



Perioperative Comparison of Preemptive and Non-Preemptive Renal Transplant Recipients

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Abstract

Objective: Preemptive transplantation cannot be performed for all patients because of the limited number of donors. This study aimed to evaluate the perioperative effects of dialysis before renal transplantation.

Methods: In this study, we retrospectively investigated 666 patients who underwent kidney transplantation at our centre. We divided patients into two groups: patients with pre-transplant dialysis (67.3%, n=448) and patients with preemptive transplant (32.7%, n=218). We carried out preoperative, intraoperative and postoperative comparisons between groups.

Results: No difference was observed in terms of intraoperative blood transfusion, crystalloid and colloid requirement, inotropic-vasopressor agent administration and hemodynamic parameters between the patients with pre-transplant dialysis and preemptive transplant. It was observed that dialysis requirement, delayed graft function and acute rejection development were significantly higher during the postoperative period in patients who underwent dialysis before transplantation. In patients with non-preemptive transplant, the decrease of serum creatinine levels at the first postoperative month was more prominent when compared to patients with preemptive transplant; however, that difference disappeared in the first year follow-up. No significant difference was found for serum albumin levels and proteinuria alterations of the patients in long-term follow-up. Additionally, patient and graft survival comparisons between patients with non-preemptive and preemptive transplant on three-year follow-up revealed no significant difference.

Conclusion: We think that preemptive transplantation treatment is a better option for patients with end-stage renal failure since patients with preemptive transplantation appear to have less metabolic function impairment, complication risk and more successful outcomes in terms of cost-effectiveness.

Keywords: Dialysis, perioperative evaluation, preemptive transplantation, renal transplantation

Introduction

Chronic kidney disease (CKD) is a pathophysiological process that is characterised by abnormal renal function and progressive degradation of glomerular filtration rate. As a result, chronic irreversible renal failure, in other terms, end-stage renal failure (ESRD), occurs. Dialysis or renal transplantation (RTx) can be performed under the title of renal replacement therapy to patients with ESRD. RTx is being suggested to be superior to dialysis treatment in the literature in terms of quality of life and survival of the patient (1). Dialysis duration in the pre-transplant period is known to affect the survival rate and long-term outcomes (2-4). While preemptive RTx refers to the transplantation performed before any dialysis intervention, non-preemptive RTx refers to the transplantation performed after haemodialysis or peritoneal dialysis treatment was done. Because of the limited number of organ donors, not all patients with ESRD have the chance to undergo preemptive RTx, and some patients receive dialysis until an appropriate organ is obtained for transplantation. Various studies reported that graft loss and mortality rates are higher in patients with non-preemptive transplant compared to patients with preemptive transplant. Nonetheless, it was also reported that there is no relationship between pre-transplant dialysis status and graft loss or mortality rates.

Our single-centre study aimed to compare perioperative outcomes of the patients with non-preemptive and preemptive transplant.

Methods

Ethical approval

We evaluated 909 patients with ESRD who had undergone RTx between 2010 and 2016. The study was started after ethical approval was granted by the regional research ethics committee (Ref: 70904504/566 No.: 850). Of 909, 243 patients who did not fulfil the inclusion criteria were excluded from the study; the remaining 666 patients were included.

Study design

Inclusion criteria involved renal transplantation due to end-stage renal failure, absence of additional solid organ failure other than CKD, and accompanying malignancy. On the other hand, exclusion criteria included concomitant organ failure, other organ transplantations performed simultaneously or at different times, missing data related to pre-transplant, post-transplant or intraoperative periods.

Age, gender, body weight, cause of ESRD, immunosuppressive regimen, biochemistry panels, intraoperative crystalloid and colloid administration, blood transfusion requirement, central venous pressure (CVP), mean arterial pressures (MAP) at the beginning, in the middle and at the end of the surgery, postoperative dialysis requirement, graft injury evaluation considering the RIFLE criteria, occurrence of acute rejection and survival parameters were retrospectively collected.

We divided 666 patients into two groups: group 1 for preemptive RTx recipients (n=218, 32.7%) and group 2 for non-preemptive RTx recipients (n=448, 67.3%) according to the sufficient data derived.

Anaesthetic approach

The same anaesthesia crew applied a standardised anaesthesia protocol for all patients. It involved IV weight-dependent midazolam 0.05 mg kg⁻¹ for premedication, fentanyl 2 µg kg⁻¹, pentothal 3-5 mg kg⁻¹, rocuronium bromide 0.4-0.6 mg kg⁻¹ for anaesthesia induction and desflurane 4%-6% (medical air 60% in oxygen), remifentanyl 0.5 µg kg⁻¹ min⁻¹ and rocuronium bromide 0.1 mg kg⁻¹, with volume control ventilation in a circle system for maintenance of anaesthesia.

In addition to the standard ASA monitoring, all graft recipients received arterial catheterisation through mostly radial artery, while internal jugular vein catheterisation for evaluating CVP due to the co-morbid condition.

Statistical analysis

All data were analysed using Statistical Package for the Social Sciences version 20 (IBM SPSS Corp.; Armonk, NY, USA). Data were expressed as n (%), mean±standard deviation (SD) or median (min-max), as appropriate. P val-

Table 1. The baseline characteristics of the patient groups

	Preemptive recipients	Non-preemptive recipients	p
Age (mean±SD)	36.30±16.27	35.20±15.54	0.425
Gender (N, %)			0.728
Male	141 (64.7%)	297 (66.3%)	
Female	77 (35.3%)	151 (33.7%)	
N.S.: not significant; SD: standard deviation			

ues <0.05 were considered statistically significant. Pearson chi-square analysis was performed for categorical variables. The normality assumptions were controlled by the Shapiro-Wilk test.

Results

The mean±SD for the ages of preemptive and non-preemptive groups were 36.30±16.27 and 35.20±15.54, respectively. Gender was not a significant determinant for both groups (Table 1). The causes for ESRD were high blood pressure (n=92, 13.8%), diabetes mellitus (n=65, 9.8%) and glomerulonephritis (n=54, 8.1%) in general. The distribution of the causes with respect to patient groups was as follows: among preemptive recipients group, 32 patients had high blood pressure (14.7%), 23 patients had diabetes mellitus (10.6%) and 22 patients had glomerulonephritis (10.1%); among non-preemptive recipient group, 60 patients had high blood pressure (13.7%), 42 patients had diabetes mellitus (9.6%) and 36 patients had urological causes (8.2%).

When patients were categorised as adults (age > 17 years, n=576) vs. paediatric (age <17, n=90) group, preemptive transplantation ratios were 35.6% and 32.3%, respectively, and no significant difference was found between preemptive and non-preemptive transplantation rates.

Intraoperative data

Intraoperative blood transfusion was required for 21% and 15.6% of patients who underwent preemptive and non-preemptive transplantation, respectively. The quantitative value of intraoperative blood transfusion was 3.74±9.26 mL kg⁻¹ in preemptive recipients and 2.93±8.58 mL kg⁻¹ in non-preemptive recipients. Intraoperative crystalloid administration was 47.82±27.30 mL kg⁻¹ and 45.01±31.70 mL kg⁻¹ in preemptive and non-preemptive transplant recipients, respectively. Whereas colloid use was 26.94±113.24 mL kg⁻¹ in patients with preemptive transplant, it was 45.02±150.76 mL kg⁻¹ for non-preemptive recipients. Intraoperative inotropic-vasopressor agent administration was required in 1.2% of preemptive recipients and 4.6% of patients with non-preemptive transplant, but the aforementioned meaningful clinical data revealed no significant difference between the two groups.

Considering hemodynamic variables, while CVP values at the beginning (beg), in the middle (mid) and at the end (end) of surgery in preemptive recipients were 12.07 ± 3.85 mmHg, 13.57 ± 4.02 mmHg and 12.88 ± 3.95 mmHg, respectively; while the CVP values in patients with non-preemptive transplant were 11.3 ± 4.34 mmHg, 13.01 ± 4.54 mmHg and 12.30 ± 4.85 mmHg, respectively. In preemptive recipients, CVP values at the beginning of surgery were found significantly higher than the values of patients with non-preemptive transplant ($p=0.03$). The CVP alterations were obtained for different time intervals during the operation by calculating the differences considering the aforementioned time intervals. For the CVP values of the preemptive recipients, an increase of 1.50 ± 2.49 mmHg (for the beg-mid interval), a decrease of 0.69 ± 2.52 mmHg (for the mid-end interval), and an increase of 1.27 ± 3.78 mmHg (for the beg-end interval) were found. Similarly, an increase of 1.98 ± 2.84 mmHg, a decrease of 0.70 ± 3.34 mmHg and an increase of 0.80 ± 1.27 mmHg were found for the same time intervals in the identical order in patients with non-preemptive transplant. For both preemptive and non-preemptive recipients, the alteration of an increasing pattern for CVP values was identified meaningful ($p=0.001$). The CVP differences the time intervals were not different between the two groups. The MAP values and the

heart rates throughout the operation that were recorded for these intervals did not have any significant difference between the two groups (Table 2).

Biochemistry panel

Serum creatinine levels at preoperative period, postoperative first month, sixth month and first year were measured as 4.95 ± 2.03 mg dL⁻¹, 1.80 ± 8.04 mg dL⁻¹, 1.32 ± 0.72 mg dL⁻¹ and 1.25 ± 0.45 mg dL⁻¹, respectively, in preemptive recipients; and 7.04 ± 6.69 mg dL⁻¹, 1.17 ± 0.69 mg dL⁻¹, 1.37 ± 0.81 mg dL⁻¹ and 1.35 ± 0.77 mg dL⁻¹, respectively, in non-preemptive recipients. The serum creatinine levels of preemptive recipients were significantly lower than those of non-preemptive transplant recipients during the preoperative period ($p=0.0001$).

Serum albumin levels at preoperative period, postoperative first month, sixth month and first year in preemptive recipients were measured as 4.29 ± 0.61 g dL⁻¹, 4.25 ± 0.74 g dL⁻¹, 4.50 ± 0.40 g dL⁻¹ and 4.55 ± 0.31 g dL⁻¹, respectively; and in non-preemptive recipients, 4.09 ± 0.87 g dL⁻¹, 4.32 ± 0.42 g dL⁻¹, 4.50 ± 0.40 g dL⁻¹, 4.63 ± 0.40 g dL⁻¹, respectively. Serum albumin levels of preemptive recipients were significantly higher during the preoperative period ($p=0.006$). Proteinuria levels in the pre-

Table 2. The baseline characteristics of intraoperative data

Intraoperative data		Preemptive recipients	Non-preemptive recipients	p
Blood transfusion requirement (n, %)		35 (21%)	58 (15.6%)	0.140
Blood transfusion (mL kg ⁻¹ , mean±SD)		2.93±8.58	3.74±9.26	0.110
Crystalloid usage (mL kg ⁻¹ , mean±SD)		47.82±27.30	45.01±31.70	0.422
Colloid usage (mL kg ⁻¹ , mean±SD)		26.94±113.24	45.02±150.76	0.165
Inotropic-vasopressor agent usage (n, %)		2 (1.2%)	17 (4.6%)	0.05
CVP (mmHg, mean±SD)	Beginning	12.07±3.85	11.3±4.34	0.03
	Middle	13.57±4.02	13.01±4.54	0.163
	End	12.88±3.95	12.30±4.85	0.091
	p	*0.001	*0.001	
CVP alterations (mmHg, mean±SD)	Beg-Mid	1.50±2.49	1.98±2.84	0.137
	Mid-End	-0.69±2.52	-0.70±3.34	0.404
	Beg-End	1.27±3.78	0.80±1.27	0.210
Mean arterial pressure (mmHg, mean±SD)	Beginning	108.73±17.84	106.10±18.17	0.186
	Middle	92.85±13.14	92.72±15.26	0.554
	End	94.67±15.62	93.94±13.71	0.617
Heart rate (bpm)	Beginning	84.40±16.35	85.97±17.26	0.302
	Middle	74.64±14.77	77.78±16.09	0.079
	End	77.57±14.10	79.41±16.15	0.273

N.S.: not significant; SD: standard deviation, *:The alteration within different groups showed an increasing pattern for CVP values by time

Table 3. The baseline characteristics of biochemistry panel

Biochemistry panel		Preemptive recipients	Non-preemptive recipients	p	
Serum creatinine (mg dL ⁻¹ , mean ± SD)	Preoperative	4.95±2.03	7.04±6.69	0.0001	
	Postoperative	First month	1.80±8.04	1.17±0.69	0.826
		Sixth month	1.32±0.72	1.37±0.81	0.916
		First year	1.25±0.45	1.35±0.77	0.885
Serum albumin (g dL ⁻¹ , mean ± SD)	Preoperative	4.29±0.61	4.09±0.87	0.006	
	Postoperative	First month	4.25±0.74	4.32±0.42	0.811
		Sixth month	4.50±0.40	4.50±0.40	0.374
		First year	4.55±0.31	4.63±0.40	0.467
Proteinuria (g day ⁻¹)	Preoperative	7.26±10.21	8.04±7.42	0.0001	
	Postoperative	First month	4.26 ± 3.22	4.38±3.35	0.966
		Sixth month	3.31±3.35	4.41±3.41	0.03
Postoperative need for dialysis (n, %)		1 (0.5%)	25 (5.6%)	0.001	
Delayed graft function (n, %)		1 (0.5%)	25 (5.6%)	0.001	
Occurrence of acute rejection (n, %)		7 (3.2)	50 (11.2%)	0.0001	
Survival (2010–2014)	First year	99%	97.7%	N.S.	
	Second year	99%	97.7%		
	Third year	99%	97.2%		
N.S.: not significant; SD: standard deviation					

operative period, postoperative first month and postoperative sixth month in preemptive recipients were 7.26±10.21 g day⁻¹, 4.26±3.22 g day⁻¹, 3.31±3.35 g day⁻¹, respectively; while in patients with non-preemptive transplant, the levels were measured as 8.04±7.42 g day⁻¹, 4.38±3.35 g day⁻¹ and 4.41±3.41 g day⁻¹, respectively. The proteinuria levels in non-preemptive recipients were found out to be significantly higher than those in preemptive patients during the preoperative period (p=0.0001) and at the postoperative sixth month (p=0.03).

These statistically significant differences mentioned above reached similar values for both groups at the postoperative first and sixth months.

Postoperative data

The need for dialysis in the postoperative period was found to be statistically lower in preemptive recipients than in non-preemptive recipients (0.5% of preemptive recipients (n=1) and 5.6% of non-preemptive recipients (n=25), p=0.001). The delayed graft function in the post-transplant period was found significantly lower in preemptive recipients than in non-preemptive recipients (0.5% of preemptive recipients and 5.6% of non-preemptive recipients, p=0.001).

The occurrence of acute rejection was found significantly lower in preemptive recipients than in non-preemptive recip-

ients (3.2% of preemptive recipients and 11.2% of non-preemptive recipients, p=0.0001) (Table 3).

Discussion

RTx is still the best treatment of ESRD. Because of the insufficient number of donors and the addition of new patients to the waiting list each year, non-transplant renal replacement therapies are becoming more crucial for patients with ESRD to continue living. Currently, the expected lifetime of patients with ESRD significantly increases because of the improvement of renal replacement therapy techniques (5). A number of studies show that the function of the transplanted kidney in the early period is related to intraoperative perfusion characteristics and urinary output (6-8).

Maintaining adequate intravascular volume level is one of the most substantial factors to preserve the graft kidney (6, 7, 9). Although some reports suggested crystalloid support over 100 mL kg⁻¹ and CVP maintenance between 10 and 17 mmHg for adequate volume support, 45 and 50 mL kg⁻¹ of volume support and 10-15 mmHg of CVP are reported to be sufficient for adequate perfusion (6, 7, 9-11). Mildly elevated systolic blood pressure is another factor in graft kidney preservation. We suppose that preoperative dialysis and appropriate fluid management maintain the low CVP values at the beginning of the surgery

in non-preemptive recipients. There was no difference in the intraoperative parameters of preemptive and non-preemptive transplant recipients other than the initial CVP.

Lower serum creatinine, higher serum albumin and lower proteinuria levels in preemptive recipients during the preoperative periods have been considered to result from shorter ESRD durations observed for these recipients.

Higher proteinuria levels of non-preemptive recipients are suggested to stem from the selectivity impairment of the native kidney because of long dialysis periods.

In the literature, preemptive kidney transplants were reported to be associated with better postoperative graft functions and longer survivals of the transplanted kidney (2, 12-17). In the study conducted by Cosio et al. (2), pre-transplant dialysis treatment was demonstrated to be an essential indicator of post-transplant mortality and graft loss. Another study reported a 37% increase in graft loss rates in patients who had been undergoing dialysis for 6-12 weeks before transplantation compared to preemptive transplant recipients (15). A similar study by Mange et al. (14) identified a correlation between pre-transplant dialysis durations and graft loss. Another study involving two different recipients for cadaveric kidney transplantation emphasised that ten-year graft survival was significantly longer in patients who received dialysis less than six months, compared to the patients who received dialysis for more than two years (15).

Yoo et al. (18) reported that one-year, five-year and ten-year survival rates of the grafts in patients with preemptive transplantation were significantly better than patients who had received dialysis before transplantation. They suggested that pre-transplant dialysis modality (haemodialysis or peritoneal dialysis) did not affect graft and patient survival. In another study (19), preemptive transplants in the paediatric patient group were shown to be significantly effective in increasing graft survival. Another study carried out with 8481 patients between 1994 and 1997 reported a 52% reduction in graft loss in preemptive transplantation (14).

Some authors also have pointed out that there is no difference in terms of long-term graft survival and mortality rates between patients with preemptive transplant and those receiving pre-transplantation dialysis. Unsal et al. showed that there is no statistically significant difference between preemptive transplants and patients having dialysis during the pre-transplant period in terms of patient survival and graft survival in the first and the third year (20). In the same study, the survival rates of the patients in the first year were 96.3% in the dialysis group, 98.9% in the preemptive group, and the rates in the third year were 95.7% in the dialysis group and 98.9% in the preemptive group. Another study on patients younger than 45 years old (21) showed no significant difference in patient

survival between preemptive transplant recipients and dialysis patients in the pre-transplant period. The investigation on 35,511 patients from European Dialysis and Transplantation Association and European Kidney Association registry between 1985 and 1992 showed no statistically significant difference in graft and patient survival between patients with pre-transplant dialysis and preemptive transplant (22).

There are numerous studies about the effects of dialysis on the immune system and rejection development during the post-transplant period in the literature. Descamps-Latscha et al. (23) demonstrated that patients with long-term dialysis had significantly higher immune system impairment compared to patients with short-term dialysis, and similarly, Kaul et al. (24) found that T lymphocyte proliferation was significantly higher in patients receiving haemodialysis. These results were associated with acute rejection and graft loss in patients with dialysis during the pre-transplant period. In patients having dialysis in the pre-transplant period, delayed graft function has been shown to vary between 4% and 9.7%; while in preemptive transplants, it has been shown to range between 2%-3% and 7.7% (14, 25-27).

Conclusion

In general terms, dialysis requirement and acute rejection development were found to be higher during the postoperative periods due to metabolic deterioration, immunologic system activation and delayed graft function status in the patients who had received dialysis before the transplantation. We concluded similar results in the this study; yet, according to the biochemical results obtained, no significant difference was found between the two groups in the postoperative first and sixth months. In terms of biochemical data obtained, a significant difference between patients with pre-transplant dialysis and preemptive transplant was solely found for short-term follow-up; but not for long-term follow-up. We suggest that preemptive transplantation has better outcomes in patients with ESRD as it is associated with less metabolic function impairments, complication risks and more cost-effective results.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Akdeniz University Medical Faculty (Ref: 70904504/566 No.: 850, Date: 12/12/2018).

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

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