INFLUENCE OF DONOR AGE ON RENAL GRAFT FUNCTION IN FIRST SEVEN POST TRANSPLANT DAYS

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Abstract

Increasing gap between demand and availability of human kidneys for transplantation has forced a re-evaluation of the limits on donor age acceptability. The present study included 74 patients who underwent kidney transplantation in University Clinical Centre Tuzla. In an observational cohort study we assessed impact of donor age on post transplant renal function by analyzing following parameters: 24 hour urine output, creatinine clearance (Cr Cl) and glomerular filtration rate (GFR). Depending on donor age recipients were allocated in to two groups. Group I included patients who received renal graft from donors age up to 55 years, and Group II encountered recipients who received renal graft from donors older than 55 years. Our goal was to determine whether donor age over 55 years significantly diminishes renal graft function in first seven post transplant days. No statistically significant difference was found between Group I and II regarding 24 hour urine output. From second to fifth postoperative day creatinine clearance values were higher in the group of patients who received kidney from donors older than 55 years (47±19, 1 vs. 44, 4±20, 8). On the fifth, sixth and seventh post operative day GFR was significantly higher in patients who received renal graft from donors age up to 55 years ($p<0,0161$). Our data showed no significant difference in observed variables between the two groups, thus indicating that utilization of renal grafts from donors' age > 55 years is acceptable and may considerably expand the donor pool.

KEY WORDS: donor age, renal graft function, early post transplant period.

Introduction

The donor's age has significant influence on the outcome of kidney transplantation. Advanced donor age is associated with worsening of initial graft function and poor long term outcome after transplantation (1). Kidneys from donors older than 55 years carry increased risk for development of post transplant anuria, acute and chronic rejection (2). Cardiovascular complications represent the leading cause of death in transplant recipients with long term functioning graft. Advanced donor age is associated with increased morbidity and mortality related to cardiovascular complications (3). According to data from the United Network for Organ Sharing, the rates of graft loss and patient death among recipients of grafts from donors 70 years of age or older are 24% and 21% higher, compared to rates among recipients of grafts from donors 60 to 69 years of age (4). In the research conducted by Nakatani et al. (5) which included 53 cadaveric transplantations, a five year graft survival was 82.6% when the donor age was under 60, while in donors 60 years and over survival was 42. 1%. The poorer graft survival of aged kidneys has been attributed to a greater susceptibility to ischemia-reperfusion injury, which makes allograft more predisposed to acute graft rejection and delayed graft function (6). With age, structure of organ changes due to hypertension, atherosclerosis or diabetes, thus making an organ less suitable for transplantation. Aged kidneys have decreased nephron mass which is considered to be one of the causes of early graft dysfunction as well as chronic rejection (7). Increasing gap between demand and availability of human kidneys for transplantation has forced a re-evaluation of the limits on donor age acceptability. Considering the limited value of serum creatinine in assessment of renal function, immediately before harvesting, histopathological analysis of renal tissue is necessary. Biopsy finding is leading factor in evaluation of the viability of a kidney for transplantation (8). Multiple studies imply that kidneys from donors older than 60 years can be used for transplantation, provided that no more than 15% of glomeruli in pre transplantation biopsy are sclerotic (9). Kidneys from donors older than 60 years of age can provide excellent renal func¬tion for up to three years after transplantation, on condition that they are allocated as single or dual transplants according to biopsy findings before transplantation and that kidneys showing more severe, chronic changes on biopsy are discarded (10). The aim of this study is to determine the effect of donor age on renal graft function in first seven post transplant days.

Materials and Methods

This is an observational cohort study that involved 74 adult kidney transplant recipients. Seventy patients received living donor kidney trans¬plant and four patient received kidney transplant from a deceased donor. Depending on donor age recipients were allocated in to two groups. Group I included patients who received renal graft from donors age up to 55 years, and Group II encountered recipients who received renal graft from donors older than 55 years. All patients were assessed as ASA IV (American Society of Anaesthesiologists) physical status. Balanced anaesthesia was used in all transplant patients. All transplantations were planned and executed in accordance with previously established transplantation protocol. Day prior to surgery all patients were dialyzed and transferred to Intensive Care Unit (ICU). Subclavian central venous catheter was inserted to all patients, immunosuppressive, anti ulcerant, antibiotic treatment were started as well as deep venous thrombosis prophylaxis. Continuous monitoring of central venous pressure (CVP), arterial pressure and oxygen saturation of blood, were applied. In order to assess renal graft function, fol¬lowing variables were evaluated in each patient during first seven post transplant days: GFR (ml/min), Cr Cl (ml/min) and 24 h urine output. GFR was calculated using following formula:

$$GFR = 270 \times Creatinine^{-1,007} \times Age^{-0,18} \times Urea^{-0,169} \times 0,755 \text{ (female)}. \quad (11)$$

Creatinine clearance was calculated by using formula proposed by Cockcroft and Gault, which is formula widely used to detect onset of renal insufficiency:

$$Cr\ Cl = (140\text{-age}) \times BW\ (kg) / (72 \times \text{creatinine})\ (18). \quad (12)$$

Statistical analysis

The statistical analysis was performed using Student t-test and Pearson correlation test, p-value of 0,05 or less was considered statistically significant.

Results

The study was conducted in University Clinical Centre Tuzla. It included 74 patients mean age 32, 9±9, 7 years, 51 were males and 23 females. Mean donor age was 49, 2±12, 2 years, 48 donors were younger and 26 were older than 55 years.

As showed in Table 1. during first three postoperative days average values of daily urine output were higher in Group II, but no statistically significant difference was noted. Starting with fourth postoperative day 24 hour urine output is higher in Group I, still no statistical significance was found (Table 1.)

	Group I	Group II	
Post operative day	24 hour urine output	24 hour urine output	p
Day 1	5080±4041	5174±3762	0,92
Day 2	5728±3240	6314±3030	0,45
Day 3	5162±2440	5319±2266	0,44
Day 4	4511±2296	4428±1919	0,79
Day 5	3840±1906	3479±1521	0,78
Day 6	3265±1639	2963±1590	0,88
Day 7	3029±1651	2627±1502	0,87

TABLE 1. Correlation between average values of 24 hour urine output and donor age

First post transplant day no difference in Cr Cl was established between the observed groups (21, 2±9, 5 vs. 21,1±9, 5). From second to fifth postoperative day Cr Cl values were higher in the group of patients who received kidney from donors older than 55 years (47±19, 1 vs. 44, 4±20, 8). After the fifth day values of Cr Cl were higher in recipients receiving renal graft from donors younger than 55 years, but no statistical significance was found (54, 4±20, 5 vs. 58, 9±24, 2) (Table 2.)

	Group I	Group II	
Post operative day	Cr Cl	Cr Cl	p
Day 1	21,1±9,5	21,2±9,5	0,972
Day 2	23,7±14	25,7±10,2	0,464
Day 3	35,3±18,7	37,6±16,4	0,601
Day 4	44,4±20,8	47±19,1	0,579
Day 5	48,7±21,3	47,2±15,8	0,731
Day 6	58,9±24,2	54,4±20,5	0,401
Day 7	64,1±23,9	62,1±20,2	0,702

TABLE 2. Correlation between average values of creatinine clearance and donor age

During first four post operative days GFR was almost equal in both observed groups (p=0, 584). On the fifth, sixth and seventh post operative day GFR was significantly higher in patients who received renal graft from donors age up to 55 years (p<0, 0161) (Table 3.)

	Group I	Group II	
Post operative day	GFR	GFR	p
Day 1	17,6±7,7	16,1±6,7	0,409
Day 2	20,8±14,7	20,2±9,9	0,821
Day 3	31,2±18,9	29,1±13,3	0,584
Day 4	40,2±21,9	36,8±14,9	0,433
Day 5	44,5±24,1	37,3±13,7	0,105
Day 6	54,7±27,8	43,5±17,1	0,035
Day 7	60,5±30,9	50,4±18,2	0,0161

TABLE 3. Correlation between average values of GFR and donor age

Discussion

Increased need and permanent organ donor shortage led to expansion of donor pool, donors older than 60 years are currently accepted in living related and in cadaveric transplantation (13, 14). In Spain renal grafts from elderly donors (> 60 years) constitute 40% of all kidney transplants (15). Study carried out by Akinlolu et al. (16) demonstrated that use of marginal kidneys prolongs recipient's life from 3 to 9 years, depending on characteristics of recipient, compared to candidates who remained on maintenance dialysis treatment waiting for an ideal donor. In this study we sought to determine whether donor age significantly influences renal graft function in first seven post transplant days. Patients were allocated according to donor age in to two groups: Group I patients who received renal graft form donors' age ≤ 55 years and Group II patients whose donors were older than 55 years. Variables evaluated in this research were: 24 hour urine output, creatinine clearance and GFR, assessment of these parameters in early postoperative period was considered to have prognostic importance regarding later graft survival. Several analyses demonstrate the importance of events such as: dialysis requirement during first week defined as delayed graft function, slow graft function (creatinine > 3mg/dl/day) and creatinine reduction ratio at day 2, during early post transplant period. These variables are associated with early and late graft loss, and there for useful in prediction of long term outcome (17, 18). The principal finding in the study conducted by Johan et al. (19) is that kidneys from older donors are more likely to undergo acute rejection episodes in the early post transplantation period compared with kidneys from younger donors. Transplant recipients of kidneys from older donor have higher incidence of delayed graft function and may double incidence of acute rejection compared to patients with immediate diuresis (20). Efficient post transplant urine production is marker of satisfactory graft function; decline in urine output indicates suboptimal graft function and often requires dialysis (21). Terasaki et al. (22) preformed an analysis of 43 172 adult cadaver donor transplants assessing joint effect of donor age, HLA mismatch, recipient sex, race, age, original disease, donor death cause, cold ischemia time and transplant year. They noted that increased first day anuria, dialysis requirement and discharge serum creatinine values correlate with donor age. Incidence

of post transplant anuria is higher in kidneys from donors younger than 5 and older than 55 years (23). Vianello et al. (24) examined influence of donor age on the outcome of kidney transplantation in 169 patients allocated in three groups according to donor age: low donor age (12 to 25 years), medium donor age (26 to 50 years) and high donor age (51 to 66 years) group. Immediate diuresis was more frequent in low donor age group compared to other two groups, but multivariate analysis showed that it was a weak positive prognostic factor for graft outcome. Though 24 hour urine output was somewhat higher in Group I after the fourth post transplant day, we found no statistically significant difference between Groups I and II, in our research. Woo et al. (25) examined records from United States Renal Data System compiled in period 1996 to 2000 year, in order to determine differences in renal graft survival rate among 32 557 recipients divided in two groups (donors age < 55, and donors age ≥55 years). They examined initial GFR, established 6 month after transplantation and stability of GFR during first post transplant year. Compared to recipients of donors < 55 years, recipients of donors ≥ 55 years established lower initial GFR and had less stabile GFR in first post transplant year. Fernandez-Fresendo et al. (26) analyzed correlation between GFR in early post transplant period and appearance of post transplant hypertension. There is research indicated that patients with lower values of GFR in early post transplant period more frequently developed post transplant hypertension compared to patients with normal GFR. Considering that cardiovascular complications present leading cause of death in kidney transplant patients, development of hypertension in early post transplant period can be considered valuable predictor of graft survival. In current analysis GFR was similar in booth observed groups during first four postoperative days. Starting with the fifth day GFR was significantly higher in Group I. Rao et al. (27) established that Cr Cl calculated one month post transplant was significantly lower in the older donor group (> 50 years) compared to control group (donors between 11 and 50 years of age), long term renal function was also assessed and there finding was that older donor age is associated with inferior post transplant outcome. Federico et al. (28) analyzed interaction between donor age, delayed graft function and chronic allograft nephropathy. They found delayed graft function to be more frequent in elderly donors; in addition the 3 month and 1 year serum creatinine values were significantly higher in elderly donor group, although renal function remained stable during this period. Patrick et al. (29) found that values of serum creatinine measured at 1 and 10 years indicate slightly diminished renal function in recipients of kidneys from donors older than 50 years, graft and patients survival at 1, 5 and 10 years were slightly better in kidneys harvested from younger donors, but observed difference was not significant. There conclusion was that kidneys obtained from donors older than 50 years are suitable for transplantation. In our research, on the first post transplant day Cr Cl did not differ significantly between the groups, while from the second to fifth postoperative day Cr Cl was higher in the recipients of kidneys harvested from donors older than 55 years. Study done by Remuzzi et al. indicates that the survival of kidney grafts obtained from donors older than 60 years allocated for single or dual transplantation, was similar to that of single grafts from younger donors. Renal function recovery was prompt; Cr Cl was stabile and urinary protein excretion within the normal range (10). The current study implies that function of renal grafts obtained from donors older than 55 years doesn't differ significantly during first seven post transplant days, compared to kidney transplants that came from donors younger than 55 years. In view of poor survival and life quality of patients on dialysis and the growing need for transplantation, our results indicate that donors older than 55 years should be included in transplantation, with careful consideration of existing donor selection criteria.

Conclusion

Successful renal transplantation improves life quality compared to long term dialysis treatment and it is the best treatment for patients with end stage renal disease. Our data showed no significant difference in observed variables between the two groups, thus indicating that utilization of renal grafts from donors' age > 55 years is acceptable and may considerably expand the donor pool. Decision whether or not to use an older donor kidney should be based on individual characteristics of donor, as well as other factors related to the standard clinical criteria for transplantation.

List of Abbreviations

Cr Cl	-	creatinine clearance
GFR	-	glomerular filtration rate
ASA	-	American Society of Anaesthesiologists
ICU	-	Intensive Care Unit
CVP	-	central venous pressure
BW	-	body weight

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