Short-Term and Long-Term Outcomes of Kidney Transplantation in Diabetic and Nondiabetic Patients

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ABSTRACT

Introduction: The purpose of this study was to compare the short-term and long-term kidney transplant outcomes in diabetic and nondiabetic patients.

Materials and Methods: We studied all kidney recipients in Golestan hospital, Ahwaz, from 1995 to 2003. The patients were divided into two groups of diabetic and nondiabetic, and 1-year, 2-year, and 5-year survival rates of the patient and the kidney were evaluated. We also evaluated and compared the causes of death between these two groups.

Results: There were 50 diabetic patients with a mean age of 51 years, and 350 nondiabetic patients with the mean age of 29 years old (P = .03). One-year, 2-year, and 5-year graft survival rates were 90% versus 91.5%, 86% versus 89%, and 76% versus 83% in diabetic and nondiabetic patients, respectively (P = .19). The patient survival rates were 92% versus 93%, 88% versus 91%, and 76% versus 84% in diabetic and nondiabetic patients, respectively. The most common cause of death was myocardial infarction in diabetic patients (50%), and septicemia among the nondiabetic ones (50%). The most common cause of kidney allograft loss was patient's death (75%) in diabetic patients and kidney rejection (40%) in nondiabetics.

Conclusion: Long-term kidney transplantation results have been significantly improved comparing with other studies. Thus, kidney transplantation is recommended as the treatment of choice in diabetic patients with end-stage renal disease. However, a complete evaluation of cardiac problems for these patients is recommended before the surgery.

KEY WORDS: diabetes, nephropathy, kidney transplantation, kidney allograft survival

Introduction

The incidence rate of diabetic nephropathy, the most common cause of end-stage renal disease (ESRD) in most developed countries, is 30% to 35% in both types of diabetes mellitus (DM).[1,2] Although, it is more common in type 1 DM, because of the higher prevalence of type 2 DM in general population, the average age of diabetic patients with ESRD is approximately 60 years.[3]

End-stage renal disease is the cause of death among about 60% of diabetic patients[4]; but, they can benefit from kidney and pancreas transplantations. In the United States, 7.1%, 75.4%, and 17.5% of diabetic ESRD patients are under the treatment of peritoneal dialysis, hemodialysis, and kidney transplantation, respectively.[2] The patient and kidney allograft survival has improved during the recent years.[5] In a study in the United States, published in 1991, survival rates of patient and kidney allograft at 10 years were 40% and 32% in

diabetic patients, and 61% and 51% in nondiabetic patients, respectively.[6] In another study, the 10-year allograft survival rate in diabetic patients with matched HLA typing has been reported to be 62%, while it has been 89% in nondiabetic patients.[7] Also, it has been shown that 1-year survival rate of diabetic and nondiabetic patients are the same (90%), but the allograft survival is 10% less in diabetic patients.[8]

Overall, diabetic ESRD patients have significantly improved following kidney transplantation regarding the survival and quality of life, compared to those maintaining on dialysis.[9] However, diabetic patients have a poorer outcome when compared with nondiabetics, and a strenuous effort is warranted to improve kidney transplantation outcome in these patients. To take the first steps, we reviewed the short-term and long-term outcomes of diabetic and nondiabetic kidney recipients in our transplant center.

Materials and Methods

The records of all kidney transplant recipients in Golestan Hospital, Ahwaz, from 1995 to 2003, were reviewed to compare the outcomes in patients with and without diabetes. Patients with new-onset diabetes mellitus after kidney transplantation were excluded. All of the patients had been completely assessed for cardiovascular disorders. Electrocardiography, Echocardiography, stress test or thallium scan, and coronary arteries angiography had been performed in diabetic recipients preoperatively. Coronary artery bypass had been done, if necessary. Nondiabetic candidates had been examined by electrocardiography, chest radiography, and echocardiography, and other assessments would have been done in case of the presence of vascular involvement in other parts of the body or clinical evidence of ischemic heart disease.

All the patients were under triple immunosuppressive regimen of cyclosporine (4 mg/kg to 5 mg/kg), azathioprine (2 mg/kg) and prednisolone (12.5 mg). Since 2001, all patients received mycophenolate mofetil (cellcept) with the dose of 2 g instead of azathioprine. All diabetic patients (with types 1 or 2) were under the treatment with insulin. All of the patients were examined monthly in the first posttransplant year and every 2 months thereafter. Reviewing the patients' records, data including age, sex, history of diabetes mellitus, duration of diabetes before transplantation, type of diabetes, history of hemodialysis, donor type, graft loss and its cause, death and its cause, serum creatinine level, and follow-up duration were collected and analysed.

Statistical analysis of the data was performed using SPSS software (Statistical Package for the Social Sciences, version 11.5, SPSS Inc, Chicago, Ill, USA) and S-plus software (S-PLUS 7, Insightful Corporation, Seattle, USA). The chi-square test, Kaplan-Meier method, and log-rank test were performed for comparisons and analyses of survival. Graft loss (death-censored) was considered the graft survival endpoint, and patient's death of any cause was considered the patient survival endpoint. A P value less than 0.05 was considered significant.

Results

The mean follow-up of the patients was 17 ± 13.4 months in diabetic and 21.5 ± 19 months in nondiabetic patients ($P = .23$). Four hundred patients were assessed, of whom 50 were diabetic and 350 were nondiabetic.

In diabetic patients group, 35 (70%) were males and 15 (30%) were females. The mean age of them was 51.0 ± 15.2 years (range, 16 to 63 years). Diabetes had been diagnosed for a mean duration of 17 ± 2.3 years (range, 12 to 24 years). Diabetic patients had been treated by hemodialysis for a mean 10 ± 3.3 conservative months (range, 4 to 18 months) before transplantation. Twenty patients had type 1 diabetes, and 30 had type 2 diabetes.

In the group of nondiabetic patients, 232 (66.3%) were males and 118 (33.7%) were females. The mean age of these patients was 29 ± 2.3 years (range, 6 to 67 years), which was significantly lower than the age of diabetic patients ($P = .03$), and they had been treated by conservative hemodialysis for 12 ± 7.5 months (range, 5 to 19 months).

Kidney donors were alive in both groups. Ten kidney donors (20%) in diabetic group and 109 (31%) in the nondiabetic group were living-related and others were living-unrelated ($P = .002$)

One-year graft survival rate was 90% and 91.5% in diabetic and nondiabetic patients, respectively, and the 2-year survival rate was 86% and 89%, respectively ($P = .50$ and $P = .37$). The 5-year graft survival rate was 76% and 83% in diabetic and nondiabetic groups ($P = .19$).

The 1-, 2-, and 5-year patient survival rates for diabetic kidney recipients were 92%, 88%, and 76%, respectively, while they were 93%, 91%, and 84% for nondiabetic patients (P = .14; P = .09; P = .08).

Of diabetic patients, 4 (8%) and 2 (4%) died during the first and second posttransplant years, and totally, 12 (24%) died within 5 years after transplantation. Causes of death among these patients included myocardial infarction (in 6 patients), septicemia (in 4 patients), lung Kaposi's sarcoma (in 1 patient), and liver failure (in 1 patient). Of nondiabetic patients, 25 (7.1%) and 6 (1.7%) died during the first and second posttransplant years, and totally, 56 (16%) died within 5 years after transplantation. Causes of death were septicemia (in 28 patients), myocardial infarction (in 14 patients), liver failure (in 6 patients), malignancies (in 4 patients), and other diseases (in 4 patients).

Of diabetic patients, 5 lost their kidney allograft function during the first year, 2 during the second year, and 12 within the first five years. In 9 out of 12 mortality cases in this group, the patients had a normal kidney function at death, while allograft renal artery thrombosis, acute kidney rejection, and extensive ureteral necrosis had developed at death in 3 patients (25%).

Of nondiabetic patients, 30 lost their kidney function within the first year, 10 within the second year, and 60 within the first 5 years. In 14 (25%) mortality cases, the patients died with a normal kidney function, while in 42 (75%), acute kidney rejection (in 22 patients), allograft renal artery thrombosis (in 11 patients), urine leakage (3 patients), recurrence of primary disease in transplanted kidney (in 3 patients), and other involvements of kidney (in 2 patients) had developed at death.

The remainder in both groups had a normal kidney function, 90% of whom had a serum creatinine level lower than 2 mg/dL, and 10% had a creatinine level higher than 2 mg/dL but did not require dialysis.

Discussion

Our diabetic kidney recipients had comparable patient and graft survivals with nondiabetic patients, being over 75% at 5 years.

Life expectancy of diabetic patients on hemodialysis has improved during recent years. The 5-year survival rate of these patients in Germany has been reported less than 10% for type 2 diabetes mellitus in early 1990s,[10] but it has been reported to be 30% to 50% in eastern Asian countries during the recent years.[2] Peritoneal dialysis is the treatment of choice in diabetic patients; however, it mostly increases the 2-year survival.[11]

There is a consensus these days that medical rehabilitation of diabetic kidney recipients is preferred to dialysis.[9] Survival rate of diabetic patients with a transplanted kidney is lower than nondiabetic kidney recipients.[5-7,12] However, diabetic patients benefit from kidney transplantation more than dialysis, because survival rate of diabetic patients under treatment of hemodialysis is very low.

Rimmer and colleagues have reported the poor results of kidney transplantation in diabetic patients in 1985. The 1- and 2-year graft survival was 37% and 13%, and patient survival was 48% and 24% in 30 patients.[12] This may be resulted from poor surgical techniques and the absence of potent immunosuppressive drugs in 1980s, and performing transplantation in patients with cardiovascular problems. Fischel and coworkers have evaluated 10-year results of kidney transplantation in diabetic patients in 1991.[6] They concluded that patient and graft survival rates are poorer in diabetic patients in long run. The results of our 5-year study on diabetic recipients did not differ from those of nondiabetic patients; however, the 10-year survival may be influenced by several vascular defects in different organs in diabetic patients. Douzdjian and colleagues[5] have studied the patient and graft survival rates in diabetic kidney recipients in 1995. The graft survival rates in 63 diabetic patients were 76% and 49% at 1 and 5 years, while they were 89% and 63% in 80 nondiabetic patients, respectively.

It seems that short-time survival rates of diabetic patients and their transplanted kidneys are improving; however, the long-time survival rate is still lower in these patients comparing with nondiabetic patients.[8,9] The most important cause of poor long-term results of transplantation among these patients is their death because of coronary artery disease, left ventricular hypertrophy, and hypertension after the transplantation.[13]

Despite the higher mean age (by about 22 years) of diabetic patients and the lower percent of living-related donors in this group of our

study, the short-term survival rate of graft was good in these patients. Acceptable short-term results may be because of accurate and complete evaluation of diabetic patients before transplantation, especially complete cardiovascular evaluation and elimination of diabetic patients with advanced cardiovascular complications from the transplantation program. Another effective factor in our study is the difference between the donors. In addition, all of our patients had received kidneys from living donors, while in other studies cadaveric kidney transplantation is dominant[14,15]; transplantation results are much better with living donors. On the other hand, our national program for kidney transplantation, which is based on living-unrelated donors, has minimized the period of dialysis required in ESRD patients, leading to less associated cardiovascular complications.

Finally, long-term results of transplantation in our center were slightly poorer in diabetic patients comparing with nondiabetic patients, but this difference was not significant.

Conclusion

The treatment of choice in diabetic patients with ESRD is kidney transplantation or combined transplantation of kidney and pancreas, and the results of hemodialysis and peritoneal dialysis are drastically poorer. Complete preoperative cardiovascular evaluation of these patients including coronary arteries angiography and coronary bypass (if needed) is recommended to improve the outcome of transplantation.

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