Our Experiences in Kidney Transplantation and Monitoring of Kidney Graft Outcomes

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Abstract

Aim of kidney transplantation is to keep the functions of graft as long as possible, with an improvement of survival and quality of patients' lives. Aim of this article was to show the outcome of kidney transplantation in patients who were treated and monitored on Institute of Nephrology, CCU of Sarajevo in period between 1996 and 2004. and to identify the factors which can interfere with graft surviving. Retrospective analysis of data from the register of kidney transplanted patients was done. In the mentioned period 29 kidney transplants were performed, and at the same time 15 previously transplanted patients (total of 44) were monitored. Patients were followed until death or graft insufficiency. Most often cause of chronic renal failure before the transplantation were glomerular diseases (31,8% cases), and chronic pyelonephritis in 29,5% cases. Living-donor related kidney transplantation was performed in 56,8% of patients, living-donor unrelated in 27,3% of patients and cadaveric in 15,9% of patients. Post-transplant complications occurred in 29,5% of patients. Analysis of graft surviving on 12 months, 5 years and 10 years monitoring showed functional grafts in 87,5%, 80% and 75,0% of patients. Cumulative survival of patients on one year monitoring is 100%, on 5 year 100%, and on 10 year 93,8%. Primary causes of graft function loss were recurrent kidney diseases. Three patients (6,8%) died due to concomitant diseases, irrespective of the transplantation. Kidney transplantation is a successful treatment of a chronic renal failure with a high percentage of patients survival and long term graft survival, but also with serious post-transplant complications.

KEY WORDS: kidney transplantation, survival, complications

INTRODUCTION

The number of patients with the end stage of renal disease (ESRD) in Bosnia and Herzegovina is constantly increasing. According to the information from the Bosnia and Herzegovina Renal Register for the year 2003, on renal replacement therapy there are 1954 patients in our country, with prevalence of patients undergoing chronic dialysis therapy 432 per one million people (1) . Although kidney transplantation is the most effective compensation option of the eccrinic and endocrine functions of kidneys, which has it's aim in the improvement of survival as well as the quality of life of patients with ESRD, the number of performed transplanatations in our country is very low due to various reasons.

AIM

The aim of this article is to show the outcome of kidney transplantation with patiens who were treated and monitored on Institute of Nephrology, Clinical Center University of Sarajevo in period between 1996. and 2004. and to identify the factors which can interfere with graft surviving.

PATIENTS AND METHODS

Retrospective analysis of data from the register of kidney transplantations, which refers to 44 patients with kidney transplantations, was done. All patiens were followed until death or graft insufficiency. The average of monitoring of patients is 8,15 years (between 1 and 22 years). There were 4 patients on Pronisone + Azathioprine immunosuppressive regimen, 2 patients on Cyclosporin monotherapy, 18 patients on Cyclosporin + Azathioprine + Pronisone combination therapy, 17 patients on Cyclosporin + Mycophenolate Mofetil + Pronisone combination therapy and finally 3 patients on Prograf + Mycophenolate Mofetil + Pronisone combination therapy. There were evaluated following variables: the source of kidney (living or cadaveric donor), the age and the gender of donor and recipient, etiology of the end stage renal failure (ESRD), duration of the previous dialysis treatment, the presence of delayed graft function (DFG), acute rejection, recurrent kidney diseases, Cytomegalovirus (CMV) infection, immunosuppressive treatment, with monitoring of the serum creatinine, clearance of creatinine, and 24 hours proteinuria and blood sugar level. The results were analysed with descriptive statistical methods for each variable. The Student t – test was used to test the difference between the middle values ($p < 0,05$ was considered as being significant). Multivariate analysis was determination method of relation between the individual variables and graft surviving.

RESULTS

In the period from 1996. to 2004. kidney transplantation was performed on 29 of our patients (24,1% in Bosnia and Herzegovina and 34,5% in India), and at the same time 15 of our previously transplanted patients were monitored (in total 44).

Causes of the ESRD before the kidney transplantation are shown on figure 1. The most often causes of the ESRD before the transplanation were glomerular diseases (32%) and chronic pyelonephritis (30 %). Living-donor related kidney transplantation (Tx) was performed in 56,8% of patients, living-donor unrelated in 27,3% of patients and cadaveric in 15,9% of patients (Table 1).

Demographic characteristics of patients are shown on Table 2, referring to the average age of donors and recipients of the organ at the time of transplantation and their gender structure. Analysis of recipient distribution accordig to the gender shows that the percentage between the genders is almost equal in all observed groups (3:1

LIVING-DONOR RELATED TX	56,8%
LIVING-DONOR UNRELATED TX	27,3%
CADAVERIC TX	15,9%

TABLE 1. Kidney transplantations types

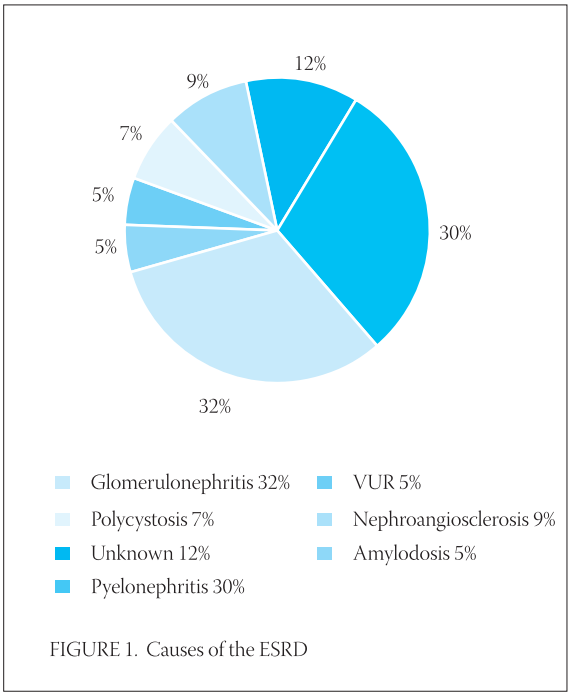

FIGURE 1. Causes of the ESRD

	LIVING RELATED TX	LIVING UNRELATED TX	CADAVERIC TX
AGE OF DONOR	47,78±11,01	26,0±3,39 (p=0,0001)	
	13 M : 12 Ž	12 M : 0 Ž	
AGE OF RECIPIENT	31,92±7,6	40,44±8,0	46,2±13,23
	72,0% M : 28,0% Ž	72,7% M : 27,3% Ž	71,4% M : 28,6% Ž

TABLE 2. Demographic characteristics of patients

	LIVING RELATED TX	LIVING UNRELATED TX	CADAVERIC TX
DIALYSIS TREATMENT (YEARS)	2,10±1,25 (1,0-4,5 y)	2,96±3,91 (0,3-13,0 y)	5,33±2,51 (3-8 y)

TABLE 3. Duration of the dialysis treatment

	DGF PRESENT	DGF ABSENT
LIVING RELATED TX	8,7 %	91,3 %
LIVING UNRELATED TX	16,7 %	83,3 %
CADAVERIC TX	16,7 %	83,3 %

TABLE 4. Frequency of occuring the DGF

	AR PRESENT	AR ABSENT
LIVING RELATED TX	20,0 %	80,0 %
LIVING UNRELATED TX	16,7%	83,7 %
CADAVERIC TX	0,0 %	100 %

TABLE 5. Frequency of occuring the acute graft rejection

	ARI	CMV INFECTION	THROMBOEMBOLISM	MALARIA
LIVING RELATED TX	8,0 %	12,0 %	-	-
LIVING UNRELATED TX	-	16,7 %	16,7 %	8,3 %
CADAVERIC TX	14,3 %	-	-	-

TABLE 6. Other postransplantation complications

in favor of men). Ratio between mail and femail donors in a group of living related transplantation is almost the same, while in the group of living unrelated transplantation we have the absolute presence of mail donors. The average life span between the group of living unrelated transplantation (26,0±3,39) and living unrelated transplantation (47,78±11,01) statistically differs significantly (p=0,00001).

The average dialysis treatment before the transplantation is shown on the table 3, which shows that the shortest duration of the dialysis treatment is in a group of living related transplantation.

Post-transplant complications had 29,5% of patients. The delayed graft function (DGF) had 11,3% of patients (table 4). This post-transplant complication was present in the same percentage in cadaveric and living unrelated transplantation (16,7%) and it was twice more often in comparison with the group of living related transplantation (8,7%).

The acute rejection (AR) manifested in 15,9% of patients and in almost same ratio between the groups of living related and living unrelated transplantation (table 5).

Frequency of occuring other complications in the early period after transplantation is shown in the table 6. The acute renal insufficiency (ARI) occured in 6,8% of patients, and the reasons for this clinical syndrom were urosepsa (Escherichia coli), CMV infection, sepsis due to flegmone of foot (Staphylococcus aureus).

Within the observed population 11,3 % of patients had CMV infection. The recidive thromboembolism and the malaria infection occured in the group of living unrelated transplantation. Mentioned complications are shown in comparison with the number of patients within a certain forms of transplantation.

Survival analysis for 12 months, 5 years and 10 years show that proper functional graft during the first post-transplant year is present in 87,5% of cases, in patients on 5 year monitoring in 80% of cases, and in patients on 10 years of monitoring in 75% of cases (figure 2). Survival of patients on one year monitoring is 100%, 5 years of monitoring 100% and 10 years of monitoring 93,8%. Predictable time to the graft insufficiency is 7,3 years.

Five patients (12,5%) had graft insufficiency at the end of the first post-transplant year. Regressive analysis of graft

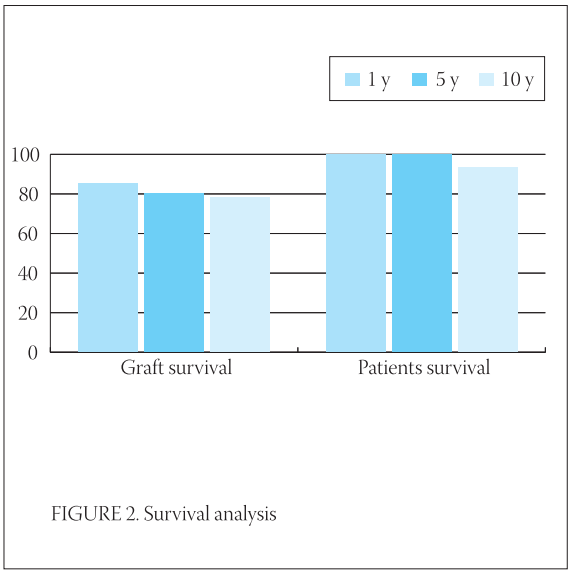

FIGURE 2. Survival analysis

	ODDS RATIO	P VALUES
ACUTE REJECTIONS	0,09	0,003
DGF	0,087	0,002
DONOR > 50 YEARS	0,0526	<0,001
LOW HLA MACH	0,0000022	<0,001
MMF	0,235	0,014

TABLE 7. Multivariate analysis of graft survival

MEMBRANOPROLIFERATIVE GN TYPE II	5 %
MEMBRANOUS GN	5 %
AMYLOIDOSIS OF KIDNEYS	5 %

TABLE 8. Diseases recurrence on graft – graft lost

NUMBER OF PATIENTS	AGE AT THE MOMENT OF GRAFT LOST (Y)	DURATION OF THE GRAFT SURVIVAL (Y)	DURATION OF POST TX SURVIVAL OF PATIENTS (Y)	CAUSES OF GRAFT LOST
8 (18,2%)	37,0±10,1 (21-49)	8,6±7,2 (3-22)	11,5±6,3 (3-22)	- transmitted diseases 37,5% - not taking medications 12,5% - CAN 12,5% - death with function graft 37,5%

TABLE 9. Characteristics of patients with graft lost

TOTAL OF PATIENTS	DECEASED	CAUSES OF DEATH	NUMBER (%)
44 (100%)	3 (6,8%)	Cirrhosis hepatis	1 (2,2%)
		Alzheimer	1 (2,2%)
		CVI	1 (2,2%)

TABLE 10. Causes of death

survival (table 7) showed that the risks of graft insufficiency within the first year after the transplantation refer to the appearance of the acute rejection (p=0,003),

Primary cause of the graft function lost in patients on 5 years of monitoring are recurrent kidney diseases (15% of patients, table 8), while chronic allograft nephropathy - CAN (12,5% of patients) is main cause of losing graft function in patients on 10 years of monitoring .

In overall period in 18,2% of patients graft lost occurred. Recurrent kidney diseases and death with functional graft were the most common cause of late graft lost. Causes and duration of graft survival and patients in the group with lost grafts is shown in table 9.

In observed population of patients, 3 patients (6,8%) died due to comorbidity, all with functional renal graft. Causes of mortality are shown on table 10. Median of patients survival is 16,7 years.

Malignicy of the skin (basocellulare epithelioma) appeared in one patient, 10 years after the transplantation and post-transplant diabetes in 4 patients (9,0%).

DISCUSSION

In post-war period transplant program is limitted on living related kidney transplantation and is very modest in quantity due to the lack of living donors. This work is an attempt to show the experiences in the field of kidney transplantations in our Center, and mostly covers patients who were transplantated outside of the country, and afterwards monitored in our hospital. Living unrelated transplantation in India (34,5%) was performed in almost 1/3 of the cases, with various complications after transplantation. Leading basic causes of ESRD before transplantation are chronic glomerulonephritis and chronic pyelonephritis, as well as in patients on dialysis treatment in our country (1). More than a half of performed transplantations are living related transplantations. The age of donors and recipients are in oposite relation between living related and living unrelated transplantation, where in the case of living related transplantation the average

age of donors is bellow 50 years, while recipients are younger (30,92±7,6 years), and in the case of living unrelated transplantation donors are very young (26,03±3,39) and recipients are in a middle age (40,44±8,0). Cadaveric kidney accepted the oldest patients in the observed population of patients (46,2±13,23). More kidney transplantation was performed in men in comparison with women. However, no difference was observed in distribution of donors according to the gender in all forms of transplantation (3:1 in favor of men). Early complications during the first year after transplantation were cumulative present in 29,5% of patients, AR in 15,9% of patients, DGF in 11,3%, CMV infection in 11,3% of patients, ARI in 6,8% of patients. The delayed graft function is more present in cadaveric and living unrelated transplantation (possible causes longer duration of dialysis before the transplantation and many hepatitis positive patients, older age, HLA-mismatching), while AR is almost equal in living related and living unrelated transplantation (possible causes HLA-mismatching and early not usage of MMF). In estimation of graft survival, serum creatinin <170 μmol/l, proteinuria less then 0,5 g/d and stable clinical condition, were taken as parametars of satisfying graft function (2). In observed population of patients proper functional graft at the end of the first year was present in 87,5% of patients. In the study of Mc Laren with associates one year graft survival is 93,0% (3). Based on UNOS (United Network for Organ Sharing) data register 1996-2001, Gjertson says that one year graft survival in living related transplantation is 94,0%, and that smaller centers (< or = 100 grafts) have rang of one year survival 87-100% (4). Hariharan with his associates confirmed that one year graft survival from living donors increased from 88,8% in 1988 to 93,5% u 1996, and cadaveric grafts from 75,7 to 87,7% (5). One year outcome of grafts in our patients is much better in the group of living related transplantation (91,66%) than in the group of all observed patients (87,5%). Multiple logistic regressive analysis confirmed that 5 factors influence the appearance of graft insufficiency within the first year, and those are AR (p=0,003), DGF (p=0,002), low HLA matching (p<0,001), donors older than 50 years (p<0,001) and no usage of MMF in immunosuppression (p=0,014). Significant connection of AR with bad graft outcome was proven in the study of Toki and his associates (2). Strongly connnection of graft survival with DGF or epizodes of AR was found also by Gjertson in his study about living kidney transplantation (4). The most of the authors recognize donors age as an independent risk factor of graft survival (6,7). Spanish authors found significantly higher values of creatinin and proteinuria on 3rd and 12th post-transplant month where donors were older then 60 (8). They also confirm that the donors age had significant effect on graft survival and patients survival, due to more often appearance of DGF. Similar to our results, Pascual and his associates confirmed that the donor older than 50 years is connected to worse graft outcome (9). Same authors highlight positive effect of MMf on one year survival, as well as the 3 year survival, especially in combination with tacrolimus (91,0%). Five years of graft survival in our population of patients is 80,0%, and 10 years survival 75,0%. Recurrent kidney diseases are the main cause of graft loss in 5 years of monitoring and CAN in 10 years of monitoring. In 5 years European multicentric study, which compared the effects of tacrolimus with original formulation of cyclosporin, 5 years graft survival was 67,9%, thus 65,9% (10). Serum creatinin > 130 μmol/l in 6th and 12th month after transplantation and changes in serum creatinin > 42,75 μmol/l between 6th and 12th month, were related with the declining of 5 years graft survival. Mortality of our monitored patients is 6,8% and refer to comorbidity conditions (cerebrovascular insult, cirrhosis hepatis, Alzheimer) with median of survival of 16,7 years. Group of Spanish authors registered mortality of 8,9% after the first transplantation year and the most often cause of death were cardiovascular diseases, malignicy and infectious diseases (11). Similar data were previously published by other authors (12, 13). Post-transplant aterogenic factors are traditional risk factors (14,15). Post-transplant diabetes mellitus (PTDM), which is considered to be the consequence of reduced secretion of insulin and/or increase of insulin resistence (16), increases the risk of graft loss and is related with the increase of cardiovacular morbidity and mortality (17). The incidence of PTDM is between 2-50% (18), so we can say that the percentage presency of PTDM in population of our patients (9%) is satisfying..

Conclusion

- Renal transplantation is successful treatment option of chronic renal failure with a high percentage of survival of patients and long term survival of graft.
- Small number of our patients received kadaveric kidney.
- Factors that can interfere with graft survival are AR, DGF, donor older than 50 years of age, HLA matching and absence of MMF in immunosuppressive regimen.
- The most common causes of graft loss are recurrent kidney diseases, CAN and lethal outcome with functional graft

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