



## Kidney Transplant Recipients with Functioning Grafts for More than 15 Years

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### ABSTRACT

**Background.** Renal transplantation is the best renal replacement therapy because it significantly improves patient survival. The developments in transplantation and increasing number of patients with end-stage renal disease (ESRD) have unmasked long-term complications secondary to immunosuppressive drugs and chronic renal failure.

**Methods and Results.** Eighty-six renal transplant recipients with grafts that have functioned more than 15 years were included in the study. This cross-sectional retrospective analysis of demographic, clinical, and laboratory findings was conducted in 3 Turkish transplantation centers. The mean age was  $30.4 \pm 10.2$  years at the time of the transplantation. The mean time between the transplantation and the study was  $19.1 \pm 3.6$  years. At the time of the study, mean creatinine level was  $1.52 \pm 0.60$  mg/dL, 70.09% of the patients displayed glomerular filtration rates  $<60$  mL/min/1.73 m<sup>2</sup>. Urinary protein excretion was  $0.57 \pm 0.65$  g/d. Hypertension and hyperlipidemia were the most common comorbid diseases. Twelve patients had diabetes and 9 cardiovascular disease. Seventeen patients had been diagnosed with skin and 5 with non-skin cancer.

**Conclusions.** As the number of recipients with long-term functioning grafts increases, long-term complications become evident, particularly chronic renal failure. Survivors should be evaluated regularly and treated early for risk factors and complications to improve long-term graft and patient survival.

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**R**enal transplantation significantly improves the survival of patients with end-stage renal disease (ESRD). Developments in immunosuppressive therapy have decreased the rates of acute rejection episodes but not long-term graft survival. The increasing number of patients with ESRD will augment the number with long-term functioning allografts.<sup>1</sup> Unfortunately, these patients have risks of complications secondary to immunosuppression and chronic kidney disease (CKD). The aim of the present study was to evaluate the demographic features and long-term complications among transplant patients with grafts surviving more than 15 years.

### MATERIALS AND METHODS

This cross-sectional study was performed in 3 transplantation centers in Turkey, including recipients with grafts that had functioned more than 15 years. Each center reviewed patient records to collect retrospectively demographic, clinical, and laboratory data, including those at the time of the last visit. Graft function was evaluated by serum creatinine level and estimated creatinine

clearance calculated with the Modification of Diet in Renal Disease formula.<sup>2</sup> Urinary protein excretion was obtained as spot morning urine protein:creatinine ratios that were calculated by dividing the urinary protein by the urine creatinine concentration.

All comorbid conditions were recorded carefully by the researcher at each center. Patients having a blood pressure  $>140$  mm Hg systolic and 80 mm Hg diastolic or under antihypertensive therapy at the time of the last visit were defined to be hypertensive.

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The diagnosis of new-onset diabetes after transplantation (NODAT) was based on a fasting plasma glucose concentration of  $\geq 126$  mg/dL, repeated random blood glucose values  $\geq 200$  mg/dL, or the use of antidiabetic drugs.<sup>3</sup> Hyperlipidemia (HL) was defined as levels of low-density lipoprotein (LDL) cholesterol and triglyceride  $>100$  mg/dL and  $>200$  mg/dL, respectively or the use of antihyperlipidemic drugs.<sup>4</sup> Cardiovascular disease (CVD) was defined as coronary artery, cerebrovascular, and/or peripheral vascular disease. Other complications, such as a history of malignancy, chronic hepatitis, osteoporosis, and/or avascular necrosis (AVN), were recorded from the patients' charts. Medications prescribed on the last visit were also recorded.

Data were analyzed with the Statistical Package of Social Science, software, version 15.0, for Windows. Continuous variables were presented as mean  $\pm$  SD, categorical variables as number and percentage.

## RESULTS

Eighty-six patients were examined from 3 transplantation centers; 47 were male. The overall mean age at the time of the transplantation was  $30.4 \pm 10.2$  years. The mean time between the transplantation and the study was  $19.09 \pm 3.60$  years. The mean donor age was  $39.8 \pm 12.1$  years. The transplantation was from a living donor in 79.1% of recipients. The mean number of HLA mismatches was  $2.06 \pm 1.53$ . The primary immunosuppressive regimen consisted of corticosteroid (CS)/azathioprine (AZA;  $n = 3$ ), CS/cyclosporine (CsA) in 1, and CS/AZA/CsA in the other subjects. Eight patients received antithymocyte globulin or OKT3 as induction therapy. The acute rejection rate in the first year was 16.27%. At the time of the last visit, 36 patients were prescribed AZA/CsA and 11 mycophenolate mofetil/CsA, 11 a tacrolimus-based regimen, and 7 amantadine target of rapamycin inhibitor-based regimen.

The laboratory parameters recorded at the last visit are listed in Table 1. Mean creatinine level was  $1.52 \pm 0.60$  mg/dL. Estimated glomerular filtration rate (GFR) was  $51.38 \pm 17.92$  mL/min/1.73 m<sup>2</sup>, with 70.09% of subjects displaying a GFR  $<60$  mL/min/1.73 m<sup>2</sup>. Spot urine protein:creatinine ratio was  $0.57 \pm 0.65$ .

Hypertension (HT) was the most common comorbid disease, with a prevalence of 89.53% (Table 2). Mean

**Table 2. Comorbid Conditions of the Patients at the Time of the Study**

HT	89.53%
HL	80.23%
NODAT	13.95%
CVD	10.46%
Cancer	
Skin cancer	19.77%
Non-skin cancer	5.81%
Osteoporosis	22.09%
AVN	9.30%
Chronic HBV infection	6.98%
Chronic HCV infection	24.42%

Abbreviations: HT, hypertension; HL, hyperlipidemia; NODAT, New-onset diabetes after transplantation; CVD, cardiovascular disease; AVN, avascular necrosis; HBV, hepatitis B virus; HCV, hepatitis C virus.

systolic and diastolic blood pressures were  $132.18 \pm 18.0$  and  $82.65 \pm 10.71$  mm Hg, respectively. HL was observed in 80.23% of patients. Levels of LDL cholesterol and triglycerides were  $123.58 \pm 51.14$  mg/dL and  $142.70 \pm 78.24$  mg/dL, respectively. Triglyceride levels were  $>200$  mg/dL in 13 and LDL cholesterol  $>100$  mg/dL in 59 patients. Forty patients were prescribed antihyperlipidemic treatment. Twelve patients had diabetes and 9 cardiovascular disease. A total of 18 skin cancers were diagnosed in 17 patients (2 malignant melanomas, 4 Kaposi sarcomas, 8 squamous cell cancers, and 4 basal cell cancers) and 6 non-skin cancers in 5 patients (2 thyroid cancers, 2 renal cell cancers, 1 sarcoma, and 1 breast cancer). Osteoporosis was diagnosed in 22.09% of patients and avascular necrosis in 9.30%. There were chronic hepatitis B and C infections in 6.98% and 24.42% of subjects, respectively.

## DISCUSSION

Because renal transplantation is the best renal replacement treatment for patients with ESRD, it is mandatory to increase graft and patient survivals. Long-term graft survival is as important as short-term survival for recipients. The increase in the number of the transplanted patients and improvements in short-term kidney transplant survival have augmented the cohort of patients living with a functioning graft for years. These long-term survivors are exposed to the risk of long-term complications. The present study evaluated the demographic characteristics of patients with graft survival for more than 15 years and their long-term complications. Most recipients were middle-aged and had received the transplant from a living donor. The patients were followed for a mean of  $19.09 \pm 3.60$  years. Most patients displayed estimated GFR levels  $<60$  mL/min/1.73 m<sup>2</sup>. The most common complications were HT and HL. Skin and non-skin cancers were diagnosed in 17 and 5 patients, respectively.

In this study, the mean serum creatinine concentration was  $1.52 \pm 0.60$  mg/dL and estimated GFR,  $51.38 \pm 17.92$  mL/min/1.73 m<sup>2</sup>. Spot urine protein:creatinine ratio was  $0.57 \pm 0.65$ . Almost 70% of the patients displayed low GFR

**Table 1. Laboratory Findings of the Patients at the Time of the Study**

Urea (mg/dL)	$52.14 \pm 23.87$
Creatinine (mg/dL)	$1.52 \pm 0.60$
GFR (mL/min/1.73 m <sup>2</sup> )	$51.38 \pm 17.92$
Fasting glucose (mg/dL)	$94.05 \pm 21.35$
Uric acid (mg/dL)	$7.05 \pm 1.60$
Albumin (g/dL)	$4.24 \pm 0.37$
Hemoglobin (g/dL)	$12.63 \pm 1.83$
Total cholesterol (mg/dL)	$195.87 \pm 40.94$
Triglyceride (mg/dL)	$142.70 \pm 78.24$
LDL cholesterol (mg/dL)	$123.58 \pm 51.14$
HDL cholesterol (mg/dL)	$53.16 \pm 14.89$
Spot urine protein:creatinine ratio	$0.57 \pm 0.65$

Abbreviations: GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, Low-density lipoprotein.

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