

# Peritoneal dialysis after renal transplant failure

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## ABSTRACT

**Background:** Controversy remains over the optimal dialysis technique following renal transplant failure.

**Aim:** To compare clinical outcomes between patients beginning peritoneal dialysis after renal transplant failure and the remaining patients on peritoneal dialysis.

**Methods:** A retrospective evaluation of all patients beginning peritoneal dialysis at our centre between October 1985 and 31 December 2005.

**Results:** 336 patients began peritoneal dialysis: 32 after renal transplant failure (group I), 180 as first renal replacement therapy (group II) and 124 after haemodialysis (group III). Group I patients were younger ( $37\pm 12$  years old vs.  $51\pm 15$  and  $48\pm 15$  years old, in groups II and III;  $p<0.001$ ). Group I had more prevalence of anuria than group II (group I 31.3%, group II 8.9%;  $p<0.001$ ) and had more total renal replacement therapy time than group III (group I  $123\pm 89$  months, group III  $68\pm 96$  months;  $p<0.001$ ). Patient survival at 12 and 24 months was 93% / 83%, 92.5% / 82.4% and 88.9% / 75% in groups I, II and III, respectively ( $p=0.13$ ). Technique survival at 12 and 24 months was 86.4% / 82.3%, 82.2% / 73.5% and 83.8% / 77.0% in groups I, II and III ( $p=0.82$ ). During follow-up 127 patients were transferred to haemodialysis: 12 (9.4%) in group I, 69 (54.3%) in group II and 46 (36.3%) in group III. The causes of transfer showed no significant differences between the groups: peritonitis (group I 66.7%, group II 36.2%, group III 37.0%;  $p=0.12$ ) and ultrafiltration failure (group I 25%, group II 20.3%, group III 28.3%;  $p=0.61$ ). Peritonitis free survival at 12 and

24 months was 65.6% / 45.1%, 66.4% / 42.3% and 54.8% / 37.6% in groups I, II and III ( $p=0.36$ ).

**Conclusions:** Patients commencing peritoneal after renal allograft failure experienced outcomes comparable with other peritoneal dialysis patients. Peritoneal dialysis is a suitable choice after renal transplant failure.

## Key-Words:

Peritoneal dialysis; renal transplant failure.

## INTRODUCTION

Although efforts are being made to improve the long-term survival of renal allografts, the success of kidney transplantation is limited by a finite half-life<sup>1</sup>. While the number of failing grafts per 1000 patients per year dropped in the 1990s from 50 to 40, the absolute number has increased due to the cumulative growth of transplant (Tx) programmes<sup>2</sup>. It is estimated that 2-3% of transplants fail each year, requiring a return to dialysis<sup>3</sup>. In Portugal, according to the registry of the Portuguese Society of Nephrology, renal allograft failure patients represented 2.7% of the total number of patients beginning dialysis in 2000 and this number increased to 4.8% in 2005. Renal allograft failure thus represents a growing cause for entering a dialysis programme. This population is a unique group with specific risk factors, including a longer duration of end-stage renal disease, immunosuppression and more rapid loss of residual renal function<sup>4,5</sup>. The question of the best renal replacement therapy in these patients

remains an open one. An initial study by Sasal *et al.*<sup>4</sup> suggested that peritoneal dialysis (PD) was associated with increased mortality and technique failure in this population. Later, Schiffi<sup>6</sup> also reported higher complication rates and technique failure in this group of patients. Further studies<sup>1,5,7-10</sup>, however, gathered evidence suggesting that PD is at least as good as haemodialysis (HD) after allograft failure.

This issue still needs to be highlighted to persuade clinicians to give graft failure patients an opportunity to choose the renal replacement modality.

The aim of this study is to analyse our centre's experience, comparing the outcomes of patients with allograft failure coming to PD with those of other PD patients, either beginning renal replacement therapy or transiting from HD.

## ■ PATIENTS AND METHODS

In this retrospective single-centre study, all patients starting PD at the Hospital Geral de Santo António, Oporto, Portugal, between 1 October 1985 and 31 December 2005 were identified from our data base. Three groups were established: group I – Patients starting PD after renal allograft failure (including patients with an intermediate time in HD < 6 months), group II – patients starting PD as first renal replacement therapy choice (including patients with an intermediate time in HD < 6 months) and group III – patients starting PD after HD (including all patients in HD > 6 months). Data were collected until death or PD dropout. Demographic data, co-morbidities (namely diabetes and hypertension), previous time of renal replacement therapy (including transplant), percentage of anuric patients (defined as glomerular filtration rate, GFR, < 1ml/min) at initiation of PD and reason for choosing PD were determined. Patient survival, technique survival, peritonitis free survival and reasons for PD dropout were evaluated.

Results were expressed as frequencies and percentages for categorical variables, mean  $\pm$  SD (median) for continuous variables. Distributions of categorical variables across the groups were compared using the  $\chi^2$  test and continuous variables using the t-test.

Survival curves were calculated using the Kaplan-Meier method. *P*-values were considered significant if < 0.05. Statistical analysis was performed using SPSS statistical software.

## ■ RESULTS

During the period of the study 336 patients began PD in our centre: thirty-two in group I, one hundred and eighty in group II and one hundred and twenty-four in group III.

### ■ Baseline characteristics

Table I lists the patient characteristics of the three groups, recorded at the time of entry into the PD programme.

There were some dissimilar characteristics between the groups. Group I patients were significantly younger than the remaining groups, but had more total renal replacement therapy time than group III and more prevalence of anuria than group II. HTA was more prevalent in group I and II but we found no difference in the prevalence of diabetes and BMI between the groups (Table I). In terms of the reason for beginning PD, we established two major groups: patients beginning PD as an option or because of vascular access problems. We found no differences between groups I and II. In group III, patients transiting from HD, vascular access problems were a major cause of PD initiation. We focused our comparison between groups I and II, as the latter, including incident PD patients in whom PD was the first renal replacement therapy, were likely to have better outcomes.

### ■ Patient survival

The number of deaths and the analysis of the causes of death are presented in Table II.

The Kaplan-Meier survival curves (Fig. 1) did not differ significantly between the three groups. Patient survival at 12 and 24 months was 93% / 83%, 92.5% / 82.4% and 88.9% / 75% in groups I, II and III ( $p=0.13$ ).

**Table I**

Baseline characteristics of the study population

	Group I	Group II	Group III	P (three groups)	P (I vs. II)
Patients (n)	32	180	124		
Female gender (%)	78	60	65		
Age (years)	37±12	51±15	48±15	<0.001	0.001
Total renal replacement therapy time (months)	123±89 (105)	–	68±96 (42)	<0.001	<0.001
Diabetes	7 (21.9%)	56 (31.1%)	37 (20.6%)	0.028	0.40
Hypertension	21 (65.6%)	124 (68.9%)	64 (51.6%)	0.014	0.70
BMI (kg/m <sup>2</sup> )	23.2±4.8	24.0±4.7	25.7±4.6	0.44	0.11
Anuria	10 (31.3%)	16 (8.9%)	77 (62%)	<0.001	0.002
Reason for PD					
Vascular access problem	17 (53%)/	53 (30%)/	95 (77%)/		
patient option	15 (47%)	98 (54%)	26 (21%)	<0.001	0.073

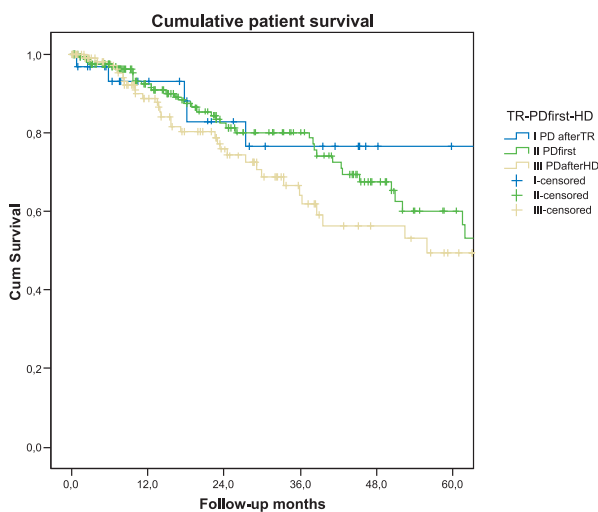
Group I – PD after graft failure; Group II – PD-first; Group III – PD after haemodialysis

**Table II**

Causes of death

	Group I	Group II	Group III	P (three groups)	P (I vs. II)
Death	5 (16%)	39 (22%)	36 (29%)	NS	NS
Cause of death					
Infectious event	1	9	7	NS	NS
Cardiovascular event	3	21	21	NS	NS
Other	1	9	8	NS	NS

Group I – PD after graft failure; Group II – PD-first; Group III – PD after haemodialysis; NS – non significant



**Figure 1**

Comparison of patient cumulative survival in the three groups (p=0.13).

### Death-censored technique survival

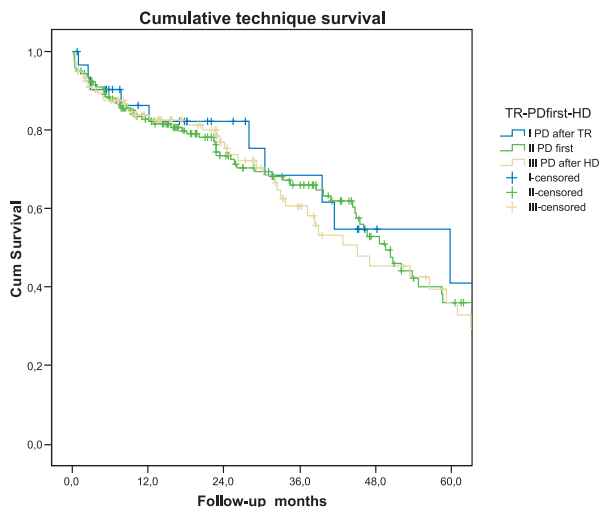
Death-censored technique survival at 12 and 24 months was 86.4% / 82.3%, 82.2% / 73.5% and 83.8% / 77% in groups I, II and III (p=0.82). The Kaplan-Meier survival curves (Fig. 2) did not differ significantly between the three groups.

### Death-censored peritonitis free survival

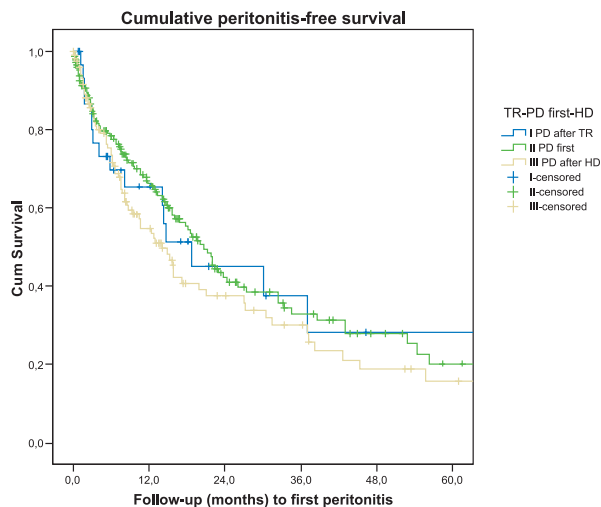
The peritonitis free survival at 12 and 24 months was 65.6% / 45.1%, 66.4% / 42.3% and 54.8% / 37.6% in groups I, II and III (p=0.36). The Kaplan-Meier survival curves (Fig. 3) did not differ significantly between the three groups.

### Causes of PD drop out

During the follow-up period, 127 patients were transferred to haemodialysis (Table III).



**Figure 2**  
Comparison of death-censored technique survival in the three groups (p=0.82).



**Figure 3**  
Comparison of death-censored peritonitis free survival in the three groups (p=0.36).

**Table III**

Causes of PD drop out

	Group I	Group II	Group III	P (three groups)	P (I vs. II)
<b>HD transfer</b>	N=12	N=69	N=46		
<b>Cause of transfer</b>					
Peritonitis	8	25	17	NS	NS
UF failure	3	14	13	NS	NS
Other	1	30	16	NS	NS

Group I – PD after graft failure; Group II – PD-first; Group III – PD after haemodialysis; NS – non significant

In analysing the causes of transfer, we chose to evaluate two major reasons for transfer: peritonitis and ultrafiltration (UF) failure. There was a trend toward a higher frequency of peritonitis as a cause of drop out in the failed transplant group (66.6% vs. 36.2% and 37% in groups II and III), which did not attain statistic significance (p=0.14). There was no significant difference in ultrafiltration failure rates between the groups.

## DISCUSSION

Despite the ever increasing number of patients returning to dialysis after renal allograft failure, there is a limited amount of evidence as to the best renal replacement therapy in this population.

An initial study by Sasal *et al.*<sup>4</sup> compared 42 patients starting PD after renal allograft failure with 43 randomly selected incident PD patients who had never been transplanted before. They found a significantly higher mortality rate, an increased risk of infectious events and a trend towards higher technique failure in the post-transplant group.

However subsequent works by different authors were unable to validate these results. Davies<sup>5</sup> in a sub-analysis of the Stoke PD Study compared 28 patients starting PD after graft failure with 469 incident PD patients. There was no difference in the frequency of co-morbidities, but transplanted patients were significantly younger. Comparing patient survival between the two groups, patients in the failed transplant group showed better survival curves. This

difference disappeared when an adjustment for age was made. Death-censored technique survival was not different between the two groups. The most striking difference between the groups was the more rapid loss of residual renal function in the failed transplant patients. The study also compared the 28 patients starting PD after failed allograft with 17 patients with failed allograft who began HD in the same period. Again, survival was not different between the two groups, though the median survival tended to be longer in the PD patients. Duman *et al.*<sup>7</sup> compared 34 patients with failed graft starting PD with 82 incident PD patients. Again there was no difference in patient and technique survival between the two groups, although in the failed transplant group there was a shorter time to the first episode of peritonitis, a higher peritonitis rate and a higher number of peritonitis episodes per patient.

More recently a large scale multicentre comparison of PD outcomes between patients with failed grafts and failed native kidneys was made<sup>1</sup>, using data from the ANZDATA registry. This involved comparison between 309 PD episodes after renal allograft failure and 13638 PD episodes after native kidney failure. On multivariate analysis PD patients with failed allograft had comparable mortality, death-censored technique failure and peritonitis free survival. In this study a secondary analysis was performed in a subset of 5496 PD patients for whom peritoneal transport status was included as a covariate. The results were similar to the remaining analysis.

The evidence presented thus far suggests that PD is an adequate renal replacement therapy in the post-Tx population and that these patients fare at least as well as incident PD patients. There are, however, few studies that directly compare PD and HD in the post-Tx set. Apart from Davies<sup>5</sup>, the only study that we know to analyse this issue is a recent work by Jonge *et al.*<sup>8</sup>. They compared 21 patients starting PD after renal Tx failure with 39 patients starting HD after renal Tx failure. There were no significant baseline differences between the groups. The outcome in both groups was not significantly different, although there was a slight trend towards higher patient survival in the PD patient group.

This study evaluates our centre's experience in an attempt to assess if the post-transplant population experienced any significant difference in outcomes

on PD compared to the remaining PD patients. As in the Davies study<sup>5</sup>, our transplanted population (group I) was significantly younger than the population in the remaining groups, but we did not find a survival advantage in this population. Similarly to some of the studies described above<sup>1,5</sup>, we did not find any significant difference in terms of overall survival and technique survival between the patients coming from transplant (group I) and incident PD patients (group II). Neither did we find any difference in peritonitis-free survival between the groups. This might seem a distressing result since many of the post-Tx patients are still on immunosuppressors and might therefore be prone to infectious events. We did indeed find a trend towards a higher frequency of peritonitis as a cause of drop out in the failed transplant group, which reinforces the need for higher clinical surveillance. There was no difference in the time to the first peritonitis episode nor a higher risk of death due to infectious intercurrents; cardiovascular events being the main cause of death in all the groups. This is comparable with the results of the ANZDATA group<sup>1</sup> study that specifically addressed this issue. It examined the risk of developing peritonitis on multivariate analysis, and failed-Tx was not found to be a risk factor.

Inevitably there are several shortcomings to our retrospective analysis. Firstly, we compared populations with different overall renal replacement therapy time. It would be interesting to directly compare PD with HD in the post-Tx setting in order to find out if renal replacement therapy choice had any impact on survival. We documented a higher prevalence of anuria in patients beginning PD after renal graft failure, in comparison with new PD patients. But we were unable to retrieve data on residual renal function time course and to assess if, in the post-Tx setting, there was indeed a quicker loss of diuresis as was shown by Davies<sup>5</sup> and if that had any impact on survival. We also had no data on immunosuppressors or immunosuppression stepping-down in the patients coming from renal Tx. It would be interesting to find out the optimum immunosuppression to achieve both minimum risk of infections and rejection symptoms and maximum preservation of residual renal function. Finally, we had no data on peritoneal transport status and were therefore unable to compare the populations in terms of this issue. This might be a subject worth exploring, since a recent study<sup>11</sup> comparing peritoneal transport status before

and after kidney transplant in patients who had been on PD before Tx and were returning to PD after renal graft failure, showed that peritoneal function upon reinitiating PD was similar to that seen pre-Tx; a tendency towards decreased small solute transport after renal transplantation was observed. These observations suggested that the transplantation period with immunosuppressive treatment might have beneficial effects on peritoneal transport, acting as a peritoneal rest period.

In conclusion, the results of our study show that patients starting PD after renal allograft failure experienced patient survival, death-censored technique survival and peritonitis free survival comparable with incident PD patients and patients transiting from HD. PD therefore appears to be a safe renal replacement therapy choice in the post-transplant setting, reinforcing the need to offer this modality as part of an integrated strategy of renal replacement therapy.

**Conflict of interest statement.** None declared.

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