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Original Paper

Early Start Peritoneal Dialysis: Technique Survival in Long-Term Follow-Up

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Key Words
Peritoneal dialysis • Unplanned peritoneal dialysis • Acute peritoneal dialysis

Abstract
Background/Aims: Peritoneal dialysis (PD) has gained interest over the last decade as a viable option for early start dialysis. It is still unknown if shorter break-in periods and less time for proper patient evaluation and training could influence technique survival in comparison to planned-start PD. ***Methods:*** A prospective and observational study that compared technique survival in a cohort of patients who started either early or planned PD. Early start PD was defined as break-in period from 3 to 14 days with no previous nephrologist follow-up or patient training. ***Results:*** A total of 154 patients were included (40 as early start PD), followed by a median time of 381 days. Comparing early vs. planned-start PD, groups were similar concerning age 56 (40; 70) vs. 48 (32; 63) years, p=0.071, body mass index (BMI) 23.3 ± 4.2 vs. 23.8 ± 4.0 kg/m^2, p=0.567 and male gender (60 vs. 48%, p=0.201), respectively. Comparing early vs. planned-start groups, there were no differences regarding PD dropout for peritonitis (7.5 vs. 11.4%, p=0.764), catheter dysfunction (12.5 vs. 17.5%, p=0.619) and patient burnout (0 vs. 4.4%, p=0.328), respectively. Less patients in early start group quit PD for peritoneal membrane failure in comparison to planned-start group (2.5 vs. 16.7%, p=0.026). In multivariate cox-regression analysis, the only factors independently associated with technique failure were BMI>25 kg/m^2 (p=0.033) and Diabetes Mellitus (p=0.013), whereas no differences regarding early vs. planned-PD start were observed (p=0.184). ***Conclusion:*** Despite the adverse scenario for initiating dialysis, early start PD had similar outcomes in comparison to planned-start PD in long-term follow-up.

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Introduction

Peritoneal dialysis (PD) is a well-established treatment for end-stage renal disease (ESRD). Even though such statement is widely accepted, it is only valid in a planned background, when patient is adequately followed-up by a multi-professional team, with proper training and, most importantly, with a reliable and timely insertion of peritoneal catheter [1].

The difficulties of combining all these factors might partially explain why hemodialysis (HD) through a central venous catheter (CVC) is considered the default renal replacement therapy in the context of urgent-start dialysis. Other contributing factors are the relative difficulty of obtaining a rapid insertion of a peritoneal catheter, concerns regarding possible complications associated with short break-in periods for starting PD and the relative ease of CVC insertions [2]. However, starting unplanned HD using CVC is independently associated with bloodstream infection and mortality in incident dialysis patients [3, 4]. Yet, the risk of septicemia is similar for PD catheters and arteriovenous fistula [3].

In the last decade, many studies have provided enough evidence to support PD as a feasible therapy for urgent/early start dialysis. They have reported an overall low risk for mechanical complications or peritonitis [5-11]. However, most studies that compared planned vs. urgent/early start PD have focused on short-term outcome measures.

Starting PD at the emergency environment is a stressful event, far from ideal conditions. Shorter training and break-in periods and possibly inaccurate clinical and social evaluation could lead to more technique failure or burnout at long-term. For this purpose, we conducted a study that aimed to evaluate technique survival in a cohort of patients that have started either early or planned-PD.

Materials and Methods

Statement of ethics

All patients gave written informed consent. This study was approved by local ethics committee (CAPpesq #45163715400000068).

Patients

Patients were divided into 2 groups: early start PD and planned-start PD. They were enrolled in this prospective and observational study from December 2010 to January 2018 at Hospital das Clínicas, University of São Paulo. Early start PD was defined as break-in period from 3 to 14 days after catheter insertion, with no previous nephrologist follow-up or patient/family training. Planned-start PD was defined as break-in period > 14 days after catheter placement, regardless of previous nephrologist follow-up.

The PD catheter used was a straight, double-cuffed Tenckhoff catheter, inserted either percutaneously by nephrologists (Seldinger technique) or videolaparoscopically by surgeons.

All patients were treated with lactate-buffered glucose dialysate. PD was performed either by Homechoice™ automated cycler machine (Baxter Inc., Deerfield, USA) or PD-NIGHT Peritoneal Dialysis Machine™ (Fresenius Medical Care, Brazil). In early start group, dwell volume was 1000 mL during the first week and was gradually increased up to 2000 mL over the first month, whereas in planned-start PD dwell volume ranged from 1500 to 2000 ml.

Outcomes

The main outcome was technique survival comparing early start and planned-start PD patients. Technique failure was defined as transitioning from PD to HD due to the following causes: peritoneal membrane failure, peritonitis, catheter dysfunction and patient burnout.

Follow-up

All patients were followed over the study period. The following outcomes were assessed in the remaining patients: death, kidney transplantation, renal function recovery and technique failure.

Statistical analysis

Normally distributed variables are expressed as mean ± standard deviation, while skewed variables are expressed and median and (25; 75) percentiles. Categorical variables are expressed as percentage. Comparisons between groups were evaluated by unpaired *t* test, Mann-Whitney test or Chi-square test, as appropriate. Technique survival was evaluated in whole group and also stratified by early or planned-start PD by Kaplan-Meier and Cox regression analyses. Statistical analysis was performed using SPSS software package, v. 22 (SPSS Inc., Chicago, IL, USA).

Results

Patients characteristics and follow-up

A total of 154 patients initiated PD during study period (40 as early start PD). Baseline characteristics of the population are described in Table 1. Median follow-up time was 381 days. Patients have been included in early start PD more frequently since 2014 in our service, and therefore the follow-up period was slightly lower in this group in comparison to planned-start group. The etiology of ESRD was different between groups, as heart failure was significantly more prevalent in early start group (p=0.016). Nine patients in this group had no defined etiology of ESRD, whereas only 10 in planned-start PD group (p=0.023). Nephrologists inserted more catheters in planned-start in comparison to early start group. Four patients from early start group and eight patients from planned-start group had early technique failure, defined as PD dropout within 3 months after dialysis initiation. There were no differences regarding dialysis indication between groups.

Table 1. Characteristics of study population, according to PD initiation. BMI: body mass index, GN: glomerulonephritis, DM: Diabetes Mellitus, AH: arterial hypertension, ADPKD: autossomic dominant polycystic kidney disease. * p < 0.05 between groups, CKD-MBD: chronic kidney disease-mineral and bone disorder

Variable	Whole cohort	Early start PD (n=40)	Planned-start PD (n=114)	p
Age (years)	50 (34; 65)	56 (40; 70)	48 (32; 63)	0.071
Follow-up (days)	381 (179; 757)	219 (115; 642)	418 (197; 810)	0.053
BMI (kg/m^2)	23.7 ± 4.1	23.3 ± 4.2	23.8 ± 4.0	0.567
Gender (% male)	51	60	48	0.201
Catheter inserted by nephrologists (%)	70	56	77	0.012
Etiology (%)				0.025
GN	28.6	27.5	28.9	
DM	25.3	20	27.3	
AH	23.4	17.5	25.4	
Urological	5.8	5	6.1	
Nephrotoxicity	2.6	0	3.5	
Heart Failure*	1.3	5	0	
Unknown*	12.3	22.5	8.8	
ADPKD	0.6	2.5	0	
Dialysis indication (%)				0.212
Uremia	71	73	70	
Fluid overload	24	27	23	
Complications of CKD-MBD	5	0	7	

Urgent vs. planned PD

As shown in Table 2, there were no differences in kidney transplantation and renal function recovery rates when comparing early start and planned-start groups. Technique failure was significantly more observed in planned PD group, as a result of more cases of peritoneal membrane failure (2.8%

Table 2. Outcomes, according to PD initiation. pts: patients, HD: hemodialysis, PM: peritoneal membrane

Outcomes	Whole cohort	Early start PD (n=40)	Planned-start PD (n=114)	p
Deaths (%)	7.1	10	6.1	0.477
Kidney transplantation (%)	14.3	5.0	17.5	0.065
Renal function recovery (%)	3.9	5.0	3.5	0.650
Conversion to HD (%)	36.4	15	43.9	0.001
Time for HD conversion (days)	365 (214; 821)	300 (183; 808)	365 (208; 836)	0.652
Peritonitis (%)	10.4	7.5	11.4	0.764
Time for peritonitis (days)	493 (262; 881)	749 (214; 987)	478 (271; 873)	1.000
PM. failure (%)	13	2.5	16.7	0.026
Catheter dysfunction (%)	16.2	12.5	17.5	0.619
Burnout (%)	3.2	0	4.4	0.328
Catheter replacement (%)	14.9	5	18.4	0.042

vs 17.9% in early start and planned-start PD groups, respectively, p=0.024). PD dropout for peritonitis, catheter dysfunction and burnout were similar between groups. Catheter replacement was higher in planned-start PD group. Deaths were similar between groups: 11.1% in early start and 6.6% in planned-start PD (p=0.382).

Technique failure

At univariate analysis (Table 3), patients who presented technique failure were more likely to have Diabetes Mellitus (DM). Technique failure was more frequent in the planned-start PD group.

The analysis of technique failure according to PD start group, censored by death, kidney transplantation and renal function recovery obtained by Kaplan-Meier curve showed no differences between groups (Log-Rank test, $\chi^2 = 2.187$, p = 0.139), as shown in Fig. 1a. In Cox regression analysis, only overweight, defined as body mass index (BMI) > 25 kg/m^2, and DM were statistically associated with technique failure (Table 4 and Fig. 1b). Early technique failure, defined as catheter dysfunction less than 90 days after catheter placement was observed in 4 patients from early-start group and in 8 patients from planned-start group (p=0.51). Additionally, there was no difference regarding catheter placement techniques (surgical or percutaneous) in these 12 patients (6 for each group).

Table 3. Univariate analysis: risk factors for technique failure. BMI: body mass index

Covariate	Technique failure (n=56)	No technique failure (n=98)	p
Age (years)	53 (31; 65)	49.5 (35; 65)	0.377
BMI > 25 kg/m^2 (%)	46.3	31.9	0.111
Diabetes Mellitus (%)	35.7	19.4	0.034
Early start PD (%)	10.7	34.7	0.001
Catheter inserted by nephrologists (%)	76.8	66.3	0.118

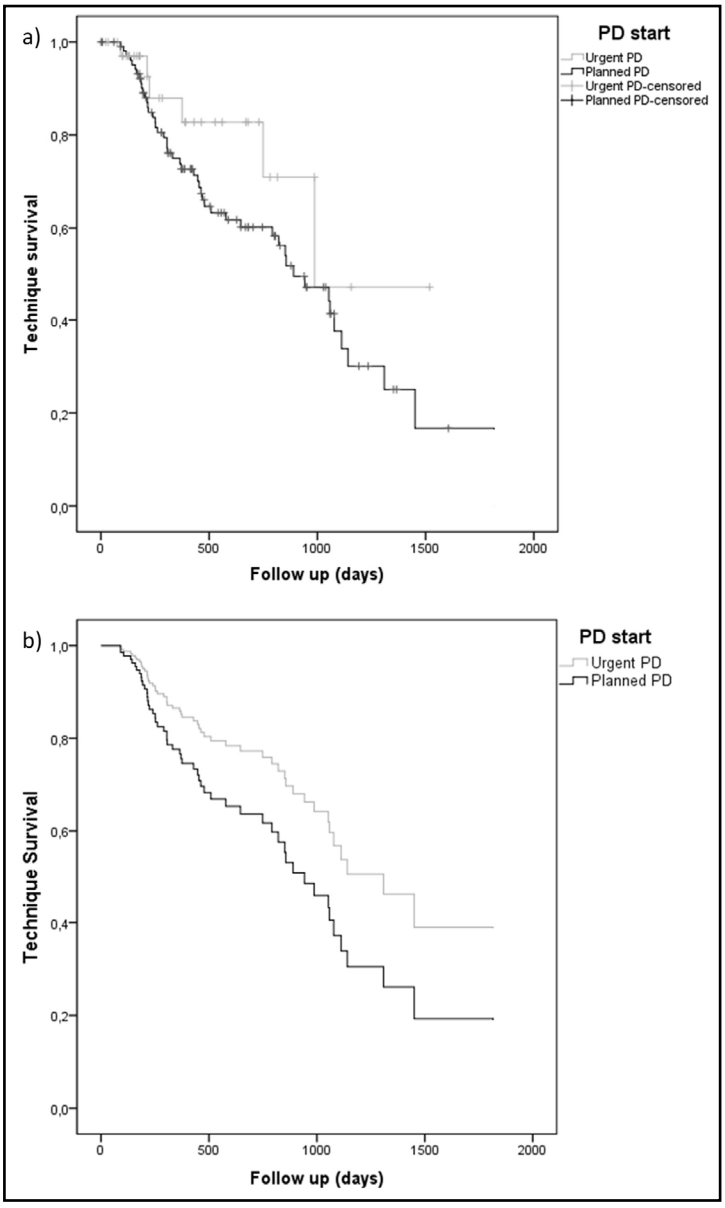

Fig. 1. Technique survival plot, according to PD start: a) non-adjusted Kaplan-Meier and b) Adjusted Cox regression analysis.

Discussion

This study prospectively evaluated a cohort of patients that have either started early or planned PD. The main outcome was technique survival, which was not different between groups, whereas DM and BMI > 25 kg/m^2 were the only variables associated with PD dropout. The risks for peritonitis, catheter dysfunction or patient burnout were similar for early or planned-start PD.

Table 4. Cox-regression analysis for PD failure. Covariates: BMI > 25 kg/m^2, diabetes mellitus and PD group (early start vs planned-start). BMI: body mass index, PD: peritoneal dialysis

Variables	Beta coefficient	p	Hazard Ratio	95,0% CI	
				Lower	Upper
BMI > 25 kg/m^2	-0.600	0.033	0.549	0.316	0.952
Diabetes Mellitus	-0.723	0.013	0.485	0.274	0.859
PD start	0.580	0.184	1.785	0.759	4.198

Despite the efforts of avoiding unplanned dialysis initiation, approximately 60 to 70% of patients start dialysis under suboptimal conditions, without definitive vascular access or adequate follow-up by nephrologists [12]. Starting urgent HD with CVC is associated with poor outcomes, including higher risk of bloodstream infection, longer hospitalization and increased mortality in comparison to PD or planned-start HD [3, 4].

In the last decade, many studies have described the use of urgent-start PD, defined as initiation of dialysis within 14 days after catheter insertion [13]. Different protocols have been reported, including less than 72h of break-in periods,[6, 8, 10, 11, 14] and surgical catheter insertion [5, 7, 15]. In general, these studies have reported overall low complication rates [3, 11, 15]. Recently, Blake and Jain have proposed a new definition for urgent-start PD, relegating this term exclusively to break-in periods shorter than 72h. Early start PD is a newly proposed term for patients who can wait from 3 to 14 days to initiate PD after catheter placement, since they do not truly require to start dialysis immediately [16].

Catheter dysfunction is a major concern in the context of early dialysis since delays in initiating dialysis procedure might potentially lead to severe complications. In urgent/early start PD, both surgical and percutaneous catheter insertions have been described and the prevalence of catheter dysfunction reported varied from 13.3 to 28.9% for surgical [1, 13, 14] and from 11 to 25.7% for percutaneous placement [2, 5-8]. In this current study, 12.5% of early start group changed dialysis method for persistent catheter dysfunction, whereas early catheter replacement was more prevalent in planned-start PD. Such finding is more likely attributable to the characteristics of our service, since nephrologists usually insert more catheters in outpatients, which was more frequent in the planned-PD group.

Another concern regarding early PD break-in is peritonitis, an important cause of PD dropout and mortality [17]. Overall, studies have reported a prevalence of peritonitis ranging from 0 to 15.4% in urgent-start PD [2, 5, 6, 8, 10]. In this study, peritonitis led to conversion to HD in 7.5% of urgent-start group population, again not different from planned-start PD.

Peritoneal membrane failure was more frequent in planned-start HD. This is possibly a result of the longer follow-up period of this group. In early start PD, only 2.5% of patients had to quit PD for this reason, but median follow-up was only of 219 days. No patient withdrew from PD due to burnout in this group.

Undoubtedly, there are additional challenges when initiating PD urgently. The decision of choosing a dialysis method in a few days or even in a few hours, and the complexity of analyzing the best option under adverse conditions, could lead to a wrong choice, increasing cases of dropout from PD. Such technique survival has already been assessed elsewhere: Povlsen et al. analyzed technique survival at 3 months in their urgent-start PD patients compared to planned-start group and found similar results (86.7 vs. 90%) [10]. In this present study, technique survival in early start PD group was 83.7%, which is an encouraging result, given the longer follow-up period.

In order to adjust outcomes in both groups, once the follow-up period of planned-start PD group was longer in comparison to early-start group, we used the Cox regression analysis. In this case, only DM and BMI > 25 kg/m^2 were independently associated with technique

failure, regardless of PD onset modality. However, even using an approach censuring patients to 1.5 years, which equals the period of follow-up between groups, does not modify the results of the Cox analysis (data not shown), reinforcing our findings of similar technique survival comparing early-start and planned-start PD. These findings are in line with data obtained from Australia and New Zealand Dialysis and Transplant Registry (ANZDATA): McDonald et al. found that BMI > 25 kg/m^2 was associated with technique failure [18]. More recently, See et al. described that the factors associated with technique failure, defined as transfer to HD or death, were age older than 70 years, DM or vascular disease, prior renal replacement therapy, late referral to a nephrology service or management in a smaller center [19].

Finally, two studies have assessed patient survival in urgent-PD: Lobbedez et al. found that patient survival at 1 year to be 83% [9], whereas Koch et al. described a survival of 69.7% after 6 months [14]. In our study, 10% of early start PD group died during follow-up.

This study has some limitations. It was an observational, single-center study with a relatively small sample size. There was no randomization between groups and some outcomes could be influenced by differences regarding baseline characteristics, which it is impossible to overcome since early start cannot be avoided. Additionally, even though the follow-up period of planned-start was longer than the early start group, we have followed patients for a relatively longer period in comparison to other studies. Another strength of this study is the fact that all patients received similar medical treatment in both groups, which reinforces our findings. Finally, to the best of knowledge, this is the first study that included patients that fit the recently created definition of early PD start.

Conclusion

Despite the adverse scenario for initiating dialysis, early start PD had similar outcomes in comparison to planned-start PD, after a relatively long follow-up period. This study brings one more piece of evidence to support PD as an alternative treatment for renal replacement therapy in the context of urgent/early start dialysis.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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