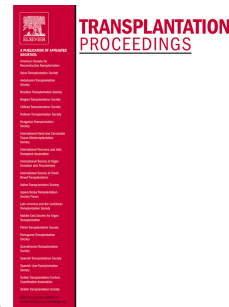


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A paired analysis of the outcome after kidney transplantation in peritoneal (PD) and hemodialysis (HD) patients

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Key words: kidney transplantation, peritoneal dialysis, hemodialysis, paired kidney analysis

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Abbreviations: AR – acute rejection, ATG - polyclonal anti-thymocyte, AZA – azathioprine, CABG - coronary artery bypass graft, CCI – Charlson Comorbidity Index, CIT – cold ischemia time, CsA – cyclosporine, DGF – delayed graft function, DM – diabetes mellitus, eGFR – estimated glomerular filtration rate, 4-point MDRD formula ( $\text{mL}/\text{min}/1.73\text{m}^2$ ), HD-hemodialysis, MM – number of HLA mismatches, MMF- mycophenolate mofetil, NODAT - new onset diabetes after transplantation, P-prednisone PD – peritoneal dialysis, PTCA - percutaneous transluminal coronary angioplasty, RTx – renal transplantation SCC - Serum creatinine concentration ( $\text{mg}/\text{dl}$ ), TAC – tacrolimus, THYMO – thymogloglobuline, TIT – total ischemia time, UTI – urinary tract infection, WIT – warm ischemia

## Abstract

The impact of dialysis modality before transplantation (HD or PD) on outcomes is not clear.

We retrospectively analyzed the impact of dialysis modality on post-transplantation follow up. To minimize the donor bias, a paired kidney analysis was applied. 133 pairs of peritoneal dialysis (PD) and hemodialysis (HD) patients transplanted in our center between 1994 and 2016 who received kidneys from the same donor were included.

HD patients were significantly older (44 vs 48 years), but the Charlson Comorbidity Index was similar (3.12 vs 3.46) in both groups. The groups did not differ significantly with respect to immunosuppressive protocols and the number of mismatches 2.96 vs 2.95.

One-year patient (98% vs 96%) and graft (90% vs 93%) survival was similar in PDP and HDP group. The Kaplan-Meier curves of patients and graft survival did not differ significantly. DGF and AR occurred significantly more often in the HD recipients. Graft vessel thrombosis resulting in graft loss occurred in 9 PD (6.7%) and in 4 HD (3%) patients ( $p>0.05$ ). Creatinine serum concentration and eGFR (MDRD) one-month, one-year, and at last visit, did not differ.

On multivariate analysis, factors significantly associated with graft loss were: graft vessels thrombosis, DGF, graft function one month after transplantation. On univariate analysis the age, coronary heart disease, graft loss were associated with death. Amongst these factors only coronary heart disease ("Model 1") and graft loss were significant predictors of death on multivariate analysis.

Conclusion: Long-term outcome of renal transplantation is similar in patients coming from either PD or HD. Those groups of patients differ in some aspects, such as susceptibility to vascular thrombosis in PDP, and to DGF and AR in HDP.

## INTRODUCTION

Renal transplantation remains the treatment of choice for many patients with end-stage renal disease (ESRD). Studies examining the association between dialysis modality, i.e. hemodialysis (HD) or peritoneal dialysis (PD), and patient and graft survival after transplantation have shown ambiguous results. Some studies reported that there was no association between dialysis modality and the patient and graft outcome after transplantation [1-6]. However, Goldfarb-Rumyantzev et al. in 92,844 US ESRD patients, observed that kidney transplant recipients on PD before transplantation had a lower risk of death, and a lower risk of (death-censored) graft failure than HD patients [7]. Molmar et al. in 12,416 HD and 2,092 PD US patients found that PD recipients had lower mortality, but similar graft loss or delayed graft function [8]. On the other hand, Snyder et al. in 22,776 US ESRD patients noticed that death censored graft failure was 1.15 times higher in PD vs HD patients, but mortality and overall graft failure rates were not different. In that study, transplantation in PD patients was more frequently associated with early, but not late, graft failure. In those patients for whom data on the cause of early graft failure was available, graft thrombosis was more frequent in PD patients [9]. Similar observations were also reported in the studies of Ojo et al., Murphy et al. and van der Vliet et al. [10-12]. Vats et al. analyzing 1,090 PD and 780 HD children, found that graft loss resulting from vascular thrombosis was more common in children who were on PD before transplantation [13]. Martins et al. in the most recent study, analyzing the impact of dialysis modality on the outcome of simultaneous pancreas-kidney transplantation (SPKT) in type 1 diabetic patients, found that transplantation in PD patients was more frequently complicated with intra-abdominal infection leading to pancreatic loss, and with renal thrombosis with an adverse impact on graft survival [14]. The effect of dialysis modality on early post-transplant infections also remains controversial. While some studies have noted a higher incidence of infections in PD patients in the first month after transplant [15] others failed to show differences in the rate of post-transplant infections in PD and HD patients [16].

The primary goal of this single-center study was to analyze short and long-term outcomes of kidney transplantation in pre-transplant PD and HD patients. We also studied the incidence of

postoperative complications, with a focus on post-transplant vascular thrombosis, infectious complications and delayed graft function. In order to minimize the impact of donor variability and bias, paired kidney analysis was applied.

## MATERIALS AND METHODS

Peritoneal dialysis patients (n=207) constituted 13.7% (207 from 1505) of all kidney transplantations performed in Gdansk Transplantation Center between December 1994, when the first patient dialyzed by means of PD was transplanted, and December 2016. 133 of those peritoneal dialysis patients (PDP) who had a paired kidney recipient from the same donor, who was on hemodialysis (HDP) before transplantation, were included in the analysis. Patients who sequentially underwent both dialysis modalities were excluded from the study. Only patients receiving few hemodialysis sessions before starting long-lasting PD were accepted. Patients receiving second and next KTx were excluded from the study.

### Statistical Analyses

Quantitative variables were presented as means with standard deviations (SD) or medians with inter-quartile range (IQR). Qualitative data was shown as numbers and percentages.

Continuous variables were compared using Student's t-test or Wilcoxon-Mann-Whitney test, whereas chi-square test or Fisher's exact test were applied for categorical variables.

Survival curves were plotted by using the Kaplan-Meier method. Differences in survival between PD group and HD group were compared using log-rank [17] test and Renyi's test (supreme version of the weighted log-rank test) [18]. The reverse Kaplan-Meier estimator [19] was used to evaluate median follow-up. Univariate and multivariate models were based only on Cox proportional hazards regression [20]. Results from the Cox regressions were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs).

Multivariate Cox proportional hazards models were built using the following strategies: only significant

variables (P value of 0.05 or less) with univariate models (model 1), and forward selection (model 2).

The assumption of proportionality hazards was evaluated by including time-dependent interactions of each variable, and tested using Schoenfeld residuals [21].

In order to verify the linearity of continuous covariates, the martingale residuals [2022] with LOESS (local polynomial regression) curve were plotted.

The goodness of fit of multiple regression was assessed using Akaike's information criterion (AIC). The 2-tailed tests were carried out at a significance level of  $p \leq 0.05$ .

All statistical analyses were performed using R package version 3.2.3.

## RESULTS

### Recipient Characteristics

The PDP group consisted of 133 (65 male, 68 female) patients aged between 12 and 71 (mean  $44.42 \pm 15.1$ ) years. The HDP group also constituted 133 (86 male, 47 female) patients aged between 19 and 81 (mean  $48.88 \pm 15.5$ ). The PDP patients were significantly younger (t-Student Test,  $p=0.04$ ), but with regard to the Charlson comorbidity index (CCI) [23, 24] we found no differences in the number of comorbidities between PDP and HDP patients (3.12 vs 3.46).

The underlying renal diseases in the PDP and HDP groups included chronic glomerulonephritis (38.5% vs 31.8%), chronic interstitial nephritis (6.2% vs 7.7%), diabetic nephropathy (14.6% vs 15.5%), cystic kidney disease (7.7% vs 11.6%), hypertensive nephropathy (12.3% vs 14.0%), and not known and others about 20% in both groups.

Dialysis time before transplantation was significantly shorter in PDP than in HDP group ( $20.35 \pm 17$  vs  $33.55 \pm 36$  mo.;  $p<0.05$ ).

The frequency of diabetes type 1 and 2 was equal in PDP and HDP (15/9;  $p>0.05$ ). The time on the waiting list for PDP recipients (mean  $4.9 \pm 5$ ; range 1 day to 23 mo.) and HDP (mean  $5.2 \pm 8$ ; range 1

days to 45 mo.) was not different ( $P > 0.05$ ) – available data from years 2011-2016. The PDP and HDP groups did not differ with respect to types of immunosuppressive protocols, mean total ischemia time (14h 33' vs 14h 48') and panel reactive antibody titers (6.1/3.1% vs 4.6/1.2% historical and current, respectively).

Patients characteristics were performed in Tab. 1.

#### Donor Characteristics

The donors for PDP and HDP recipients (87 male, 52 female) were aged between 15 and 74 (mean  $43.3 \pm 14$ ) years. Their mean eGFR (Cockcroft-Gault) level was  $114.2 \pm 45$  mL/min/1.73 m<sup>2</sup>. The cause of donor death was traumatic in 42%, cerebrovascular in 52% and other factors accounted for 6% of the deaths. According to deceased-donor score (A,B,C,D) the categories of donors were as follows: A - 41; B - 50; C - 36; D - 1; no data - 5 in the PDP group and A - 40; B - 49; C - 38; D - 1; no data - 5 for the HDP group. The groups slightly differed due to the fact that in deceased-donor score, the number of mismatches between donor and recipient is therefore also taken into account [25].

#### Post-transplantation follow-up in PDP and HDP Groups

The post-transplantation follow-up for the PDP and HDP groups is presented in Table 2. The groups (PDP vs HDP) differ significantly with respect to the incidence of delayed graft function (DGF). 28 (21.05%) PDP patients, and 57 (42.86%) HDP patients experienced DGF ( $P < 0.05$ ). DGF was defined as the need for hemodialysis during the first week after transplantation. The incidences of acute rejection (AR) were significantly fewer in the PDP (14.3% vs 32.3%) in PDP vs HDP, respectively;  $p < 0.05$ . AR was not always biopsy-proven, so the probability of mis-diagnosis of AR in patients suffering from DGF was probable.

The most common complications were infections: urinary tract infections and cytomegalovirus (CMV), and also new onset diabetes after transplantation (NODAT). PDP and HDP had a similar rate of bacterial infections (mostly urinary tract infection) ( $p > 0.05$ ), and the duration of the first hospitalization was



slightly longer in HDP group (24.1 vs 22.2 days,  $p>0.05$ ). The number of cardiovascular complications was small, and similar in both groups.

Among the surgical complications, the most common were lymphoceles, hematomas, urinary fistulas, ureter obstructions and graft vessels thrombosis. The amount of early graft vessel thrombosis was higher in PDP as compared to HDP: 6, 7.2% vs 3% ( $p>0.05$ ).

On univariate analysis PD was not a risk factor for graft vessel thrombosis (Tab. 3)

In multivariate “forward model” analysis (Tab. 4). PD can be directed as an independent risk factor for graft vessels thrombosis, the risk was almost 3 times higher than in HDP ( $p=0.09$ ).

#### Comparison of graft function in the PDP and HDP Groups

A comparison of the concentration of serum creatinine and eGFR measured at a few time points after transplantation (after 1 months, after 12 months, and during the last ambulatory control, was similar in both groups, test  $P>0.05$  – Tab. 5. During long-term follow-ups patients were losing their grafts mainly due to IF/TA, and suspicion of non-compliance to medications.

#### Comparison of Patient Survival and Graft Survival

During the follow-up (0.5 to 23 years) 8 and 12 patients died in PDP and HDP groups, respectively. Causes of death were mainly malignancy and cardiovascular diseases (Table 6).

The groups (PDP vs HDP) did not differ significantly from each other with respect to 1-year patient survival (98% vs 96%) and 1-year death censored graft survival (90% vs 93%) and 1-year graft survival (89% vs 90%). The Kaplan-Meier curves of patients and graft and death-censored graft survival did not differ significantly (Fig 1,2,3).

During follow-up there were a total of 20 death events - estimated median length of follow-up was 46 months (95% CI: 26-57) .

On univariate analysis, factors significantly associated with death-censored graft loss were: DGF, graft vessels thrombosis, infections (mainly UIT) and graft function one month after transplantation, the independent predictors upon multivariate analysis were: DGF, graft vessels thrombosis and eGFR (Table 7, 8). DGF, graft vessels thrombosis, graft function one month after transplantation were independent factors of graft loss (Table 9, 10). On univariate analysis the age, coronary heart disease, graft loss were associated with death. Amongst these factors only coronary heart disease ("Model 1") and graft loss were significant predictors of death on multivariate analysis.

(Table 11, 12).

## DISCUSSION

Previous single-center studies have brought contradictory results in estimation of the influence of pre-transplant dialysis modality on transplantation outcome in recipients receiving grafts from the same donor. Our study groups PDP and HDP were comparable in respect of comorbidities, gender and CCI, mean age of HDP group was higher. Patients received kidneys from donors with excellent kidney function and were given similar types of initial immunosuppressive protocols. Short and long-term medical care was performed by the same transplant team. This methodological factor mitigates the confounding influence of differences in demographic and clinical characteristics of donors, as well as different transplant center surgical and medical protocols, on the results. The groups (PDP vs HDP) did not differ significantly from each other with respect to 1-year patient survival and 1-year death censored graft survival and 1-year graft survival.

While some studies have failed to find a difference in outcomes [1,2,3,4,5,6], others have found PD to have some beneficial effects after renal transplantation compared to HD [7, 8, 9]. In our center, PDP had a

similar to HDP one-year patient survival (98% vs 96%), one-year death censored graft survival (90% vs 93%) and one-year graft survival (89% vs 90%). The Kaplan-Meier curves showing long-term follow-up (0.5-23 years) patients and graft survivals did not differ significantly in PDP and HDP (Fig 1, 2, 3).

Cardiovascular, and most other, complications listed in table 2 were observed in similar frequency in PDP and HDP; Infectious complication were equally common in both groups. Graft function in both groups did not differ, both early and late, after transplantation. Similar numbers of patients died during the follow-up; main causes of death (cardiovascular disease or neoplasm) were not different.

However, the studied groups have differed in certain aspects. Some studies have shown PDP to experience fewer incidences of DGF (8, 9, 26, 27) the others have not (4). In our center, in quite well-matched groups, we confirmed that PDP experienced significantly less DGF. In PDP we also diagnosed a significantly fewer number of ARs, although the diagnosis was usually based on clinical symptoms and doppler US, and in HDP experiencing much more frequently DGF, the number of ARs could be overestimated. On the other hand, DGF may predispose to rejection [20].

PD patients have been reported to be more likely to have allograft vascular thrombosis, compared to patients treated with HD [10-14]. The incidence of vascular thrombosis at our center was higher in PDP as compared to HDP but not significantly (multivariate “forward model” analysis the risk in PDP was almost 3 times higher than in HDP).

What is to be noticed is that among PDP were more individuals with type 1 diabetes (DM1) (11 vs 7% in PDP and HDP respectively), but none of patients with thrombosis suffered from DM 1. In HDP thrombosis occurred in three patients, and none of them was diabetic. Martins et al. in his recent study analyzing the impact of dialysis modality on the outcome of simultaneous pancreas-kidney transplantation (SPKT) in DM1 patients, found that transplantation in PD patients was more frequently complicated with renal thrombosis with an adverse impact on survival [14]. There are several risk factors for vascular thrombosis in solid organ transplantation; such as multiple vessels, technical problems during anastomosis, very young pediatric donors or elderly donors, thrombocytosis, hemoconcentration, hypotension and the existence of a previous transplant and hypercoagulable states [10,29]. Diabetes itself

has been considered an additional risk factor for thrombosis [30]. Controversies still exist whether PD by itself predisposes to a thrombophilic state [10]. However, patients with vascular access problems are referred more often to PD, possibly due to a pre-existing prothrombotic state in some of them. Robertson et al. [31] and Scheffert et al. [29] reported potential beneficial effects of aspirin and low-dose heparin started in the early post-operative period, at the expense of a higher risk of bleeding in PKT. Schenker et al. have found better results using low molecular-weight heparin [32].

In our transplant center low molecular-weight heparin is a standard in post-operative protocols. However, taking into consideration our, and other authors', observations, both in kidney transplantation and PKT, the use of small doses of aspirin could be conceivable.

Our results show that short and long-term patients and graft survival are independent of the pre-transplant dialysis modality. Those groups of patients differ in some aspects, such as susceptibility to vascular thrombosis in PDP, and to DGF and AR in HDP. As PD first strategy, besides pre-emptive transplantation, in ESRD patients is advised, the risk of renal thrombosis should be taken into consideration and appropriate measures undertaken.

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- Fig 1. Patient survival (Kaplan-Meier) in days for PDP and HDP group of patients  
Fig 2. Death censored graft survival (Kaplan-Meier) in days for PDP and HDP groups  
Fig 3. Graft survival (Kaplan-Meier) in days for PDP and HDP groups



Table 1. Characteristics of Peritoneal Dialysis Pairs (PDP) (n=133) who had their kidney donor Hemodialyzed Pairs (HDP) (n=133)

| Comorbidities (n)                                | PDP                 | HDP                 | Significance        |
|--|---------------------|---------------------|---------------------|
| Coronary artery disease (treated conservatively) | 9                   | 11                  | ns                  |
| Coronary artery disease (treated by PTCA)        | 6                   | 3                   | ns                  |
| Coronary artery disease (treated by CABG)        | 4                   | 3                   | ns                  |
| Cerebral stroke                                  | 2                   | 2                   | ns                  |
| Peripheral artery disease                        | 2                   | 4                   | ns                  |
| Type 1 diabetes mellitus                         | 15                  | 9                   | ns                  |
| Type 2 diabetes mellitus                         | 5                   | 12                  | ns                  |
| viral hepatitis                                  | HBV-4               | HBV-1               | ns                  |
|  | HCV-1               | HCV-11              | Fisher Test, p<0.05 |
| Charlson Comorbidity Index                       | 3.12                | 3.46                | ns                  |
| Estimated 10 year survival                       |                     |                     |                     |
| End point  | PDG                 | HDG                 |                     |
| Graft loss [95% CI]                              | 0.674 [0.562-0.809] | 0.593 [0.470-0.748] |                     |
| Death censored graft loss [95% CI]               | 0.716 [0.606-0.845] | 0.648 [0.520-0.808] |                     |
| Death [95% CI]                                   | 0.907 [0.832-0.988] | 0.852 [0.760-0.956] |                     |
| <b>Immunological characteristics</b>             |                     |                     |                     |
| Number of HLA mismatches (n)                     | 2.97                | 2.94                |                     |
| Immunosuppressive protocols (n)                  | 14                  | 16                  |                     |
| AZA, CsA, P                                      | 1                   | 2                   |                     |
| AZA, TAC, P, ATG induction                       | 0                   | 1                   |                     |
| AZA, CSA, P, ATG induction                       | 5                   | 3                   |                     |
| AZA, TAC, P                                      | 50                  | 35                  |                     |
| MMF, CsA, P                                      | 46                  | 51                  |                     |
| MMF, TAC, P                                      | 5                   | 2                   |                     |
| MMF, CsA, P, induction (anti-CD25)               | 8                   | 10                  |                     |
| MMF, TAC, P, induction (anti-CD25)               | 0                   | 2                   |                     |
| MMF, CsA, P, ATG induction                       | 0                   | 0                   |                     |
| MMF, TAC, P, ATG induction                       | 0                   | 0                   |                     |
| CsA, sirolimus, P,                               | 1                   | 1                   |                     |
| CsA, sirolimus, P, ATG induction                 | 0                   | 2                   |                     |
| Everolimus, TAC, P, induction (anti-CD25)        | 1                   | 1                   |                     |
| THYMO, csa, mmf                                  | 0                   | 4                   |                     |
| Everolimus, CsA, P, induction (anti-CD25)        | 0                   | 1                   |                     |
| THYMO, TAC, mmf, P                               | 0                   | 0                   |                     |
| TAC, sirolimus, P, ATG induction                 | 1                   | 0                   |                     |
| No data  | 1                   | 0                   |                     |

Table 2. Summary of one-year post-transplant follow-up in PDP and HDP patients

| Parameter | Peritoneal Dialysis | Hemodialysis Pairs | Significance |
|-----------|---------------------|--------------------|--------------|
|-----------|---------------------|--------------------|--------------|

|   | Pairs (PDP)<br>n (%) | (HDP)<br>n (%) |        |
|---|----------------------|----------------|--------|
| Delayed graft function                            | 28 (21.05)           | 57 (42.86)     | p<0.05 |
| Acute rejection (not biopsy-proven)               | 19 (14.28)           | 43 (32.33)     | p<0.05 |
| Graft vessel thrombosis                           | 9 (6.7)              | 4(3)           | ns     |
| Urological complications                          | 9 (6.8)              | 7 (5.3)        | ns     |
| Cytomegalovirus infection (CMV)                   | 20 (15.0)            | 13 (9.8)       | ns     |
| Other infections (mostly urinary tract infection) | 37 (27.8)            | 33 (24.8)      | ns     |
| New onset diabetes after transplantation (NODAT)  | 16 (12.0)            | 13 (9.8)       | ns     |
| Duration of the first hospitalizations            | 21.98 ± 10           | 23.62 ± 14     | ns     |

T-student test, Fisher test; *NS*, non-significant

Table 3. Univariate Cox regression analysis of factors related to graft vessel thrombosis

|                                   | Univariate model  |         |
|-----------------------------------|-------------------|---------|
| Variables                         | HR (95% CI)       | P value |
| PD                                | 2.29 (0.70-7.43)  | 0.17    |
| Age                               | 0.98 (0.94-1.01)  | 0.23    |
| Male gender                       | 0.33 (0.10-1.06)  | 0.06    |
| AR                                | 1.48 (0.46-4.81)  | 0.51    |
| DGF                               | 7.46 (2.05-27.12) | <0.01   |
| WIT                               | 1.03 (0.98-1.07)  | 0.26    |
| CIT                               | 1 (1-1)           | 0.14    |
| TIT                               | 1 (1-1)           | 0.13    |
| MM                                | 1.03 (0.65-1.62)  | 0.91    |
| PRA current                       | 1 (0.96-1.06)     | 0.82    |
| Lymphocele                        | 2.15 (0.48-9.69)  | 0.32    |
| CMV infection                     | 2.10 (0.58-7.65)  | 0.26    |
| Bacterial infections (mainly UTI) | 0.82 (0.23-2.99)  | 0.77    |
| Reoperation                       | 1 (0.97-1.05)     | 0.66    |
| Duration of hospitalization       | 1 (0.97-1.05)     | 0.66    |

|   |                  |      |
|---|------------------|------|
| after RTx   |                  |      |
| CsA   | 0.71 (0.23-2.17) | 0.55 |
| Tac   | 1.29 (0.43-3.85) | 0.64 |
| Induction therapy (ATG,<br>Thymoglobulin,<br>basiliximab) | 1 (0.22-4.54)    | 0.99 |
| Coronary heart disease                                    | 1.02 (0.13-7.86) | 0.98 |
| SCC one month after RTx                                   | 0.84 (0.24-2.97) | 0.79 |
| eGFR one month after RTx                                  | 0.97 (0.94-1.01) | 0.19 |
| DM  | 0.98 (0.22-4.4)  | 0.98 |

Table 4. Multivariate Cox regression analysis of factors related to graft vessel thrombosis

|             | Model 1 (AIC: 134.41) |         | Model 2 “forward” (AIC: 129.89) |         |
|-------------|-----------------------|---------|---------------------------------|---------|
| Variables   | HR (95% CI)           | P value | HR (95% CI)                     | P value |
| DGF         | 7.46 (2.05-27.12)     | <0.01   | 10.06 (2.73-37.03)              | <0.01   |
| PD          | -                     | -       | 2.95 (0.85-10.17)               | 0.09    |
| Male gender | -                     | -       | 0.36 (0.11-1.24)                | 0.10    |

Table 5. Changes of eGFR and changes in plasma creatinine concentration in Peritoneal Dialysis Patients (PDP) (n=133) who had their kidney donor Hemodialyzed Pairs (HDP) (n=133)

| Period of time                             | eGFR (4p MDRD) |           | Creatinine concentration (mg/dl) |           |
|--|----------------|-----------|----------------------------------|-----------|
|  | PDP Group      | HDP Group | PDP Group                        | HDP Group |
| 1 month                                    | 51.95          | 51.91     | 1.47                             | 1.52      |
| 12 months                                  | 56.31          | 57.76     | 1.38                             | 1.38      |
| Last visit (observation time 0.5 to 22 mo) | 56.81          | 59.17     | 1.47                             | 1.44      |

Abbreviations: MDRD, Modification of Diet in Renal Disease abbreviated formula

Table 6. Causes of death during post-transplant follow-up in PDP and HDP patients

| Parameter       | Peritoneal Dialysis Pairs (PDP)<br>n=133  | Hemodialysis Pairs (PDP)<br>n=133  |
|-----------------|---|--|
| Causes of death | 8 deaths<br>1- lung cancer<br>1-myeloma multiplex<br>2- cerebral stroke<br>1- sclerosing encapsulating peritonitis<br>1-cns and lung aspergillosis<br>1 – colon cancer<br>1-no data | 12 deaths<br>1- stomach cancer<br>1- sepsis<br>3- cardiovascular (myocardial infarction)<br>1-pulmonary embolism<br>1-neuroendocrine neoplasm<br>5-no data |

Table 7. Univariate Cox regression analysis of factors related to death censored graft loss

| Variables   | Univariate model   |         |
|---|--------------------|---------|
|   | HR (95% CI)        | P value |
| PD  | 0.99 (0.57-1.73)   | 0.98    |
| Age   | 0.99 (0.97-1.01)   | 0.21    |
| Male gender #   | 1.44 (0.80-2.57)   | 0.22    |
| AR  | 1.27 (0.71-2.27)   | 0.42    |
| DGF   | 3.06 (1.75-5.35)   | <0.01   |
| WIT   | 1.01 (0.98-1.04)   | 0.46    |
| CIT   | 1 (1-1)            | 0.22    |
| TIT   | 1 (1-1)            | 0.21    |
| MM  | 1.12 (0.85-1.48)   | 0.43    |
| PRA current   | 1 (0.98-1.03)      | 0.89    |
| Lymphocele  | 1.61 (0.72-3.60)   | 0.25    |
| CMV infection   | 1.08 (0.50-2.30)   | 0.85    |
| Bacterial infections (mainly UTI)#  | 0.45 (0.21-0.96)   | 0.04    |
| Reoperation   | 1.88 (0.84-4.22)   | 0.13    |
| Duration of hospitalization after RTx   | 1.023 (1.007-1.04) | <0.01   |
| CsA   | 0.90 (0.50-1.62)   | 0.72    |
| Tac   | 1.27 (0.69-2.33)   | 0.45    |
| Coronary heart disease  | 1.15 (0.36-3.72)   | 0.81    |
| SCC one month after RTx   | 1.75 (1.08-2.81)   | 0.02    |
| eGFR one month after RTx  | 0.99 (0.98-1.01)   | 0.48    |
| DM  | 1.38 (0.69-2.77)   | 0.7     |
| Graft vessels thrombosis  | 86.73 (34.04-221)  | <0.01   |
| # violation of proportional hazards assumption, * assumption of linearity might (seems to) be slightly violated |                    |         |

Table 8. Multivariate Cox regression analysis of factors related to death censored graft loss

|                                       | Model 1 (AIC: 391.51) |         | Model 2 “forward” (AIC: 389.54) |         |
|---------------------------------------|-----------------------|---------|---------------------------------|---------|
| Variables                             | HR (95% CI)           | P value | HR (95% CI)                     | P value |
| DGF                                   | 2.14 (1.16-3.94)      | 0.01    | 2.14 (1.16-3.95)                | 0.01    |
| Duration of hospitalization after RTx | 1.00 (0.98-1.03)      | 0.85    | -                               | -       |
| SCC one month after RTx               | 1.74 (0.96-3.17)      | 0.07    | 1.80 (1.08-3)                   | 0.02    |
| eGFR one month after RTx              | -                     | -       | -                               | -       |
| Graft vessels thrombosis              | 93.41 (32.26-270.54)  | <0.01   | 95.78 (33.94-270.32)            | <0.01   |

Table 9. Univariate Cox regression analysis of factors related to graft loss

|                                   | Univariate model |         |
|-----------------------------------|------------------|---------|
| Variables                         | HR (95% CI)      | P value |
| PD                                | 0.93 (0.56-1.52) | 0.75    |
| Age                               | 1 (0.98-1.02)    | 0.90    |
| Male gender                       | 1.69 (1-2.88)    | 0.05    |
| AR                                | 1.20 (0.71-2.02) | 0.50    |
| DGF                               | 2.62 (1.59-4.29) | <0.01   |
| WIT                               | 1.01 (0.99-1.04) | 0.42    |
| CIT                               | 1 (1-1)          | 0.21    |
| TIT                               | 1 (1-1)          | 0.19    |
| MM                                | 1.07 (0.83-1.38) | 0.58    |
| PRA current                       | 0.99 (0.97-1.03) | 0.90    |
| Lymphocele                        | 1.48 (0.70-3.13) | 0.30    |
| CMV infection                     | 1.30 (0.69-2.44) | 0.42    |
| Bacterial infections (mainly UTI) | 0.73 (0.41-1.30) | 0.28    |
| Reoperation                       | 1.50 (0.68-3.32) | 0.32    |

|   |                     |       |
|---|---------------------|-------|
| Duration of hospitalization after RTx *   | 1.02 (1-1.04)       | 0.01  |
| CsA   | 0.87 (0.51-1.49)    | 0.618 |
| Tac   | 1.16 (0.67-2.03)    | 0.59  |
| Induction therapy (ATG, Thymoglobulin, basiliximab)   | 1.65 (0.78-3.53)    | 0.19  |
| Coronary heart disease  | 1.50 (0.60-3.76)    | 0.39  |
| SCC one month after RTx *   | 1.73 (1.13-2.67)    | 0.01  |
| eGFR one month after RTx *  | 0.99 (0.98-1.01)    | 0.68  |
| DM  | 1.63 (0.89-2.97)    | 0.11  |
| Graft vessels thrombosis  | 56.59 (23.88-134.1) | <0.01 |
| # violation of proportional hazards assumption, * assumption of linearity might (seems to) be slightly violated |                     |       |

Table 10. Multivariate Cox regression analysis of factors related to graft loss

|                                       | Model 1 (AIC: 510.05) |         | Model 2 “forward” (AIC:506.42) |         |
|---------------------------------------|-----------------------|---------|--------------------------------|---------|
| Variables                             | HR (95% CI)           | P value | HR (95% CI)                    | P value |
| DGF                                   | 1.98 (1.16-3.38)      | 0.01    | 1.96 (1.15-3.35)               | 0.01    |
| Duration of hospitalization after RTx | 1 (0.97-1.02)         | 0.87    | -                              | -       |
| SCC one month after RTx               | 1.75 (1.03-2.99)      | 0.04    | 1.76 (1.10-2.82)               | 0.02    |
| Graft vessels thrombosis              | 63.18 (23.41-170.49)  | <0.01   | 68.58 (26.10-180.19)           | <0.01   |
| DM                                    | -                     | -       | 1.88 (1.02-3.45)               | 0.04    |

Table 11. Univariate Cox regression analysis of factors related to death

| Variables   | Univariate model  |         |
|---|-------------------|---------|
|   | HR (95% CI)       | P value |
| PD  | 0.82 (0.33-2.03)  | 0.67    |
| Age   | 1.05 (1.01-1.08)  | 0.02    |
| Male gender   | 1.68 (0.64-4.40)  | 0.29    |
| AR  | 1.06 (0.42-2.7)   | 0.90    |
| DGF   | 1.21 (0.49-3.02)  | 0.68    |
| WIT   | 1.02 (0.98-1.06)  | 0.43    |
| CIT   | 1 (1-1)           | 0.38    |
| TIT   | 1 (1-1)           | 0.36    |
| MM  | 0.79 (0.52-1.20)  | 0.26    |
| PRA current   | 0.99 (0.93-1.06)  | 0.73    |
| Lymphocele  | 1.73 (0.50-5.98)  | 0.38    |
| Bacterial infections (mainly UTI)                   | 2.09 (0.87-5.06)  | 0.10    |
| Reoperation   | 1.29 (0.29-5.61)  | 0.73    |
| Duration of hospitalization after RTx               | 1.02 (0.99-1.04)  | 0.14    |
| CsA   | 0.61 (0.24-1.56)  | 0.30    |
| Tac   | 1.36 (0.53-3.53)  | 0.52    |
| Induction therapy (ATG, Thymoglobulin, basiliximab) | 1.02 (0.24-4.44)  | 0.98    |
| Coronary heart disease                              | 4.48 (1.47-13.64) | <0.01   |
| SCC one month after RTx                             | 1.36 (0.59-3.15)  | 0.47    |
| eGFR one month after RTx                            | 0.99 (0.97-1.02)  | 0.83    |
| DM  | 2.32 (0.88-6.12)  | 0.09    |
| Graft loss  | 20 (4.61-86.67)   | < 0.01  |



Table 12. Multivariate Cox regression analysis of factors related to death

| Variables              | Model 1 (AIC: 144.46) |         | Model 2 “forward” (AIC: 141.61) |         |
|------------------------|-----------------------|---------|---------------------------------|---------|
|                        | HR (95% CI)           | P value | HR (95% CI)                     | P value |
| Age                    | 1.03 (0.99-1.07)      | 0.06    | 1.03 (0.99-1.08)                | 0.09    |
| MM                     | -                     | -       | 0.67 (0.41-1.09)                | 0.11    |
| UTI                    | -                     | -       | 2.94 (1.19-7.28)                | 0.02    |
| Coronary heart disease | 4.72 (1.21-18.39)     | 0.03    | 3.41 (0.85-13.69)               | 0.08    |
| Graft loss             | 21.41 (4.93-92.88)    | <0.01   | 26.45 (6.04-115.89)             | <0.01   |

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A paired kidney analysis was applied to evaluate the impact of dialysis modality on post-transplantation follow up in 133 pairs receiving grafts from the same donor.

Long-term transplantation outcome is similar in patients coming from either PD or HD.

PD and HD groups differ in some aspects, such as susceptibility to vascular thrombosis in PD, and to DGF and AR in HD.