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Original Paper

Hemodialysis or Peritoneal Dialysis, Which Is Better for Patients with Delayed Graft Function?

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Key Words
Hemodialysis • Peritoneal dialysis • Kidney transplantation • Delayed graft function

Abstract
Background/Aims: Hemodialysis (HD) or peritoneal dialysis (PD) is an important renal replacement method in patients with delayed graft function (DGF) after kidney transplantation; however, it is not clear which dialysis modality is superior. This study determined the impact of different dialysis modalities on patients with DGF. ***Methods:*** It was a single-center, retrospective and descriptive study. We performed 673 kidney transplants from donors after cardiac death (DCD) between January 2010 and December 2016 at our center and 138 (20.5%) recipients developed DGF after transplantation. We classified the recipients into two groups according to post-transplant dialysis: DGF-HD (n=96) and DGF-PD (n=42). We analyzed the outcomes of the different dialysis modalities 30 days and 1 year post-transplantation. ***Results:*** There were no differences in baseline factors between patients with post-transplant HD (n = 96) or PD (n = 42). There were 10 patients with conversion from PD to HD during DGF. The DGF-PD patients had a higher rate of treatment failure than the DGF-HD patients (23.8% vs. 0%, p <0.001), peritonitis (7.1% vs. 0%, p = 0.027), and longer duration of dialysis dependence (10.5 vs. 9 days, p = 0.003). There was no statistically significant difference between both groups with respect to acute rejection, hemorrhage, and patient and graft survival at 1 year. ***Conclusion:*** In renal transplant recipients with DGF, post-transplant PD led to increased treatment failure. PD did not result in rapid recovery of transplanted renal function, and had a high probability of peritonitis.

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Introduction

Delayed graft function (DGF) continues to be one of the early complications following post-renal transplantation. The reported frequency of DGF of donors after cardiac death (DCD) kidney transplants greatly varies worldwide (10%–61%) [1–4]. Since 2010, DCD have become the major source of kidneys used in transplants in China. The incidence of DGF is significantly higher than in the past (28%–41%) [5, 6]. DGF is associated with significant morbidity, including increased risks of acute allograft rejection, prolonged hospitalization, higher health care costs, and poorer graft survival [7–9]. Factors associated with an increased risk of DGF include donor (prolonged cold ischemia, donor age >55 years, anoxia, and higher terminal serum creatinine concentration) and recipient factors (hypovolaemia, panel-reactive antibodies > 50%, inherited thrombophilia, pre-transplant diabetes mellitus, and increased body mass index [BMI]) [7, 8].

The effect of pre-transplant dialysis modality on graft and patient survival, however, is controversial [10–14]. In addition, it is unclear whether or not the type of post-transplant dialysis modality in renal transplant recipients with DGF affects restoration of renal function, peri-operative complications, or patient and graft survival. Peritoneal dialysis (PD) has several advantages, including wide availability, ease of performance, non-vascular access placement, ability to remove large amounts of fluid in hemodynamically unstable patients, no need for anticoagulation, fewer complications of hemorrhage, and gradual, but effective correction of acid-base and electrolyte imbalance [15]. Compared with PD, hemodialysis (HD) has a higher dialysis efficacy and better capacity control, but a greater impact on hemodynamics and an increased tendency to bleed. At present, only one study has shown the effect of post-transplant dialysis modality in renal transplant recipients with DGF on 1-year outcomes. It was concluded that using PD increased the risk of wound infection/leakage and required less dialysis time post-operatively [4], but the failure rates of HD and PD treatment were not analyzed.

The aim of this study was to determine the effect of the type of post-transplant dialysis modality on treatment failure rate, duration of dialysis dependence, and 30-day and 1-year outcomes in patients who developed DGF after kidney transplantation.

Materials and Methods

Study population

We conducted a single-center, retrospective and descriptive study consisting of 692 DCD kidney transplantations performed between January 2010 and December 2016 at the Kidney Disease Centre of the First Affiliated Hospital at the Medical College of Zhejiang University. The exclusion criteria were as follows: previous or concurrent transplantation of an organ other than a kidney; a positive cross-match; panel of reactive antibodies (PRA) ≥20%; and malignant tumors. According to exclusion criteria, 19 cases were excluded and 673 cases were included in the study. One hundred and thirty-eight (20.5%) patients developed post-transplantation DGF. The definition of DGF in this study was the need for HD or PD (excluding hyperkalemia) within 7 days post-operatively from renal transplantation [7, 16]. PD patients used continuous ambulatory PD (CAPD), while HD patients used intermittent HD (IHD) before renal transplantation. All the patients used the same dialysis modality (PD or HD) before and after kidney transplant. The patients were divided into two groups based on pre-transplant dialysis, as follows: DGF-HD group (n=96); and DGF-PD group (n=42). These patients were followed for at least 1 year.

Immunosuppression

All recipients underwent induction therapy with anti-thymocyte globulin (ATG) or interleukin-2 receptor antagonist (basiliximab). Standard triple-drug immunosuppression was initiated mainly with prednisone, a calcineurin inhibitor (CNI) (tacrolimus: trough level, 4–10ng/ml; or cyclosporine: trough level, 150–300 ng/ml) within 12 months post-operatively, plus mycophenolate mofetil or enteric-coated

mycophenolate sodium. Anti-rejection therapy after the diagnosis of acute rejection consisted of a 3–5day course of methylprednisolone (6–10 mg/kg/day).If first-line treatment failed, the recipients were treated with anti-thymocyte globulin (1.0 mg/kg/day x 5days) or plasma exchange therapy for a diagnosis of humoral rejection.

Data collection and definitions

Demographics, clinical characteristics, and parameters in donors and recipients were collected from the kidney transplantation electronic database and medical records. Background donor factors were collected, and included age, gender, BMI, cardio-pulmonary resuscitation, continuous renal replacement therapy, hypertension, cold ischemia time, warm ischemia time, pre-operative creatinine level (pre-transplant), urine volume (24 hours pre-transplant), Intensive Care Unit (ICU) hospitalization, and cause of donor death. Background recipient factors were collected, and included age, gender, BMI, hepatitis B infection rate, diabetic status, Human histocompatibility leukocyte antigen (HLA), status, pre-operative duration of dialysis, use of immunosuppressants, and the primary disease. Operative outcomes were collected, and included the number of treatment failures (dialysis changed from PD to HD or HD to PD after kidney transplantation for various reasons), days until dialysis independence, days the post-operative serum creatinine level declined to 2mg/dl, acute rejections, hospitalizations, re-hospitalizations, pulmonary infections, urinary tract infections, post-operative peritonitis, wound infections or leakage, acute left heart failure, gastrointestinal hemorrhage, perirenal hematomas, herpes zoster outbreak, myelosuppression, new-onset diabetes, and patient and graft survival within 30 days and 1 year. The serum creatinine level and estimating glomerular filtration rate (eGFR) were determined within 7 days, 14 days, 30 days, 3 months, and 1 year.

The eGFR was estimated by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [11]. Height and weight were measured on the day of surgery.

Statistics

Statistical analysis was performed with SPSS 19.0 (Inc., Chicago, Ill., USA) and graphics were generated with GraphPad Prism (GraphPad Software 5.0; San Diego, CA, USA). Continuous variables were expressed in the text as mean values with standard deviations (SDs). Medians were used to show the days before dialysis independent, and the days before post-operative serum creatinine declined under 2.0 mg/dL. Categorical variables were presented as frequencies with percentages. Comparisons between the two groups were performed using Student's t-test for normally distributed continuous data, the Mann–Whitney U test for skewed continuous data and chi-squared test for categorical data. The Kaplan-Meier method was used to analyze graft and patient survival, the days before dialysis independent and the days before post-operative serum creatinine declined under 2.0 mg/dL. Multivariable Cox regression was used to analyze factors that may influence the days before dialysis independent. Selection of the variables including donor and recipient characteristics (in Table 1) has been done using stepwise approach. A p value ≤ 0.05 was required to achieve statistical significance.

Ethics

The study was approved by the First Affiliated Hospital of Zhejiang University Ethics Committee Board (Reference Number: 2018-032), and all of the involved activities conformed to the ethical guidelines of the Declaration of Helsinki. Informed consent was obtained from all patients.

Results

673 cases were included in the study between January 2010 and December 2016. DGF developed in 138 (20.5%) recipients. Of the 138 recipients, 96 and 42 were undergoing HD and PD, respectively, prior to renal transplantation.

There was no difference in baseline data with respect to any donor demographic or clinical factors (Table 1). Compared with HD recipients, recipients on PD required less time on dialysis before transplantation (51.5 vs. 38.1 months, p = 0.001; Table 1). There were no significant differences between the groups with respect to the type of induction therapy and immunosuppression.

There were 10 conversions from PD to HD after kidney transplantation. The reasons for the change in modality from PD to HD were attributed to acute left heart failure (five cases; an average of 13 days post-operatively), wound infections and leakage (four cases, an average of 31 days post-operatively), and abdominal dialysis tube occlusion (one case, 3 days post-operatively). Of the five patients who converted dialysis modality due to heart failure, four were high transporters and one was a high average transporter. The remaining 37 patients were high average, low average, and low transporters. The PD program of these five acute left heart failure patients before conversion to HD: 2.5% of the peritoneal dialysate 1000ml was kept in the abdominal cavity for 1.5-2 hours, 8-10 times a day. The PD program of four wound infections and leakage patients before conversion to HD was a standard CAPD. One abdominal dialysis tube occlusion patient was converted to HD after treatment failure (changing his position and urokinase

Table 1. Demographic or clinical factors of (a) donors and (b) recipients for DCD kidney transplantation BMI = body mass index; CPR = cardio-pulmonary resuscitation; CRRT = continuous renal replacement therapy; ICU=Intensive Care Unit; HLA = human histocompatibility leukocyte antigen; ATG = anti-thymocyte globulin; FK = tacrolimus; EC-MPS= enteric-coated mycophenolate sodium; MMF = mycophenolate mofetil

Factor	Hemodialysis	Peritoneal dialysis	p value
(a) Donor	N=74	N=37	
Gender (% male)	66(89.2)	29(78.4)	0.126
Age (yr)	39.1±15.1	36.1±16.9	0.353
Height (cm)	163.3±20.5	157.8±30.2	0.259
Weight (kg)	62.6±15.9	58.8±19.8	0.275
BMI (kg/m2)	23.0±3.6	22.2±3.5	0.239
CPR (%)	14(18.9)	7(18.9)	1.000
Hypertension (%)	12(16.2)	4(10.8)	0.633
Warm ischemia times (min)	9.4±5.4	11.3±9.2	0.177
Cold ischemia times (hr)	7.4±3.5	6.9±3.4	0.494
Preoperative creatinine (μmol/l)	142.2±111.6	125.1±73.9	0.408
Pre-transplant urinary volume (mL/24 h)	2844.7±1551.8	2452.8±1747.8	0.240
ICU hospitalization (days)	5.8±5.5	5.6±6.6	0.853
CRRT (%)	3(4.1)	1(2.7)	1.000
Pediatric donor (%)	6(8.1)	5(13.5)	0.369
Cause of death (%)			0.721
Craniocerebral trauma	42(56.8)	18(48.6)	
Stroke	22(29.7)	13(35.1)	
Other	10(13.5)	6(16.2)	
(b) Recipient	N=96	N=42	
Gender (% male)	66(68.8)	22(52.4)	0.066
Age (yr)	44.9±10.5	43.2±13.3	0.480
Height (cm)	166.6±6.9	164.1±10.1	0.147
Weight (kg)	60.2±10.1	57.9±12.2	0.284
BMI (kg/m2)	21.7±3.2	21.4±3.3	0.690
Hepatitis B (%)	8(8.3)	5(11.9)	0.509
Diabetic (%)	2(2.1)	2(4.8)	0.755
HLA (MM)	2.9±1.2	3.0±1.1	0.737
Pre-transplant dialysis duration (months)	51.5±28.8	38.1±18.1	0.001
Basiliximab/ATG (%)	32.3/67.7	38.1/61.9	0.508
FK/cyclosporine (%)	90.6/9.4	90.5/9.5	1.000
MMF/EC-MPS (%)	45.8/54.2	54.8/45.2	0.334
Primary disease (%)：			0.323
Glomerulonephritis	85.4	92.9	
Polycystic kidney	6.3	0	
Hypertensive nephropathy	2.1	4.8	
Diabetic nephropathy	2.1	0	
Other	4.1	2.3	

Table 2. 30-d and 1-y outcomes in renal transplant recipients with delayed graft function using peritoneal dialysis or hemodialysis * These were analysed using Kaplan-Meier method

Outcome	HD (n=96)	PD (n=42)	p value
Treatment failure (%)	0(0)	10(23.8)	<0.001
Days until dialysis independence (days)	9.0	10.5	0.003*
Postoperative serum creatinine recovered to 2mg/dl (days)	27	27	0.875*
Acute rejection at 1 year (%)	6(6.3)	2(4.8)	1.000
Hospitalization(days)	29.7±16.9	39.6±31.6	0.128
re-hospitalization	38(39.6)	20(47.6)	0.379
Graft survival at 30 days (%)	97.9%	95.2%	0.376*
Patients survival at 30 days (%)	99.0%	100%	0.508*
Graft survival at 1 year (%)	92.7%	85.7%	0.176*
Patients survival at 1 year (%)	96.9%	97.6%	0.814 *

injection into the dialysis tube). No patients in the HD group converted to PD post-operation, see Table 2. Fistula occlusion occurred in one patient. Vascular access of the patient was changed to a temporary catheter in the internal jugular vein. There were no differences between the two groups in bleeding-related complications, see Table 3. Two patients with gastrointestinal bleeding continued HD by adjusting the anticoagulation method. There was no conversion from HD to PD due to refractory hypotension. Thus, DGF-PD patients had a higher rate of treatment failure than DGF-HD patients (23.8% vs. 0%, p <0.001; Table 2). Compared with DGF-HD, DGF-PD patients had a higher incidence of peritonitis (7.1% vs. 0%, p = 0.027; Table 3). All the three patients had clinical signs of peritoneal inflammation and peritoneal fluid leukocyte count of>0.1 * 10^9/L. The peritoneal fluid culture of two patients was Escherichia coli and one patient was negative for culture. Patients with peritonitis were controlled by antibiotics and continued PD. Peritonitis was not the cause of PD conversion to HD in the study. Compared with DGF-HD, DGF-PD patients had a longer duration of dialysis dependence (10.5 vs. 9 d, p = 0.003, Fig. 1). Among the donor and recipient characteristics in the Table 1, dialysis mode and warm ischemia time were independent factors influencing dialysis dependent time over 30 days. Compared with hemodialysis treatment, peritoneal dialysis treatment have a 3.259 hazard ratio (95% CI 1.030–10.314, P=0.044) for dialysis dependent time over 30 days post-transplantation. Donor with a longer warm ischemia time (hazard ratio= 1.053, 95% CI 1.007–1.100, P=0.022) was other risk factor for dialysis dependent time over 30 days post-transplantation, see Table 4. At 30 days and 1 year post-transplantation, there was no statistically significant difference between the groups with respect to patient and graft survival after transplantation in patients who developed DGF (Fig. 2); renal function of graft was detailed in Fig. 3.

Renal transplant recipients who developed DGF were categorized into three groups depending on the first and the last dialysis modality used after transplantation HD-HD (n = 96), PD-PD (n = 32), and PD-HD (n = 10). PD-HD was associated with the highest risk of overall graft failure, whereas PD-PD was associated with the highest survival of overall graft among the three groups (p<0.001). The proportion of graft survival in the HD-HD group was 92.7%, 100% in the PD-PD group, and 40% in the PD-HD group at 1 year. The proportion of patient survival was similar in all groups at 1 year (HD-HD, 96.9%; PD-PD, 100%; and PD-HD, 90%. p=0.243).

Table 3. Complications in renal transplant recipients with delayed graft function using peritoneal dialysis or hemodialysis

Outcome	HD(n=96)	PD(n=42)	P
Total infection rate at 1 year (%)	48(50)	25(59.5)	0.302
Pulmonary infection at 30 days (%)	17(17.7)	7(16.7)	0.882
Pulmonary infection at 1 year (%)	35(36.5)	17(40.5)	0.654
Urinary tract infection at 30 days (%)	3(3.1)	3(7.1)	0.541
Urinary tract infection at 1 year (%)	7(7.3)	4(9.5)	0.917
Postoperative peritonitis (%)	0(0)	3(7.1)	0.027
Wound infection or leakage (%)	6(6.3)	4(9.5)	0.845
Acute left heart failure (%)	2(2.1)	4(9.5)	0.129
Gastrointestinal hemorrhage (%)	2(2.1)	1(2.4)	1.000
Perirenal hematoma (%)	0(0)	1(2.4)	0.304
Herpes zoster (%)	2(2.1)	2(4.8)	0.755
Myelosuppression (%)	7(7.3)	5(11.9)	0.376
New-onset diabetes (%)	4(4.2)	3(7.1)	0.755

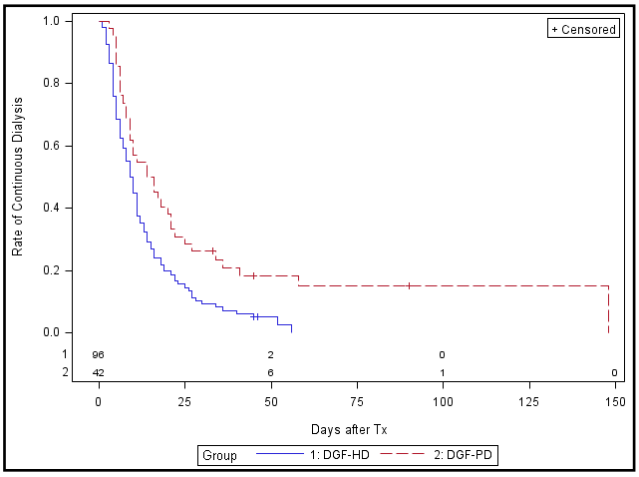

Fig. 1. Days until dialysis independence of DGF-HD and DGF-PD patients. Compared with DGF-HD, DGF-PD patients had a longer duration of dialysis dependence (10.5 vs. 9 d, p = 0.003).

Discussion

DGF is a common complication in the early stage of renal transplantation. In selecting the mode of transitional dialysis, the clinician usually chooses the same pre-transplant dialysis method after the patient develops DGF; however, it remains unknown whether or not HD or PD is superior.

PD patients have a relatively high incidence of malnutrition and continue PD after transplantation because of abdominal loss of nutrients and the influence of abdominal distension on appetite, which is the cause of wound infections and leakage. The treatment failure rate of PD includes peritoneal infections, malnutrition, inflammation, cardiovascular mortality, volume overload, glucose exposure, adequacy of solute removal, peritoneal access, and peritoneal physiology [17]. Our study showed that the treatment failure rate of the PD group was significantly higher than the HD group for the following three reasons: acute left heart failure; wound infections and leakage; and the abdominal dialysis tube was occluded. Of the five patients who converted the mode of dialysis due to heart failure, four were high transporters and one was a high average transporter. Peritoneal function was relatively poor for the ultrafiltration of water. After changing to HD, cardiac function in the five patients significantly improved with dehydration. Special attention should be paid to capacity control during DGF of high transporters and timely conversion of the dialysis mode to avoid heart failure if necessary. We only had one case of a PD patient with automated PD (APD) after surgery. Indeed,

Table 4. Multivariate Cox regression analysis determined risk factors for post-transplant dialysis time over 30 days. The characteristics of donor: gender, age, BMI, warm ischemia times, cold ischemia times, preoperative creatinine, pre-transplant urinary volume, ICU hospitalization time, cause of death and rate of cardio-pulmonary resuscitation, hypertension, continuous renal replacement therapy, pediatric donor and the characteristics of recipient: gender, age, BMI, pre-transplant dialysis time, post-transplant dialysis modality (HD or PD), HLA mismatch, induction therapy, immunosuppressive agents and rate of Hepatitis B, diabetes mellitus were analyzed. Variables of $p < 0.2$ were included in multivariate Cox regression model. BMI = body mass index; ICU=Intensive Care Unit; CRRT = continuous renal replacement therapy; HD= Hemodialysis, PD= Peritoneal dialysis, HLA = human histocompatibility leukocyte antigen

Factor	Dialysis time <30days (=117)	Dialysis time >=30days (n=21)	P value	Multivariate analysis between post-transplant dialysis time below and over 30 days		
				Hazard ratio	95% CI	P value
Donor characteristics						
BMI (kg/m2)	23.24±3.45	21.95±4.54	0.063			0.547
Warm ischemia times (min)	9.58±5.53	12.90±10.77	0.175	1.053	1.007-1.100	0.022
Preoperative creatinine (μmol/l)	149.52±114.53	106.23±52.97	0.157			0.252
ICU hospitalization (days)	5.69±5.40	6.05±7.86	0.134			0.319
CRRT (%)	2(1.7%)	4(19%)	0.005			0.089
Recipient characteristics						
Dialysis mode (1=HD, 2=PD)	86/31	10/11	0.022	3.259	1.030-10.314	0.044
Hepatitis B (%)	9(7.7%)	4(19.0%)	0.113			0.603
HLA (MM)	2.79±1.15	3.43±1.21	0.028			0.089

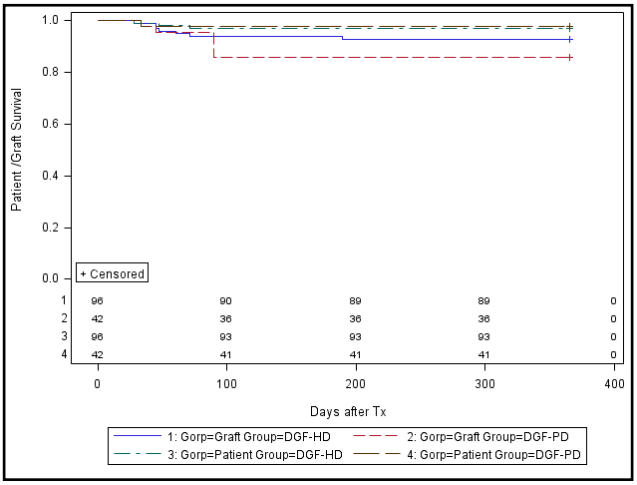

Fig. 2. Patient and graft survival at 1 year of DGF-HD and DGF-PD patients. There was no statistically significant difference in patient (DGF-HD vs DGF-PD: 96.9% vs 97.6%, p=0.814) and graft survival (DGF-HD vs DGF-PD: 92.7% vs 85.7%, p=0.176) between the two groups (Tx: transplantation).

APD may be better than CAPD for water removal. APD might reduce the rate of treatment failure because of poor capacity control. HD was not converted to PD due to hemorrhage, which may be better for capacity control. HD did not significantly affect hemorrhagic complications, which may be related to the anti-coagulation property of citrate *in vitro* and the reduced effect on blood coagulation. Three cases of peritonitis did not convert from PD into HD, and were quickly controlled with antibiotics. In this study, peritonitis was not the cause of treatment failure. PD had an effect on incision healing after transplantation. Incision complications were the second most common cause of treatment failure in the current study. The worst prognosis for PD-HD suggested that the early conversion to HD may improve the prognosis if PD led to complications. PD-PD was associated with the lowest risk of overall graft failure compared with other groups.

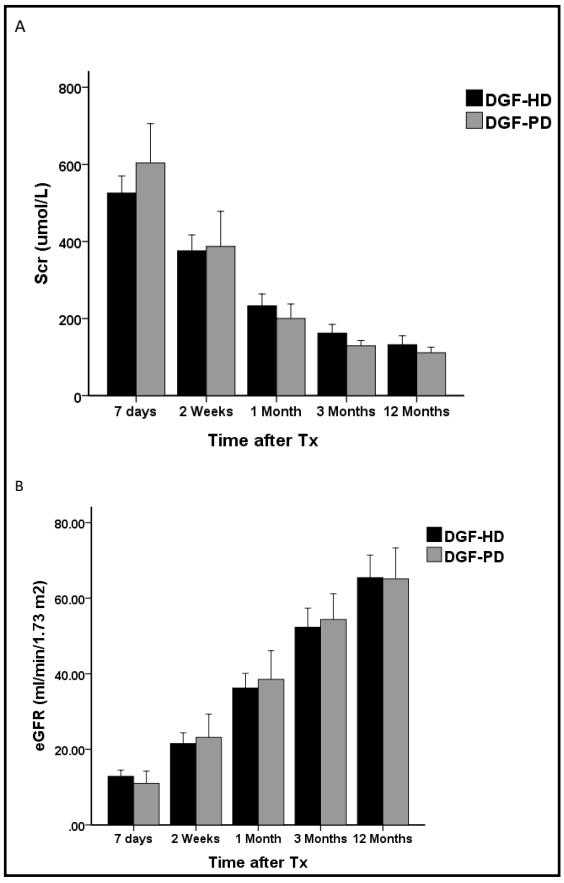

Fig. 3. Renal function (A: Serum creatinine and B: estimating glomerular filtration rate (eGFR)) of DGF-HD and DGF-PD patients at 1 year. There was no statistically significant difference in renal function between the two groups (Tx: transplantation).

It has been suggested that the occurrence of infections after transplantation may differ between PD and HD patients; however, there is no consensus on the outcome. Infective complications and patient mortality have been reported to be higher with PD [18, 19]. In contrast, some studies have reported fewer bacterial and hepatitis infections in PD patients after transplantation, and a similar rate of other infections in HD and PD patients [20, 21].In our study there was a higher incidence of post-transplantation peritonitis in recipients who underwent pre-transplant PD, which may increase the likelihood of abdominal infections. In addition, establishing immunosuppression led to changes in intestinal micro-ecology and migration of intestinal bacteria after transplantation.

It has been hypothesized that residual renal function may be better preserved in PD patients [20, 21], and consequently PD patients may have a higher glomerular filtration rate (GFR) at the time of kidney transplantation. Nevertheless, long-term graft function, as measured by eGFR at different times throughout the first post-transplant year, also had similar results in these groups in our study. The number of days the serum creatinine level recovered to 2mg/ml was similar in the two groups post-transplantation. The HD group had a shorter duration of dialysis dependence after DGF. The PD group had no advantage because the influence on hemodynamics was less. It is our opinion that if hypotension does not occur, intermittent HD does not significantly affect recovery of the transplanted kidney. Due to poor capacity control, heart failure might affect the renal blood supply, which is not conducive to recovery of renal function. In addition to dialysis modality, warm ischemia time is also a risk factor for postoperative dialysis-dependent time more than 30 days. But other donor (such as cold ischemia times) and recipient (body mass index and diabetes) characteristics that might affect the duration of DGF are not associated with postoperative dialysis-dependent time

more than 30 days. This might be related to relatively short cold ischemia time (average 7.3 hours) of the kidneys, and relatively low body mass index (average 21.6) and the proportion of diabetes (2.9%) in the recipients in the study.

Our study had the expected limitations of a retrospective study. Even though we adjusted for a number of patient characteristics, the possibility of residual confounding could not be excluded. First, in patients without specific preferences or contraindications for one of the dialysis modalities, the preference of the nephrologist/center may influence the final choice for PD or HD before transplantation [22]. Second, all the patients used the same dialysis modality (PD or HD) before and after kidney transplant. Furthermore, all measured baseline demographic and clinical factors were similar between the groups and those factors that may have differed, such as donor DCD race and lifestyle, may have had an impact upon the outcome.

In summary, in renal transplant recipients with DGF, post-transplantation PD led to increased treatment failure. PD did not exhibit the advantage of rapid recovery of transplanted renal function, but PD had a high probability of peritonitis. DGF-PD patients should be converted to HD in a timely fashion when complication arises.

Disclosure Statement

All authors declare that they have no conflict of interest.

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