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Recipient Related Prognostic Factors for Graft Survival after Kidney Transplantation. A Single Center Experience

Alina ELEC [1], Horaţiu COLOSI [2,*], and Mihai LUCAN [1]

[1] Clinical Institute of Urology and Renal Transplantation, 4-6 Clinicilor Street, Cluj-Napoca, Romania.
[2] Medical Informatics Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, 6 Louis Pasteur Street, Cluj-Napoca, Romania.
E-mails: alina.elec@yahoo.com; hcolosi@umfcluj.ro; mihailucan@renaltransplant.ro

* Author to whom correspondence should be addressed; Tel.: +40264431697; Fax: +40264593847

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Abstract
Background and Aim. Advanced chronic kidney disease (CKD) severely impairs life expectancy and quality of life in affected patients. Considering its benefits, renal transplantation currently represents the optimal treatment solution for end stage kidney disease patients. Pre-transplant assessment aims to maximize the graft and patient survival by identifying potential factors influencing the post-transplant outcome. The aim of this study has been to analyze recipient related prognostic factors bearing an impact on graft survival.
Material and Methods. We analyzed the graft outcomes of 426 renal transplantations performed at the Clinical Institute of Urology and Renal Transplantation of Cluj-Napoca, between January 2004 and December 2008. Variables related to recipient and to potential donor/recipient prognostic factors were studied using univariate and multivariate analysis.
Results. Graft survivals at 1, 3, 5 and 7 years were 94.01%, 88.37%, 82.51% and 78.10%, respectively. Chronic rejection (41.11%) and death with a functioning graft (18.88%) were the main causes of graft loss. In uni and multivariate analysis the recipient related variables found to influence the renal graft outcome were: peritoneal dialysis, pre transplant residual diuresis, grade I hypertension, severe iliac vessel atheromatosis, ischemic heart disease, stroke history, dyslipidemia and denutrition. The worst graft outcomes have been found for recipients on peritoneal dialysis, with anuria, hypotension, severe iliac atheromatosis, ischemic heart disease, stroke history, dyslipidemia and a poor nutritional status.
Conclusion. The type of dialysis, the pre transplant residual diuresis, recipient arterial blood pressure, iliac vessel atheromatosis, ischemic heart disease, stroke history, dyslipidemia and denutrition significantly influence graft survival.

Keywords: Kidney transplantation; Graft survival; Prognostic factors; Renal graft recipient

Introduction

The prevalence of chronic kidney disease (CKD) in Romania lies at around 7% of the general population [1]. The treatment options for these patients are dialysis or kidney transplantation. Despite improvements in technology, dialysis is a poor substitute for normal renal function.

Renal transplantation exhibits numerous benefits such as: improved patient survival rate to 87% vs 30% for dialyzed patients at 5 years following the start of treatment, correction of CKD induced metabolic anomalies such as uremia, vitamin D and mineral metabolism, anemia, improved the quality of life by no machine dependency, return to full time employment, improved exercise

capacity and sexual function and, except for the first year, renal transplantation implies lower costs than dialysis [2,3]. Thus, it currently represents the optimal treatment solution for end stage kidney disease patients [2]. However, there is little evidence to suggest how and which CKD patients should be selected to have maximum benefit from kidney transplantation [2] and prognosis of renal failure remains difficult at the individual level [4].

Pretransplant assessment needs to evaluate medical eligibility for transplantation, particularly the evaluation of prognostically important cardiovascular diseases, to ensure that a renal transplant is surgically, urologically and immunologically possible, to identify necessary pre transplant medical or surgical interventions, to determine and inform the patient about the short and long term risks and benefits [2]. Pretransplant assessment aims to maximize the graft and patient survival by identifying the potential factors influencing the outcome.

The aim of this study has been to investigate the above mentioned factors, as well as other recipient related prognostic factors bearing a potential impact on renal graft survival.

Materials and Methods

Target Population, Sampling And Investigated Variables

From the targeted population of kidney transplanted patients, we studied a total of 426 patients, representing all patients with renal transplantation (from both living and deceased donors) performed between January 2004 and December 2008 in Cluj-Napoca, at the Clinical Institute of Urology and Renal Transplantation.

The study was conducted prospectively, as an observational study of graft survival. The follow up period ended in December 2011, thus, the minimum follow-up was 3 years.

Graft survival time was defined as the time between the date of transplantation and the date of graft failure. Graft failure was defined as one of the following events: return to dialysis, retransplantation or death with functioning graft. The graft survival was evaluated at different moments of the follow up: week 1 (W1), month 1 (M1), month 3 (M3), month 6 (M6), year 1 (Y1), year 3 (Y3), year 5 (Y5), year 7 (Y7), and last visit (LV). The graft function was evaluated at each before mentioned moment by serum creatinine level (mg/dl) and estimated glomerular filtration rate (GFR) (ml/min/1.73m^2) computed according to the 4 parameters Modified Diet in Renal Disease formula (MDRD4) which estimates GFR using serum creatinine, age, race, and gender [5].

The following variables related to the recipient have been investigated: age (years), gender, body mass index (BMI), ABO blood group, panel reactive antibody percentage (PRA), time on the waiting list (months), primary renal disease, pre transplant dialysis modality and duration (months), dialysis related complications, cardiovascular factors (high arterial blood pressure following the JNC 7 classification, ischemic cardiopathy, left ventricular hypertrophy, use of antihypertensive drugs, iliac vessels atheromathosis, stroke), diabetes before transplantation, dyslipidemia, denutrition, hepatitis B or C virus infection, cytomegalovirus (CMV) serological status, pre operative urinary tract infection (UTI), and transplanted side.

In order to investigate potential donor/recipient relationships, the following variables have also been studied: donor/recipient age ratio, gender mismatch, BMI ratio, ABO mismatch (all grafts were ABO compatible but one), HLA mismatch, CMV mismatch (R+/D+, R+/D-, R-/D+, R-/D-).

All patients had a negative complement-dependent cytotoxicity (CDC) test and/or ELISA crossmatch before transplantation. Antilymphocyte antibodies were used as induction therapy. For maintenance of immunosupression the following medications have been used: steroids, anticalcineurine inhibitors (mainly tacrolimus, few of them cyclosporine) and mycophenolate mophetil or mycophenolic acide. All patients received standard antifungal, antibacterial and cytomegalovirus prophylaxis.

Statistical Analysis

Quantitative variables have been described using mean values, standard deviations (SD), as well as their range. Categorical variables have been described using absolute and relative frequencies as well as the 95% confidence intervals (95% CI) of the latter.

Graft survival has been investigated using the Kaplan-Meier method. Statistical univariate and multivariate analyses were performed using SPSS 16.0. Hazard ratios (HR) and their 95% CI have been computed for the investigated prognostic factors.

In all cases, the statistical significance level has been considered at $\alpha=0.05$.

Results

In the studied sample, 303 patients (71.12%) received a graft from a living donor (154 patients, 36.15% from living related donors, 149 patients 34.97% from living unrelated donors) and 123 patients (28.87%) from a deceased standard criteria donor. Graft survival at 1, 3, 5 and 7 years follow up were 94.01%, 88.37%, 82.51%, 78.10%, respectively (figure 1). Ninety grafts (21.12%) were lost during the follow up. The main causes of graft loss were chronic rejection (41.11%), death with a functioning graft (18.88%), acute rejection (13.33%), recurrence of the primary renal disease (10%), graft thrombosis (5.55%), infection (5.55%), calcineurin inhibitor (CNI) toxicity (4.44%) and polyoma virus nephropathy (1.11%).

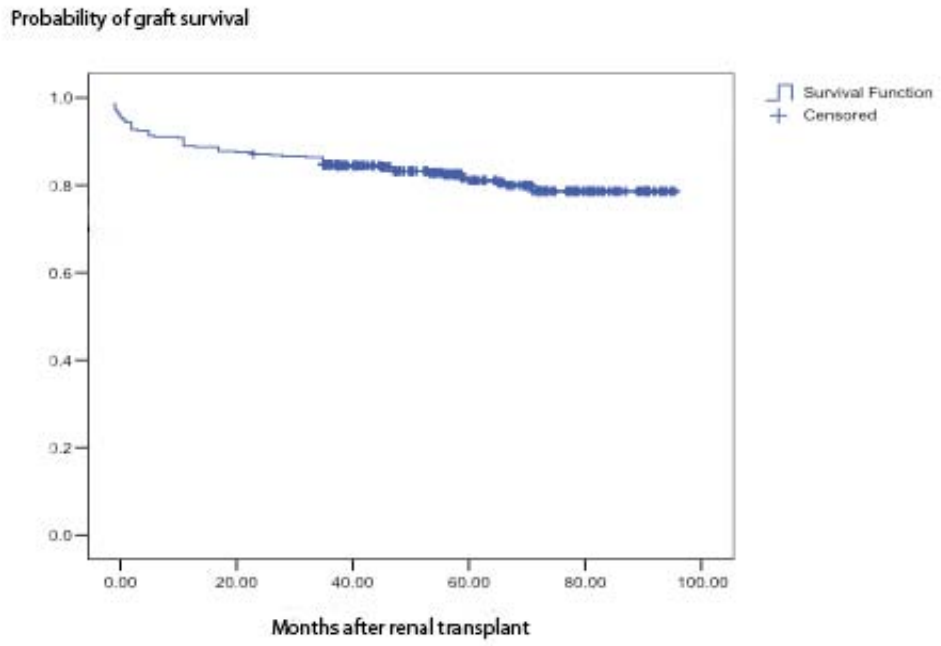

Figure 1. Graft survival function in the studied sample

The main descriptive statistics found for the studied sample are presented in tables 1 and 2.

Results of univariate analysis regarding predictors of graft survival are presented in tables 3 and 4.

Table 1. Recipient characteristics

Predictors	Mean ± SD or n	Range or % ± 95% CI
Age (years)	36.97 ± 12.83	3-65
Gender M/F	236/190	55.4 / 44.6 ± 4.72
Body mass index (BMI)	23.84 ± 8.66	14.10-176
PRA I	128	30 ± 4.35
PRA<10%	91	21.4 ± 3.89
PRA 10-50%	28	6.6 ± 2.36
PRA >50%	9	2.0 ± 1.33
PRA II	128	30 ± 4.35
PRA<10%	105	24.6 ± 4.09
PRA 10-50%	17	4.0 ± 1.86
PRA >50%	6	1.4 ± 1.12
Time on waiting list (months)	9.80 ±11.14	0-65
Primary renal disease	426	100 ± 0
Glomerular disease	255	59.9 ± 4.65
Tubulointerstitial disease	105	24.6 ± 4.09
Cystic disease	32	7.5 ± 2.5
Vascular disease	15	3.5 ± 1.75
Diabetes	12	2.8 ± 1.57
Other/hereditary disease	7	1.6 ± 1.19
Risk of recurrence	426	100 ± 0
Catastrophically recurrent renal disease	5	1.2 ± 1.03
Sistemic disease	34	8.0 ± 2.58
Primary glomerulonephritis and Alport	229	53.8 ± 4.73
No recurrent renal disease	158	37.1 ± 4.59
Type of dialysis	426	100 ± 0
Hemodialysis (HD)	315	73.94 ± 4.17
Peritoneal dialysis (DP)	61	14.31 ± 3.33
Pre dialysis	50	11.73 ± 3.06
Time on dialysis (months)	30.17 ± 33.79	0-216
Pre transplant diuresis	426	100 ± 0
Yes (>200ml)	268	62.9 ± 4.59
No (<200ml)	158	37.1 ± 4.59
Complications of dialysis	426	100 ± 0
Mineral bone disease	101	23.7 ± 4.04
Anemia	81	19.2 ± 3.74
Dialysis access failure	56	13.1 ± 3.2
Uremic neuropathy	15	3.52 ± 1.75
None	172	40.4 ± 4.66
Recipient arterial blood pressure (BP)	426	100 ± 0
Normal (BP→120/80mmHg)	63	14.8 ± 3.37
Prehypertension (BP →139/89 mmHg)	125	29.3 ± 4.32
Hypertension gr I(BP →159/99mmHg)	156	36.6 ± 4.57
Hypertension gr II (BP>/=160/100mmHg)	61	14.3 ± 3.32
Hypotension (BP<110/60mmHg)	21	4.9 ± 2.05
Iliac vessels atheromatosis	426	100 ± 0
Mild	70	16.4 ± 3.52
Moderate	77	18.1 ± 3.66
Severe	33	7.7 ± 2.53
Absent	246	57.7 ± 4.69

Table 1. (*continuation*) Recipient characteristics

Predictors	Mean ± SD or n	Range or % ± 95% CI
Ischemic heart disease	426	100
Yes	90	21.1 ± 3.87
No	336	78.9 ± 3.87
Stroke	425	99.7 ± 0.52
Yes	14	3.3 ± 1.7
No	411	96.5 ± 1.75
Left ventricular hypertrophy (LVT)	425	99.7 ± 0.52
Yes	101	23.8 ± 4.04
No	324	76.2 ± 4.04
Antihypertensive treatment	426	100 ± 0
With calcium channel blockers	258	60.6 ± 4.64
Without calcium channel blockers	68	16.0 ± 3.48
None	100	23.5 ± 4.03
Diabetes mellitus	426	100 ± 0
Yes	21	4.9 ± 2.05
No	405	95.1 ± 2.05
Dyslipidemia	426	100 ± 0
Yes	167	39.2 ± 4.64
No	259	60.8 ± 4.64
Denutrition	426	100 ± 0
Yes	38	8.9 ± 2.7
No	388	91.1 ± 2.7
Hepatitis B virus infection (VHB)	426	100 ± 0
Positive	33	7.7 ± 2.53
Negative	383	89.9 ± 2.86
Old infection	10	2.3 ± 1.42
Hepatitis C virus infection (VHC)	426	100 ± 0
Positive	60	14.1 ± 3.3
Negative	366	85.9 ± 3.3
Cytomegalovirus (CMV) Ig G	426	100 ± 0
Positive	407	95.5 ± 1.97
Negative	19	4.5 ± 1.97
Urinary tract infection (ITU)	426	100 ± 0
Yes	53	12.4 ± 3.13
No	373	87.6 ± 3.13
Transplanted side	425	99.7 ± 0.52
Right	257	60.3 ± 4.65
Left	168	39.4 ± 4.64

In univariate analysis the following recipient related variables significantly ($p<0.05$) influenced the renal graft outcome: the type of dialysis, the pre-transplant residual diuresis, recipient arterial blood pressure, iliac vessel atheromatosis, ischemic heart disease, the presence of stroke in the patient's medical history, dyslipidemia and denutrition.

The recipient's anthropometric parameters (age, gender and BMI), the time spent on dialysis or the time on the waiting list, primary renal disease, relapse risk, dialysis complications, the presence of diabetes or preexisting hepatitis B or C virus infection, immunizations, CMV status, urinary tract infections (UTI) and the transplanted side did not influence the graft outcome ($p>0.1$).

Results of multivariate analysis regarding predictors of graft survival are presented in Table 5.

Table 2. Donor/recipient relationship characteristics

Predictors	Mean ± SD or n	Range or % ± 95% CI
Age ratio *(donor/recipient)*	1.32 ± 0.78	0.19-10.33
BMI ratio *(donor/recipient)*	1.09 ± 0.24	0.50-2.31
ABO mismatch	425	99.7 ± 0.52
Identical ABO group	294	69.0 ± 4.39
Compatible ABO group	131	30.8 ± 4.38
Gender ratio (recipient-donor)	425	99.7 ± 0.52
F←F	86	20.2 ± 3.81
F←M	105	24.6 ± 4.09
M←F	109	25.6 ± 4.14
M←M	125	29.3 ± 4.32
Mismatch	425	99.7 ± 0.52
0	5	1.2 ± 1.03
1	6	1.4 ± 1.12
2	17	4.0 ± 1.86
3	118	27.7 ± 4.25
4	109	25.6 ± 4.14
5	117	27.5 ± 4.24
6	53	12.4 ± 3.13
CMV ratio (recipient/donor)	426	100 ± 0
+/+	404	94.8 ± 2.11
+/-	3	0.7 ± 0.79
-/+	18	4.2 ± 1.9
-/-	1	0.2 ± 0.42

Table 4. Predictors of graft survival related to the recipient-donor relationship

Predictors	df	Log rank (χ^2)	Hazard ratio (HR)	HR 95% CI	p Value
Age ratio *(donor/recipient)*	1	-	1.15	0.93-1.41	0.181
BMI ratio *(donor/recipient)*	1	-	0.61	0.24-1.55	0.303
ABO mismatch	1	2.56	-	-	0.109
Gender ratio	3	6.43	-	-	0.092
Mismatch	6	8.44	-	-	0.207
CMV ratio	1	0.83	-	-	0.362

* significant at $p<0.05$; ** significant at $p<0.01$; [a] borderline significance; df – degrees of freedom

Multivariate Cox regression analysis showed that the significant factors contributing to graft survival were: type of dialysis (peritoneal dialysis HR 4.58 vs hemodialysis HR 3.71 and preemtive patients HR 0.27), pre-transplant diuresis (absent HR 1.83), grade I hypertension following JNC7 classification (HR 0.39) vs hypotension (HR 1.37), ischemic heart disease (presence HR 1.99). A tendency towards statistical significance has also been observed for grade II arterial hypertension (p=0.086), severe iliac atheromatosis (p=0.089) and denutrition (p=0.098).

Table 3. Predictors of graft survival related to recipients

Predictors	df	Log rank (χ^2)	Hazard ratio (HR)	HR 95% CI	p Value
Age	1	-	0.99	0.97-1.01	0.657
Gender	1	1.01	-	-	0.313
BMI	1	-	1.00	0.98-1.02	0.834
PRA I	2	0.28	-	-	0.869
PRA II	2	0.60	-	-	0.739
Time on the waiting list	1	-	1.00	0.98-1.02	0.911
Primary renal disease	5	3.21	-	-	0.667
Risk of recurrence	3	0.28	-	-	0.963
Type of dialysis	2	6.65	-	-	0.036*
HD vs Pre dialysis	1	5.70	-	-	0.016*
DP vs Pre dialysis	1	6.98	-	-	0.008**
Time on dialysis	1	-	1.00	0.99-1.01	0.110
Pre transplant diuresis	1	12.83	-	-	0.000**
Complications of dialysis	4	1.34	-	-	0.854
Recipient arterial blood pressure	4	10.98	-	-	0.027*
normotension vs HTA gr I	1	3.99	-	-	0.046*
Prehypertension vs hypotension	1	5.19	-	-	0.023*
HTA gr I vs hypotension	1	8.67	-	-	0.003**
HTA gr II vs hypotension	1	5.56	-	-	0.018*
Iliac vessel atheromatosis	3	15.60	-	-	0.001**
mild vs severe	1	7.85	-	-	0.005**
moderate vs absent	1	4.03	-	-	0.045*
severe vs absent	1	13.56	-	-	0.000**
Ischemic heart disease	1	17.80	-	-	0.000**
Stroke	1	6.37	-	-	0.012*
LVH	1	0.35	-	-	0.553
Antihypertensive treatment	2	3.08	-	-	0.214
Diabetes	1	1.28	-	-	0.258
Dyslipidemia	1	4.58	-	-	0.032*
Denutrition	1	3.69	-	-	0.054[a]
VHB	2	1.31	-	-	0.518
VHC	1	1.16	-	-	0.281
CMV Ig G	1	1.96	-	-	0.161
Urinary tract infection	1	0.83	-	-	0.360
Transplanted side right/left	1	0.03	-	-	0.958

* significant at $p<0.05$; ** significant at $p<0.01$; [a] borderline significance; df – degrees of freedom

Table 5. Multivariate analysis of factors influencing graft outcome

Predictors	df	HR	HR 95% CI	p Value
Type of dialysis				
Hemodialysis (HD)	1	3.71	1.17-11.83	0.026
Peritoneal dialysis (PD)	1	4.58	1.31-16.09	0.017
Pre dialysis	1	0.27	0.08-0.86	0.026
Pre transplant diuresis				
Yes (>200ml)	1	0.55	0.35-0.88	0.011
No (<200ml)	1	1.83	1.16-2.90	0.010
Recipient arterial blood pressure				
Normotension TA→120/80	1	0.72	0.30-1.75	0.479
Prehypertension →139/89	1	0.56	0.25-1.29	0.172
HTA gr I →159/99	1	0.39	0.17-.89	0.025
HTA gr II >/=160/100	1	0.43	0.16-1.13	0.086
Hypotension TA<110/60	1	1.37	0.57-3.31	0.479
Iliac vessel atheromatosis				
mild	1	0.74	0.35-1.55	0.425
moderate	1	1.21	0.67-2.17	0.531
severe	1	1.87	0.91-3.86	0.089
absent	1	1.23	0.60-2.53	0.565
Ischemic heart disease				
Yes	1	1.99	1.18-3.34	0.010
No	1	0.48	0.29-0.81	0.006
Stroke				
Yes	1	1.46	0.58-3.65	0.420
No	1	0.69	0.27-1.72	0.420
Dyslipidemia				
Yes	1	1.41	0.89-2.24	0.148
No	1	0.71	0.45-1.13	0.148
Denutrition				
Yes	1	1.74	0.90-3.34	0.098
No	1	0.58	0.30-1.11	0.098

df – degrees of freedom

Discussion

The aim of our study has been reached by univariate and multivariate analysis of prognostic factors with a potential influence on graft survival.

Due to patient follow-up periods varying between a maximum of 8 years and a minimum of 3 years, a limitation of our study has been the relatively high number of censored observations, especially among later included patients. However, this 3 to 8 year follow-up of all 426 patients that have been transplanted over a period of 5 years in the targeted renal transplantation center succeeded in raising 90 complete observations, which in turn allowed us to outline the following results regarding prognostic factors of renal graft survival.

Recipient age. The recipients in our study were relatively young (table 1). In univariate analysis no significant link was found between recipient age and graft survival or between donor/recipient age ratio (table 2) and graft survival. As stated in literature, recipient age alone can not be considered a barrier to transplantation if medical and surgical assessment is satisfactory [2]. However, extreme ages (<5 and >65 years) are considered high risk categories for graft failure due to a higher

immunological risk and potential surgical problems in the first case and to the risk of death with a functioning graft in the second [2].

Gender. Female donor to male recipient is reported in literature to have the worst results in graft survival by the reduced nephron mass of the graft [6]. All four possible donor-recipient combinations (female to female, male to female, female to male, male to male) were analyzed in our study, but no significance in graft survival for any of them has been found.

Body mass index (BMI). Mild obesity (BMI>25) before transplantation has a negative impact on long-term renal graft and patient survival [7]. The average BMI in our study was in the normal range (table 1) and the donor BMI was close to the recipient BMI (table 2), potentially explaining the fact that the BMI was not found to be a risk factor for graft failure.

Blood group, sensitization and time on the waiting list. The median time on the waiting list was less than a year (table 1). The short waiting time was correlated to the fact that most of the transplants were performed from living donors (71.12%) so the surgery could be conveniently scheduled. Factors reported in literature to be associated with longer waiting times, including age > 50 years, blood group O and high peak panel reactive antibody (PRA) levels >50% [8] were not common in our data: few recipients were > 50 years old (17.13%) or had a PRA> 50% (table 1). Blood groups A+ and O+ were the two most frequent blood types having almost similar proportions of graft survival (84.6% respective 86.4%).

Primary renal disease and relapse risk. Renal diseases with a potential relapse on the graft have been reported to be associated with a worse outcome in graft survival. Data on patterns of recurrence, risk factors for recurrence and the implications for patient and graft outcomes after recurrence allow rational decisions regarding who should receive a transplant, when, how many times, and from what donor source [9]. The most common causes of end stage renal disease (ESRD) in our study were glomerular (59.9%). We divided primary renal disease into four categories, according to the type of nephropathy and to the relapse risk (catastrophic relapse risk, systemic disease, primary glomerulonephritis and renal disease with no recurrence risk). Most of the primary renal diseases in our sample corresponded to intermediate/low relapse risk (primary glomerulonephritis (53.8%) or no recurrence risk diseases (37.1%). No significant difference in graft survival was found concerning the type of primary renal disease ($p=0.667$) or the stratified relapse risk ($p=0.963$).

Type of dialysis. Comparing different types of treatment for ESRD patients undergoing kidney transplantation, we noticed that preemptive patients had a superior graft survival (94%) over dialysed patients (78% HD and 74.5% PD patients). The shortage of cadaveric donors or the absence of a willing living donor made the preemtive transplantation less frequent in practice (only 11.73 % of the recipients were on pre dialysis at the transplant moment). In other reports [10] neither HD nor PD affected the outcome of renal transplantation. In our study, a small difference in graft survival in favor of hemodialysis (78%, HR 3.71) vs peritoneal dialysis (74.5%, HR 4.58) was observed. The cardiovascular associated morbidities of the peritoneal dialyzed patients may explain these results.

Time on dialysis and dialysis complications. The longer patients receive dialysis, the more dialysis related complications can occur, the greater the risk for post transplantation morbidity, mortality and graft loss [11]. In our study, mean dialysis duration was less than 3 years (30 months), with a range between 0-216 months. The two most frequent dialysis complications (hyperparathyroidism and anemia) were present in 23.7% respectively 19.2% of the studied patients, with no impact on graft survival ($p=0.854$).

Pre transplant recipient diuresis >200 ml/24 hours was associated with a higher graft survival (85.8%) vs only 71.5% in patients with <200ml/24 hours diuresis ($p<0.001$). This result may be explained by the fact that anuria means a small, nonfunctional bladder with increased risk of posttransplant urinary fistula and graft dysfunction.

Recipient arterial blood pressure. Worse outcomes were found when the BP was low (61.9% in hypotension, 74.6% in normotension) and improved with moderate increase in BP (79.8% in prehypertension, 84.5% in grade I HTA patients). This result confirms that it is better to have a slightly increased arterial blood pressure (to be able to obtain a normal renal graft blood flow) rather than a lower BP, which predisposes to hypo-perfusion and delayed graft function. However, an increase in BP >160/100 mmHg seemed to be no longer an advantage.

Ischemic heart disease was associated with a decreased rate of graft survival (65.9% if present vs 84.7% in its absence). Thus, effective prevention and management of cardiovascular disease in kidney transplant recipients allows increasing patient longevity and quality of life, in addition to improving graft survival. The high prevalence of cardiovascular complications in kidney transplant recipients can be explained by cardiovascular risk factors present before transplantation, in addition to the development of new risk factors and worsening of preexisting risk factors after transplantation [12].

Iliac vessel atheromatosis. The best outcome is obtained when the patient has mild or no atheromatosis at the iliac vessel level. Traditional independent risk factors for atherosclerotic cardiovascular disease include cigarette smoking, hypertension, dyslipidemia, male gender, diabetes mellitus, and advancing age. Kidney disease introduce additional cardiovascular risks that typically do not operate in the general population such as abnormal mineral metabolism and hyperparathyroidism responsible of arterial medial calcification, oxidant stress and inflammation, hyperhomocysteinemia [2,12]. Optimal presurgical evaluation of potential kidney recipients is necessary for successful renal transplantation. In cases of severe atherosclerotic disease in the distal abdominal aorta and pelvic vessels, the surgeon has the options of disqualifying the potential recipient, abandoning the procedure, performing orthotopic renal transplantation, or reconstructing the pelvic vessels [13]. An increasing trend of HR with the severity of iliac vessel atheromatosis has been found in our study as well, although in our multivariate analysis the level of statistical significance has only been approached for severe iliac vessel atheromatosis.

Stroke. We found a significant decrease in renal graft survival in patients who had a stroke in their medical history (57.1% in patients with stroke history vs 81.5% in patients with no history of stroke).

Diabetes. In literature, type 1 and 2 diabetic patients presented higher survival rates after transplant in comparison to the dialysis therapy, although the prevalence of cardiovascular events and infectious complications remain higher than in the general population [14]. Kidney recipients with DM had worse patient and graft survival rates compared to no diabetic patients. These findings suggested that kidney transplant patients presenting with any type of DM should be more closely followed [15]. In our study, only 21 graft recipients (4.9%) had diabetes in their medical history, and no significant influence of DM in total graft survival could be observed in these patients ($p=0.258$).

Dyslipidemia. Dyslipidemia has been found in literature to be a significant risk factor for the development of atherosclerotic disease and of chronic allograft rejection [17]. While patients with chronic kidney disease (CKD) are at higher risk for cardiovascular disease (CVD) than patients in the general population, dyslipidemia represents a potentially modifiable risk factor for CVD in patients with CKD. PD patients have a somewhat more atherogenic lipid panel than hemodialysis patients. This may be due to the near universal use of glucose-containing peritoneal dialysate and subsequent absorption of glucose across the peritoneal membrane [16]. In our study, the presence of dyslipidemia in renal graft recipients was associated with a lower graft survival (75.4% vs. 83.7 % in its absence, $p=0.032$).

Patient denutrition has resulted from our study to be potentially associated with graft failure (survival rate 68.4% in its presence vs. 81.7% in its absence, however with only a borderline tendency towards statistical significance of $p=0.054$).

Hepatitis B or C virus infection. Hepatitis B virus (HBV) infection can adversely affect the clinical outcome of kidney transplantation. After the introduction of antiviral agents, better long-term outcomes of HBV-positive recipients have been obtained [18]. Other results published in literature showed that pretransplant minimal HCV infection had no detrimental effect on the short-term patient and graft survival but more complications have occurred so it was suggested that kidney transplant recipients with minimal HCV infection be monitored for severe systemic bacterial infections and new onset of posttransplant diabetes mellitus [19]. In our study, Hepatitis B and C virus infection was present in 10% respective 14.1% of the recipients. The presence of HBV or HCV infections did not decrease graft survival compared to non-infected recipients, during the follow-up period of our study.

Cytomegalovirus infection. Cytomegalovirus (CMV) is one of the most important infections in renal transplant recipients. Exposure to the virus, as indicated by the presence of detectable IgG anti-CMV antibodies in the plasma, increases with age in the general population and is present in more than two-thirds of donors and recipients prior to transplantation [2]. It is therefore common for the donor and/or recipient to be CMV-positive at the time of transplantation. The risk of developing CMV disease is based on donor and recipient CMV exposure and immunosuppression intensity [20]. All four recipient/donor possibilities (R+/D+, R+/D-, R-/D+, R-/D-) were analyzed in our study, but most of the cases were in recipient positive/donor positive category (94.8%) which meant a low/moderate risk of CMV disease (10-30%).

Urinary tract infection. Urinary tract infections (UTI) before transplantation were present in 12.4% of the studied cases. Univariate analysis showed no impact of UTI on graft survival. The major risk factors for UTI in the renal transplant recipient before transplantation include anatomic abnormalities of the native kidneys (such as vesicoureteral reflux, stones) and neurogenic bladder especially in diabetic patients. Nephrectomy before kidney transplantation in chronic renal parenchymal infection, renal stones, or obstructive uropathy with chronic infection can be useful in preventing serious infections after renal transplantation [13].

Transplanted side. More than half of our patients (60.3%) received the kidney in the right iliac fossa (the preferred side to place the kidney due to the more accessible right iliac vein). No significant difference in graft survival was found regarding the transplanted side (p=0.958).

Mismatch. When trying to match a donor to a recipient, avoidance of mismatches (MM) is used in preference to matching of HLA antigens. Transplants with 0-0-0 mismatch (MM) from living donors (LD) have superior graft survival to other LD transplants. No evidence of significant differences in outcomes between 1 haplotype matched grafts (1-1-1 MM, i.e. parent to child) and 2-2-2 MM LD grafts (i.e. unrelated LD transplants between spouses) was found in other studies [2]. In all cases, long term graft survival was at least as good as 0-0-0 MM deceased donor (DD) transplants [2]. In our study, the majority of recipients (93.2%) have been transplanted with 3 or more mismatches without a negative influence on graft survival. 303 patients, meaning 71.12%, received the graft from a living donor and only 123 patients (28.87%) received the graft from a deceased standard criteria donor, which explains the good outcome, despite multiple mismatches.

Conclusions

The type of dialysis, the amount of pre transplant residual diuresis, the arterial blood pressure of the recipient, iliac vessel atheromatosis, ischemic heart disease, stroke in the patient`s medical history, dyslipidemia and denutrition have been found to be recipient related variables significantly influencing graft survival.

The worst graft outcomes have been found in recipients on peritoneal dialysis, with anuria, hypotension, severe iliac atheromatosis, ischemic heart disease, stroke, dyslipidemia and poor nutrition status.

These factors should be carefully investigated and taken into consideration when selecting candidate patients for renal transplantation, in order to improve renal graft survival.

Conflict of Interest

The authors declare that they have no conflict of interest.

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