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ORIGINAL RESEARCH

Comparison of preemptive kidney transplant recipients with nonpreemptive kidney recipients in single center: 5 years of follow-up

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Background: For suitable patients with end-stage renal disease, kidney transplantation (KT) is the best renal replacement therapy, resulting in lower morbidity and mortality rates and improved quality of life. Preemptive kidney transplantation (PKT) is defined as transplantation performed before initiation of maintenance dialysis and reported to be associated with superior outcomes of graft and patient survival. In our study, we aimed to compare the 5-year outcomes of PKT and nonpreemptive kidney transplantation (NPKT) patients who received KT in our center, to define the differences according to complications, comorbidities, adverse effects, clinical symptoms, periodical laboratory parameters, rejection episodes, graft, and patient survival.

Methods: One hundred kidney transplantation (37 PKT, 63 NPKT) recipients were included in our study. All patients were evaluated for adverse effects, complications, comorbidities, clinical symptoms, monthly laboratory parameters, acute rejection episodes, graft, and patient survival.

Results: Acute rejection episodes were found to be significantly correlated with graft loss in both groups ($P = 0.02$ and $P = 0.01$, respectively). Hypertension after transplantation was diagnosed by ambulatory blood pressure measurement in 74 of 100 patients. Twenty-five of 37 (67.6%) of Group 1 (PKT) recipients had hypertension while 54 of 63 (85.4%) of Group 2 (NPKT) had hypertension. The incidence of hypertension between two groups was statistically significant ($P = 0.03$), but this finding was not correlated to graft survival ($P = 0.07$). Some patients had serious infections, requiring hospitalization, and were treated immediately. Infection rates between the two groups were 10.8% for Group 1 patients and 31.7% for Group 2 patients and were statistically significant ($P = 0.02$). Infection, requiring hospitalization, was found to be statistically correlated to graft loss in only NPKT patients ($P = 0.00$).

Conclusion: While the comparison of PKT and graft and patient survival with NPKT is poorer than we expected, lower morbidity rates of hypertension and infection are similar with recent data. Avoidance of dialysis-associated comorbidities, diminished immune response, and cardiovascular complications are the main benefits of PKT.

Keywords: transplantation, preemptive, hypertension, infection, graft, survival

Introduction

End-stage renal disease (ESRD) is a severe and growing health problem worldwide. Undoubtedly, for suitable patients with ESRD, kidney transplantation (KT) is the best renal replacement therapy, resulting in lower morbidity and mortality rates and improved quality of life compared to maintenance dialysis. Despite all the advantages of kidney transplantation, most renal allograft recipients undergo a prior period of maintenance dialysis because of the inadequate donor organ pool.[1–3]

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Preemptive kidney transplantation (PKT) is defined as transplantation performed before initiation of maintenance dialysis and reported to be associated with superior outcomes of graft and patient survival compared to nonpreemptive kidney transplantation (NPKT). However, only a small part of ESRD patients receive PKT around the world.[4–6]

In our study, we aimed to compare the 5 years of outcomes of PKT and NPKT patients who received KT in our center to define the differences according to complications, comorbidities, adverse effects, clinical symptoms, periodical laboratory parameters, rejection episodes, graft, and patient survival.

Patients and methods

One hundred kidney transplantation (37 PKT, 63 NPKT) recipients were included in our study. Mean duration time on maintenance dialysis of NPKT recipients was 24 ± 18 months. The 100 kidney transplant recipients were divided into two groups; Group 1 had PKT patients while Group 2 had NPKT patients. All patients were evaluated in terms of adverse effects, complications, comorbidities, clinical symptoms, periodical laboratory parameters, acute rejection episodes, graft, and patient survival.

Demographic, clinical, and laboratory parameters for all patients were recorded. Age, sex, smoking, duration of dialysis before transplantation, body mass index, human leukocyte antigen mismatches, ambulatory blood pressure measurements, fasting glucose levels, uric acid levels, all immune suppressive regimens, and cumulative steroid dosages were recorded.

There was no difference in immunosuppression used in the two groups. Cyclosporine or tacrolimus, mycophenolate mofetil, and steroids were the primary immune suppressive agents. All recipients were administrated 500 mg of intravenous methylprednisolone just before restoration of blood flow to the allograft, and the dose of steroid was tapered to 60 mg per day over 4 days. Oral methylprednisolone 30 mg twice daily was given and tapered by 10 mg every week until the ongoing dose of 10 mg per day was reached. Cyclosporine or tacrolimus therapy was also started immediately after surgery, with dosage subsequently adjusted to maintain a trough concentration of 200–300 nanograms (ng) per mL or 10–12 ng per mL, respectively. All acute rejection episodes were proven by transplant kidney biopsy and treated with intravenous methylprednisolone 500 mg per day for 3 days. If steroid-pulsed therapy did not lead to improvement in acute rejection, intravenous antithymocyte globulin (ATG) of 2 mg per kg was administered for 5–10 days.

Statistical analyses were performed with the Statistical Package for the Social Sciences software (version 11.0, SPSS Inc, Chicago, Ill, USA). All numerical variables are expressed as the mean ± standard deviation (SD). Normality of data was analyzed by using a Kolmogorov–Smirnov test. All numerical variables with normal distribution were expressed as the mean ± SD while variables with a skew distribution were expressed as median (interquartile range). Categorical variables are given as percentages and were compared with Chi-square test. Normally distributed numeric variables were compared with independent samples of the Student's *t*-test, and skew distributed numeric variables were compared with Mann–Whitney U test. A P value < 0.05 was accepted as statistically significant.

Results

Eighty male and 20 female renal transplant recipients were included in the study. Patients were divided as PKT patients (Group 1) and NPKT patients (Group 2). The etiology of kidney failure for the patients is summarized in Table 1. All patients were followed up periodically for 5 years. Short- and long-term effects of preemptive and nonpreemptive kidney transplantation are compared between two groups. The demographic findings and the mismatches of two groups are summarized in Tables 2 and 3.

During the 5 years after transplantation, 40 patients had an acute rejection episode proven by biopsy. Some 23 patients had a single episode, while 12 had two episodes, and five patients had three episodes. Twelve (32%) PKT recipients had acute rejection; 28 (44%) NPKT recipients had acute rejection. Four biopsies showed chronic allograft nephropathy. The count of acute rejection episodes was statistically significant and found to correlate with graft loss in both groups ($P = 0.02$ and $P = 0.01$, respectively).

Twelve of 100 patients had surgical complications (urine leak, lymphocele, hematoma); 24 patients had serious

Table 1 Etiologies of ESRD

ESRD etiology	n (patient) = (%)
Unknown	16
Glomerulonephritis	27
Amyloidosis	3
Diabetes mellitus	23
Hypertension	22
Vesicoureteral reflux	3
Nephrolithiasis	2
Polycystic kidney disease	1
Pyelonephritis	3

Abbreviation: ESRD, end-stage renal disease.

Table 2 Demographic data

	Group 1 (n = 37)	Group 2 (n = 63)
Age (years)	34.02 ± 10.61	31.44 ± 10.41
Sex (%)	Male: 33 (89.2%)	Male: 47 (74.6%)
	Female: 4 (10.8%)	Female: 16 (25.4%)
Donor (%)	Living: 36 (97.3%)	Living: 46 (73%)
	Cadaveric: 1 (2.7%)	Cadaveric: 17 (27%)

infections, requiring hospitalization, and were treated immediately. Infection rates between the two groups were 10.8% for Group 1 patients and 31.7% for Group 2 patients, and were statistically significant ($P = 0.02$). Serious infection, requiring hospitalization, was found to be statistically correlated to graft loss only in NPKT patients ($P = 0.00$). Erythrocytosis was diagnosed in 22 patients. None of the patients had anemia or leukopenia. Osteopenia and osteoporosis were diagnosed with bone-mineral densitometry in seven patients. Three recipients had gouty arthritis, which was treated successfully.

Hypertension after transplantation was diagnosed by ambulatory blood pressure measurement in 74 of 100 patients. Twenty five of 37 (67.6%) of Group 1 (PKT) recipients had hypertension, while 54 of 63 (85.4%) of Group 2 (NPKT) had hypertension. The incidence of hypertension between the two groups was statistically significant ($P = 0.03$), but this finding was not correlated to graft survival ($P = 0.07$). All the complication rates for the two groups are summarized in Table 4.

Graft loss was the end point in three (8.1%) of Group 1 patients and in five (7.95%) of Group 2 patients, while death was the end point in one patient (2.7%) of Group 1 and in one (1.6%) of the Group 2 patients. There was no statistical significance between two groups for 5 years of graft and patient survival ($P = 0.36$; $P = 1.00$, respectively). An acute rejection episode was independently associated with graft survival in all transplant recipients while serious infection, requiring hospitalization, was independently associated with mortality in only NPKT recipients ($P = 0.00$).

In our study, laboratory parameters of all patients were measured in the first week, third month, sixth month, twelfth month, and yearly after transplantation. The laboratory values measured were complete blood count, C-reactive protein levels, alanine aminotransferase, aspartate aminotransferase, serum calcium, phosphorus, parathyroid hormone, serum creatinine, and blood urea nitrogen. None of the laboratory parameters were found to be related with graft loss or patient survival.

Table 3 Mismatches of the recipients

	Group 1 (n = 37)	Group 2 (n = 63)	Total (n = 100)
0 Mismatch	0	0	0
1 Mismatch	4	0	4
2 Mismatch	10	2	12
3 Mismatch	23	32	55
4 Mismatch	0	18	18
5 Mismatch	0	11	11

Table 4 Complications after transplantation

	Group 1 (n = 37)	Group 2 (n = 63)	*P*-value
Lymphocel	3 (8.1%)	9 (14.3%)	NS
Infection	4 (10.8%)	20 (31.7%)	0.02
Hypertension	25 (67.6%)	54 (85.4%)	0.03
Erythrocytosis	7 (18.9%)	15 (23.8%)	NS
CAN	0	4 (6.3%)	NS
Osteopenia/OP	5 (13.5%)	2 (3.2%)	NS
Gouty arthritis	1 (2.7%)	3 (3.2%)	NS
Malignancy	0	0	NS

Abbreviations: CAN, chronic allograft nephropathy; OP, osteoporosis; NS, not significant.

Discussion

Kidney transplantation is the best choice for treatment in ESRD patients, not only for the longer survival rates but also for the lower costs and treatment of dialysis-related comorbidities.[1–6] Eligible patients should receive PKT, which may reduce morbidity and mortality, the need for vascular access, and the cost of dialysis. Prolonged hemodialysis duration may result in cardiovascular morbidities even after successful transplantation.[7,8] In our study, we demonstrated that new onset hypertension rates were significantly higher in NPKT recipients. The mean duration of dialysis in our NPKT recipient population was 24 ± 18 months, which may be long enough to be a result of irreversible left-ventricular hypertrophy and accelerated atherosclerosis in ESRD patients. Why pretransplant dialysis continues to compromise patient survival is not entirely clear.

Mange and Weir[7] showed a 52% decrease for graft loss for PKT recipients after the first year of transplantation, compared to NPKT recipients in 8481 patients. Kasiske et al[3] also reported similar findings. In our study, although PKT recipients had better outcomes than NPKT recipients for both graft and patient survival at the end of 5 years of follow-up, the results were not statistically significant. The limited size of our study may be the reason for this insignificant result.

In our study, the mean age was 34.02 ± 10.61 years in Group 1 and 31.44 ± 10.41 years in Group 2. We aimed to exclude the old, and also the kidney recipients at high-risk

of cardiovascular disease. Surprisingly, 74% of the young kidney recipients diagnosed for new onset hypertension after transplantation. Steroid use and close follow-up with three monthly ambulatory blood pressure monitorizations after kidney transplantation may be the result of the higher rates of hypertension. Although hypertension is an important risk factor for cardiovascular morbidity and mortality, the younger age of our patients may be hiding the late complications of hypertension in the first 5 years after transplantation. While early results of our study remain insignificant for hypertensive complications in our study group, long-term follow-up results may be more similar with the literature.[17]

Gill et al[9] showed that the most important factor for graft survival in 54,582 patients was the patient survival. In our study, the 5-year follow-up showed no difference of patient survival between the two groups. The reason for similar graft survival results in PKT patients and NPKT patients may be because of our small study group, relatively short duration of follow-up, and younger age of our patients.

Complications due to hemodialysis were mainly cardiovascular disease, malnutrition, chronic inflammatory state, impaired immune response, and insufficient clearance.[10–12] Kaul et al reported that the initiation of hemodialysis led to significant improvement in T-cell proliferation, which may be associated with acute cellular rejection episodes.[13] Cacciarelli et al have shown that the incidence of acute rejection episodes was lowest in patients who had the shortest duration of dialysis.[14] In our study, neither acute rejection episodes nor graft survival was associated with duration of dialysis. Nevertheless, all these factors may be responsible for more common and serious infections, cardiovascular complications, and hypertension in NPKT recipients. In our study, we stated that the severe (requiring hospitalization) infection rates were significantly higher in the NPKT recipient group than PKT recipient group ($P = 0.02$). These findings were not different from other studies, suggesting that NPKT recipients are more prone to serious infections.[13–15] Because the initiation of dialysis has been reported to diminish immune function, this increased the risk of rejection and life-threatening infections.[16] Also, chronic inflammatory state caused by long-term contact with dialysis membranes and changes in immune status may be considered as the causes of lower graft survival rates in NPKT recipients.

Conclusion

Recent data provides convincing evidence that PKT is advantageous for patient and graft survival.[17,18] While the comparison of PKT and graft and patient survival with NPKT is poorer than we expected, the lower morbidity rates of hypertension and infection are in line with recent data.[10,18] Avoidance of dialysis-associated comorbidities, diminished immune response, and cardiovascular complications are the main benefits of PKT. Further long-term studies may be beneficial to further support our findings.

Disclosure

The authors report no conflicts of interest in this work.

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