-year follow-up and transplantation from DD aged from 50 to 59 years. In result the study population consisted of 193 KT recipients, and all cases were divided into two groups according to donor age: group A (donor age >60 years, 27 KT from 18 DD, mean age of donors 62,6 + 2,1 years, mean age of recipients 58,0 + 9,0 years), and group B (donor age <49 years, 166 KT from 98 DD, mean age of donors 35,4 + 10,2 years, mean age of recipients 40,5 + 14,7 years). Groups were compared for posttransplant outcomes and 5-year graft and patient survival.
Results. During the study period the number of transplantations from donors aged >60 years amounted to 10.5% of all transplantations. The use of elderly donors was not associated with worse early posttrransplant results; in long-term it was associated with higher patient mortality and lower rate of death-censored graft losses, however analysis of survival revealed difference only in patient 5-year survival (p=0.001).
Conclusion. KT from older donors when allocated to age-matched recipients ensures acceptable outcomes and should be continued in the future with recommendation to keep cold ischemia time as short as possible and to introduce urgent analysis of donor kidney "zero" biospy.
Key words: kidney transplantation, elderly donors, posttransplant results

INTRODUCTION

Organ transplantation has become an integral part of modern medicine, however, donor organ shortage limits its availability. At the same time the experience gained during the era of transplantation and achievments in immunosuppression give the possibility to expand limits for organ donation, including transplantation from elderly donors. Currently many countries use deceased donors kidney transplantation from elderly persons, alocating these organs to age-matched recipients (5).
Transplantation from elderly donors is associated with higher risk of transplanting organs of poorer quality and possible co-morbidities and, accordingly, poorer graft function and survival (6, 7, 10). On the other hand it gives opportunity to transplant more patients, and recent publications on this problem show that patient survival is better among transplanted patients compared with those who remain on dialysis (8). This is especially actual because during the past decade the proportion of wait-listed elderly recipients has grown significantly (4).
In Latvia organ transplantation form elderly donors started more than a decade ago and during the last years there is tendency for increase in their number: considering kidney transplantations from donors older than 60 years the rate of such transplantations increased from 10% up to 25%, and percentage of all donors older than 50 years of age is now more than 50% of all deceased donors (unpublished data from national organ procurement organization).

AIM OF THE STUDY

The aim of this study was to analyse results of kidney transplantation from elderly donors.

MATERIALS AND METHODS

Study initially included all consecutive deceased donor renal transplantations performed in a single center from 01.01.2004 till 31.12.2007. In order to ensure relieble results we excluded cases when patients were not available for five-year follow-up and cases, when patients underwent transplantation from donors from 50 to 59 years of age. After exclusion the study population consisted of 193 kidney transplantations from 116 deceased donors. Patients were divided into two groups according to donor age: group A where donor age was 60 or more years (27 transplantations from 18 donors; mean donor age 62,6 $\pm$ 2,1 years; donor gender 18 male / 9 female; mean recipient age 58,0 $\pm$ 9,0; recipient gender 16 male / 11 female) and group B (control group) where donor age was 49 years or less (166 transpla ntations from 98 donors; mean donor age 35,4 $\pm$ 10,2 years; donor gender 120 male / 46 female; mean recipient age 40,5 $\pm$ 14,7; recipient gender 85 male / 81 female) (table 1).
Patients were followed-up for 5 years. We analysed posttransplant outcomes in association of donor and recipient demographical and clinical factors, diagnosis, laboratory tests, histyological findings at donor "zero"

biopsy and cold ischemia time. All operations were performed by authors using the same organ explantation and transplantation techniques. Donor kidney "zero" biopsies were performed at donor operation by "true-cut" method. Organ conservation was performed by histidine-tryptophan-ketoglutarate solution (HTK). Data was collected from transplantation center surgical, transplant coordination and ambulatory follow-up databases and records.

Statistical analysis was performed by IBM SPSS Statistics 22 program. Parametric features are shown as mean + stAndard deviation. Groups were compared using χ^2 – test for non-parametric and ANOVA test parametric variables. Survival was analysed by Kaplan-Meier test. Results were considered statistically significant for $p < 0.05$.

RESULTS

Totally 27 kidney transplantations were performed from 18 donors ≥ 60 years of age, which amounted to 10,5% of analysed cases. Analysis of donor factors showed higher rate of non-traumatic brain death rate (56% vs. 34% in control group) and BMI (27,8 ± 2,5 vs. 24,9 ± 4,1 kg/m² in control group). Donor kidney "zero" biospy results revealed tendency towards higher percentage of glomerular sclerosis (3,0 ± 10,0 vs. 1,0 ± 4,3 % in control group, p = 0.075). Laboratory tests showed similar levels of serum creatinine and urea in both groups (table 1).

Table 1. Demographical and clinical features of study groups and posttransplant results.

Factors	Group A (elderly donors), N = 27	Group B (young donors), N = 166	p
Donor factors:			
Age, yy	62,6 ± 2,1	35,4 ± 10,2	
Gender, m/f	18 / 9	120 / 46	0.348
BMI, kg/m²	27,8 ± 2,5	24,9 ± 4,1	0.001
Non-traumatic cause of brain death, n	15 (56%)	57 (34%)	0.030
Severe hemodynamic disturbances, n	13 (48%)	97 (59%)	0.214
"0" biopsy results:			
Glomerular sclerosis, %	3,0 ± 10,0	1,0 ± 4,3	0.075
Intersticial sclerosis, %	3,9 ± 7,6	2,6 ± 5,1	0.254
Donor analyses:			
Serum creatinine, mmol/l	0,12 ± 0,06	0,11 ± 0,04	0.100
Serum urea, mmol/l	7,10 ± 3,35	6,39 ± 3,23	0.294
Recipient factors:			
Age, yy	58,0 ± 9,0	40,5 ± 14,7	<0.001
Gender, m/f	16 /11	85 / 81	0.285
Svars, kg	75,2 ± 14,6	70,2 ± 19,3	0.207
Re-transplantation, n	2 (7,4%)	18 (10,9%)	0.446
Peritoneal dialysis, n	1 (3,7%)	12 (7,3%)	0.431
Diagnoses:			
Chr.glomerulonephritis, n	13 (48,2%)	71 (42,8%)	0.375
Chr.interstitial nephritis, n	4 (14,9%)	16 (9,7%)	0.299
Diabetic nephropathy, n	2 (7,4%)	21 (12,7%)	0.342
ADPKD, n	4 (14,9%)	16 (9,7%)	0.299
Hypertensive nephropathy,n	2 (7,4%)	12 (7,3%)	0.612
Obstructive nephropathy, n	0	8 (4,9%)	0.292
Reflux nephropathy, n	0	8 (4,9%)	0.292
Other/not precised, n	2	14	

Analysis showed that in most of cases kidneys from elderly donors were allocated to older recipients (58 ± 9 years vs. 41 ± 15 years in control group, $p < 0.001$). Analysis of such recipient factors as gender, weight, type of dialysis and diagnosis showed no differences between groups (table 1).

Posttransplant results showed that cold ischemia time was similar in both groups and there was relatively higher rate of delayed graft function in group A (33,3 vs. 18,1% in control group), however, analysis failed to attain statistical significance (p = 0.063). Recipients from both groups had similar length of hospital stay after transplantation and serum creatinine level at discharge and at the end of follow-up (counted only for grafts functioning at the end of follow-up period) (table 2).

Table 2. Results of kidney transplantation in study groups.

Factors	Group A (elderly donors), N = 27	Group B (young donors), N = 166	p
Results:			
Cold ischemia time, hh	16,7 ± 3,8	16,5 ± 4,9	0.840
Delayed graft function, n	9 (33,3%)	30 (18,1%)	0.063
Hospital stay, dd	29,0 ± 8,1	26,9 ± 11,8	0.392
Acute rejection episodes, n	15 (55,5%)	73 (43,9%)	0.181
Serum creatinine (discharge), mmol/l	0,13 ± 0,05	0,13 ± 0,07	0.631
Serum creatinine (follow-up), mmol/l	0,13 ± 0,04	0,15 ± 0,06	0.270
Graft loss (death-censored), n	4 (14,8%)	54 (32,5%)	0.046
Patient death, n	10 (37,0%)	22 (13,3%)	0.005

During the follow-up period only 4 recipients of those who underwent kidney transplantation from elderly donors lost their grafts, and in control group this number was higher – 54 graft losses (14,8 vs. 32,5% accordingly, p = 0.046), however comparison of graft survival curves failed to show statistically significangt difference (Log Rank (Mantel-Cox) = 1.745 (p = 0.186) for death-censored graft 5-year survival) (fig. 1).

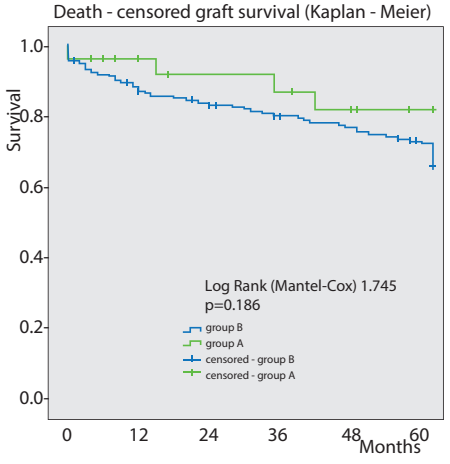


Fig. 1. Death-censored graft 5-year survival (Kaplan-Meier).

Patient death rate was significantly higher in recipients transplanted from elderly donors (37,0 vs. 13,3% in control group, p = 0.005).

Comparison patient survival (Kaplan-Meier) in both groups revealed statistically significantly lower patient 5-year survival in group A (Log Rank (Mantel-Cox) = 10.252, p = 0.001) (fig. 2).

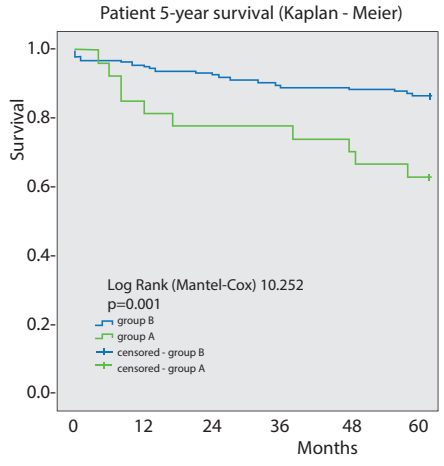


Fig. 2. Patient 5-year survival (Kaplan-Meier).

DISCUSSION

Development in kidney replacement therapy and improved results of kidney transplantation resulted in increased number of elderly recipients on waiting list and increased gap between donor organ supply and the number of recipients waiting for transplantation. The use of organs from elderly donors for age-matched recipients gives the opportunity to improve this situation and remains one of the steps for increase of the number of kidney transplantations (5). This is also recommended in the last "Guide to the quality and safety of organs for transplantation" where experts underline that age should not be the limiting factor for deceased donation, however elderly donors should be used carefully considering the higher risk worse outcomes (1). The rate of the use of kidneys from elderly donors varies between different countries, in Eurotransplant countries this rate is one of the highest and reported results show that their allocation policy is effective: local use ensures relatively low cold ischemia time and better long-term results (2).

Results of our study show that ederly donors had higher rate of non-traumatic brain injury as a cause of death and BMI ($p < 0.05$ for both) and only slight tendency to higher rate of glomerular sclerosis ($p = 0.075$), that proves that calendar age is not reliable factor in determination of contraindications for deceased donation. Kidneys from such donors were mainly allocated to elderly recipients ($p < 0.001$). Irrespective of the fact that we have mainly local allocation, the average cold ischemia time was relatively long (more than 16 hours) that may explain relatively higher rate of the delayed graft function (33,3 vs. 18,l% in controls, $p = 0.063$). Posttransplant results showed lower 5-year patient survival among recipients of elderly donors ($p = 0.001$), which can be related to higher age of these patients. In our study in patients transplanted from elderly donors we observed less frequent death-censored graft losses than in the control group, however comparison of 5-year graft survival curves did not reveal statistical significance (Log Rank (Mantel-Cox) = 1.745, $p = 0.186$). One of the possible reasons for this lower rate of graft losses may be associated with very cautious approach to selection of such donors and organs prior to transplantation. Otherwise posttransplant result were similar in both groups with similar serum creatinine levels for functioning grafts at the end of 5-year follow-up period.

Worse results and higher mortality in patients receiving their graft from elderly donors was reported also by other authors. *Cohen et al.* (2005) reported Eurotransplant results for senior program and showed siimilar graft survivals in patients transplanted from senior donors and from standart risk donors, with lower survival only in cases of KT from senior donors with developed delayed graft function in posttransplant period (2). At the same time Veroux et al. (2012) reported significantly lower graft survival in KT from older donors (9). In recent study by *Dempster et al.* (2013) authors also revealed that the use of older donors was associated with higher rate of DGF, graft losses and higher serum creatinine at 1 year after transplantation ($p < 0.05$ for all), however at the same time old donors were not associate with increased risk of patient deaths (4). In their study patient mortality was associated with older recipient age ($p = 0.03$). The possible way to improve results is to use of pre-transplant biopsy results and transplantation of two donor kidneys into the same recipient (3).

CONCLUSION

In conclusion, results of our study show that kidney transplantation from older donors when allocated to aage-matched recipients ensures acceptable outcomes and should be contienued in the future. Special attention should be paid to ensure the cold ischemia time as low as possible in order to reduce delayed graft function. The problem of urgent examination donor organ biopsy and the use of results for decision about the quality of kidney grafts is still very actual and should be solved as soon as possible. In cases when sclerosis of donor kidneys is associated with high risk to use it for for transplantation, transplant surgeon should assess the possibility of transplanting of two donor kidneys into one recipient.

Conflict of interest: None

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