

Comparison of planned-start, early-start and deferred-start strategies for peritoneal dialysis initiation in end-stage kidney disease

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ABSTRACT

Introduction: In patients with end-stage kidney disease (ESKD) suitable for peritoneal dialysis (PD), PD should ideally be planned and initiated electively (planned-start PD). If patients present late, some centres initiate PD immediately with an urgent-start PD strategy. However, as urgent-start PD is resource intensive, we evaluated another strategy where patients first undergo emergent haemodialysis (HD), followed by early PD catheter insertion, and switch to PD 48–72 hours after PD catheter insertion (early-start PD). Conventionally, late-presenting patients are often started on HD, followed by deferred PD catheter insertion before switching to PD ≥14 days after catheter insertion (deferred-start PD).

Methods: This is a retrospective study of new ESKD patients, comparing the planned-start, early-start and deferred-start PD strategies. Outcomes within 1 year of dialysis initiation were studied.

Results: Of 148 patients, 57 (38.5%) patients had planned-start, 23 (15.5%) early-start and 68 (45.9%) deferred-start PD. Baseline biochemical parameters were similar except for a lower serum urea with planned-start PD. No significant differences were seen in the primary outcomes of technique and patient survival across all 3 subgroups. Compared to planned-start PD, early-start PD had a shorter time to catheter migration (hazard ratio [HR] 14.13, 95% confidence interval [CI] 1.65–121.04, $P=0.016$) while deferred-start PD has a shorter time to first peritonitis (HR 2.49, 95% CI 1.03–6.01, $P=0.043$) and first hospital admission (HR 2.03, 95% CI 1.35–3.07, $P=0.001$).

Conclusion: Planned-start PD is the best PD initiation strategy. However, if this is not possible, early-start PD is a viable alternative. Catheter migration may be more frequent with early-start PD but does not appear to impact technique survival.

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INTRODUCTION

Peritoneal dialysis (PD) is a well-established long-term dialysis modality for patients with end-stage kidney disease (ESKD).¹ It is recommended that a PD catheter should be placed at least 2 weeks prior to the anticipated need of long-term PD treatment for a planned-start PD.² Despite wide-spread promotion of planned-start dialysis for patients with advanced chronic kidney disease, late presentation and emergent initiation of chronic dialytic therapy remains a worldwide reality, and haemodialysis

(HD) by means of a central venous catheter (CVC) is the most utilised initial modality.³ In recent years, studies on incident HD patients have identified CVC use to be directly associated with worse survival, especially in the first year of therapy.⁴ The risks of initiation of HD using CVC include bacteraemia and central venous stenosis.^{4,5} It also necessitates multiple procedures before definitive access is established.^{6,7}

In planned-start PD, the catheter is inserted electively and typically rested for several weeks following insertion

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CLINICAL IMPACT

What is New

- We compared planned-start, early-start and deferred-start peritoneal dialysis (PD). Our early-start strategy (emergent haemodialysis with early switch to PD) can be easily adopted by many centres.

Clinical Implications

- Technique and patient survival were similar across all 3 subgroups. Planned-start PD is the best PD initiation strategy. For patients who present late, the early-start strategy is a viable option.

to minimise the risk of mechanical complications, such as catheter leak.² Over this period, many patients require urgent initiation of interim HD to bridge this gap. There is significant interest in the practice of urgent-start PD, defined as the initiation of PD within 48–72 hours of catheter placement,^{8,9} which circumvents the need for temporary vascular access. The urgent-start strategy also facilitates uptake of PD and is cost-effective short term and long term.¹⁰ Several observational studies support the safety, efficacy and feasibility of this approach.^{10–18} Urgent-start PD patients exhibit a similar short-term patient survival and technique failure as the traditionally planned counterpart.^{19,20}

The successful implementation of urgent-start PD programmes requires the availability of procedurists for immediate implantation of the PD catheter and the commitment of a multiprofessional team to the routine operation of the programme.^{17,21}

To overcome the unique logistical demands for urgent-start PD, our centre adopted an early-start PD strategy. In this approach, HD is started urgently, followed by early PD catheter insertion, and PD is started within 14 days after PD catheter insertion.⁹ Compared to urgent-start PD, data are limited regarding the impact of early-start PD in new patients with ESKD.¹⁹

More often, patients who present late in ESKD are started on interim HD. If suitable for PD, PD catheter insertion and PD initiation would be deferred to a later date, termed as deferred-start PD. It would be important to evaluate how an early start-strategy compares to this more conventional deferred-start strategy.

In this observational study, we compared the clinical outcomes and relevant complications between patients

initiated on PD with planned-start, early-start and deferred start PD strategies.

METHODS

Study population

We performed a retrospective cohort study of patients with ESKD who were started on PD from 1 January 2010 to 31 October 2017. This research project was approved by the local commission of ethics in research, the SingHealth Centralised Institutional Review Board, and waiver of informed consent was obtained (CIRB Reference: 2018/2737).

Group definitions

The PD patients were divided into 3 cohorts: planned-start PD group, early-start PD group and deferred-start PD group.⁹ For planned-start PD, the PD catheter was inserted electively, rested for at least 14 days before initiating long-term PD as the first dialysis modality. In the early-start PD group, HD would be initiated first via a non-tunnelled short-term dialysis catheter for emergent indications, followed by PD catheter insertion and then switched to peritoneal dialysis 48–72 hours after insertion. In the deferred-start PD group, patients would be initiated on interim HD via a tunnelled dialysis catheter, and PD catheter insertion would be performed non-urgently before switching to PD at least 14 days after PD catheter insertion.

PD preparation and regimen

All PD catheters were inserted using the open surgical technique by surgeons experienced in PD catheter placement and all patients received preoperative antibiotic prophylaxis. Prior to initiation of PD, all patients and/or their caregivers would undergo a standardised 4-day PD training.

In the planned-start and deferred-start PD group, patients were started on a full dose of PD at least 2 weeks after PD catheter insertion. For continuous ambulatory PD, the patients were started on 4 exchanges of 2L bags per day. For automated PD, 10L of PD fluids were delivered in 5 exchanges over 10 hours nightly via a cycler. PD fluids with 1.5% dextrose was invariably the initial choice, unless poor ultrafiltration volume was already seen during the initial dwells.

For the early-start group, in the first 14 days post-catheter insertion, low-volume PD was applied using a cycler, with each fill ranging from 1–1.2L for a total of 5–6L over 8–10 hours per day. After 14 days, a full dose is prescribed as described above.

Outcome measures

Clinical characteristics recorded included patient demographics, comorbidities, date of first dialysis, date of creation of dialysis access and baseline laboratory test results on dialysis initiation.

The primary outcome of interest was technique and patient survival. Technique survival was assumed in the absence of technique failure, which was defined as long-term transfer to HD for any reason. Duration of patient survival is determined from the date of first dialysis (HD or PD). For calculation of patient survival, all deaths following dialysis initiation were included. Patient survival includes the time on HD for the early-start and deferred-start PD groups. Secondary outcomes of interest were the incidence and time-to-event for peritonitis, exit-site infection, peri-catheter leakage and catheter migration within 1 year of PD initiation. The frequency of peritonitis and number of unplanned hospitalisations in the first year of PD were also studied.

Statistical analysis

Descriptive statistics were reported as median and interquartile range (IQR) for continuous data, and as number (percentage) for categorical data. A comparison of baseline characteristics between the 3 subgroups was undertaken. Categorical data were analysed by chi-square test or Fisher's Exact test as appropriate, while continuous data were compared with the Kruskal-Wallis test.

In the primary time-to-event analysis for technique failure and patient mortality, Cox regression analysis was used to compare between the 3 main subgroups of patients and derive the survival curves. For the secondary outcomes, a time-to-event analysis using Cox regression was undertaken for the first episode of peritonitis, exit-site infection, peri-catheter leakage, PD catheter migration and hospitalisation. The hazard ratio (HR) and the 95% CI was presented, with planned-start PD as the reference group.

The incidence of peritonitis, exit-site infection, peri-catheter leakage, PD catheter migration and hospitalisation within the first year of PD was analysed by Pearson chi-square test or Fisher's Exact test where appropriate. A post hoc pairwise analysis with Bonferroni correction for multiple comparisons was planned if a significant difference was found. The number of peritonitis episodes and number of hospitalisations within the first year of PD was compared between the 3 subgroups with the Kruskal-Wallis test and if significant, Dunn's multiple comparisons test was planned.

Level of significance was set at $\alpha=0.05$. Data were processed using SPSS Statistics version 20 (IBM Corp, Armonk, US).

RESULTS

Patient characteristics

A total of 148 patients (mean age 62 years, 48% male, 90% Chinese) were enrolled in this study from January 2010 to October 2017. The baseline characteristics of these participants are listed and categorised according to the PD initiation strategy in Table 1. Among these patients, there were 57 (38.5%) planned-start, 23 (15.5%) early-start and 68 (45.9%) from the deferred-start group. A history of coronary heart disease or congestive heart failure were noted to be more frequent in the early-start PD patients, compared with the planned-start and deferred-start PD counterparts. There were otherwise no significant differences in the other baseline characteristics of the groups. Initial biochemical parameters were also similar between the groups except for serum urea. Median serum urea levels were lower in the planned-start PD group (28mmol/L) as compared to the early-start group (37mmol/L) and deferred-start group (32mmol/L) ($P<0.001$).

Primary outcomes

The survival plot for technique survival is shown in Fig. 1A. When compared to planned-start PD in the time-to-event analysis, early-start PD was similar to planned-start PD with a HR of 1.08 (95% CI 0.28–4.06, $P=0.915$). Deferred-start PD appeared to have a higher HR for technique failure at 1.60 (95% CI 0.66–3.86) but this observation was not statistically significant ($P=0.297$).

The plot for patient survival is shown in Fig. 1B. Planned-start PD patients appeared to have the best survival, while it appeared to be lower with early-start PD (HR 1.35, 95% CI 0.65–2.81, $P=0.426$) and with deferred-start PD (HR 1.62, 95% CI 0.99–2.66, $P=0.053$). However, these findings were also not statistically significant. Table 2 tabulates the results from Cox regression analysis.

Secondary outcomes

The number and proportion of patients who experienced secondary outcomes are presented in Table 3. No statistically significant differences between the subgroups were found for incidences of peritonitis, exit site infection and peri-catheter leakage within the first year of PD. The frequency of peritonitis and number of hospitalisations between the 3 subgroups in the first year on PD were also similar.

Table 1. Baseline characteristics of study cohort, stratified by how peritoneal dialysis (PD) was initiated

	All (N=148)	Planned-start PD (n=57)	Early-start PD (n=23)	Deferred-start (n=68)	P value
Male, no. (%)	71 (48)	23 (40.4)	9 (39.1)	39 (57.4)	0.113
Ethnicity, no. (%)					0.401
Chinese	90 (60.8)	38 (66.7)	16 (69.6)	36 (52.9)	
Malay	35 (23.6)	10 (17.5)	6 (26.1)	19 (27.9)	
Indian	15 (10.1)	6 (10.5)	0 (0)	9 (13.2)	
Others	8 (5.4)	3 (5.3)	1 (4.3)	4 (5.9)	
Comorbidities, no. (%)					
Diabetes mellitus	112 (75.7)	42 (73.7)	17 (73.9)	53 (77.9)	0.840
Hypertension	133 (89.9)	52 (91.2)	20 (87)	61 (89.7)	0.817
Coronary artery disease	62 (41.9)	18 (31.6)	14 (60.9)	30 (44.1)	0.054
Congestive cardiac failure	39 (26.4)	12 (21.1)	12 (52.2)	15 (22.1)	0.010
Cerebrovascular disease	30 (20.3)	11 (19.3)	6 (26.1)	13 (19.1)	0.760
Malignancy	1 (0.7)	0 (0)	0 (0)	1 (1.5)	1.000
Peripheral vascular disease	21 (14.2)	8 (14)	4 (17.4)	9 (13.2)	0.901
Age at initiation of PD, median (IQR), years	62 (53–74)	63 (53–74)	64 (55–77)	60 (53–71)	0.487
eGFR at initiation, median (IQR), mL/min/1.73m ²	5 (4–7)	6 (4–9)	6 (5–7)	5 (3–7)	0.006
Serum urea at initiation of dialysis, median (IQR), mmol/L	31 (26–39)	28 (22–33)	32 (27–38)	37 (29–45)	<0.001
Days on HD, median (IQR)	26 (0–61)	0 (0)	18 (12–33)	67 (43–119)	<0.001
Duration of follow-up on PD, median (IQR), years	2.8 (0.9–4.4)	3.2 (1.3–6.2)	1.3 (0.7–3.3)	2.5 (0.7–4.2)	0.014

eGFR: estimated glomerular filtration rate; HD: haemodialysis; IQR: interquartile range; PD: peritoneal dialysis

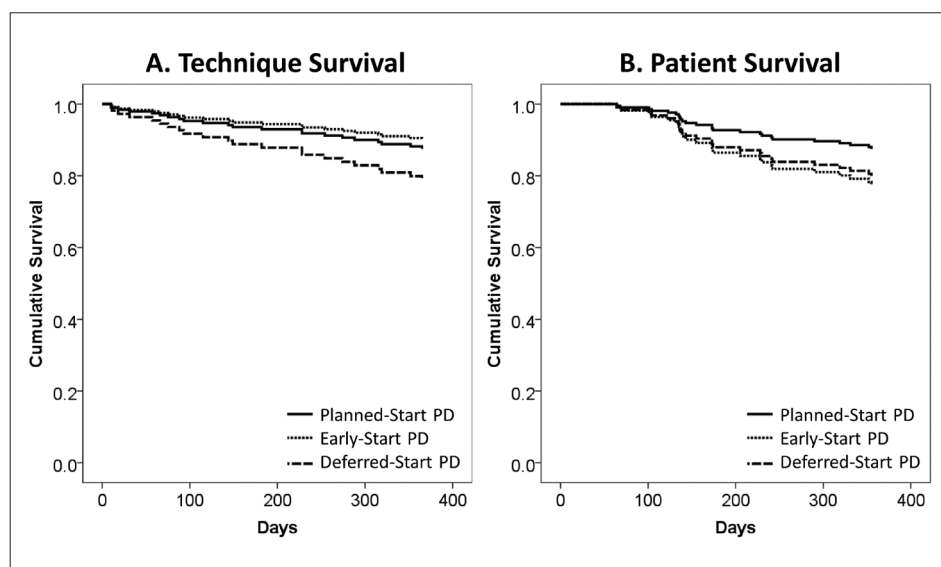


Fig. 1. Survival plot from Cox regression analysis for primary outcomes of interest in (A) Technique survival and (B) patient survival, comparing between planned-start peritoneal dialysis (PD), early-start PD and deferred-start PD.

Table 2. Results of cox regression analysis of primary and secondary outcomes

Outcome (total events)	Subgroup	Number of events No. (%)	Hazard ratio	95% CI for hazard ratio		P value
				Lower	Upper	
Technique failure (n=22)	Planned-start	7 / 57 (12.3)	-	-	-	-
	Early-start	2 / 23 (8.7)	1.08	0.28	4.06	0.915
	Deferred-start	13 / 68 (19.1)	1.60	0.66	3.86	0.297
Patient mortality (n=31)	Planned-start	7 / 57 (12.3)	-	-	-	-
	Early-start	7 / 23 (30.4)	1.35	0.65	2.81	0.426
	Deferred-start	17 / 68 (25)	1.62	0.99	2.66	0.053
Peritonitis (n=29)	Planned-start	7 / 57 (12.3)	-	-	-	-
	Early-start	5 / 23 (21.7)	2.10	0.67	6.64	0.205
	Deferred-start	17 / 68 (25)	2.49	1.03	6.01	0.043
Exit site Infection (n=16)	Planned-start	7 / 57 (12.3)	-	-	-	-
	Early-start	2 / 23 (8.7)	0.79	0.16	3.79	0.764
	Deferred-start	7 / 68 (10.3)	0.95	0.33	2.70	0.917
Peri-catheter leak (n=4)	Planned-start	3 / 57 (5.3)	-	-	-	-
	Early-start	0 / 23 (0)	0	0	0	0.989
	Deferred-start	1 / 68 (1.5)	0.32	0.03	3.11	0.328
PD catheter migration (n=10)	Planned-start	1 / 57 (1.8)	-	-	-	-
	Early-start	5 / 23 (21.7)	14.13	1.65	121.04	0.016
	Deferred-start	4 / 68 (5.9)	3.56	0.40	31.87	0.256
First hospitalisation (n=114)	Planned-start	39 / 57 (68.4)	-	-	-	-
	Early-start	19 / 23 (82.6)	1.44	0.83	2.50	0.193
	Deferred-start	56 / 68 (82.4)	2.03	1.35	3.07	0.001

CI: confidence interval

A significant difference between the 3 subgroups was noted in the number of patients who experienced PD catheter migration in the first year by chi-square test ($P=0.008$). Post hoc subgroup analysis found that the early-start PD group had a significantly higher incidence of PD catheter migration at 21.7%, as compared to 1.8% of patients in the planned-start PD group (Bonferroni corrected $P=0.011$).

Cox regression analysis of the secondary outcomes is presented in Table 2 and Fig. 2. The first episode of peritonitis was significantly earlier in the deferred-start PD group (HR 2.49, 95% CI 1.03–6.01, $P=0.043$) and a trend towards earlier peritonitis was also seen in the early-start PD group (HR 2.10, 95% CI 0.67–6.64, $P=0.205$), as compared to planned-start PD (Fig. 2A).

As reflected in Fig. 2B, time to catheter migration was significantly shorter for early-start PD, with a hazard ratio of 14.13 (95% CI 1.65–121.04, $P=0.016$). Time to first hospital admission was significantly shorter for patients in the deferred-start group (HR 2.03, 95% CI 1.35–3.07, $P=0.001$) while no differences were found between planned and early-start PD (Fig. 2C). There were no differences in the time to first exit site infection (Fig. 2D) and peri-catheter leak (Fig. 2E).

DISCUSSION

In this study, no differences were found between the 3 PD initiation strategies for our primary outcomes of interest—technique and patient survival. Planned-PD had the best secondary outcomes with a longer time to the

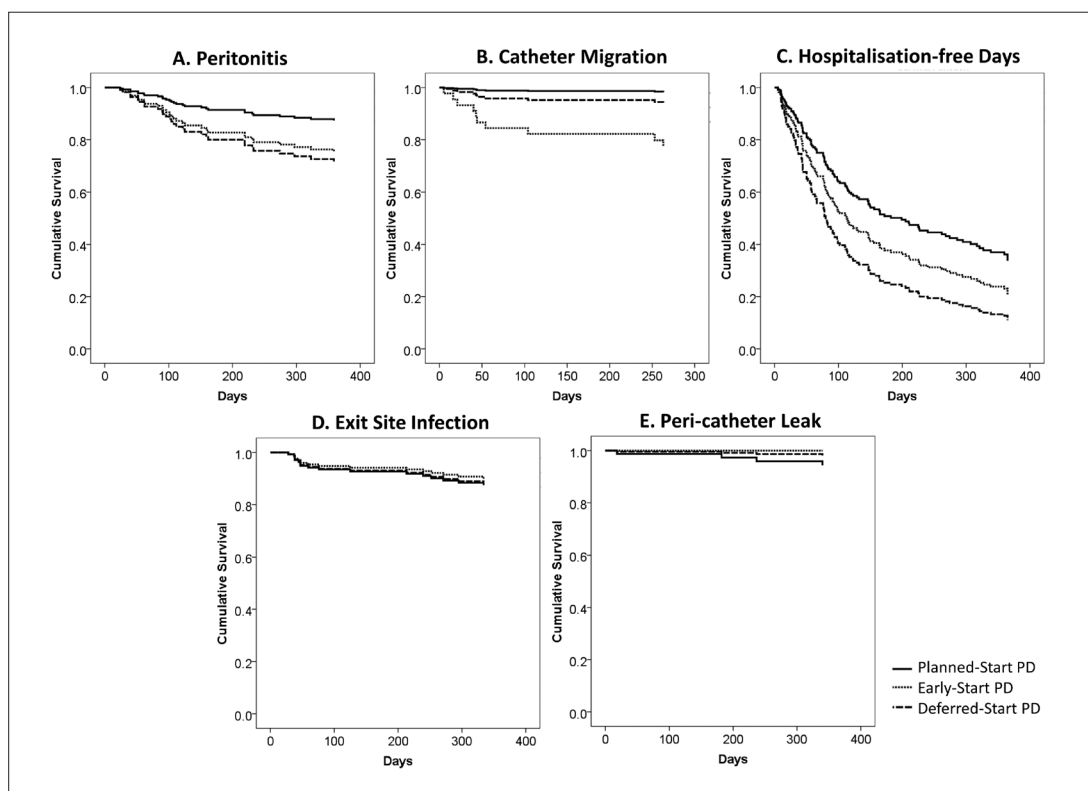


Fig. 2. Survival plot from Cox regression analysis for secondary outcomes of interest in (A) peritonitis, (B) catheter migration, (C) hospitalisation-free days, (D) exit site infection and (E) peri-catheter leak, comparing between planned-start peritoneal dialysis (PD), early-start PD and deferred-start PD.

Table 3. Complications within the first year of peritoneal dialysis (PD) initiation

	All	Planned-start PD (n=57)	Early-start PD (n=23)	Deferred-start (n=68)	P value
Patients with technique failure in the 1 st year, no. (%)	22 (14.9)	7 (12.3)	2 (8.7)	13 (19.1)	0.424 ^a
Deaths in the 1 st year, no. (%)	31 (20.9)	7 (12.3)	7 (30.4)	17 (25.0)	0.103 ^a
Patients with peritonitis within 1 year, no. (%)	29 (19.6)	7 (12.3)	5 (21.7)	17 (25)	0.201 ^a
Patients with exit-site infection within 1 year, no. (%)	16 (10.8)	7 (12.3)	2 (8.7)	7 (10.3)	0.938 ^a
Patients with peri-catheter leakage within 1 year, no. (%)	4 (2.7)	3 (5.3)	0 (0)	1 (1.5)	0.376 ^a
Patients with catheter migration within 1 year, no. (%)	10 (6.8)	1 (1.8)	5 (21.7)	4 (5.9)	0.008 ^a
Peritonitis episodes in the 1 st year, median (IQR)	0 (0)	0 (0)	0 (0–1)	0 (0–1)	0.140 ^b
Hospital admissions in the 1 st year, median (IQR)	2 (1–3)	1 (0–3)	2 (1–2)	2 (1–3)	0.336 ^b

IQR: interquartile range; PD: peritoneal dialysis

^a Fisher's Exact test

^b Kruskal-Wallis test

first episode of peritonitis. Of note, early-start PD had the highest incidence of catheter migration, but there was no increased risk for peri-catheter leak. Following initiation of dialysis, the time to first hospital admission was the shortest for patients in the deferred-start group.

Studies had consistently shown that urgent-start on PD may be associated with an increased risk of mechanical complications but with no detrimental effects on peritonitis, patient and technique survival as compared to planned-start PD.^{17,19} Our study reached similar

conclusions with early-start PD. With no differences in technique and patient survival between various strategies, the physician is given the flexibility to utilise any of the strategies based on available resources, patient's clinical circumstances and preferences. Further studies should evaluate if this strategy of early-start PD can increase long-term uptake of PD.

Early infection is a primary concern with an urgent-start strategy.¹⁰ In the present study, there was no statistically significant difference in the incidence of infectious complications within the first year of PD although the first peritonitis episode was significantly earlier in the deferred-start group while a trend towards significance was seen in the early-start group. Future studies should explore the underlying reasons for this observation and if different antibiotic prophylaxis regimens are required.

The early-start PD group had a significantly higher incidence of PD catheter migration at 21.7% compared to 1.8% of patients in the planned-start PD group, although it did not have a significant impact on technique survival. This may be a significant problem in early-start PD, as there is less time to institute conventional prescription for bowel clearance^{10,20} and wait for spontaneous repositioning. It is important to be aware of this common complication and assess early for catheter malposition if there are flow issues.

Abdominal wall complications, especially peri-catheter leakage, are major concerns in urgent-start PD.²² No peri-catheter leak occurred in our study, which could be attributed to the use of low-volume regimens, to avoid high intraperitoneal pressures in the first 14 days after catheter insertion.

PD patients previously on HD are known to have poorer survival.⁵ This was attributed to a more rapid loss of residual renal function, a major determinant of survival in PD patients.²³⁻²⁵ The median duration on HD for the deferred-start PD group is 67 days as compared to 18 days in early-start PD group. The deferred-start PD group did show a trend towards poor survival, though this did not reach statistical significance. Further studies would be needed to investigate if there was an impact on residual renal function and if this was a substantial factor affecting survival.

Besides ESKD, the early-start strategy can also be adopted for other applications of PD, such as in the management of acute kidney injury or chronic heart failure.^{26,27} When patients transit from the acute treatment phase to long-term kidney support, the early-start PD approach may be more practicable with less logistical prerequisites.

The limitation of this study lies in the single-centre observational design. The PD strategy was based on the recommendations of individual nephrologists, taking into account patient and caregiver preferences and circumstances. While individual bias cannot be avoided, our study reflects real-life clinical decision-making and the choice of PD initiation strategy is expected to have no impact on patient and technique survival. Prospective randomised trials would provide more definitive conclusions, but randomised HD vs PD study designs in ESKD patients had not been successful.²⁸ While early-start PD may strike a balance between planned-start and deferred-start PD, it remains resource- and manpower-intensive and may not be a suitable strategy in many centres.

The study was non-randomised and the patient numbers in each subgroup was small. In particular, there were only 23 patients in the early-start group. Furthermore, the event rates were low for some of the outcomes and these limitations may increase the possibility of biased results. Additional baseline clinical factors were not included in the Cox model as the number in each subgroup was small. Socio-economic factors were not included in the study.

For observational studies on the effect of dialysis initiation on mortality, lead time bias is another potential confounder. However, the lead time differences between early-start PD vs deferred-start PD were not expected to be different but may instead favour planned-start PD in terms of survival.

CONCLUSION

A planned start is the best strategy for initiation of dialysis. If this is not possible, our results suggest that early-start PD is a possible alternative that is less resource-intensive compared to urgent-start PD. With a wide choice of various PD initiation strategies, PD is a viable option in most patients who require urgent dialysis initiation.

Availability of data and materials

Individual de-identified participant data will be shared. Data that underlie the results reported in this article, after de-identification, will become available after 9 months and stored for at least 36 months following article publication. This will be provided to investigators who propose the use of data for meta-analysis with proof of approval by an independent review committee identified for this purpose. Proposals may be submitted through the corresponding author. Data will be provided without investigator support other than provision of deposited data.

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