Nephro-Urol Mon. 2011;3(4):285-290
Nephro-Urology Monthly
Journal home page: www.NUmonthly.com

Effect of Dialysis Modality on Transplantation Outcome in Living-Donor Renal Transplantation

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ARTICLE INFO

Article Type:
Original Article

Article history:
Received: 13 Apr 2011
Revised: 21 Apr 2011
Accepted: 30 Apr 2011

Keywords:
Peritoneal dialysis
Hemodialysis
Transplantation
Graft survival

ABSTRACT

Background: Peritoneal dialysis (PD) and Hemodialysis (HD) have been considered as two standard treatment methods in patients with end stage renal disease. It has been proposed that PD patients have a more protected volume status leading to a better renal transplantation outcome and lower incidence of post-transplant (DGF) delayed graft function , while HD exacerbates the immune disturbance by recurrent activation of inflammatory response, oxidative stress and free radical production that can contribute to DGF.
Objectives: In this retrospective study, we analyzed the effect of peritoneal dialysis (PD) or Hemodialysis (HD) on patients' survival, graft survival, delayed graft function (DGF), acute rejection and early and late complication after living-donor renal transplantation.
Patients and Methods: We retrospectively analyzed the data of patients who received their first living renal transplantation between December 2002 and Aril 2010. We entered only those patients who were on PD or HD for at least three months. We excluded patients who experienced DGF because of surgical complications. We allocated one or two aged and sex matched HD patients for one patient in PD group. All patients in each group were operated in a single transplant center.
Results: Of 143 patients who had their first living kidney transplant in, 69 patients (M/F 48/21 mean age: 35.3 ± 15.9 years) were in PD group and 74 patients (M/F 38/36 mean age: 40.7 ± 13.3 years) were in HD group. Mean age of donor in PD and HD group were 28.4 ± 4.4 and 29.7 ± 5.6 years. The number of diabetic patient in PD and HD groups were 11/69 (13.6%) and 16/74 (16.2%) (P = 0.4). The rate of delayed graft function, early acute rejection in PD and HD groups was as the followings: 3/69(4.3%) versus 3/74(4.1%) and 3/69(4.3%) versus 2/74 (2.7%). Comparison of overall five years patient and graft survival between the PD and HD patients showed no significant difference by log-rank test (P = 0.13 for patients survival), (P = 0.26 for grafts survival).
Conclusions: We found that the choice of dialysis modality does not influence the overall patient and graft survival and the rate of specific complications in living-donor renal transplantation.

▸ *Implication for health policy/practice/research/medical education:*
This is the first published article that reporting the complications and outcome of renal transplantation in a group of Peritoneal dialysis patients all with living donors and comparing them with a matched group of Hemdialysis patients.

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Please cite this paper as:
Ardalan M, Etemadi J, Ghabili K, Ghojazadeh M, Ghafari A, Khosroshahi HT. Effect of Dialysis Modality on Transplantation Outcome in Living-Donor Renal Transplantation. *Nephro-Urol Mon.* 2011;**3**(4):285-90.

1. Background

Peritoneal dialysis (PD) and Hemodialysis (HD) are two standard methods of treatment in patients with end stage renal disease. The effect of PD and HD on patient and graft survival after renal transplantation has been extensively debated (1, 2). Some authors suggest that peritoneal dialysis (PD) favorably affects early graft function (1, 2). Other studies reported an less favorable results for PD patients as compared with HD patients (3). It has been proposed that PD patients have a more protected volume status leading to a better renal transplantation outcome and lower incidence of post-transplant (DGF) delayed graft function (1, 2, 4-6). HD exacerbates the immune disturbance by recurrent activation of inflammatory response, oxidative stress and free radical production that can contribute to DGF (7-11). On the other hand, higher incidences of graft thrombosis have been reported in PD compared with HD patients (10, 12-15). Another study has shown no significant differences between these two

Table 1. Baseline Characteristics of the Peritoneal dialysis and Hemodialysis Groups

Characteristic	PD [a]	HD [a]	*P* value
Patients, n	69	74	NA [a]
Sex			0.028
Male	48	38	
Female	21	36	
Primary disease, No. (%)			
Glomerulonephritis	23 (33.3)	10 (13.5)	0.006
Lupus nephritis	4 (5.8)	1 (1.4)	NS (0.19)
Diabetic nephropathy	11 (13.6)	16 (16.2)	NS (0.4)
Hypertension	9 (13.0)	16 (21.6)	NS
Obstruction	1 (1.4)	14 (18.9)	0.001
Polycystic kidney disease	3 (4.3)	10 (13.5)	NS (0.08)
Stone and pyelonephritis	3 (2.1)	0 (0)	NS (0.11)
Nephro-toxins	1 (1.4)	0/74 (0)	NS
Unknown	14 (20.3)	11 (14.9)	NS
Sex			0.027
Male	55	46	
Female	14	28	
Pre-transplant virologic assessment, No. (%)			
CMV IgG (+)	69 (100)	73 (98)	NS [a]
Anti-HCV (+)	3 (4.3)	8 (10.8)	NS (0.21)
HBsAg (+)	1 (1.4)	6 (8.1)	NS (0.1)
Pre-transplantation laboratory assessment			
Hemoglubine, mg/dL	9.4 ± 1.1	9.4 ± 1.2	NS
Serum Calcium, mg/dL	9.5 ± 0.80	9.5 ± 0.83	NS
Serum phosphor	5.6 ± 1.7	5.7 ± 1.6	NS
C-reactive protein, No. (%)			
Negative	59 (85.5)	65 (87.8)	NS
One plus positive	4 (5.8)	7 (9.5)	NS
Two plus positive	4 (5.8)	2 (2.7)	NS
Three plus positive	2 (2.9)	0 (0)	NS (0.23)
Mean age of patients, y	35.3 ± 15.9	40.7 ± 13.3	NS c (0.08)
Mean time on dialysis, mo	16.4 ± 10.3	21.4 ± 11.0	NS (0.22)
Antibody induction therapy, No. (%)	2 (2.8)	3 (4.1)	NS
Mean duration of follow-up, mo	78 ± 46	79 ± 44	NS
living donors	69	74	NA
Mean age, y	28.4 ± 4.4	29.7 ± 5.6	NS

[a] Abbreviations: HD, Hemodialysis; NA, Not Available; NS, Non-significant; PD, Peritoneal dialysis

different modalities for patients' survival, graft survival and post-transplant complications (16-18). This is the first report that compares the effect of pre-transplant dialysis modality on the transplantation outcomes in a cohort of living -donor renal transplantation.

2. Objectives

In this study, we compared the influence of the pre-transplant dialysis modality (PD or HD) on the patient survival, allograft survival and early and late post transplantation complications.

3. Patients and Methods

3.1. Patients

We retrospectively analyzed the data of PD and HD patients from two adjacent centers in north-west of Iran who received their first renal transplantation between December 2002 and April 2010. All patients were transplanted in one center. We entered both adult aged and pediatric patients who had been on dialysis for at least three months before transplantation without a switch from one dialysis modality to the other. We excluded patients with primary nonfunctioning allograft (PNF) or delayed graft function (DGF) because of surgical complications. HD patients were matched for age and sex with PD patients. We found one or two matched HD patients for each patient in PD group. None of patients received combination of PD and HD. The pre-transplant hemodialysis strategy was to dialyze patients 3 times weekly for 4 hours per session, using blood flow rates of 200 – 300 mL/min and dialysate flows of 500 mL/min. All HD patients were dialyzed with biocompatible HD membrane, using standard bicarbonate-containing dialysate solution (bibag, Fresenius medical care) and acetate containing hemodialysis solution (Na:135 mmol/L,

Table 2. Primary and Secondary Endpoints in our Study

Variable	PD [a]	HD [a]	*P* value
Patients, n	69	74	NA [a]
Primary endpoints			
1-Year outcomes, %			
Graft survival	93	92	0.81
Patient survival	98	100	0.53
5-Year outcomes, %			
Graft survival	81	74	0.042
Patient survival	95	71	0.001
Complications in the early post-transplant period (< 90 days), No. (%)			
Primary nonfunctioning graft	4 (5.8)	6 (6.8)	NS [a]
Delayed graft function	6 (8.7)	9 (12.2)	NS (0.59)
Acute rejection	7 (10.1)	9 (12.2)	NS
peri-allograft lymph collection	6 (8.7)	7 (9.5)	NS
Peri-allograft urine collection	1 (1.4)	2 (2.7)	NS
Allograft thrombosis	2 (2.9)	3 (4.1)	NS
Impaired wound healing	4 (5.8)	4 (5.4)	NS
CMV infection . CMV IgM (+)	2 (2.9)	6 (8.1)	NS (027)
Long-term post-transplant complications, No. (%)			
Post-transplant Diabetes mellitus	3 (4.3)	3 (4.1)	NS
Malignancy	2 (2.9)	4 (5.4)	NS
Tuberculosis	1 (1.4)	2 (2.7)	NS
Causes of graft failure, No. (%)			
Acute rejection	3 (4.3)	2 (2.7)	NS
Primary nonfunctioning graft	3 (4.3)	5 (6.7)	NS
Delayed graft function	3 (4.3)	3 (4.1)	NS
Recurrent glomerulonephritis	1 (1.4)	1 (1.35)	NS
Chronic allograft nephropathy	3 (4.3)	6 (8.2)	NS
Death with functioning graft	2 (2.9)	3 (4.1)	NS
Others (ATN, nephrotoxin)	0 (0)	2 (2.7)	NS
Cause of death, No. (%)			
Systemic infection	2 (2.7)	5 (6.8)	NS (0.44)
Cardiovascular accident	0 (0)	2 (2.7)	NS (0.49)
Malignancy	0 (0)	2 (2.7)	NS

[a] Abbreviations: HD, Hemodialysis; NA Not Available; NS Non-significant; PD, Peritoneal dialysis

K: 1-2 mmol/L, Ca: 1.25 mmol/L, Mg: 0.5mmol/L, Chloride: 105.5 mmol/L, Acetate:35 mmol/L, Fresenius medical care) based on its availability in the units. All patients received an adequate dose of dialysis. Continuous ambulatory peritoneal dialysis (CAPD) was the only method in our PD group and they usually received 3-4 daily exchanges of 2 L PD solution. All PD patients were treated with glucose-containing solution and received an adequate dose of dialysis. All patients in each group had a panel reactive antibody below 30%. For post-transplantation immune-suppression, patients received three doses of intravenous methyl prednisolone (05-1 g/day), which was continued as oral prednisolone 1mg/kg and then tapered to 5 mg prednisolone by the end of first year. Cyclosporine was initiated at 7-8 mg/kg in two divided doses and then adjusted according to the blood levels. Mycophenolate mofetile was started and continued at 2000 mg/day. All patients received the same antimicrobial prophylaxis after renal transplantation. Pre-transplant induction therapy was used only in five patients. Three patients in HD and two patients in PD group received induction therapy with anti-interleukin-2 antibody, daclizumab (Zenapax, Roche).

3.2. Definitions

The primary endpoints of the study were graft and patient survival. The secondary endpoints included early and long-term post-transplant complications in each group. Delayed graft function (DGF) was defined if a patient needed dialysis in the first week following transplantation (19). Primary non-function (PNF) was defined if the kidney never achieved function after transplantation. Acute graft rejection (AGR) was suspected on clinical and biochemical parameters and confirmed by allograft biopsy. We only entered the cases of early AGR that happened in the first 90 days after transplantation (20).

3.3. Statistical Analysis

The results of the study were analysed by descriptive (Mean ± SD and percentage) and analytical statistical methods. Numeric variables were compared using the independent samples t-test. Patients' survival and graft survival analysis was carried out using Kaplan–Meier estimates and plot. Survival curves were compared using log rank test. Graft survival analysis was performed by censoring death with functioning grafts. Statistical significance was taken at $P < 0.05$.

4. Results

During the 9-yr period, there were 143 patients falling within the defined criteria for this study. 74 patients were on HD and 69 patients were on PD. All patients received their transplanted kidney from living related or unrelated donors. Patients who were on PD (Male/Female; 48/21, mean age; 35.3 ± 15.9 years) was younger compared with HD patients (M/F; 38/36, mean age; 40.7 ± 13.3 years) although the difference was not significance ($P = 0.08$). PD patients had a shorter pre-transplant dialysis period (16.4 ± 10.3 month) compared with HD patients (21.4 ± 11.0 month), ($P < 0.01$). The age of donors in PD group was 28.4 ± 4.4 years and in HD group was 29.7 ± 5.6 years ($P = 0.28$). Fifty five patients (55/69, 79%) in PD group and 46 patients in HD group (46/74, 62%) had male donors. All female donors, donated their organ to female or child patients. Glomerulonephritis was the main primary cause of renal failure in HD group. Diabetic nephropathy and hypertensive nephrosclerosis were the major causes of renal failure in HD patients. One patient (1.4%) in PD group and six patients (8.1%) in HD group had positive result for hepatitis-B virus infection ($P = 0.117$). The number of patients with positive hepatitis C infection (HCV) in HD and PD groups were: 3 patients (4.3%) and 8 patients (10.8 %) in succeeding ($P = 0.211$). *Table 1* shows

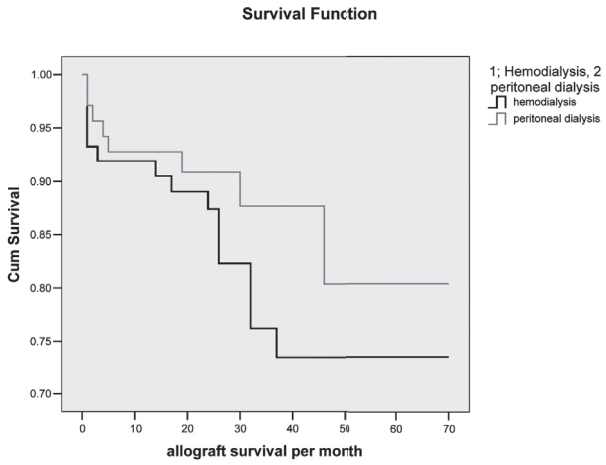

Figure 1. Patients on Peritoneal Dialysis (PD, Upper Line) Seemed to have Better 5-year Graft Survival than did the Patients on Hemodialysis (HD), However, the Comparison of the Kaplan–Meier Curves for Overall 5-year with Log-Rank Method Showed no Significant Difference ($P = 0.26$)

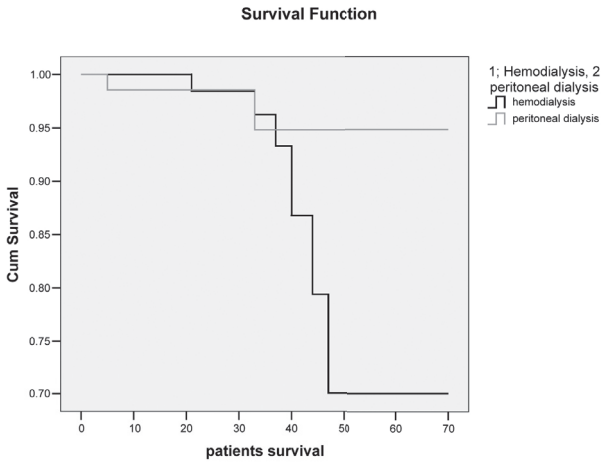

Figure 2. After 5-year Follow-up, Patients on Peritoneal Dialysis (PD, Upper Line) Seemed to have Better Survival than did the Patients on Hemodialysis (HD), However, the Comparison of the Kaplan–Meier Curves for Overall 5-year with Log-Rank Method Showed no Significant Difference ($P = 0.13$).

the basic characteristics of patients in PD and HD group and Figure 1 shows the overall 1 year and 5 year graft and patient survival rates in HD and PD groups. The overall 1year graft survival rate was 93% and 92% in PD and HD groups in succeeding *(Figure 1, Table 2)*. The overall 1 year patient survival rate was 98% for the PD group and 100% for the HD group *(Figure 2)*. The graft failure definition didn't include patient death with a functioning graft. Patients' survival dropped prominently in HD group after third year of transplantation *(Figure 2)*. At the end of the 5-year follow-up, patients on the PD seemed to have better graft and patients' survival than patients on HD. After the third year, the patient survival rate for the PD patients remained stable over the 5 years. Comparison of the Kaplan–Meier curves for overall five years graft survival and patients survival between the PD and HD patients showed no significant difference by log-rank test, (P = 0.26) and (P = 0.13) in succeeding (Figures 1 and 2, table 2). Ninety patients in the PD group 7 (10.1%) and 9 patients (12.2%) in HD group developed early acute rejection (P = 0.79). In PD group, 4 patients (4/7) responded to antirejection therapy, two patients (2/7) failed to respond and returned to peritoneal dialysis. One of these, two non-responders, a 55 year-male, developed renal allograft thrombosis. None of patient with early acute rejection in PD group died during our follow-up. In HD group with acute rejection (9 patients), 7 patients (7/9) responded to antirejection therapy. Two patients (2/9) didn't respond and lost their allograft. Both of them returned to hemodialysis and died within next three years. Renal allograft failure totally happened in 8 patient in PD group (8/69, 11.5%), 5 of them (5/69, 7.2%) returned to PD, and 3 of them (3/69, 4.3%) changed to HD modality. Sixteen patients in HD group (16/74, 21.6%) failed their allograft through the study period. Eleven of those (11/16, 14.9%) returned to HD and five patients (5/16, 6.8%) shifted to PD. Peritoneal catheter was removed at the time of transplantation in two patients (2/69, 2.9%). In remaining 64 PD patients (64/69, 92.8%), catheter was removed at end of third month of transplantation. Three patients (3/69, 2.1%) whose catheter remained up to this period were returned to PD after their early allograft failure. Impaired wound healing happened in those with lymph collection (lymphocele) or urine leakage (urinoma). All of them improved after improvement of their surgical complications. Six patients in PD group (6/69, 8.7%) and nine patients (9/74, 12.2 %) in HD group (p: 0.59) experienced DGF. Three of these patients (3/6) in PD group and 3 of patients in HD group (3/9) regained their allograft function. Primary non-functioning graft (PNF) was observed in 4 patients in the PD group (5.8%) and 5 patients in the HD group (6.8%). Only one patient in PD group (1/4) gained their allograft function after his PNF. Malignancy happened in two patients in PD group (one had Kaposi sarcoma and the other one, squamous cell carcinoma) and five patients in HD group (one squamous cell carcinoma, one Non-Hodgkin lymphoma, one renal cell carcinoma of native kidney and gastric adenocarcinoma in two patients) during our follow up period. Primary and secondary end points of our study and the rate and type of post-transplant complications in HD and PD groups have been shown in *Table 2*.

5. Discussion

In this retrospective study, we studied and compared the results of living-donor renal transplantation in a group of PD and HD patients. The PD group seemed to have better five-year's patients and graft survival. However, survival analysis revealed no overall significant differences in graft survival and patient's survival between PD and HD groups. The rates of post-transplant complications, including; delayed graft function (DGF), primary nonfunctioning graft (PNF), acute rejection (AR), surgical complications and allograft thrombosis was not significantly different between the two groups. The rate of long term complications including; post-transplant diabetes mellitus, malignancy and tuberculosis were not significantly different between two different modalities. In this study, both the HD and the PD groups were matched for demographic features of their donors. All patients in each group underwent a set of in detail clinical and laboratory examination as a renal transplant recipient. Surgical variables including operating surgical team was the same in both groups. All recipients were Iranian and received their first living renal transplantation and started with similar cyclosporine based therapy. Because all patients received their kidney from a living donor, there was no influence of cold ischemia time. We believe that we had a fitted cohort of PD and HD patients that enabled us to examine the effect of dialysis modality on the transplantation outcome. We didn't enter the results of HLA typing in our study because we aren't performing it regularly in our centers. The findings of our study in living –donor renal transplantation was consistent with the findings of previous studies in cadaveric transplantation which showed that there was no significant difference in patient survival and graft survival between HD and PD patients (10, 21, 22).

It has also been reported that the rate and severity of DGF is lower in PD in comparison with HD patients (1, 5, 6). Better preservation of residual renal function in PD patients has been proposed as the cause of this superiority (3). Patients on PD had lower rate of free radical production than patients on HD (23). In our study, the rate of DGF was lower in PD patients when compared with HD patients, although the difference was not significant. Artificial membrane of HD activates the immune system and it has been suggested as a risk factor for acute rejection (24). The rate of early acute allograft rejection (AGR) was similar between two study groups in our study. PD has been reported as a risk factor for renal allograft thrombosis (12-15). In the present study we didn't find an increased rate of allograft thrombosis

in PD patients. Pre-transplant dialysis duration has been reported as an important factor affecting the patient and graft survival. We didn't find such an effect in our study. PD patients in our study had a shorter dialysis period. It could be due to selection a bias, whereby, PD patients had a lower co-morbidities and or transplant candidate were more likely to be placed on PD (3, 22, 25, 26). There is no general agreement on the best time for PD catheter removal after transplantation. In our centers, we remove the PD catheters three months after a successful transplantation. We have two reasons for our protocol. First, it helps patients if there is any need for dialysis during the early transplantation period. Secondary, wound healing is much better when corticosteroid dosage is reduced after three months. In a few patients in our study catheter was removed during the operation. In this study, we found that the choice of dialysis modality did not influence the overall patient and graft survival in living donor renal transplantation. We also found that pre-transplant dialysis modality does not influence the short term and long term complications after living donor renal transplantation.

Financial support

The work was done without any financial support.

Conflict of interest

There is no conflict of interest in this work.

Acknowledgments

We are very grateful to the staffs of peritoneal dialysis unit of Imam Reza Hospital-Tabriz, Mrs Shahin Zolali and Mrs Sayah Melli for their great help in data collection

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