BMJ Open

Clinical outcomes of automated versus continuous ambulatory peritoneal dialysis for end-stage kidney disease: protocol of a systematic review and meta-analysis

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To cite: Shi X, Du H, Zhang Z, *et al*. Clinical outcomes of automated versus continuous ambulatory peritoneal dialysis for end-stage kidney disease: protocol of a systematic review and meta-analysis. *BMJ Open* 2022;**12**:e065795. doi:10.1136/bmjopen-2022-065795

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065795).

Received 17 June 2022
Accepted 11 October 2022

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ABSTRACT

Introduction An increasing number of studies comparing automated peritoneal dialysis (APD) with continuous ambulatory peritoneal dialysis (CAPD) in clinical outcomes have been published since the publication of a systematic review and meta-analysis including three randomised controlled trials in 2007. We will conduct a systematic review and meta-analysis to explore more clinical outcomes of APD versus CAPD for end-stage kidney disease.

Methods and analysis The protocol is conducted following the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines. Three databases—PubMed, EMBASE and the Cochrane Library—will be searched comprehensively from inception to 16 June 2022, without language restriction. Studies reporting clinical outcomes comparing APD with CAPD will be included. Two independent reviewers will screen the titles and abstracts and then obtain and assess full texts of potential relevant articles for eligibility following the inclusion and exclusion criteria. The methodological quality of included observational studies will be assessed by using the Newcastle–Ottawa Scale. The risk of bias of included randomised controlled studies will be assessed by using the Cochrane Risk of Bias tool. Relative risk for dichotomous outcomes and standard mean difference for continuous outcomes with corresponding 95% *CIs* will be pooled for summary effects. Cochrane Q test and I^2 values will be used to assess heterogeneity between studies. To assess and explore the source of heterogeneity, subgroup analyses and sensitivity analyses will be conducted, and meta-regression, funnel plot and Egger's test will be performed if there are no less than 10 studies. Analyses will be performed using STATA software, V.13.0 (STATA Corporation, College Station, Texas, USA).

Ethics and dissemination Ethics approval is not applicable as no personal information is collected from patients. The results will be published in a peer-reviewed journal or disseminated in relevant academic conferences.

PROSPERO registration number CRD42022311401.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A strength of this study is that both randomised controlled trials and observational studies will be included.
⇒ Another strength of the study is that the study design is rigorous.
⇒ The main limitation is that non-English electronic databases will not be searched, which may cause a language bias.

INTRODUCTION

Peritoneal dialysis (PD) is one of the kidney replacement therapies for patients with end-stage kidney disease (ESKD), including continuous ambulatory PD (CAPD) by manual exchanges or automated PD (APD) by using a cycler.[1–3] APD consists of many modalities, such as continuous cycling PD (CCPD), intermittent PD (IPD), nightly intermittent PD (NIPD), tidal PD (TPD) and continuous flow PD.

Historically, CAPD was considered to be more appropriate for low transporters, while APD was mainly introduced to high transporters due to the fast solute clearance. Several studies have reported the relative advantages of APD over CAPD in lower incidence of peritonitis, mortality and technique failure.[4–9]

During the past few decades, there was an increasing utilisation of APD for all transport characteristics due to patients' preference for lifestyle benefits.[10] However, the clinical superiority of APD is still controversial. The main disadvantage of APD that has been reported is the decline of residual kidney function.[11 12]

In 2007, a systematic review and meta-analysis was published for assessing comparative clinical effectiveness of APD versus CAPD for ESKD.[13] This review reported several clinical outcomes that APD appears to be more beneficial than CAPD, such as reducing the rate of peritonitis and increasing the quality of life with respect to social issues.

Nevertheless, only three randomised controlled trials (RCTs) were included, making it difficult to detect the difference of some clinical outcomes due to small size and short follow-up periods. Moreover, as 15 years have passed, more and more studies related to this topic have been reported.[4–9] Overall, there is a lack of sufficient evidence on some beneficial clinical outcomes of APD versus CAPD for patients with ESKD.

The patient population with ESKD was one of the most affected groups by the COVID-19 pandemic.[14] The International Society of Peritoneal Dialysis (ISPD) provided practical guidelines that encourage clinicians to choose PD as the maintenance dialysis modality during this pandemic.[15] ISPD standards and committee have adapted the recommendations from Peking University First Hospital for PD, in which APD with remote patient management (RPM) should be strongly recommended as the major way to manage patients on PD.[16] Given the increasing trend towards greater utilisation of APD, potential clinical benefits, patients' preference for lifestyle benefits and the favourable modality recommendation for COVID-19, exploring the clinical outcomes of APD compared with CAPD is essential.

We will conduct a systematic review and meta-analysis of studies to evaluate important clinical outcomes of APD versus CAPD for ESKD.

METHODS AND ANALYSIS

This study has been registered in the PROSPERO international prospective register of systematic reviews (CRD42022311401). This protocol is conducted following the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines.[17 18]

Search strategy

Three databases—PubMed, EMBASE and the Cochrane Library—will be searched comprehensively from inception to 16 June 2022, without language restriction. The combinations of Medical Subject Heading terms and text words will be used for literature search: "APD", "NIPD", "CCPD", "TPD", "IPD", "PD-plus", "aAPD" and all possible spellings of "ambulatory peritoneal dialysis" and "continuous ambulatory peritoneal dialysis". Full search strategy of each database is described in online supplemental file 1. Reference lists of included studies and relevant articles will be screened and experts will be consulted in the field to clarify further relevant studies. The literature search will be performed independently by two independent investigators. EndNote V.X7 (Thomson Reuters, New York, New York, USA) software will be used for literature selection. Differences will be evaluated and resolved by a third reviewer.

Eligibility criteria

We will include studies meeting the criteria as follows: (1) RCTs, quasi-RCTs and observational studies (cohort studies, case–control studies and cross-sectional studies) that comprise adult patients; (2) reported clinical outcomes comparing APD with CAPD; and (3) effect estimates of relative risk (RR) and standard mean difference (SMD) with 95% CIs that were provided or can be calculated. We will exclude the following studies: (1) other types of studies, including case reports and review articles; (2) studies conducted among paediatric recipients or animals; (3) studies on irrelevant topics or studies lacking sufficient data even after request from the authors. For studies that covered overlapping data, we will include the most comprehensive one reporting the largest sample size.

Study records

Selection process

Two reviewers will screen the titles and abstracts independently for eligibility, then will obtain and assess full texts of potential relevant articles independently following the inclusion and exclusion criteria. Discrepancies will be resolved by team discussion.

Data items

Data will be extracted by two investigators independently into a predefined standardised form. General characteristics include: (1) first author; (2) publication year; (3) sample size; (4) proportion of male; (5) age; (6) ethnicity; (7) diabetic status and (8) peritoneal solute transporter status. The primary clinical outcome measures will include: (1) frequency of PD-related infections (peritonitis, exit site and tunnel infections) and (2) mortality. The secondary primary outcome measures are: (1) hospitalisation (number of patients hospitalised, number of hospitalisation episodes and number of days of hospitalisation); (2) catheter removal; (3) quality of life; (4) technique failure; (5) switching from the original PD modality to a different dialysis modality including an alternative form of PD; (6) dialysis adequacy measures such as Kt/V and creatinine clearance (weekly); (7) residual kidney function and (8) blood pressure (systolic, diastolic and mean arterial pressure).

We will contact libraries abroad or corresponding author of relevant articles by email or buy full copies through legal means when detailed data for pooling analysis were unavailable. Any discrepancies will be resolved by consultation with a third investigator.

Quality appraisal of included reviews

The methodological quality of included observational studies will be assessed by using the Newcastle–Ottawa Scale. A score of at least 7 points is defined as high-quality study (online supplemental file 2).[19] The risk of bias of included RCTs will be assessed by using the Cochrane Risk of Bias tool without masking the study name.[20] Two reviewers will respectively evaluate each trial with 'low', 'unclear' or 'high' risk of bias. A trial will be considered as at high risk if one or more domains are evaluated to be high risk. A trial will be regarded as at low risk of bias if all domains are judged to be low risk. Otherwise, it will be

considered as at unclear risk of bias.[21] Disagreements in the scores will be resolved by team discussion.

Data analysis

RR for dichotomous outcomes and SMD for continuous outcomes with corresponding 95% *CIs* will be provided or calculated from each study. When data on the number of episodes are available, the rate ratio will be calculated as the ratio of the rate of the outcome (eg, the peritonitis rate) in the experimental treatment group (calculated by number of episodes of the outcome over unit time on PD) over the rate in the control group. Cochrane Q test and I^2 values will be used to assess heterogeneity between studies. I^2 <50% is defined as low heterogeneity, and I^2 ≥50% is defined as high heterogeneity.[22 23] The effect estimates will be calculated using a random-effects model when high heterogeneity was found (p<0.10 or I^2 ≥50%); otherwise, a fixed-effects model will be used.[24 25] The pooled effect estimates for RCTs and observational studies will be done separately in different groups. Subgroup analyses will include age, sample size, diabetic status, peritoneal solute transporter status and ethnicity. The pooled effect estimates for multi-adjusted and unadjusted risk will also be done separately in different subgroups to check the stability of the results. Sensitivity analyses will be conducted by omitting one study at one time and then pooling the data to assess the change of effect estimates. To explore the source of heterogeneity, a meta-regression will be performed if there are at least 10 studies. For clinical outcomes of at least 10 studies included, publication bias will be evaluated by funnel plot and Egger's test.[26] Egger's test with two-tailed significance level of 0.10 is considered to be statistically significant. Analyses will be performed using STATA software, V.13.0 (STATA Corporation, College Station, Texas, USA). If there are sufficient data available, the Grading of Recommendations, Assessment, Development and Evaluations approach will be used to evaluate the strength of the evidence. If there are not enough data for quantitative synthesis, we will present the main findings as a systematic review.

Patient and public involvement

Patients and the public will not be involved.

DISCUSSION

To our knowledge, this is the first protocol of systematic review and meta-analysis to evaluate the clinical outcomes of APD versus CAPD for patients with ESKD, providing a detailed analysis of the available evidence.

A published systematic review and meta-analysis in 2007 reported that APD was associated with significant lower peritonitis and hospitalisation rate compared with CAPD.[13] However, no significant differences were made in terms of other important clinical advantages, such as risk of mortality, modality switching from original PD modality to a different dialysis modality, PD catheter removal and hospital admissions. Besides, the study only included three RCTs and the clinically important outcomes may have been missed due to their small size and short follow-up periods.

There are an increasing number of trials published comparing the advantages and disadvantages of APD over CAPD. Many studies reported that APD has several advantages over CAPD such as mortality, quality of life, technique survival and peritonitis.[4–9 27 28]

During the past few decades, APD has been popular globally, especially in developed countries.[10] Technological advances, such as remote access modules in the APD field, made it easier to manage patients' dialysis prescriptions for physicians and provided increased patient treatment compliance.[29–31] Consequently, APD with RPM is increasingly valued by nephrologists and strongly recommended as a major way to manage patients on PD during the COVID-19 pandemic to increase the proportion of APD.[15 16] Accordingly, it is necessary and important to perform a comprehensive quantitative analysis to further explore the clinical outcomes of APD versus CAPD for patients with ESKD.

The strengths of this systematic review and meta-analysis are rigorous study design and comprehensive assessment regarding the important clinical outcomes of APD versus CAPD in patients with ESKD. However, the absence of more RCTs will be the main limitation of this study.

The findings of this study will be of interest to nephrologists, kidney disease-related official policymakers, as well as patients with ESKD, providing evidence as a basis for the promotion of relevant treatment choice or modality to improve the outcomes, especially quality of life of patients with ESKD.

Contributors XS, HD and ZZ conceived the study. All authors participated in designing the study. XS drafted the protocol. HD, ZZ and YZ critically revised the manuscript. All authors reviewed and approved the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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