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Factors influencing renal graft survival: 7-Year experience of a single center

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ABSTRACT

Background and objective: The demand for kidney transplants exceeds the existing supply. This leads to a recently growing interest of research in the area of factors that could prolong graft long-term outcomes and survival. In Lithuania, approximately 90% of kidney transplantations are from deceased donors. Donor organs are received and shared only inside the country territory in Lithuania; therefore, donor data is accurate and precise. This study was performed to present particularities of kidney transplantation data in Lithuania and to identify the effect of donor and recipient factors and histologic findings on renal graft outcomes. The aim of this study was to identify the effect of donor and recipient factors and histologic findings on renal graft outcomes.

Materials and methods: We analyzed the influence of deceased donor and recipient factors and histological findings on the graft function in 186 renal transplant patients. Graft survival was estimated within the first year after transplantation.

Results: The donors and recipients were older in worse eGFR group 1 year after transplantation. Dissimilarity of degree of glomerulosclerosis (GS), interstitial fibrosis (IF) and arteriolar hyalinosis (AH) were significant in inferior and superior renal function groups (GS >20% 11.4 vs. 0%, $P = 0.017$; IF 9.3 vs. 0%, $P = 0.034$; AH 69 vs. 26.2%, $P < 0.001$). Nine independent variables were significantly associated with a worse renal transplant function 1 year posttransplantation: AH (OR = 6.287, $P < 0.001$), an episode of urinary tract infection (OR = 2.769, $P = 0.020$), acute graft rejection (OR = 3.605, $P = 0.037$), expanded criteria (OR = 4.987, $P = 0.001$), female gender donors (OR = 3.00, $P = 0.014$), cerebrovascular disease caused donor brain death (OR = 5.00, $P = 0.001$), donor's age (OR = 1.07, $P < 0.001$), and recipient's age (OR = 1.047, $P = 0.022$). Worse renal graft survival 1 year posttransplantation was associated with a delayed graft function and a higher level of glomerulosclerosis in time-zero biopsy.

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Conclusions: Donor factors, such as age, female gender, brain death of cerebrovascular cause and expanded criteria donor status had a significant negative impact on the renal graft function 1 year after transplantation. Recipients' age, urinary tract infection and acute graft rejection episodes after transplantation were associated with a worse kidney function 1 year after transplantation. Lower 1-year graft survival was related to a delayed graft function (DGF) and a higher degree of glomerulosclerosis.

1. Introduction

The number of patients with end-stage renal disease (ESRD) and receiving renal replacement therapy (RRT) is growing rapidly. According to the ERA-EDTA Registry, there were 1019.8 patients per million population on RRT and 459.3 per million population (45%) after kidney transplantation in 2013 [1]. An efficient kidney transplant improves the quality of life [2], corrects metabolic consequences of chronic kidney disease (CKD) [2] and reduces the mortality risk for most patients when compared with maintenance dialysis [3,4]. It also saves treatment costs and helps to maintain social needs, whereas about 60%–70% of kidney transplant recipients successfully return to work [5]. Interest in the research of factors that could prolong graft long-term outcomes and survival is increasing worldwide. This leads to accepting older and expanded criteria donor (ECD) kidneys, individualizing immunosuppression, using molecular therapy, and searching for mechanisms of immunotolerance.

There is a lack of published data about RRT and kidney transplantation outcomes in the Baltic States: Lithuania, Latvia, and Estonia. The Baltic States are heterogenic in prevalent rates (the number of patients per million population that were receiving RRT) of RRT (719.0, 600.3, and 572.1 per million population, respectively) and number of kidney transplantations (227.8, 324.8, and 346.0 per million population, respectively) [1]. Lithuania was the first Baltic state to declare independence from the Soviet Union on 11 March 1990 and since then has made a huge progress in nephrology. A broad network of dialysis units ensures dialysis accessibility for a large ESRD patient population. Since 1996, the amount of patients with ESRD has increased 7 times, and now 491.2 patients per million population ($n = 1460$) are receiving dialysis therapy in Lithuania [1,6]. At present, the kidney transplant waiting list is approximately 175 patients, while the number of cadaveric kidneys transplanted annually remains almost stable at approximately 70. In 2013, 28 kidney transplantations per million population ($n = 77$) were performed in Lithuania. Although approximately 90% of renal transplantations are from deceased brain death (DBD) donors, the number of patients living with transplanted kidney is also growing: 11.4 kidney transplantations per million population ($n = 63$) were performed in Lithuania in 2000 [6], and there were 28 kidney transplantations per million population ($n = 77$) in 2013 [1].

We are also expanding the donor pool and improving graft long-term outcomes in Lithuanian population by using marginal donors, performing time-zero and protocol kidney biopsies, which were started in 2007. Donor organs are received and shared only inside the country territory in Lithuania; therefore, we performed this study to present particularities of kidney transplantation data in Lithuania and to identify the effect of donor and recipient factors and histologic findings on renal graft outcomes. Our goal was to compare donor and recipient characteristics and to ascertain factors related to kidney function 1 year posttransplantation and graft survival.

2. Materials and methods

The Renal Transplantation Center of the Hospital of the Lithuanian University of Health Sciences is particular, because all deceased donors whose kidneys are transplanted are prepared in this hospital; therefore, donor data is adequate and precise. Between January 2007 and December 2013, 197 cadaveric-renal transplantations were performed in our transplantation center (Departments of Nephrology and Urology). Of these transplantations, 11 were excluded as they were from donors < 18 years of age or because of incomplete clinical information. The remaining 186 patients were included in this retrospective, observational study. Recipients with ≥1-year graft survival were selected ($n = 141$) from our cohort for further analysis.

Donor data included age, gender, donor cause of death, history of hypertension, serum creatinine level before procurement, cold ischemia time and donor type (expanded criteria or standard). Information on recipient's age, gender, duration of dialysis, HLA incompatibility, underlying kidney disease, body mass index, acute rejection, posttransplantation infectious complications and diabetes mellitus was involved in analysis. Each HLA mismatch was counted equally for immunologic risk determination (example, 3 from 6; 2 from 6, etc.). Daclizumab or basiliximab with mycophenolate mofetil and steroids were used as an induction immunosuppressive therapy; maintenance immunosuppression consisted of cyclosporine or tacrolimus plus mycophenolate mofetil and steroids in all recipients. The renal transplant function was assessed by the presence of a delayed graft function (DGF) (defined as a need for dialysis within the first week after kidney transplantation [7]) and the estimated glomerular filtration rate (eGFR) at 1 year after transplantation. The values of eGFR were calculated using CKD-EPI formula.

Time-zero biopsies were performed using a 16-G needle gun on the upper kidney pole after reperfusion. Glomerulosclerosis (GS), interstitial fibrosis (IF), tubular atrophy (TA),

arteriosclerosis (AS) and arteriolar hyalinosis (AH) were registered as percentage in samples of time-zero biopsies. IF, TA, AS and AH were rated according to the 2007 Banff scoring system on allograft pathology [8,9].

The study was approved by the local ethical committee (Lithuanian Bioethics Committee BE-2-9).

All analyses were performed using SPSS software. The groups were compared using the independent samples t test and the chi-square test. Univariate and multivariate analyses were conducted using nonparametric correlations and logistic regression methods. Receiver operating characteristic (ROC) curves were used to compare the predictive value of the clinical parameters and morphologic findings on GFR at 1 year after transplantation. Graft survival 1-year posttransplantation was estimated using the Kaplan–Meier survival method for all recipients. The start point for graft survival was the date of transplantation and the end point was the need for regular dialysis or death with a functioning graft. A two-sided P value of 0.05 was considered to be statistically significant.

3. Results

3.1. Recipient and donor characteristics

The mean donor age was 44.09 ± 15.76 years (range, 7–75) with 61.1% being men. The main cause of donor death was cerebrovascular disease (63.3%). The mean time of cold ischemia was 19.6 ± 4.57 h (range, 9–32).

The average recipient age was 45.42 ± 11.13 years (range, 19–68) with 58.1% of men. DGF was observed in 31.7% of the recipients. Detailed donor and recipient characteristics are shown in Table 1.

Average duration of posttransplantation follow up was 45.60 ± 22.44 months (median, 44.19 months).

3.2. Histologic findings in time-zero biopsy

The mean number of glomeruli in time-zero biopsies was 10.49 ± 9.34 with 39.7% of biopsies containing > 10 glomeruli. The level of GS was 4.2 ± 9.59%. Any grade of TA, IF, AS and AH was observed in 10.7%, 2.8%, 39.7% and 43.5%, respectively. The majority of abnormal histologic findings were of mild degree (grade I) according to the Banff criteria [9,10]. No association between GS and IF was observed. However, we found a significant correlation between TA and IF ($r = 0.231$, $P = 0.002$). More than half (60%) of IF was identified in time-zero biopsies with any grade of TA, while only 12.2% of IF in the samples with no TA–12.2% of IF ($P = 0.018$).

3.3. Association between donor and recipient parameters, histologic findings and graft function 1 year after transplantation

The study population with ≥1 year graft survival ($n = 141$) was divided into tertiles according to the eGFR value. We performed analysis in the groups of the lower (eGFR < 40 mL/min/1.73 m^2, $n = 45$) and the upper (eGFR > 56 mL/min/1.73 m^2, $n = 49$) tertiles of the transplant function. Donor and recipient characteristics of the lower and the upper eGFR tertile groups are presented in Table 2.

There were no statistically significant differences in terminal donor serum creatinine ($P = 0.266$), sodium ($P = 0.721$), cold ischemia time ($P = 0.999$), waiting time on dialysis ($P = 0.773$), induction therapy with monoclonal antibodies ($P = 0.887$), female gender of recipients ($P = 0.905$), DGF ($P = 0.060$) and late posttransplant period urinary tract infections ($P = 0.088$) between renal function groups.

The donors and recipients were older in the lower tertile eGFR group 1 year after transplantation, 51.3 ± 14.6 years vs. 34.7 ± 15.2 years ($P < 0.001$) and 47.1 ± 8.7 vs. 41.7 ± 12.7 ($P = 0.042$), respectively.

Table 1 – Donor and recipient characteristics.

Characteristics	Value
Donors	
Age, years	44.1 ± 15.8
Gender (male/female), %	61.1/38.9
Cause of death, %	
Cerebrovascular disease	63.3
Trauma	35.6
Others	1.1
History of hypertension (yes/no), %	34.7/65.3
Terminal serum creatinine, μmol/L	97.65 ± 39.15 (88.00)
Cold ischemia time, h	19.6 ± 4.57 (20.00)
Expanded criteria donor type (yes/no), %	39.3/60.7
Recipients	
Age (years)	45.4 ± 11.1
Gender (male/female), %	58.1/41.9
History of diabetes (yes/no), %	14.5/85.5
Delayed graft function (yes/no), %	31.7/68.3
Body mass index, kg/m^2	25.14 ± 4.64 (24.39)
Acute rejection at an early postoperative period (yes/no), %	9.1/90.9
Urinary tract infection at an early posttransplant period (yes/no), %	40.9/59.1
Human leukocyte antigen (HLA) mismatch	3.35 ± 0.95 (3.00)

Values are mean ± standard deviation (median) unless indicated otherwise.

Table 2 – Donor and recipient characteristics in transplant function groups.

Characteristics	GFG < 40 mL/min/1.73 m^2	GFG > 56 mL/min/1.73 m^2
Donors		
Age, years	51.4 ± 14.6	34.7 ± 15.0
Gender (male/female), %	48.9/51.1	75.5/24.5
Cause of death, %		
Cerebrovascular disease	20.0	41.9
Trauma	80.0	58.1
History of hypertension (yes/no), %	46.7/53.3	25.6/74.4
Terminal serum creatinine, μmol/L	110.60 ± 58.32 (90.00)	94.23 ± 32.92 (87.50)
Cold ischemia time, h	19.74 ± 4.08 (21.00)	20.64 ± 4.82 (20.00)
Expanded criteria donor type (yes/no), %	60/40	25.6/74.4
Recipients		
Age, years)	47.1 ± 8.7	41.7 ± 12.7
Gender (male/female), %	64.4/35.6	63.3/36.7
History of diabetes (yes/no), %	2.2/97.8	20.4/79.6
Delayed graft function (yes/no), %	35.6/64.4	18.4/81.6
Body mass index, kg/m^2	26.36 ± 5.31 (26.03)	23.90 ± 4.40 (22.88)
Acute rejection at an early postoperative period (yes/no), %	15.6/84.4	0/100
Urinary tract infection at an early posttransplant period (yes/no), %	48.9/51.1	26.5/73.5
Human leukocyte antigen (HLA) mismatch	3.36 ± 0.81 (3.00)	5.59 ± 0.93 (3.00)

Values are mean ± standard deviation (median) unless indicated otherwise.

Dissimilarity of degree of GS, IF and AH were significant in inferior and superior renal function groups (GS >20% 11.4% vs. 0%, $P = 0.017$; IF 9.3% vs. 0%, $P = 0.034$; AH 69% vs. 26.2%, $P < 0.001$). No variance among the transplant function groups in TA ($P = 0.305$) and AS ($P = 0.334$) was observed in time-zero biopsy.

Five independent donor variables and four independent recipient variables were significantly associated with an inferior renal transplant function 1 year posttransplantation (Tables 3 and 4).

AH was an independent variable significantly associated with an inferior graft function 1 year posttransplantation (OR = 6.287, $P < 0.001$). The probability of a worse transplant function 1 year after transplantation increases with episodes of urinary tract infection (early posttransplant period) (OR = 2.769, $P = 0.020$) and acute graft rejection (late post-transplant period) (OR = 3.605, $P = 0.037$), when kidneys are transplanted from expanded criteria (OR = 4.987, $P = 0.001$), with female gender donors (OR = 3.00, $P = 0.014$) and cerebrovascular disease caused brain death (OR = 5.00, $P = 0.001$). Adding 1 year to donor's age (OR = 1.07, $P < 0.001$), the same as to recipient's age (OR = 1.047, $P = 0.022$), enlarges chances of an inferior graft function 1 year posttransplantation. The history of recipient's diabetes made an opposite influence, i.e., it decreased the probability of a worse graft function (OR = 0.087, $P = 0.022$). The results of the final model are presented in Table 5.

Donors with brain death of cerebrovascular cause were older than donors with traumatic brain injury, 50.8 ± 11.2 vs. 32.5 ± 16.6 years ($P < 0.001$). The threshold value of donor age was 36 years (sensitivity 58.7%, specificity 91.1%) derived by the ROC test (Fig. 1). Donors with cerebrovascular disease caused death were older: there were 91.1% of >36-year-old donors and 8.9% < 36 years old donors ($P < 0.001$).

In order to sort out the relation between donor kidney morphologic changes, donor factors and the renal graft function, our study population was subdivided into two groups by random selection according to the degree of glomerulosclerosis on time-zero biopsy: group I, transplants with <20% GS ($n = 170$); and group II, transplants with >20% GS

Table 3 – Donor factors associated with inferior transplant function 1 year posttransplantation.

Variable	OR	95% CI	P
Arteriolar hyalinosis	6.287	2.433–16.244	<0.001
Cerebrovascular disease caused donor brain death	5.00	1.980–12.625	0.001
Expanded criteria donor type	4.987	1.975–12.548	0.001
Donor female gender	3.00	1.254–7.177	0.014
Donor age	1.07	1.037–1.105	<0.001

Table 4 – Recipient factors associated with inferior transplant function 1 year posttransplantation.

Variable	OR	95% CI	P
Acute graft rejection (late posttransplant period)	4.259	1.091–16.627	0.037
Urinary tract infection (early posttransplant period)	2.769	1.174–6.531	0.020
Recipient age	1.047	1.007–1.089	0.022
History of diabetes	0.087	0.011–0.708	0.022

Table 5 – Multivariate logistic regression analysis of inferior renal graft function.

Variables	Odds ratio (95% CI)
Donor female gender	
No	1
Yes	2.899 (0.985–8.531)
Donor age	
<36 years	1
>36 years	1.066 (1.030–1.103)*
Urinary tract infection (early posttransplant period)	
No	1
Yes	3.865 (1.322–11.301)*

Constant = −3.549.
* $P < 0.05$.

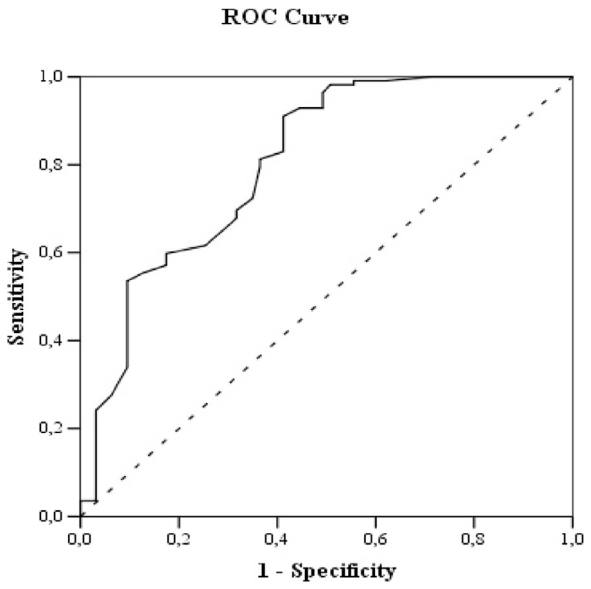


Fig. 1 – ROC curve derived from the logistic regression analysis of donor age according to the cause of death in population with ≥1 year graft survival (*n* = 141). The donors with brain death of cerebrovascular cause were older than the donors with traumatic brain injury, 50.8 ± 11.2 vs. 32.5 ± 16.6 years (*P* < 0.001). The threshold value of donor age was 36 years (sensitivity – 58.7%, specificity – 91.1%). The area under the ROC curve is 0.805, which indicates a high degree of discrimination.

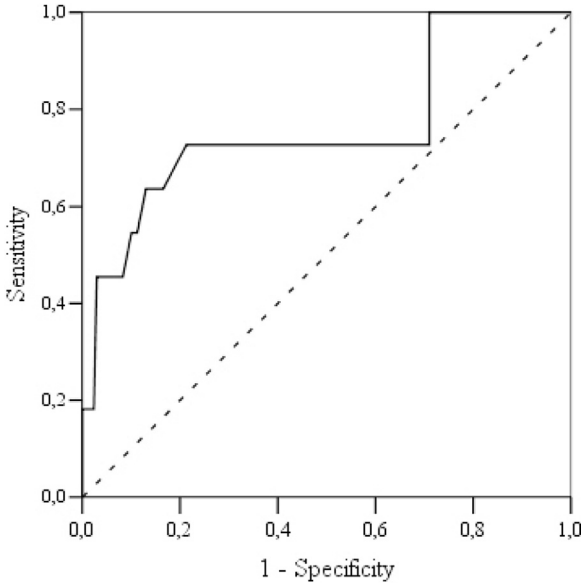


Fig. 2 – ROC curve derived from the logistic regression analysis of donor age according to the level of glomerulosclerosis (*n* = 181). There were significantly more donors older than 55 years in the >20% GS group compared with <20% GS group: 72.7% vs. 21.3% (OR = 9.852; 95% CI, 2.486–39.045, *P* < 0.001). The threshold value of donor age was 55 years (sensitivity – 72.7%, specificity – 78.7%). The area under the ROC curve is 0.763, which indicates a high degree of discrimination.

(*n* = 11). Five recipients were excluded from analysis due to a lack of biopsy data. Diffuse GS was associated with older donor age and donor arterial hypertension anamnesis, therefore with transplants from expanded criteria donors. There were significantly more donors older than 55 years in the >20% GS group compared with <20% GS group: 72.7% vs. 23.1% (OR = 9.852; 95% CI, 2.486–39.045, $P < 0.001$). The threshold value of donor age was 55 years (sensitivity 72.7%, specificity 78.7%) (Fig. 2). The rate of positive history of hypertension among donors with diffuse GS was also higher: 63.6% vs. 32.7% (OR = 3.605; 95% CI, 1.008–12.889, $P = 0.037$). A major degree of GS (>20% GS) in time-zero biopsies was seen in kidneys from expanded criteria donors (OR = 4.249; 95% CI, 1.084–16.657, $P = 0.026$). Marked GS was associated with acute rejection episodes (in early posttransplant period), 36.4 vs. 7.7% ($P = 0.002$). DGF was significantly more common in the >20% GS group compared with < 20% GS group: 90.9% vs. 9.1% (OR = 9.231; 95% CI, 1.023–83.331, $P = 0.025$). There were no statistically significant differences in the terminal donor serum creatinine level between GS groups ($P = 0.057$), donor gender ($P = 0.088$) and cold ischemia time ($P = 0.158$) (Table 6).

3.4. *Renal graft survival analysis*

The overall graft survival (by Kaplan–Meier) of 186 patients was 93.5% and 90% at 1 and 3 years after transplantation, respectively. At the end of the study, 80.1% of transplanted kidneys were still functioning, 11.3% of the recipients were returned to dialysis and 8.6% were dead with the functioning graft. The mean eGFR 1 year after transplantation was 49.68 ± 20.25 mL/min/1.73 m^2 (median 46.6 mL/min/1.73 m^2) (range, 7.1–120.8 mL/min/1.73 m^2).

Worse renal graft survival 1 year and 3 years posttransplantation was associated with a delayed graft function and a higher level of glomerulosclerosis in time-zero biopsy (Figs. 3 and 4). No significant correlation was seen between graft survival and other variables, including IF ($P = 0.202$), TA ($P = 0.569$), acute graft rejection during the early ($P = 0.305$) and the late posttransplant period ($P = 0.080$).

Table 6 – Factors associated with glomerulosclerosis level in time-zero biopsy.

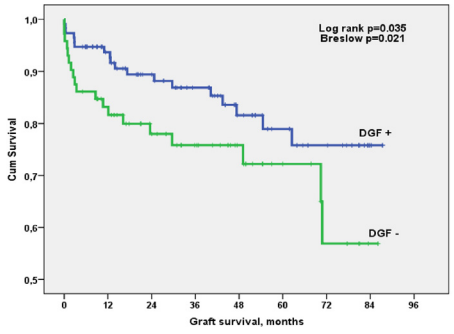
Factor	Group GS < 20%	Group GS > 20%	P
Mean donor age, years	43.6 ± 15.5	58.4 ± 14.3	0.004
Donor age > 55 years, %	21.3%	72.7%	<0.001
Donor serum creatinine, μmol/L	99.23 ± 44.19	128.00 ± 74.06	0.057
History of hypertension, %	32.7	63.6	0.037
Expanded criteria donor, %	38.6	72.7	0.026
Donor female gender, %	37.7	63.6	0.088
Cold ischemia time	19.66 ± 4.52	17.55 ± 4.81	0.158
Cerebrovascular disease caused donor brain death, %	62.3	100	0.040
Acute graft rejection (early posttransplant period), %	7.7	36.4	0.002

Values are mean ± standard deviation unless indicated otherwise.

4. Discussion

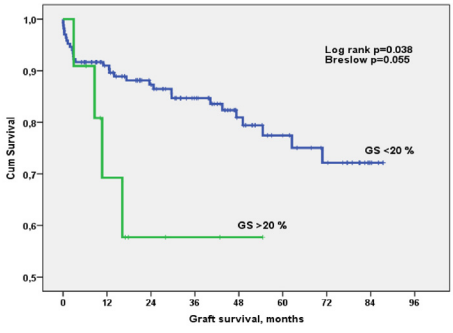
This study was carried out to identify the risk factors of the graft function that can be crucial to improve renal transplant outcomes. During the study, the effect of graft histologic changes, donor and recipient characteristics on renal allograft function and survival was evaluated.

The results of survival analysis where unexpected: many donor and recipient factors had no impact on kidney survival. However, DGF and a higher degree of GS in time-zero biopsy had a negative influence on graft survival 1 year after



Months/ Number at risk	0	12	24	36	48	60	72	84	96
DGF +	72	54	40	30	21	12	7	2	0
DGF −	114	90	73	58	40	27	19	4	0

Fig. 3 – Association of graft survival and the rate of DGF by Kaplan–Meier survival analysis. The occurrence of DGF was a risk factor for poorer graft outcomes (49.5% vs. 94.4% for 1-year survival and 75.3% vs. 86.0% for 3-year survival).



Months/ Number at risk	0	12	24	36	48	60	72	84	96
GS < 20	168	132	105	81	55	34	25	6	0
GS > 20	11	6	3	2	1	0	0	0	0

Fig. 4 – Association of graft survival and the level of GS by Kaplan–Meier survival analysis. The 1-year and 3-year graft survival rates in GS > 20% group (69.3% and 57.7%) were poorer versus in GS < 20% group (91.0% and 84.7%).

transplantation. Preceding studies have disclosed the influence of the degree of glomerulosclerosis [11–14], interstitial fibrosis [12,13], tubular atrophy [12] and AH [13] in time-zero biopsies on predicted graft survival 1 year after transplantation. Recent results determining the impact of donor histology on graft survival are questionable. Indicated associations of preimplantation kidney morphology with kidney survival are assessed by novel doubtful biopsy score [11] or in mixed study populations of circulatory death and brain death donors [13].

Our study disclosed that the probability of a lower renal allograft function was a few times higher when kidneys were accepted from female, older age and expanded criteria donors after cerebrovascular brain death transplanted to older recipients who had urinary tract infection and acute transplant rejection episodes posttransplantation. Notably, recipients with pretransplant diabetes had a better renal graft function 1 year after transplantation. However, we could not find any data about the early renal transplant function in diabetic recipients. We suggest that higher GFR can be explained by hyperfiltration characteristics to diabetes, which can be confirmed by performing further protocol graft biopsies. Each year of donor age older than 36 years as well as the female donor gender and urinary tract infection episodes at an early posttransplant period are predictors of a worse renal allograft function. However, significance of some associations was lost in multivariate analysis.

According to previous studies, donor age [11,13–16], expanded criteria donor category [11,14] and recipient age [15] showed a marked negative correlation with the renal function 1 year after transplantation. Surprisingly, we observed no differences in cold ischemia time, HLA mismatching or waiting time on dialysis in separate transplant function groups. Some studies have found that kidneys from older donors more frequently have risk factors for the development of a worse kidney function after transplantation; they have a higher incidence of DGF and loss of functional renal reserve [17,18]. In our study, deceased brain death donors were quite young, with the mean age of 44 years (the oldest donor–was 68 years old). However, the majority of these young donors died from cerebrovascular disease (63.3%). The reason for this is high cardiovascular mortality (and morbidity). Lithuania has reported the highest standardized death rate for ischemic heart diseases and a very high rate of cerebrovascular diseases among the European Union countries [19]. Moreover, older recipients' age was related to lower GFR, but the age of a recipient was not a risk factor for graft survival, as suggested by some clinical studies [20,21]. Kidneys from expanded criteria donors demonstrate a risk of graft failure or a worse transplant function, as observed in recently published series and our study [22–24]. As reported in other studies, the impact of the donor female gender on a worse transplant function may be explained by larger glomerular volumes in males, as shown in rats [25], immunologic factors as necessitating antirejection therapy or expressing more HLA antigens [26]. In our study, the gender match analysis could clarify the effect of the female donor gender. However, we had no possibility to perform weight–size matching analysis because of a lack of donor anthropometric data. The adverse role of the female donor gender is controversial and needs to be determined; besides, female donor kidneys have a worse long-time survival [27]. Our observation is in line with the recent published study of Marconi et al. [28], which presents an inferior renal graft function in 1 year after transplantation from cerebrovascular disease caused brain dead donors as compared with traumatic brain injury donors; however, donor cause of death was not identified as an independent risk factor for graft survival. Due to the impact of posttransplantation infectious complications on the transplant and patient survival [29], prevention and treatment of infections play an important role in the overall success of transplantation [30]. The data we presented in this study confirmed that urinary tract infections were responsible for increased probability of a worse graft function 1 year posttransplantation. As confirmed in many researches, acute rejection has a negative prognostic value on graft survival [31–33]. Our results agree with those recently published by Marcén et al. [34], who analyzed the data of 4,488 patients and observed that acute rejection increased the possibility of lower GFR 1 year after transplantation.

Typically, other studies evaluate the impact of donor histology on renal graft outcomes after discarding kidneys based on their morphology and predict donor risk factors in kidneys chosen for transplantation [35–37]. In our center baseline biopsy findings were not used discard deceased donor kidneys; therefore, our results reflect a complete amplitude of donor kidney morphology. Moreover, numerous studies have reported that core needle biopsies are superior to wedge biopsies [38,39]; consequently, the assessment of morphologic changes in our research is trustworthy. The majority of abnormal baseline histologic findings in our study were of mild degree: GS and IF less than 5%, and TA over 10%. Moreover, 93.9% of kidney transplants included GS less than 20%, which indicates an acceptable donor kidney status. Our results revealed that GS more than 20% was associated with expanded criteria donor type, as well as older donor age and history of arterial hypertension (both of the latter are decided as ECD parameters), and donor brain death of cerebrovascular cause. Donors older than 55 years predominantly had significant glomerulosclerosis (>20%) and, consequently, the higher degree of global glomerulosclerosis is closely linked to older donor's age.

Previous studies have revealed that severity of global glomerulosclerosis and interstitial fibrosis is related to donor age, ECD status and donor brain death of vascular origin [11,13]. Significant AH has been proved in hypertensive and diabetic cadaveric donors [13]. No evidence of interrelation between donor gender, terminal serum creatinine or cold ischemia time has been observed [11,13–16].

5. Limitations of our study

The differences in this study outcomes are presumable due to methodology of the research, number of study population, categorization of the variables, and limitation of biopsy evaluation and a lack of confounding factors control. Moreover, the course of post transplantation care and adverse events can overshadow the impact of donor and recipient factors on graft outcomes.

6. Conclusions

Our data analysis indicated that donor factors, such as age, female gender, brain death of cerebrovascular cause and

expanded criteria donor type, had a significant negative impact on the renal graft function 1 year after transplantation. Recipients' age, urinary tract infection and acute graft rejection episodes after transplantation were predictors of a worse kidney function 1 year after transplantation. We observed that marked glomerulosclerosis in graft time-zero biopsy was related to older donor age, history of arterial hypertension, expanded criteria category and cerebrovascular cause of brain death. Kidneys with a higher degree of glomerulosclerosis were associated with acute rejection episodes at an early posttransplant period. Lower 1-year graft survival was related to a higher degree of glomerulosclerosis and a delayed graft function.

Authors' contributions

R.A.: conception and design, data collection and analysis, manuscript writing and final approval of the manuscript; E.D.: conception and design, data collection and analysis, manuscript writing and final approval of the manuscript; V.K.: conception and design, critical revision and final approval of the manuscript; M.J.: conception and design, critical revision and final approval of the manuscript; L.P.: data collection, drafting of the manuscript; A.G.: data collection, drafting of the manuscript; E.S.: conception and design, critical revision and final approval of the manuscript; A. I.B.: conception and design, critical revision and final approval of the manuscript. All authors made significant intellectual contributions and approved the final manuscript.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Conflicts of interest

The authors declare that they have no conflicts of interest.

REFERENCES

[1] Kramer A, Pippias M, Steel VS, Bonthuis M, Abad Diaz JM, Afentakis N, et al. Renal replacement therapy in Europe: a summary of the 2013 ERA-EDTA Registry Annual Report with a focus on diabetes mellitus. Clin Kidney J 2016;9:1–13.

[2] Landreneau K, Lee K, Landreneau MD. Quality of life in patients undergoing hemodialysis and renal transplantation – a meta-analytic review. Nephrol Nurs J 2010;37(Jan/Feb):37–44.

[3] Schnuelle P, Lorenz D, Trede M, Van Der Woude FJ. Impact of renal cadaveric transplantation on survival in end-stage renal failure: evidence for reduced mortality risk compared with hemodialysis during long-term follow-up. J Am Soc Nephrol 1998;9:2135.

[4] Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med 1999;341:1725–30.

[5] The Order No. V-1462 of 31 December 2014 of the Minister of Health of the Republic of Lithuania ''On the approval of 2015–2025 years transplantation programs''.

[6] Ziginskiene E, Kuzminskis V, Bumblyte IA, Santockiene L, Dalinkeviciene E, Kardauskaite Z, et al. Parallels in development of hemodialysis service and kidney transplantations in Lithuania during 1996–2005. Medicina (Kaunas) 2007;43(Suppl. 1):114–20.

[7] Port FK, Bragg-Gresham JL, Metzger RA, Dykstra DM, Gillespie BW, Young E, et al. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. Transplantation 2002;74(9):1281.

[8] Racusen LC, Solez K, Colvin RB, Bonsib SM, Castro MC, Cavallo T, et al. The Banff 97 working classification of renal allograft pathology. Kidney Int 1999;55(2):713–23.

[9] Solez K, Colvin RB, Racusen LC, Haas M, Sis B, Mengel M, et al. Banff 07 classification of renal allograft pathology: updates and future directions. Am J Transplant 2008;8 (4):753–60.

[10] Snoeijs MG, Buurman WA, Christiaans MH, van Hooff JP, Goldschmeding R, van Suylen RJ, et al. Histological assessment of preimplantation biopsies may improve selection of kidneys from old donors after cardiac death. Am J Transplant 2008;8:1844–2185.

[11] Kosmoliaptsis V, Salji M, Bardsley V, Chen Y, Thiru S, Griffiths MH, et al. Baseline donor chronic renal injury confers the same transplant survival disadvantage for DCD and DBD kidneys. Am J Transplant 2015;15(3):754–63.

[12] De Vusser K, Lerut E, Kuypers D, Vanrenterghem Y, Jochmans I, Monbaliu D, et al. The predictive value of kidney allograft baseline biopsies for long-term graft survival. J Am Soc Nephrol 2013;24(11):1913–23.

[13] Arias LF, Blanco J, Sanchez-Fructuoso A, Prats D, Duque E, Sáiz-Pardo M, et al. Histologic assessment of donor kidneys and graft outcome: multivariate analyses. Transplant Proc 2007;39:1368–70.

[14] Kayler LK, Mohanka R, Basu A, Randhawa P. Correlation of histologic findings on preimplant biopsy with kidney graft survival. Transpl Int 2008;21:892–8.

[15] Fischer-Frohlich CL, Kutschmann M, Feindt J, Schmidtmann I, Kirste G, Fruhauf NR, et al. Influence of deceased donor and pretransplant recipient parameters on early overall kidney graft-survival in Germany. J Transplant 2015. article ID 307230, 10 pp..

[16] Carter JT, Lee CM, Weinstein R, Lu AD, Dafoe DC, Alfrey EJ. Evaluation of the older cadaveric kidney donor: the impact of donor hypertension and creatinine clearance on graft performance and survival. Transplantation 2000;70:765–7701.

[17] Cosio FG, Henry M, Pesavento TE, Ferguson RM, Kim S, Lemeshow S. The relationship between donor age and cadaveric renal allograft survival is modified by the recipient's blood pressure. Am J Transplant 2003;3:340–7.

[18] Oppenheimer F, Aljama P, Peinado CA, Guirado L. The impact of donor age on the results of renal transplantation. Nephrol Dial Transplant 2004;19(3). iii11–iii15.

[19] Cardiovascular Diseases Statistics. Eurostat website: http://ec.europa.eu/eurostat/statisticsexplained/index.php/File:Standardised_death_rates_%E2%80%94_diseases_of_the_circulatory_system,_residents,_2013_(per_100_000_male-female_inhabitants).png [last accessed 01.03.17].

[20] Moghani-Lankarani M, Assari S, Sharifi-Bonab M, Nourbala MH, Einollahi B. Does age of recipient affect outcome of renal transplantation? Ann Transplant 2010;15(2):21–6.

[21] Nunes P, Mota A, Parada B, Figueiredo A, Rolo F, Bastos C, et al. Do elderly patients deserve a kidney graft? Transplant Proc 2005;37(6):2737–42.

[22] Merion RM, Ashby VB, Wolfe RA, Distant DA, Hulbert-Shearon TE, Metzger RA, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. J Am Med Assoc 2005;294(21):2726–33.
[23] Resende L, Guerra J, Santana A, Mil-Homens C, Abreu F, da Costa AG. Impact of donor age on renal allograft function and survival. Transplant Proc 2009;41(3):794–6.
[24] Fraser SM, Rajasundaram R, Aldouri A, Farid S, Morris-Stiff G, Baker R, et al. Acceptable outcome after kidney transplantation using ''expanded criteria donor'' grafts. Transplantation 2010;89(1):88–96.
[25] Remuzzi A, Puntorieri S, Mazzoleni A, Remuzzi G. Sex related differences in glomerular ultrafiltration and proteinuria in Munich–Wistar rats. Kidney Int 1988;34:481–6.
[26] Vereerstraeten P, Wissing M, De Pauw L, Abramowicz D, Kinnaert P. Male recipients of kidneys from female donors are at increased risk of graft loss from both rejection and technical failure. Clin Transplant 1999;13(2):181–6.
[27] Glyda M, Czapiewski W, Karczewski M, Pieta R, Oko A. Influence of donor and recipient gender as well as selected factors on the five-year survival of kidney graft. Pol Przegl Chirur 2011;83:188–95.
[28] Marconi L, Moreira P, Parada B, Bastos C, Roseiro A, Mota A. Donor cause of brain death in renal transplantation: a predictive factor for graft function? Transplant Proc 2011;43(1):74–6.
[29] Dupont PJ, Manuel O, Pascual M. Infection and chronic allograft dysfunction. Kidney Int Suppl 2010;119:S47–53.
[30] Al-Hasan MN, Razonable RR, Kremers WK, Baddour LM. Impact of Gram-negative bloodstream infection on long-term Allograft survival after kidney transplantation. Transplantation 2011;91(11):1206–10.
[31] Koo EH, Jang HR, Lee JE, Park JB, Kim SJ, Kim DJ, et al. The impact of early and late acute rejection on graft survival in renal transplantation. Kidney Res Clin Pract 2015;34:160–4.
[32] Jung CW, Park KT, Kim SY, Kim SJ, Kim MG, Jo SK, et al. Clinical outcomes in kidney transplantation patients from deceased donors with acute kidney injury. Transplant Proc 2013;45(8):2941–5.
[33] Opelz G, Dohler B. Influence of time of rejection on long-term graft survival in renal transplantation. Transplantation 2008;85:661–6.
[34] Marcén R, Morales JM, Fernández-Rodriguez A, Capdevila L, Pallardó L, Plaza JJ, et al. Long-term graft function changes in kidney transplant recipients. NDT Plus 2010;3(2):ii2–8.
[35] Kasiske BL, Stewart DE, Bista BR, Salkowski N, Snyder JJ, Israni AK, et al. The role of procurement biopsies in acceptance decisions for kidneys retrieved for transplant. Clin J Am Soc Nephrol 2014;9(3):562–71.
[36] Remuzzi G, Cravedi P, Perna A, Dimitrov BD, Turturro M, Locatelli G, et al. Long-term outcome of renal transplantation from older donors. N Engl J Med 2006;354:343–52.
[37] Fernandez-Lorente1 L, Riera L, Bestard O, Carrera M, Goma M, Porta N, et al. Long-term results of biopsy-guided selection and allocation of kidneys from older donors in older recipients. Am J Transplant 2012;12:2781–8.
[38] Mazzucco G, Magnani C, Fortunato M, Todesco A, Monga G. The reliability of pre-transplant donor renal biopsies (PTDB) in predicting the kidney state. A comparative single-centre study on 154 untransplanted kidneys. Nephrol Dial Transplant 2010;25:3401–8.
[39] Haas M, Segev DL, Racusen LC, Bagnasc SM, Melancon JK, Tan M, et al. Arteriosclerosis in kidneys from healthy live donors: comparison of wedge and core needle perioperative biopsies. Arch Pathol Lab Med 2008;132:37–42.