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# Comparison of outcomes of incremental vs. standard peritoneal dialysis: a systematic review and meta-analysis

Shuang Xu<sup>1</sup>, Weifei Wu<sup>2</sup> and Jing Cheng<sup>1\*</sup>

## Abstract

**Background** Incremental peritoneal dialysis (IPD) refers to the use of less than standard full-dose peritoneal dialysis (SPD) in end-stage renal disease patients. While the use of IPD is being reported in the literature, its safety and efficacy vs. SPD is unclear. We hereby performed a systematic review of studies comparing mortality, peritonitis, technique survival, anuria-free survival and residual renal function (RRF) between IPD and SPD.

**Methods** All comparative studies published on PubMed, Embase, CENTRAL, Scopus, and Web of Science databases from inception to 5th September 2023 and reporting on given outcomes were eligible.

**Results** Ten studies were included. Definitions of IPD were heterogenous and hence mostly a qualitative synthesis was undertaken. Majority of studies found no difference in patient survival between IPD and SPD. Meta-analysis of crude mortality data also presented no significant difference. Peritonitis and technique survival were also not significantly different between IPD and SPD in the majority of studies. Data on RRF was conflicting. Some studies showed that IPD was associated with the preservation of RRF while others found no such difference.

**Conclusion** IPD may be a safe alternative to SPD in incident dialysis patients. There seems to be no difference in patient survival, peritonitis, and technique survival between the two modalities. However, the impact of IPD on RRF is still questionable. Evidence is heterogeneous and conflicting to derive firm conclusions.

**Keywords** Dialysis, Renal failure, Mortality, Technique survival, Peritonitis

## Introduction

End-stage kidney disease (ESKD) is a major public health problem affecting around 4–7 million individuals around the world [1]. The need for renal replacement therapy for survival imposes enormous socioeconomic pressure on both the patients as well as health care setups globally. In about 80% of patients, the initial choice is hemodialysis but is associated with a high risk of mortality and rapid loss of residual renal function (RRF) in the initial months of maintenance dialysis [2–6]. Contrastingly, peritoneal dialysis (PD) offers lower mortality rates owing to the maintenance of RRF while providing more or less equivalent long-term survival as compared to hemodialysis

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[HD] [7, 8]. Nevertheless, while the number of patients requiring renal replacement therapy has grown exponentially, those enrolled in PD have not correspondingly increased. Lack of patient education, risk of catheter-related complications, shortage of trained manpower, and lack of support for assisted PD are important factors limiting the uptake of PD [9].

The concept of incremental PD (IPD) was first reported in the year 1997 and consisted of starting maintenance dialysis with PD but with lower-dose prescription rather than the full dose i.e. standard PD (SPD) while maintaining individualized clearance goals [10]. The dosage is gradually increased as the RRF declines by changing the dwell time, volume and number of exchanges [11, 12]. IPD can be implemented in both continuous ambulatory PD (CAPD) and ambulatory PD (APD) achieving the therapeutic goals of renal replacement therapy at a reduced cost [12]. Recommendations by the International Society for Peritoneal Dialysis (ISPD) in 2020 recommended the usage of IPD for improving patient experience and providing high-quality, goal-directed PD [13]. The presumed advantages of IPD like longer preservation of RRE, reduced costs, and reduced time on PD have prompted its utilization in several countries worldwide. However, these advantages are still debatable and it is unclear if PD should be started at a reduced dosage or full-dose. Several comparative studies on IPD vs. SPD have been published in the past decade [14–16], however, there has not been an attempt to pool published evidence. We hereby attempted to perform a comprehensive systematic review and meta-analysis to analyze the efficacy and safety of IPD vs. SPD.

## Materials and methods

### Search protocol

The present study was reported by the guidelines of PRISMA [17] and registered on PROSPERO (CRD42023458440). All studies published on PubMed, Embase, CENTRAL, Scopus, and Web of Science databases were searched from inception to 5th September 2023. Only English-language studies were eligible. It was conducted by an experienced medical librarian along with one study reviewer. The search strategy included MeSH/Emtree terms and free keywords namely: “low dose”, “incremental”, “peritoneal dialysis”, “incremental dialysis”, “survival” “ and “mortality”. Details can be found in Supplementary Table 1. All search results were downloaded into EndNote X8 (Thompson ISI Research soft, Philadelphia, Pennsylvania), a reference manager software. Duplicate articles were identified and excluded. All remaining unique citations underwent screening by two reviewers. Full texts of articles found important were downloaded and further screened based on inclusion criteria.

### Inclusion criteria

Both reviewers independently checked the eligibility of studies based on the following criteria:

1. Any study design conducted on patients undergoing PD without any age restriction.
2. Comparing outcomes of IPD with SPD. We did not predefine IPD and accepted the criteria mentioned in the included studies.
3. Outcomes included all-cause mortality, peritonitis, technique survival, anuria-free survival, and RRE.

Studies comparing IPD with HD, not reporting any outcomes, on urgent-start PD, and single-arm studies were excluded.

All studies underwent final screening based on these criteria. The reviewers resolved any disagreements (if any) involving the study selection by discussion. In the end, one reviewer undertook a hand search of the reference list of included studies for any possible inclusions. In two studies were found to use the same database and had same or overlapping study duration, the study reporting the maximum outcomes was to be included.

### Data extraction

A pre-defined data collection form was used by the reviewers to collect data. It included the author and publication information, location, IPD and SPD definition, duration of IPD, follow-up, sample size, age, gender details, diabetics, creatinine, baseline renal function, haemoglobin, albumin, baseline 24-hour urine output, and drug use. The second reviewer then cross-checked the data for correctness. All endpoint data based on the inclusion criteria was extracted. We did not predefine any endpoints and all definitions reported by the included studies were acceptable.

### Study quality

The Newcastle-Ottawa Quality Assessment Scale (NOS) was selected for assessing individual study bias of observational studies [18]. The scale intends to rate selection bias, comparability of the exposed and unexposed groups, outcome assessment, and completeness of follow-up. Points are awarded based on pre-determined questions and the final score of each study can be 0 meaning the highest risk of bias up to 9 meaning the lowest risk of bias. The Cochrane risk of bias-2 tool was used to examine risk of bias in randomized controlled trials (RCT) [19]. Two reviewers were involved in the risk of bias analysis and disagreements were resolved by discussion.

### Statistical analysis

Quantitative synthesis was planned if a minimum of three studies were available for each outcome. If outcomes were reported on different scales or without 95% confidence intervals (CI), meta-analysis was not conducted. Outcome data was extracted as a crude ratio or adjusted ratio. Both data were to be pooled separately. Crude dichotomous data was pooled to obtain.

RR and 95% CI. Subgroup analysis was conducted based on study design. A random-effects model was chosen because of anticipated heterogeneity. The chi-square test judged the heterogeneity between studies; the  $I^2$  statistic was also calculated. The  $I^2$  statistic gives the percentage of the variability in effect size based on heterogeneity rather than sampling error. Any value  $>50\%$  was considered substantial heterogeneity. “Review Manager” (RevMan, version 5.3; Nordic Cochrane Centre (Cochrane Collaboration), Copenhagen, Denmark; 2014) was the software used. Values of  $p < 0.05$  were considered to be statistically significant. Owing to a low number of studies funnel plot was not generated for publication bias. GRADE approach (Grading of Recommendations Assessment, Development and Evaluation) was used to assess certainty of evidence.

## Results

### Search results

The final number of articles obtained from all databases was 2016. Unique articles amongst these were 992. The reviewers eliminated 973 studies based on initial screening. Nineteen underwent full-text analysis and ten were selected for the meta-analysis [14–16, 20–26] (Fig. 1).

### Baseline details of studies

Study details and baseline data of participants at the start of PD are presented in Tables 1 and 2. All were retrospective studies and only one was an RCT. One study was a secondary analysis of an RCT. The studies published between 2013 and 2023 included patients from India, Italy, China, Korea, Australia, the USA and Portugal. The RCT of Yan et al [24] compared 3 vs. 4 exchanges/day of CAPD with a follow-up of two years. Hayat et al [20] compared  $<56$  L/week vs.  $\geq 56$  L/week of PD fluid exchange with a follow-up of about two years. In the retrospective studies, there was a wide variation in what was defined as IPD. Most studies however, considered  $\leq 3$  dwells of CAPD per day as IPD. Jeloka et al [22] reported IPD as one icodextrin exchange/day. Huang et al [14] defined IPD as CAPD  $< 8$  L/day with no patient receiving it for  $< 7$  days a week. SPD was defined as  $\geq 4$  exchanges on CAPD per day in four studies. In three studies,  $\geq 3$  exchanges/day was considered as SPD. Four studies did not report the duration of IPD. In the remaining studies, it ranged from one year to 2.5 years. A total of 1540

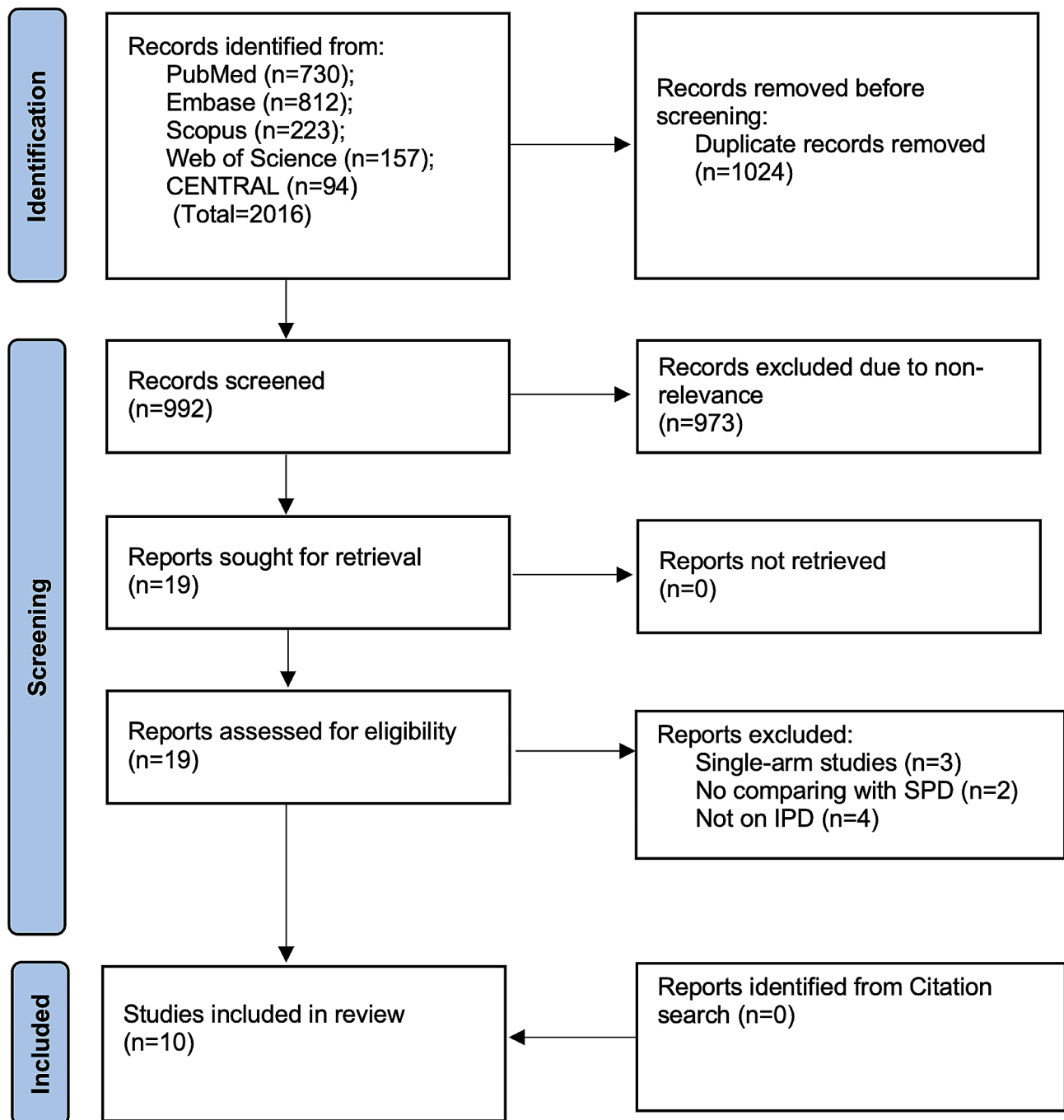
patients were on IPD while 1837 were on SPD. The mean age was above 40 years in both IPD and SPD groups across studies. Majority of studies had a male predominance in the sample. The percentage of diabetics was  $< 50\%$  across studies. However, in the study of Jeloka et al [22] and Naljayan et al [21]  $> 50\%$  of patients in both the IPD and SPD groups were diabetics. GFR was  $\leq 10$  ml/min/1.73m<sup>2</sup> in most studies, both in IPD and SPD. GFR was significantly better in the IPD group vs. the SPD group in the study of Lee et al [15]. No such difference was noted in the remaining studies. The follow-up duration varied from 17 months to a maximum of 12 years. On examination of study quality of observational studies, the reviewers gave one study 5 points, three studies scored 6 points, while the remaining got 8 points. The study of Yan et al [24], being an RCT, was assessed by the Cochrane risk of bias tool. There were “some concerns” regarding the randomization process and missing outcome data, high risk of bias for outcome assessment, but low risk of bias for deviations from intended interventions, and selection of reported result. Overall the RCT was classified as having high risk of bias.

### Mortality

Outcome data reported by studies is presented in Table 3. Much of the data was not amenable to a meta-analysis. Since crude mortality rates were reported by five studies, we decided to pool them together. No statistically significant difference was noted in mortality rates between IPD and SPD (RR: 0.84 95% CI: 0.46, 1.55  $I^2=28\%$ ). The results were non-significant for both the single RCT and non-RCTs (Fig. 2). GRADE assessment of evidence showed certainty of evidence was “very low” for both the RCT and non-RCTs (Supplementary Table 2). All-cause mortality adjusted for confounders was reported by Lui et al [16] (HR: 0.79 95% CI: 0.58–1.09) and Lee et al [15] (HR: 0.504 95% CI: 0.230–1.104) but without any statistically significant difference between the two groups. Naljayan et al [21] also reported the incidence rate ratios (IRR) of mortality rates in both CAPD and APD groups. No statistically significant difference in mortality was noted between IPD and SPD for CAPD (IRR: 0.68; 95% CI: 0.43–1.06) and APD (IRR: 0.62; 95% CI: 0.34–1.14) groups. As noted in Table 3, except for the study of Jeloka et al [22] which noted better survival with IPD, the remaining studies also noted no statistically significant difference in patient survival between IPD and SPD.

### Peritonitis

Peritonitis was reported as an outcome of eight studies. Lee et al [15] found a statistically significant lower risk of peritonitis in patients undergoing IPD as compared to SPD. The incidence of peritonitis was 1/18 patient-year in IPD patients and 1/7 patient-year in the SPD group



**Fig. 1** Study flowchart

( $p=0.002$ ). However, all remaining studies noted no statistically significant difference in the risk of peritonitis with either modality.

**Technique survival**

Six of the ten studies reported on technique survival. In the study of Fernandez et al [26], 5/57 IPD patients and 8/30 patients SPD patients had technique failure. Mechanical complications with SPD (2/30) were also

significantly higher as compared to IPD (0/57) in their study. Overall, the authors noted superior technique survival with IPD ( $p=0.026$ ). None of the remaining five studies noted a statistically significant difference in technique survival between the two modalities.

**Anuria-free survival**

Three studies reported on anuria-free survival. Yan et al [24] in their RCT noted no statistically significant

**Table 1** Details of included studies

Study	Location	Excluded patients	IPD definition	SPD definition	Duration of IPD	Follow-up	NOS score
Hayat 2023 <sup>#</sup> [20]	Australia	NR	< 56 L/week of PD fluid	≥ 56 L/week of PD fluid	NR	19.5 m	8
Nalajyan 2023* [21]	USA	Body weight < 40 kg, prior limb amputation, or GFR > 20 mL/min/1.73m <sup>2</sup> during the first 4 weeks on PD	CAPD: < 4 daily exchanges, 3–7 days a week and < 2 L dwell volume of 4 exchanges. APD: with last fill, 3–6 treatment days/week, without last fill 3–7 treatment days/week	Greater dose than IPD	NR	12 m	8
Liu 2023* [16]	China	Transferred from maintenance HD or kidney transplantation failure; withdrawal within six months after PD initiation; incomplete data on daily PD exchanges; failure to satisfy the definition of IPD or SPD; incomplete data	≤ 3 × 2 L daily exchanges during the six months of CAPD inception, seven days per week	≥ 4 × 2 L daily exchanges, seven days per week at the initiation of CAPD	12.2 [4.8–30] m	59.6 [32.4–90.3] m	8
Fernandes 2023 [26]	Portugal	NR	CAPD: less than 4 dwells daily, less than 2 L dwell volume, and/or treatment less than 7 days/week; APD: without a long dwell, less than 10 L daily delivered, and/or treatment for less than 7 days/week	Greater dose than IPD	NR	23 [15–35] m	6
Lee 2021* [25]	Korea	Started HD before the PD catheter insertion, had done PD with an automated cycler, or had a total duration of PD less than 6 months	Two or three manual exchanges per day	Initiation of CAPD with four exchanges with 2 L per day, seven days a week	24.1 [15.4–36.8] m	Up to 12 years	8
Huang 2021 [14]	Australia	PD technique failure within 30 days	CAPD < 8 L/day and APD without a last fill; no participants were prescribed a < 7 days/week PD regimen	NR	NR	17–20 m	6
Lee 2019* [25]	Korea	Total duration of PD < 6 months, initiation of PD at another hospital, urine volume of < 200 mL per day at the time of initiating PD, previous HD, and incomplete data	1–2 dwells per day on CAPD, 7 days a week, and a peritoneal Kt/V < 1.7 per week, but a total Kt/V ≥ 1.7 per week	Initiation of PD with 3 or more exchanges per day for CAPD, 7 days a week	2.6 [1.6–4.5] years	5.9 [3.3–7.8] years	8
Yan 2016 <sup>^</sup> [24]	China	History of maintenance HD or kidney transplantation, anticipated life expectancy less than 6 months, active malignancy, acute infection, significant heart failure, or other severe diseases	CAPD 3 exchanges/day	CAPD 4 exchanges/day	NR	2 years	-
Sandrine 2016 [23]	Italy	Non-renal indication for PD, < 6 months of follow-up	1–2 dwell times per day on CAPD	3–5 dwell times per day, 7 days a week for CAPD	17 [10–30] m	Up to 5 years	6
Jeloka 2013 [22]	India	HIV, hepatitis B, and hepatitis C patients	1 icodextrin exchange/day	3 × 2 L exchanges of glucose-based dialysate	18.8 ± 4.7 m	Up to 5 years	5

PD, peritoneal dialysis; APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; DM, diabetes mellitus; IPD, incremental peritoneal dialysis; SPD, standard peritoneal dialysis; HD, hemodialysis; GRF, glomerular filtration rate; HIV, human immunodeficiency virus; NR, not reported; L, litres; Kt/V, K, dialyzer clearance of urea, t – dialysis time, V – volume of distribution of urea

\*propensity matched

<sup>^</sup> RCT

<sup>#</sup>secondary analysis of RCT

**Table 2** Characteristics of the sample

Study	Groups	Sample size	Age (years)	Female (%)	DM (%)	Creatinine (mg/dl)	GFR (ml/min /1.73m <sup>2</sup> ); mean ± SD	Hb (g/L); mean ± SD	Alb (g/L); mean ± SD	24 h-UF (mL)	Urine output (mL/day); mean ± SD or Median [IQR]	ACEI/ARB use (%)
Hayat 2023 [20]	IPD SPD	45 109	NA	NA	NA	NA	7.9±3.2 7.3±2.7	NA	NA	NA	1810±730 1380±610	NA
Naljayan 2023 [21] (CAPD)	IPD SPD	107 107	57.1 58	50.5 42	53.3 61.7	NR	12.5±3.7 13±3.7	NR	NR	NR	NR	NR
Naljayan 2023 [21] (APD)	IPD SPD	722 722	57 56.9	33.9 38.9	56.4 58.6	NR	11.8±3.9 11.6±4	NR	NR	NR	NR	NR
Liu 2023 [16]	IPD SPD	285 502	46.5 47	48.8 47.2	22.8 23.7	NR	4.9±2.45 4.6±2.7	109±20 109±19	36.9±4.6 36.9±4.6	80 300	850 [500–1250] 800 [500–1200]	40 46
Fernandes 2023 [26]	IPD SPD	57 30	NR	NR	NR	NR	NR	NR	NR	NR	1650 [1225–2150] 1100 [400–1500]	NR
Lee 2021 [25]	IPD SPD	39 78	58.2 58.2	41 39.7	38.5 37.2	7.3±2.7 10.2±3.9	8.3±3.8 5.9±3.4	96±10 91±14	35±4 35±5	NR	748.6±395.8 597.4±441.7	NR
Huang 2021 [14]	IPD SPD	42 54	60.6 61.4	39 17	28 52	457µmol/L±NR 496µmol/L±NR	10.1±2.5 9.7±3.3	NR	NR	300 300	1700 [1500–2000] 1400 [1000–1800]	37 41
Lee 2019 [25]	IPD SPD	176 171	49.2 48.2	47.7 49.7	33 30.5	NR	6.9±3 6.5±2.4	NR	NR	NR	1576±595.2 1451±494.8	79 70.2
Yan 2016 [24]	IPD SPD	70 69	53.2 53	54 48	21 19	NR	5.7±2.9 6.4±2.8	NR	NR	NR	1465±525 1602±570	NR
Sandrini 2016 [23]	IPD SPD	29 76	63 59	45 34	NR	NR	5.7±1.3 5.4±1.8	NR	NR	NR	NR	NR
Jeloka 2013 [22]	IPD SPD	13 28	58 58.2	38.5 21.5	69.2 64.2	8±2.4 8.8±2.5	7.8±2.6 7.9±1.7	96±11 98±15	34±4 33±7	NR	1265±216 551±504	NR

APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; DM, diabetes mellitus (any type); IPD, incremental peritoneal dialysis; SPD, standard peritoneal dialysis; GFR, glomerular filtration rate; Hb, hemoglobin; Alb, Albumin; m, months; UF, Ultrafiltrate; NR, not reported; NA, not available; SD, standard deviation; IQR, interquartile range

**Table 3** Endpoints reported by included studies

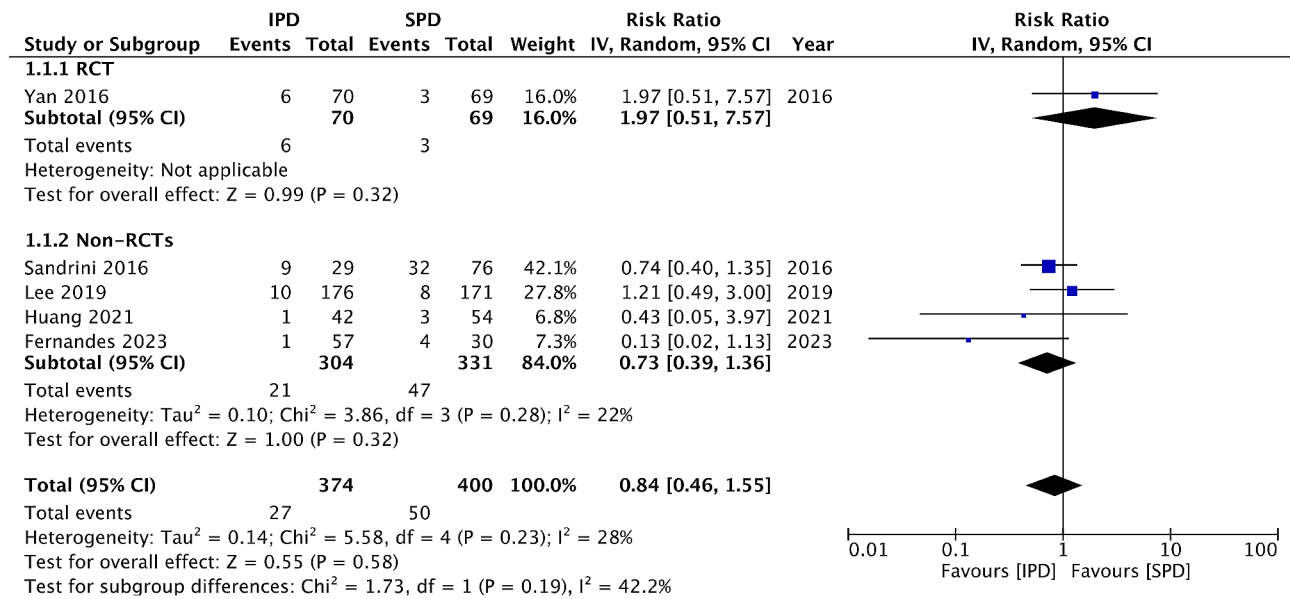
Study	Endpoints	Definition	Result
Hayat 2023 [20]	Residual renal function	NR	No statistically significant difference between IPD and SPD. IPD: $3.2 \pm 2.9$ mL/min/1.73 m <sup>2</sup> , SPD: $3.4 \pm 2.8$ mL/min/1.73 m <sup>2</sup> at 24 months (mean $\pm$ SD).
	All-cause mortality	NR	No statistically significant difference between IPD and SPD. CAPD: (IRR: 0.68; 95% CI: 0.43–1.06), APD: (IRR: 0.62; 95% CI: 0.34–1.14).
	GFR values at follow up	NR	No statistically significant difference between IPD and SPD. Values not reported.
Liu 2023 [16]	Peritonitis	Two or more of the following symptoms and signs: (1) persistent abdominal pain or turbidity of PD effluent; (2) the total amount of leukocytes in the PD effluent over 100/ $\mu$ L and the proportion of neutrophil granulocytes over 50%; and (3) positive results from an etiological examination of PD effluent	No statistically significant difference between IPD and SPD. Peritonitis rates in both IPD and SPD groups was 0.14/patient-year.
	Technique survival	PD patients who did not ( $\geq 3$ months) switch to HD because of inadequate dialysis	No statistically significant difference between IPD and SPD. Values not reported.
Fernandes 2023 [26]	All-cause mortality	NR	No statistically significant difference between IPD and SPD (HR: 0.79; 95% CI: 0.58–1.09).
	Anuria free survival	Anuria was defined as patients with urine volume less than 100 mL per day for at least three months	Significantly better with IPD (HR: 0.72; 95% CI 0.58–0.91)
	GFR $\geq 5$ mL/min	NR	Significantly better with IPD (OR: 12.66; 95% CI 1.37–116.97)
	Peritonitis	NR	No statistically significant difference between IPD and SPD. IPD: 0.25/patient-year, SPD: 0.29/patient-year.
Lee 2021 [15]	Technique failure	NR	Significantly lower with IPD (HR: 0.17; 95% CI: 0.05–0.63)
	All-cause mortality	NR	Significantly lower with IPD. Values not reported.
	Renal creatinine clearance	NR	Significantly better with IPD. IPD: 45.2 [18.8–64.3] mL/min/1.73m <sup>2</sup> , SPD: 19.2 [8.9–36.9] mL/min/1.73m <sup>2</sup> (median and IQR values after 24 months).
	Renal urea clearance	NR	Significantly better with IPD. IPD: 0.77 [0.42–1.4], SPD: 0.42 (0.14–0.63) (median and IQR values of k <sub>T</sub> V per week after 24 months).
	Peritonitis	Signs and symptoms of peritoneal inflammation and peritoneal effluent with a white blood cell count of $> 100$ cells/ $\text{mm}^3$ and a polymorphonuclear leukocyte count of $> 50\%$	Significantly lower with IPD. IPD: 1/18 patient-year, SPD: 1/7 patient-year.
Huang 2021 [14]	Technique survival	NR	No statistically significant difference between IPD and SPD. Values not reported.
	All-cause mortality	NR	No statistically significant difference between IPD and SPD (HR: 0.504; 95% CI: 0.230–1.104)
	Technique survival	Time to transfer to haemodialysis or death, censored for kidney transplantation, renal function recovery or transfer to another treating centre	No statistically significant difference between IPD and SPD (HR: 0.87; 95% CI: 0.30–2.51).
Patient survival	Renal creatinine clearance	Average of creatinine and urea clearance, corrected for body surface area and expressed as L/week/1.73m <sup>2</sup>	No statistically significant difference between IPD and SPD. IPD: -1.34 (95% CI: -2.32 – -0.12) L/week/1.73m <sup>2</sup> /month, SPD: -0.89 (95% CI: -2.73 – -0.55) L/week/1.73m <sup>2</sup> /month.
	Renal urea clearance	NR	No statistically significant difference between IPD and SPD. IPD: -0.02 (95% CI: -0.05–0.01) k <sub>T</sub> V per month, SPD: -0.01 (95% CI: -0.05–0.00) k <sub>T</sub> V per month
	Peritonitis	NR	No statistically significant difference between IPD and SPD. IPD: 0.12 (95% CI: 0.06–0.23) episodes/patient-years SPD: 0.23 (95% CI: 0.14–0.37).
	Technique survival	NR	No statistically significant difference between IPD and SPD. Values not reported.

**Table 3** (continued)

Study	Endpoints	Definition	Result
Lee 2019 [25]	Technique survival	Transfer to hemodialysis and death directly related to PD-related complication	No statistically significant difference between IPD and SPD. Time to technique survival-IPD: 2.7 years, SPD: 2.9 years.
	All-cause mortality	NR	No statistically significant difference between IPD and SPD. IPD: 10.9 events/1000 person years, SPD: 7.6 events/1000 person years.
Yan 2016 [24]	Anuria free survival	Anuria defined as urine volume of < 100 mL per day	Significantly lower risk with IPD. (HR: 0.61 95% CI: 0.43–0.88)
	Peritonitis	ISPD 2006 guidelines	No statistically significant difference between IPD and SPD. IPD: 0.10 (95% CI: 0.08–0.13) episode/patient-years, SPD: 0.10 (95% CI: 0.08–0.12) episode/patient-years
	Anuria free survival	Anuria defined as urine volume of < 100 mL per day for > 1 month	No statistically significant difference between IPD and SPD. Patients developing anuria- IPD: 15, SPD: 16.
	Technique survival	NR	No statistically significant difference between IPD and SPD. IPD: 1 failures, SPD: 2 failures.
Sandrini 2016 [23]	Patient survival	NR	No statistically significant difference between IPD and SPD. IPD: 6 deaths, SPD: 3 deaths.
	Peritonitis	ISPD 2006 guidelines	No statistically significant difference between IPD and SPD. IPD: 0.13 episodes per year, SPD: 0.20 episodes per year.
	Patient survival	NR	No statistically significant difference between IPD and SPD. IPD: 9 deaths, SPD: 32 deaths.
Jeloka 2013 [22]	Peritonitis	NR	No statistically significant difference between IPD and SPD. IPD: 1/135 episode/patient-months, SPD: 1/46 episode/patient-months.
	Residual renal function	Mean of creatinine renal clearance and urea renal clearance	Significantly better with IPD. IPD: 4.36 ± 2.96 SPD: 2.03 ± 2.55 (mean ± SD)
	Patient survival	NR	Significantly longer in IPD. IPD: 42.84 SE-7 months, SPD: 25.19 SE-9.2 months.
Jeloka 2013 [22]	Patient survival	NR	Lower in the IPD group, significance unknown. IPD: 1 episode in 56.22 patient-months, SPD: 1 episode in 25.29 patient-months
	Peritonitis	NR	

IPD, incremental peritoneal dialysis; SPD, standard peritoneal dialysis; HD, hemodialysis GFR, glomerular filtration rate; APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; IRR, incident rate ratio; CI, confidence intervals; NR, not reported; HR, hazard ratio; OR, odds ratio; IQR, interquartile range. SE: standard error; SD < standard deviation





**Fig. 2** Meta-analysis of crude mortality rates between IPD and SPD

difference between IPD and SPD for anuria-free survival. However, the two retrospective studies of Lui et al [16] and Lee et al [25] found statistically significant better anuria-free survival with IPD. Huang et al [14] also noted no statistically significant difference in residual urea and creatinine clearance at the end of follow-up between the two groups. On the other hand, Fernandez et al [26] found that renal urea and creatinine clearance were statistically significant higher with IPD in the first two years of follow-up. GFR was also found to be superior to IPD in the first two years. Sandrini et al [23] reported longer preservation of RRF with IPD as compared to SPD. Naljayan et al [21] found no difference in GFR values in the one-year follow-up between IPD and SPD with both CAPD and APD. Hayat et al [20] also noted no statistically significant difference in RRF and urine volumes between IPD and SPD.

**Discussion**

The use of IPD has been suggested as an alternative treatment strategy such that the combination of reduced dose and RRF leads to sufficient small solute clearance reducing the burden of uremic symptoms [12]. As the RRF declines with time, the dose of PD is also correspondingly increased to SPD. IPD offers an advantage of gentle prescription at PD initiation leading to an easier transition to full-dose by offering a more personalized and flexible treatment regimen. It also reduces the disruption faced by incident dialysis patients with a better quality of life [27]. However, whether it is as efficacious and safe as SPD is still unclear. Our systematic review and meta-analysis hereby present the first formal, updated, and comprehensive comparative evidence on the outcomes of IPD and

SPD. A total of ten recent studies including both RCTs and non-RCTs were analyzed to generate exhaustive evidence on patient survival, technique survival, peritonitis, and preservation of RRF between the two groups. We did not limit ourselves to RCTs as first, there were just two in literature (of which one is a secondary analysis of an RCT); and second, it would not have generated all-encompassing evidence on the differences between IPD and SPD. Nevertheless, due to methodological variations, differences in IPD definitions, and varied presentation of data, much of the review involved a qualitative rather than a quantitative analysis. A pooled analysis was conducted only for mortality rates which showed no statistically significant difference between the two modalities. Our results concur with the prior systematic review of Garofalo et al [28] who pooled together one study on IPD and ten studies on incremental HD and compared it with standard dialysis in a single meta-analysis only to note no statistically significant difference in mortality. Their study also showed lower mean loss of RRF with incremental PD and HD when compared with standard dialysis but with only one study on PD. Similar results have been noted in a narrative review as well [29].

Despite IPD being an old concept from the 1990s, its definition is still unclear [10]. The same was noted in the included studies where none of the studies were homogenous in defining IPD. As per the recent ISPD guidelines<sup>3</sup>, IPD can be any dose of PD which is less than the full-dose while achieving the kidney clearance target and prescribed to increase the dose as and when RRF declines. However, what constitutes SPD is subject to regional variations and body habitus. In Asian populations, SPD may be considered as 3 exchanges of 2 L/day

while in Western countries SPD consists of 4 exchanges of 2 L/day on CAPD or equivalent on APD with a long dwell [29–31]. Such variation was noted in the studies in our review with Yan et al [24] from China comparing 3 vs. 4 exchanges/day while Hayat et al [20] from Australia comparing based on total volume exchange/week. Thus, it is clear from the current literature that IPD cannot be based on a singular cut-off and is based on patient population, individual lifestyle and clearance requirements. Furthermore, even in a single region, IPD can be delivered in several ways depending on fill volume, number of exchanges, and dry periods for PD [27].

Patient survival assumes precedence in cases of ESKD. Initiating IPD can entail the hazard of under-dialysis and reduced small solute clearance. Also, IPD has a small margin of safety in terms of peritoneal clearance if RRF declines. Failure to increase the dose promptly based on RRF can increase the risk of complications, fluid overload and mortality. There can be “therapeutic inertia” on the part of the physician due to inadequate monitoring or due to the patient’s reluctance to get the PD prescription changed or increased from what they are used to [29, 32]. Nevertheless, this systematic review did not note any statistically significant difference in survival between IPD and SPD groups. Meta-analysis of crude mortality rates failed to show any statistically significant difference between the two groups. Also, qualitative synthesis of studies reporting adjusted data failed to show any statistically significant difference in patient survival. The only study of Jeloka et al [22] which noted better survival with IPD has important bias due to the small sample size and selection of participants.

The number of exchanges during PD is an important risk factor for peritonitis [33]. In CAPD, reduced exchanges and fewer connections can decrease the risk of contamination. Also, prolonged dwell time for a single bag of dialysate positively affects the peritoneal defence status [34]. Therefore, theoretically, IPD may reduce the risk of peritonitis. Indirectly, it may also prolong the utilization of PD as peritonitis is a major reason cited by PD drop outs [35]. Nevertheless, a quantitative analysis to assess peritonitis risk between the two modalities was not possible in this review as the risk is directly proportional to the number of exchanges and dwell times. The variations in the IPD definitions amongst the included studies were too critical for a meta-analysis. During qualitative synthesis, we noted that except for one study [15], no study reported a statistically significant difference in the risk of peritonitis between IPD and SPD. Likewise, technique failure did not show any statistically significant difference between IPD and SPD across most studies. The study of Lee et al [15] found a statistically significant lower risk of peritonitis in the IPD group. Despite being a propensity score matched analysis, their study

could include only 39 patients in the IPD group, which is a major limitation in the interpretation of results. Also, technique survival and peritonitis can be influenced by catheter insertion techniques, patient education, and rigorous follow-up and care. These practices may not be similar across studies, especially in the case of retrospective studies.

Clearance obtained by RRF as compared to PD can have important clinical implications. A study by Bargman et al. evaluating the relative contribution of RRF on patient outcomes has shown that per 5 L/week per 1.73 m<sup>2</sup> increment of GFR improves patient survival by 12% [36]. Maintaining RRF also has cardiovascular implications by improving fluid status, blood pressure control, and reducing left ventricular hypertrophy [29]. Han et al [37] have shown that preservation of RRF also reduces the risk of peritonitis. Liao et al [38] have found that the rate of decline of RRF is a strong marker for all-cause mortality and technique failure in PD. The length and number of dialysis sessions and intradialytic hypotension have been identified as markers of RRF in hemodialysis patients [39]. Observational studies have shown that twice-weekly or incremental HD leads to the preservation of RRF as compared to thrice-weekly or standard hemodialysis [40, 41]. Similarly, a major advantage postulated for IPD vs. SPD is the preservation of RRF. However, analysis of studies comparing IPD vs. SPD for RRF demonstrated mixed outcomes. The RCTs of Yan et al [24] and Hayat et al [20] noted no statistically significant difference in anuria-free survival and RRF respectively between IPD and SPD. However, several observational studies did note better RRF with IPD. Importantly, evidence from observational studies cannot be relied upon due to selection bias. Most of the studies did not use propensity score matching for adjusting baseline variables. It is plausible that physicians may have prescribed IPD to healthier patients leading to bias in the outcomes. Based on current data, this review cannot determine if IPD leads to the preservation of RRF and there is a need for further RCTs on this subject.

There are other limitations to the review as well. The overall number of studies was not very high. Too many methodological differences, especially regarding IPD definition, study type, study population, exclusion criteria, follow-up period, etc., prevented a comprehensive quantitative analysis. The endpoints reported by the studies were also not numerically amenable to quantitative synthesis due to variability in reporting. Most of the data was observational and from medical records, therefore prone to bias. The method of selection of IPD patients was also not mentioned in studies. We were unable to differentiate the outcomes of CAPD and APD due to a lack of sufficient data from the studies. Also, it was unclear what were the outcomes in PD patients who subsequently

underwent hemodialysis or kidney transplantation, as separate data for such patients was not reported. Lastly, important outcomes like cardiovascular diseases and pulmonary infections could not be assessed due to lack of data from the included studies.

Nevertheless, this systematic review presents a comprehensive qualitative analysis of outcomes with IPD and SPD. It sheds light on the limitations of current literature while also presenting important evidence for physicians who can make informed decisions. We believe the current review will encourage further research on the efficacy and safety of IPD vs. SPD in a more rigorous study design. Future studies should include comparable equivalent groups of patients for whom the observations should start at the beginning of PD. Such studies should report all the outcomes included in this review after sufficiently long follow-up to provide robust evidence.

## Conclusions

IPD may demonstrate comparable outcomes as SPD in incident dialysis patients. There seems to be no difference in patient survival, peritonitis, and technique survival between the two modalities. However, the impact of IPD on RRF is still questionable. Evidence is heterogeneous and conflicting to derive firm conclusions.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12882-024-03669-w>.

Supplementary Material 1

Supplementary Material 2

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Not applicable.

## Author contributions

SX conceived and designed the study. SX, WW, and JC collected the data, performed the literature search, and analyzed the data. SX was involved in the writing of the manuscript. All authors have read and approved the final manuscript.

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## Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request. Our paper is a systematic review, the Clinical Trial Number is not required.

## Declarations

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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## References

1. Lv JC, Zhang LX. Prevalence and disease burden of chronic kidney disease. *Adv Exp Med Biol*. 2019;1165:3–15. [https://doi.org/10.1007/978-981-13-8871-2\\_1](https://doi.org/10.1007/978-981-13-8871-2_1).
2. Eckardt K-U, Gillespie IA, Kronenberg F, Richards S, Stenvinkel P, Anker SD, et al. High cardiovascular event rates occur within the first weeks of starting hemodialysis. *Kidney Int*. 2015;88:1117–25. <https://doi.org/10.1038/ki.2015.117>.
3. Thomas B, Wulf S, Bikbov B, Perico N, Cortinovis M, Courville de Vaccaro K, et al. Maintenance Dialysis throughout the World in Years 1990 and 2010. *J Am Soc Nephrol*. 2015;26:2621–33. <https://doi.org/10.1681/ASN.2014101017>.
4. Zareba W. Initiation of dialysis: trigger or cause of cardiovascular events? *Kidney Int*. 2015;88:942–4. <https://doi.org/10.1038/ki.2015.271>.
5. Yaprak B, Arslan N, Alataş H. Multiple factors influencing mortality in hemodialysis patients. *Eur Rev Med Pharmacol Sci*. 2023;27:1095–103. [https://doi.org/10.26355/eurev\\_202302\\_31212](https://doi.org/10.26355/eurev_202302_31212).
6. Arslan N. Association of cardiometabolic risks with body composition in hemodialysis patients. *Eur Rev Med Pharmacol Sci*. 2023;27:2469–76. [https://doi.org/10.26355/eurev\\_202303\\_31780](https://doi.org/10.26355/eurev_202303_31780).
7. Marrón B, Remón C, Pérez-Fontán M, Quirós P, Ortiz A. Benefits of preserving residual renal function in peritoneal dialysis. *Kidney Int Suppl*. 2008;S42–51. <https://doi.org/10.1038/sj.ki.5002600>.
8. Yeates K, Zhu N, Vonesh E, Trpeski L, Blake P, Fenton S. Hemodialysis and peritoneal dialysis are associated with similar outcomes for end-stage renal disease treatment in Canada. *Nephrol Dial Transpl*. 2012;27:3568–75. <https://doi.org/10.1093/ndt/gfr674>.
9. Teitelbaum I, Finkelstein FO. Why are we not getting more patients onto peritoneal Dialysis? Observations from the United States with Global implications. *Kidney Int Rep*. 2023;8:1917–23. <https://doi.org/10.1016/j.ekir.2023.07.012>.
10. PG B. Incremental peritoneal dialysis. *Perit Dial Int*. 2020;40. <https://doi.org/10.1177/0896860819895362>.
11. Guest S, Leyboldt JK, Cassin M, Schreiber M. Kinetic modeling of incremental ambulatory peritoneal Dialysis exchanges. *Perit Dial Int*. 2017;37:205–11. <https://doi.org/10.3747/pdi.2016.00055>.
12. Reddy YNV, Mendu ML. The role of incremental peritoneal Dialysis in the era of the advancing American kidney Health Initiative. *Clin J Am Soc Nephrol*. 2020;15:1835–7. <https://doi.org/10.2215/CJN.03960320>.
13. Brown EA, Blake PG, Boudville N, Davies S, de Artega J, Dong J, et al. International Society for Peritoneal Dialysis practice recommendations: prescribing high-quality goal-directed peritoneal dialysis. *Perit Dial Int*. 2020;40:244–53. <https://doi.org/10.1177/0896860819895364>.
14. Huang LL, Mah JY, Howard J, Roberts MA, McMahon LP. Incremental peritoneal dialysis is a safe and feasible prescription in incident patients with preserved residual kidney function. *Nephrol (Carlton)*. 2022;27:74–81. <https://doi.org/10.1111/nep.13962>.
15. Lee SM, Min YS, Son YK, Kim SE, An WS. Comparison of clinical outcome between incremental peritoneal dialysis and conventional peritoneal dialysis: a propensity score matching study. *Ren Fail*. 2021;43:1222–8. <https://doi.org/10.1080/0886022X.2021.1960564>.
16. Liu R, Ye H, Peng Y, Yi C, Lin J, Wu H, et al. Incremental peritoneal dialysis and survival outcomes: a propensity-matched cohort study. *J Nephrol*. 2023;36:1907–19. <https://doi.org/10.1007/s40620-023-01735-4>.
17. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int J Surg*. 2021;88:105906. <https://doi.org/10.1016/j.ijsu.2021.105906>.
18. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M et al. Oct. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. [http://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). Accessed 30 2020.
19. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 6. Cochrane; 2019. <https://doi.org/10.1002/9781119536604>.
20. Hayat A, Cho Y, Hawley CM, Htay H, Krishnasamy R, Pascoe E, et al. Association of Incremental peritoneal dialysis with residual kidney function decline in patients on peritoneal dialysis: the balANZ trial. *Perit Dial Int*. 2023;43:374–82. <https://doi.org/10.1177/08968608231175826>.

21. Nalajayan M, Hunt A, McKeon K, Marlowe G, Schreiber MJ, Brunelli SM, et al. Use of incremental peritoneal dialysis: impact on clinical outcomes and quality of life measure. *J Nephrol.* 2023;36:1897–905. <https://doi.org/10.1007/s40620-023-01703-y>.
22. Indian J Nephrol. 2013;23:276–9. <https://doi.org/10.4103/0971-4065.114496>.
23. Sandrini M, Vizzardì V, Valerio F, Ravera S, Manili L, Zubani R, et al. Incremental peritoneal dialysis: a 10 year single-centre experience. *J Nephrol.* 2016;29:871–9. <https://doi.org/10.1007/s40620-016-0344-z>.
24. Yan H, Fang W, Lin A, Cao L, Ni Z, Qian J. Three Versus 4 daily exchanges and residual kidney function decline in Incident CAPD patients: a Randomized Controlled Trial. *Am J Kidney Dis.* 2017;69:506–13. <https://doi.org/10.1053/ajkd.2016.08.019>.
25. Lee Y, Chung SW, Park S, Ryu H, Lee H, Kim DK, et al. Incremental peritoneal Dialysis may be beneficial for preserving residual renal function compared to full-dose peritoneal Dialysis. *Sci Rep.* 2019;9:10105. <https://doi.org/10.1038/s41598-019-46654-2>.
26. Fernandes A, Matias P, Branco P. Incremental peritoneal dialysis: is it better for preservation of residual kidney function and clinical outcomes? *Clin Nephrol.* 2023;99:11–7. <https://doi.org/10.5414/CN110958>.
27. Qureshi MA, Hamidi S, Auguste BL. Five things to know about incremental peritoneal Dialysis. *Can J Kidney Heal Dis.* 2023;10:20543581231192748. <https://doi.org/10.1177/20543581231192748>.
28. Garofalo C, Borrelli S, De Stefano T, Provenzano M, Andreucci M, Cabiddu G, et al. Incremental dialysis in ESRD: systematic review and meta-analysis. *J Nephrol.* 2019;32:823–36. <https://doi.org/10.1007/s40620-018-00577-9>.
29. Cheetham MS, Cho Y, Krishnasamy R, Jain AK, Boudville N, Johnson DW, et al. Incremental Versus Standard (Full-Dose) peritoneal Dialysis. *Kidney Int Rep.* 2022;7:165–76. <https://doi.org/10.1016/j.ekir.2021.11.019>.
30. Yu X, Chen J, Ni Z, Chen N, Chen M, Dong J, et al. Number of daily peritoneal Dialysis exchanges and mortality risk in a Chinese Population. *Perit Dial Int.* 2018;38(Suppl 2):S53–63. <https://doi.org/10.3747/pdi.2017.00283>.
31. Diaz-Buxo JA, Youngblood BP, Torres AM. Delivered Dialysis Dose with PD Plus Therapy. *Am J Nephrol.* 1998;18:520–4. <https://doi.org/10.1159/000013398>.
32. Auguste BL, Bargman JM. Incremental peritoneal dialysis: new ideas about an old approach. *Semin Dial.* 2018;31:445–8. <https://doi.org/10.1111/sdi.12712>.
33. Bieber SD, Burkart J, Golper TA, Teitelbaum I, Mehrotra R. Comparative outcomes between continuous ambulatory and automated peritoneal dialysis: a narrative review. *Am J Kidney Dis.* 2014;63:1027–37. <https://doi.org/10.1053/ajkd.2013.11.025>.
34. de Fijter CW, Verbrugh HA, Oe LP, Peters ED, van der Meulen J, Donker AJ, et al. Peritoneal defense in continuous ambulatory versus continuous cyclic peritoneal dialysis. *Kidney Int.* 1992;42:947–50. <https://doi.org/10.1038/ki.1992.371>.
35. Chaudhary K. Peritoneal Dialysis Drop-out: causes and Prevention Strategies. *Int J Nephrol.* 2011;2011:434608. <https://doi.org/10.4061/2011/434608>.
36. Bargman JM, Thorpe KE, Churchill DN. Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. *J Am Soc Nephrol.* 2001;12:2158–62. <https://doi.org/10.1681/ASN.V12102158>.
37. Han SH, Lee SC, Ahn SV, Lee JE, Kim DK, Lee TH, et al. Reduced residual renal function is a risk of peritonitis in continuous ambulatory peritoneal dialysis patients. *Nephrol Dial Transpl.* 2007;22:2653–8. <https://doi.org/10.1093/ndt/gfm242>.
38. Liao C-T, Chen Y-M, Shiao C-C, Hu F-C, Huang J-W, Kao T-W, et al. Rate of decline of residual renal function is associated with all-cause mortality and technique failure in patients on long-term peritoneal dialysis. *Nephrol Dial Transpl.* 2009;24:2909–14. <https://doi.org/10.1093/ndt/gfp056>.
39. Wong J, Vilar E, Davenport A, Farrington K. Incremental haemodialysis. *Nephrol Dial Transpl.* 2015;30:1639–48. <https://doi.org/10.1093/ndt/gfv231>.
40. Zhang M, Wang M, Li H, Yu P, Yuan L, Hao C, et al. Association of initial twice-weekly hemodialysis treatment with preservation of residual kidney function in ESRD patients. *Am J Nephrol.* 2014;40:140–50. <https://doi.org/10.1159/000365819>.
41. Lin Y-F, Huang J-W, Wu M-S, Chu T-S, Lin S-L, Chen Y-M, et al. Comparison of residual renal function in patients undergoing twice-weekly versus three-times-weekly haemodialysis. *Nephrol (Carlton).* 2009;14:59–64. <https://doi.org/10.1111/j.1440-1797.2008.01016.x>.

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