

# Urgent-start peritoneal dialysis and patient outcomes: a systematic review and meta-analysis

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**Abstract.** – **OBJECTIVE:** The present study was aimed at illustrating short- or long-term patient outcome among individuals with urgent-start peritoneal dialysis (PD) compared with those with conventional PD.

**MATERIALS AND METHODS:** We searched the PubMed, EMBASE, Cochrane Controlled Trials Register and China National Knowledge Infrastructure databases. Cohort studies were investigated comparing the effects of urgent start of PD (<14 days after catheter insertion) to those of conventional start of PD (≥14 days after catheter insertion). Risks of bias across studies were evaluated using Newcastle-Ottawa Quality Assessment Scale. We calculated the pooled risk ratios and mean differences with 95% confidence intervals for dichotomous data and continuous data, respectively.

**RESULTS:** Six studies involving 1,242 patients were identified. Compared with conventional PD, urgent-start PD was not associated with a high mortality (RR: 1.25, 95% CI: 0.92 to 1.69;  $I^2=0\%$ ,  $p=0.99$ ) and a higher prevalence of overall mechanical complications (RR: 1.79, 95% CI: 0.85 to 3.78;  $p=0.12$ ;  $I^2=64\%$ ,  $p=0.02$ ). However, urgent-start PD was associated with a higher prevalence of leakage (RR: 6.72, 95% CI: 2.11 to 21.32;  $I^2=0\%$ ,  $p=0.60$ ). In terms of infectious complications, data analysis of the fixed-effects model showed no difference between the two groups. (RR: 1.36, 95% CI: 0.90 to 2.05,  $p=0.14$ ), regardless of peritonitis (RR: 1.36, 95% CI: 0.90 to 2.05,  $p=0.14$ ;  $I^2=0\%$ ,  $p=0.70$ ) or other infections (RR: 1.15, 95% CI: 0.49 to 2.69,  $p=0.99$ ;  $I^2=0\%$ ,  $p=0.75$ ).

**CONCLUSIONS:** Urgent-start PD was not associated with a higher risk of mortality and dialysis-related complications. However, compared with conventional PD, an urgent start of PD may increase the risk of a leak.

Key Words

Renal failure, Peritoneal dialysis, Outcome, Meta-analysis.

## List of Abbreviations

CI: confidence intervals; CNKI: China National Knowledge Infrastructure; ESRD: end-stage renal disease; MD: mean difference; RR: risk ratio; SMD: standardized mean difference

## Introduction

With the continuously rising global burden of end-stage renal disease, the need for renal replacement therapy has increased<sup>1</sup>. Commonly used treatment options include hemodialysis, peritoneal dialysis and kidney transplantation. Among the choices, peritoneal dialysis has been an attractive therapeutic option due to its relatively low cost. However, the use of peritoneal dialysis in some countries has increased but has fallen in other countries<sup>2</sup>. The main determination of peritoneal dialysis as a proportion of all dialysis use is policy maker guidance. Economic incentives, therapeutic simplicity, reduced requirements for technical support and electricity, and a reduced need for trained medical staff are the major advantages of peritoneal dialysis<sup>3,4</sup>. Additionally, for patients with a late referral, peritoneal dialysis is more beneficial. Patients with end-stage renal disease (ESRD) in countries with limited health service tend to be referred late and without pre-dialysis education, requiring unplanned dialysis or an ‘urgent start’. Usually, an international society of peritoneal dialysis recommends to wait for 2 weeks prior to catheter access where possible and dialysis therapy earlier than two weeks after catheter insertion is defined as an urgent start<sup>5,6</sup>. Compared with acute central venous catheter insertion for unplanned hemodialysis, urgent-start peritoneal dialysis is the preferred

modality for these patients because of the high infection-related mortality associated with acute central venous catheter insertion<sup>7,8</sup>. A previous study also revealed that urgent-start hemodialysis was an independent predictor of short-term (30-day) dialysis-related complications<sup>9</sup>. Until now, whether urgent-start peritoneal dialysis affects the short- or long-term patient outcome compared with conventional peritoneal dialysis remains inconclusive. Most researches have suggested that urgent-start PD is safe and practicable<sup>6,9-11</sup>, and an in-hospital education program in those patients may lower the incidence of complications even further<sup>12</sup>. The present study was aimed at illustrating the patient outcomes among individuals with urgent-start PD compared with those with traditional PD.

## Materials and Methods

### Methods

All analyses were based on previously published studies, thus no Ethical approval and patient consent are required.

### Search Strategy and Study Selection

We performed a search of the medical literature in the PubMed (up to November 2017), EMBASE (1980 to November 2017), Clinical Trials Registry (<http://clinicaltrials.gov/>) (date of search: 2, November 2017), and China National Knowledge Infrastructure (CNKI) databases (date of search: 2, November 2017). Studies on peritoneal dialysis were identified using the terms *peritoneal dialysis and observational study* (either as medical subject heading (MeSH) and free text terms). We also searched the reference lists of original reports, reviews, case reports, guidelines and meta-analyses of studies involving peritoneal dialysis (retrieved through the electronic searches) to identify studies that had not yet been included in the computerized databases. We set no language or publication date restrictions. The literature was evaluated by two authors (XJZ and CLM) independently with the following eligibility criteria: 1) cohort studies (retrospective or perspective); 2) adult patients with probable end-stage renal disease preferring or accepting peritoneal dialysis; 3) studies comparing the effects of urgent-start peritoneal dialysis (<14 days after catheter insertion) and conventional peritoneal dialysis (≥14 days after catheter insertion); and 4) studies providing data

on patient/renal outcomes or the prevalence of adverse events. All peritoneal dialysis protocols were considered. When more than one publication of one cohort study was found, we used the latest publication. We excluded studies with the following properties: 1) enrolled patients undergoing any type of hemodialysis intervention; 2) patients who had undergone any type of peritoneal dialysis previously; 3) patients with a history of any abdominal surgery; and 4) any other interventions conducted only in the exposure group or control group. We attempted to contact the original investigators to obtain further information if necessary. Any disagreement between review authors was resolved by consensus and was adjudicated with the support of a third review author (Bo).

### Outcome Assessment

The primary outcome assessed was mortality. The secondary outcomes included dialysis adequacy (Kt/V), laboratory test results (hemoglobin, iron saturation, parathyroid hormone, phosphorus, calcium, and albumin levels) and incidence of complications (including both mechanical and dialysis-related complications).

### Data Extraction

All data were extracted independently by two review authors (XJZ and CLM) in a predesigned form (Microsoft Office Excel 2016; Microsoft Corp, Redmond, Washington, USA). The data extraction were then checked by a third review author (Bo). The following data were extracted for each trial: first author and publication year; number of centers; geographical location of the study; study population; sample size; proportion of female patients; primary disease; interventions in the exposure and control groups; details of catheter insertion; dialysis protocol; duration of follow up; mortality; and outcome assessment during the study. The data were extracted as intention-to-treat analyses, where all dropouts were assumed to be treatment failures, whenever trial reporting allowed this.

### Assessment of the Risk of Bias

The assessment of the risk of bias was performed by two review authors (XJZ and CLM) independently using the Newcastle-Ottawa Quality Assessment Scale<sup>13</sup>, with disagreements resolved by discussion. Using the Newcastle-Ottawa Quality Assessment Scale, the studies scored a maximum of nine points on items in-

cluding the selection of subjects, comparability between groups, and ascertainment of the outcome of interest.

### **Statistical Analysis**

Heterogeneity among studies was assessed using the  $I^2$  statistic and  $\chi^2$ -test (assessing the  $p$ -value). If the  $p$ -value was less than 0.10 and  $I^2$  exceeded 50%, we considered heterogeneity to be substantial. Additionally, the origin of heterogeneity was analyzed. For clinical heterogeneity, sensitivity analyses and sub-group analyses were performed. Alternatively, we used the random-effects model. When heterogeneity was not substantial or obvious, clinical heterogeneity was eliminated and the fixed-effects model was used to combine the data. Dichotomous data were summarized as the risk ratio (RR). Continuous data were pooled as the mean difference (MD) if the outcome-measuring methods and units were identical among the studies; otherwise, the standardized mean difference (SMD), along with 95% confidence intervals (CIs), were used.  $p < 0.05$  was considered statistically significant.

Review Manager (RevMan) [Computer program], Version 5.3. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012), was used to generate Forest plots for outcomes with 95% CIs as well as funnel plots. The funnel plots were assessed for the evidence of asymmetry and possible publication bias or other small study effects.

### **Role of the Funding Source**

The National Nature Science Fund of China played no role in the study design, data collection and analysis, preparation or review of the manuscript or in the decision to submit the manuscript for publication.

## **Results**

Our initial search yielded 1,128 records, 117 of which appeared to be relevant to the systematic review and were retrieved for further assessment (Figure 1). Of these, 111 were excluded for various reasons, leaving six eligible articles involving 1,242 patients, among which four studies were in English and two were in Chinese<sup>11,14-18</sup>.

### **Study Characteristics and Risk of Bias**

Table I summarizes the characteristics of the included studies. Among the 1,242 subjects in-

cluded, 579 were male and 663 were female. The mean age was 53.95 years. All of the studies implied a retrospective study design. The follow-up duration ranged from 90 days to 10 years. The patients in the exposure group were defined to begin dialysis 14 days after catheter insertion. Detailed dialysis protocols were unavailable in most studies. Disease prior to ESRD was described in detail in only one study<sup>15</sup>. Patients with various primary diseases (chronic glomerular nephritis, hypertensive nephropathy, diabetic nephropathy, SLE and ADPKD) were included. No study reported a dialysis adequacy comparison, which was one of our interested outcomes.

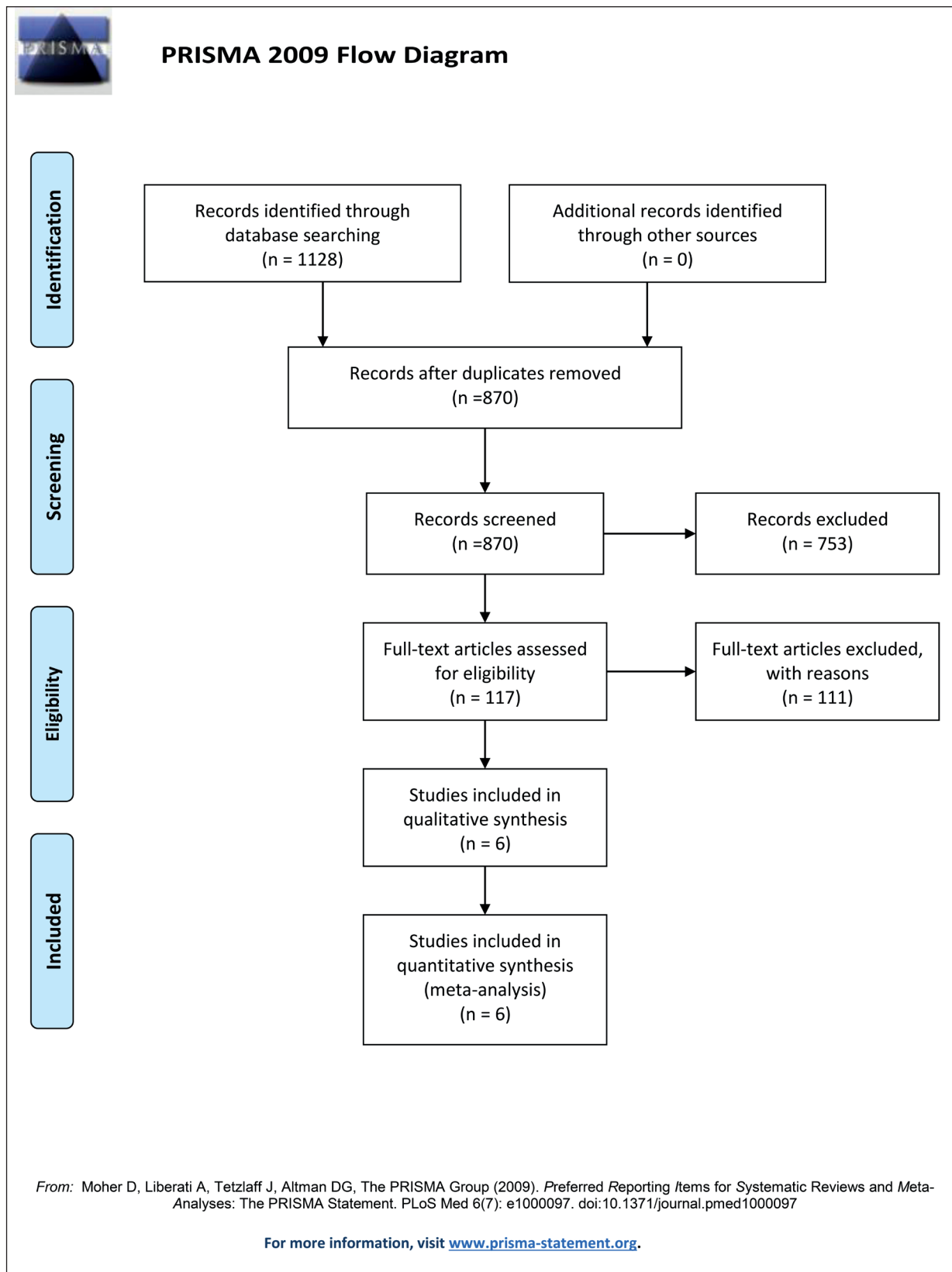
### **Risk of Bias**

The risk of bias ratings for each study was assessed using the Newcastle-Ottawa Quality Assessment Scale. In the domains of comparability and outcome, all of the included studies were awarded full stars. However, due to the report flaw, all of the studies failed to demonstrate that the outcome of interest (e.g., peritonitis) was not present at the start of the study. The risk of bias evaluation of each study was identical (seven stars) and represented a high quality of methodology and subsequent low risk of bias (Table II).

### **Effects of Exposure**

#### *Mortality*

Mortality was the primary outcome of this review, while only two retrospective cohort studies collecting data for six and ten years reported this<sup>15,16</sup>. An insufficient number of events were observed in other studies with a relatively short duration of follow up. Overall, no significant difference was found between the exposure and control groups (RR: 1.25; 95% CI: 0.92 to 1.69;  $I^2=0\%$ ,  $p = 0.99$ ) (Figure 2). These two studies were conducted in mainland China and Taiwan, respectively. The patient baseline data were not comparable in one study<sup>15</sup>. The authors of this report suggested that, compared with the control group, the patients in the urgent-start PD group were younger ( $52.6 \pm 17.3$  vs.  $56.1 \pm 15.3$  (y)) but had worse renal and liver function (eGFR:  $5.36 \pm 2.03$  vs.  $6.50 \pm 2.50$  (mL/min/1.73 m<sup>2</sup>)), (ALB:  $34.0 \pm 5.7$  vs.  $36.2 \pm 5.9$  (g/L)), (Prealbumin:  $289.8 \pm 88.1$  vs.  $312.6 \pm 74.0$  (mg/L)) and more severe anemia (Hb:  $76.9 \pm 18.8$  vs.  $80.8 \pm 17.9$  (g/L)). The difference in the patients' baseline data may be attributed to the selection bias of the non-randomized study. However, in a worse clinical background, the mortal-



**Figure 1.** Flow diagram of the literature search and study selection. From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097. For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).

**Table I.** Characteristics of the included studies.

Study	N	Mean age	Race	Mean follow-up time (month)	Intervention	Outcome
Pai 2016 (Pai et al., 2016)	149	55.6 ± 13.9	Chinese (Taiwan)	30.5 ± 24.9	Urgent starters vs Delayed starters	Peritonitis rates, peritoneal dialysis technique survival and patient survival
Povlsen 2016 (Povlsen & Ivarsen, 2006)	104	58.7±17.2	Not mentioned	3	Acute start vs planned start	Infectious and mechanical complications; technique survival
Liu 2013 (Liu et al., 2013)	657	53.6±16.8	Chinese	not mentioned	Urgent group vs planned group	Catheter dysfunctions, peritonitis, technique survival, patient survival
Ghaffari 2012 (Ghaffari, 2012)	27	47.9±15.9	not mentioned	3	Urgent-start PD vs non-urgent-start PD	Short-term (90-day) clinical outcomes and complications
Zhang 2017 (Zhang et al., 2017)	165	56.73±10.9	Chinese	3	Observation group vs control group	Catheter related complications and peritonitis
See 2017 (See et al., 2017b)	104	50.9±14.1	Caucasian, Asian, Aboriginal, other	not mentioned	Urgent-start vs conventional	Early complications; technique failure and time to the first episode of peritonitis.

ity of urgent-start PD was comparable to that of the control group, as Liu et al<sup>15</sup> suggested. In the other work, no significant difference was found in the patients' baseline condition between groups.

#### *Prevalence of complications*

##### *Mechanical complication*

Six studies involving 1,242 patients reported different types of mechanical complications (Figures 3 and 4). The mechanical complications studied included leaks, catheter blockage, migration and prevalence of catheter replacement. Obvious heterogeneity was found ( $I^2=64%$ ,  $p=0.02$ ). Analysis of the data in the random-effects model showed that the incidence of overall mechanical complications was comparable in the two groups (RR: 1.79; 95% CI: 0.85 to 3.78;  $p=0.12$ ) (Figure 3). However, in subgroup analyses according to the specific complication, we

found that urgent-start PD was associated with a higher incidence of leaks (RR: 6.72; 95% CI: 2.11 to 21.32;  $I^2=0%$ ,  $p=0.60$ ) (Figure 4A). No higher prevalence of catheter blockage and migration was found in the urgent-start PD group (RR: 2.80; 95% CI: 0.49 to 15.98;  $I^2=0%$ ,  $p=0.38$ ) (Figure 4B) and (RR: 1.28; 95% CI: 0.17 to 9.87;  $I^2=53%$ ,  $p=0.14$ ) (Figure 4C), respectively. No significant difference in the prevalence of catheter replacement with surgery was found (RR: 2.36; 95% CI: 0.19 to 29.01;  $I^2=83%$ ,  $p=0.01$ ) (Figure 4D). We also performed sensitivity analysis using random effects model when pooling the leaks data: (RR: 8.38; 95% CI: 2.30 to 30.54;  $I^2=0%$ ,  $p=0.73$ ).

##### *Dialysis-related complications*

Infectious complications are major dialysis-related complications. Infectious complications included peritonitis and exit-site infection.

**Table II.** Risk of bias

Study	Selection	Comparability	Outcome
Pai 2016 (Pai et al., 2016)	*	*	*
Povlsen 2006 (Povlsen & Ivarsen, 2006)	*	*	*
Liu 2013 (Liu et al., 2013)	*	*	*
Ghaffari 2012 (Ghaffari, 2012)	*	*	*
Zhang 2017 (Zhang et al., 2017)	*	*	*
See 2017 (See et al., 2017b)	*	*	*

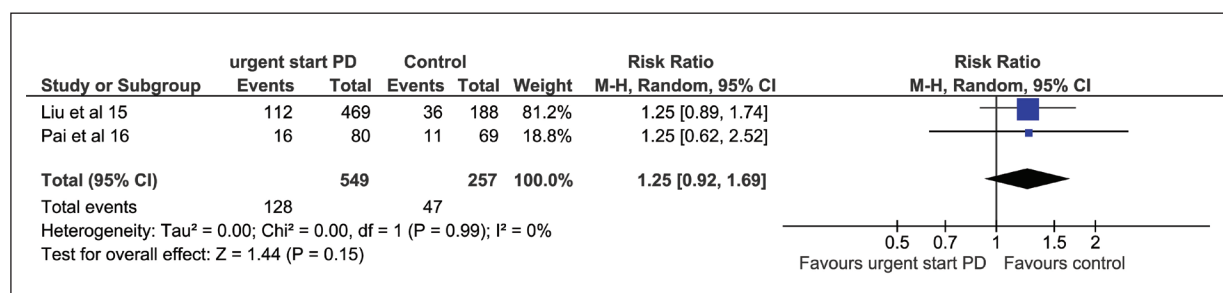


Figure 2. Mortality level among participants with urgent-start PD vs. the control.

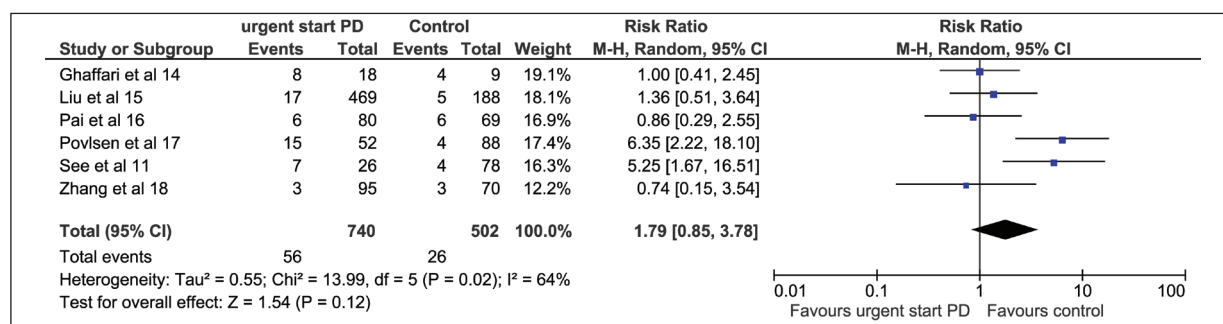


Figure 3. Overall mechanical complications among participants with urgent-start PD versus the control.

Five studies involving 585 patients reported infectious complications. No obvious heterogeneity was found ( $I^2=0\%$ ,  $p=0.75$ ). Analysis of data in the fixed-effects model showed no difference in the infectious complications between the two groups (RR: 1.36, 95% CI: 0.90 to 2.05,  $p=0.14$ ) (Figure 5). Among the four studies, four reported the occurrence of peritonitis and three reported other infections. No difference in these two subgroups was found (RR: 1.36, 95% CI: 0.90 to 2.05,  $p=0.14$ ;  $I^2=0\%$ ,  $p=0.70$ ) (peritonitis, Figure 6A) and (RR=1.15, 95% CI: 0.49 to 2.69,  $p=0.99$ ;  $I^2=0\%$ ,  $p=0.75$ ) (other infections, Figure 6B).

Publication bias

No evidence of publication bias for the primary outcome was indicated by visual inspection of the funnel plots (not shown).

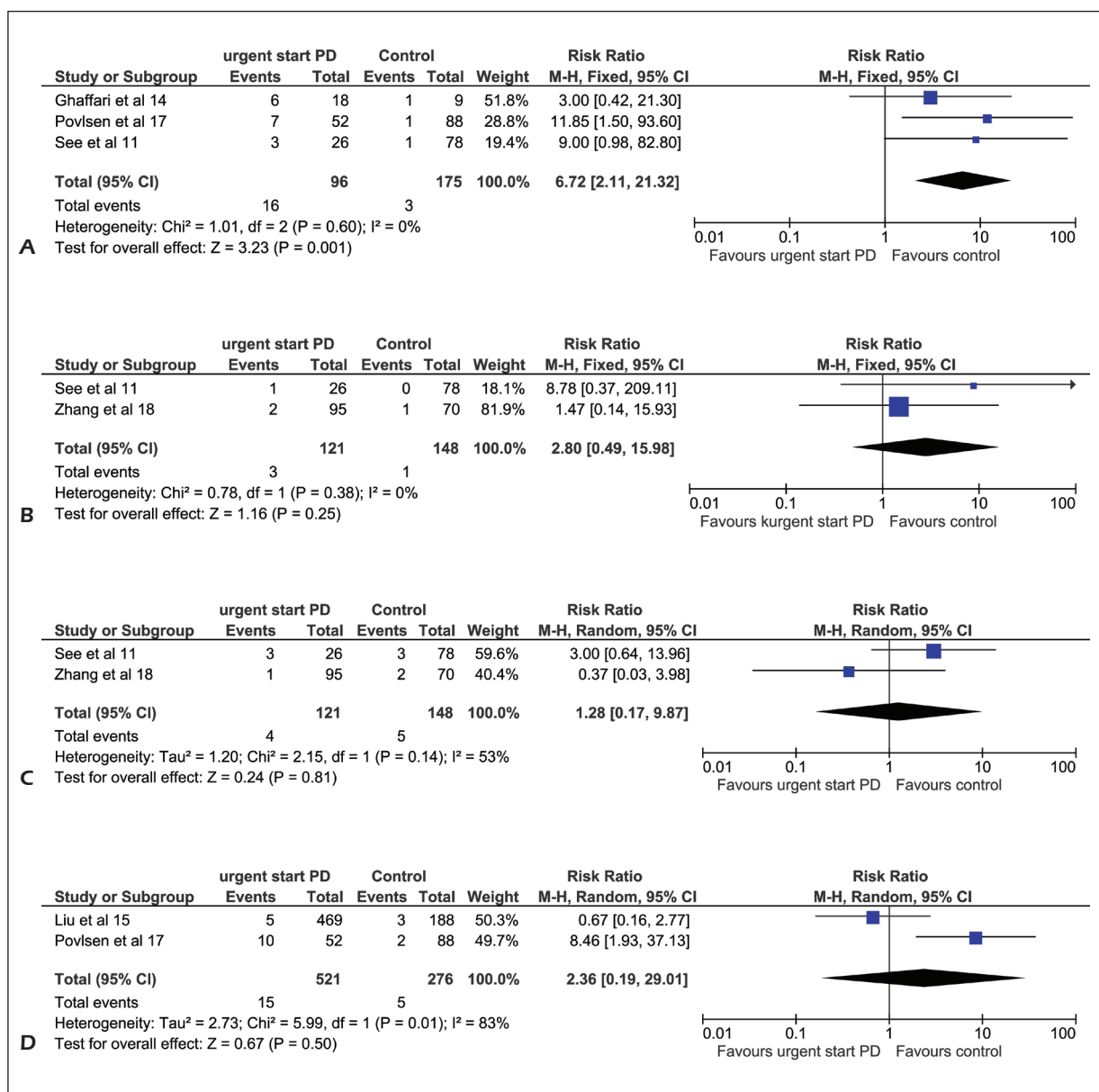
Discussion

This systematic review and meta-analysis provide evidence for the efficiency and safety of urgent-start PD. We included six cohort studies involving 1,242 subjects. All of the included studies were retrospective. The non-random study design

prevented us from drawing causal conclusions. The available data suggested that urgent-start PD was not associated with a higher risk of mortality and dialysis-related complications. However, compared with conventional PD, urgent start PD may increase the risk of leaks. No higher risk of other mechanical complications, including blockage and catheter migration, was found. Although dialysis adequacy was our outcome of interest, an insufficient number of studies were focused on this result. Due to the limited data, we do not know whether urgent-start PD affects dialysis adequacy.

In most cases, hemodialysis is the preferred choice for patients in urgent need of dialysis. However, with the anti-indication of hemodialysis or limited medical resources, urgent-start PD is a competitive choice. Compared with conventional PD, researchers are concerned about the potential higher incidence of complications and, consequently, higher mortality. Some studies have focused on this topic, but many of them are retrospective. In addition, non-randomized patient selection may introduce selection bias to the studies.

To our knowledge, this is the first systematic review or meta-analysis evaluating the efficiency and safety of urgent-start PD. We provide a



**Figure 4.** **A**, Leaks among participants with urgent-start PD vs. the control. **B**, Blockage among participants with urgent-start PD vs. the control. **C**, Migration among participants with urgent-start PD vs. the control. **D**, Prevalence of catheter replacement with surgery among participants with urgent-start PD vs. the control.

comprehensive overview examining the effectiveness outcomes and safety outcomes for urgent-start PD and have conducted a meta-analysis where methodologically appropriate. We revealed that urgent-start PD is not associated with higher mortality and higher risk of complications except for leaks. The results suggested that urgent-start PD may serve as a treatment option in certain cases.

Our research has several limitations. First, due to the non-random study design, selection bias

may affect the results of the present meta-analysis. However, we assumed that this may not exaggerate the efficacy and safety of urgent-start PD because, compared with conventional PD, more severe patients were usually allocated to urgent-start PD, which is typically under evaluated compared to urgent start PD. Second, the duration of follow-up was relatively short and various among the included studies. Two studies did not report the duration of follow-up, which indicated the flaw of the included studies. The mortal-

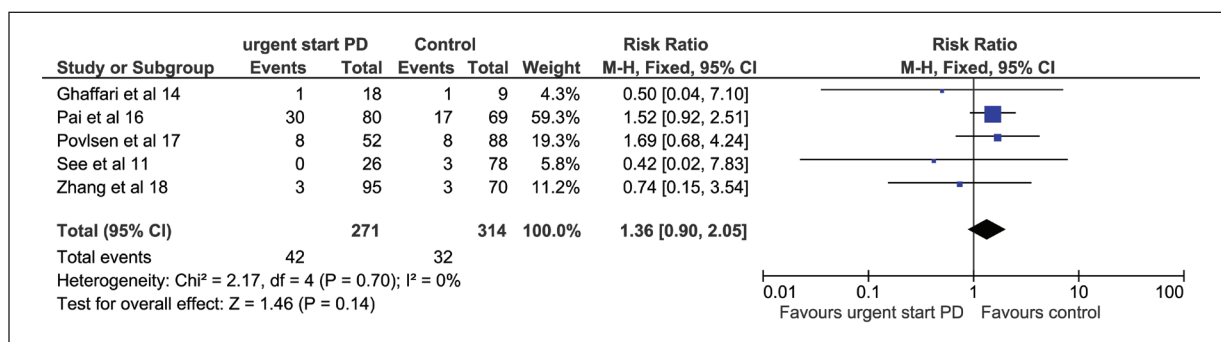


Figure 5. Incidence of infectious complications among participants with urgent-start PD vs. the control.

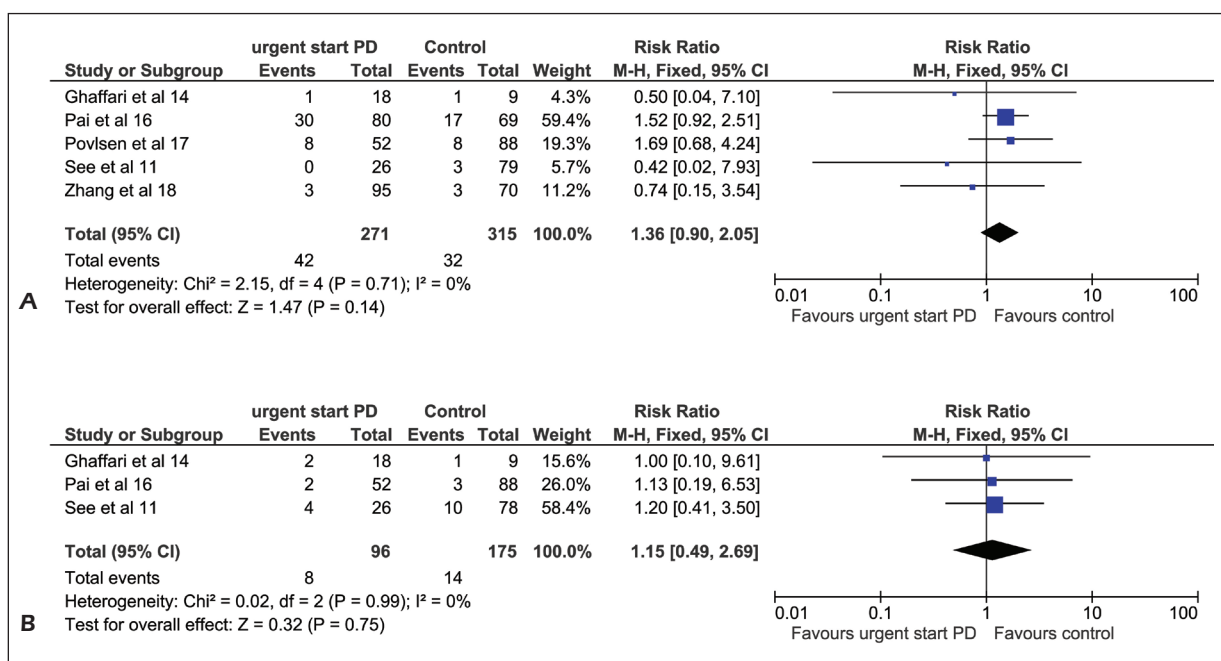


Figure 6. **A**, Occurrence of peritonitis among participants with urgent-start PD vs. the control. **B**, Occurrence of other infectious complications among participants with urgent-start PD vs. the control.

ity was reported in only two studies, limiting the confidence in drawing a conclusion. Third, it was impossible to evaluate the dialysis adequacy because no other study has reported these findings. In addition, no study has focused on dialysis protocol optimization in urgent-start PD patients. The lack of detailed evidence limits the application of the results of this article.

### Conclusions

Urgent-start PD was not associated with higher risk of mortality and dialysis-related complications. But only two studies with limited sample size re-

ported mortality as results, the conclusion should be treated cautiously. Compared with conventional PD, urgent start PD may increase the risk of leaks. No higher risk of other mechanical complications, including blockage and catheter migration, was found. The findings of this review also suggest that further research evaluating the dialysis adequacy and detailed dialysis protocol of urgent-start PD should be undertaken. Additionally, long-term adverse events and mortality should also be investigated.

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### Conflict of Interests

None disclosed. The results presented in this paper have not been published previously in whole or part.

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