REVIEW ARTICLE

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Clinical effect of different dialyzers used in patients with kidney disease: a meta-analysis of randomized clinical trials

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INTRODUCTION

As an effective treatment for end-stage renal disease, hemodialysis has been used in clinic for more than 80 years and it is an effective measure for treating acute and chronic renal failure[1]. The incidence and prevalence of chronic kidney disease and kidney failure are increasing worldwide. In the United States, the number of people receiving dialysis has risen by about 20,000 cases per year[2]. Dialyzer is a necessary instrument for each hemodialysis. Blood (inside the membrane) convects with dialysis fluid (outside the membrane) in the dialyzer to remove toxic substances such as creatinine and urea from the patient's body through a concentration gradient or pressure gradient. At present, there are various kinds of dialyzer membrane materials commonly used in clinical practice, including polyether sulfone (PES), polysulfone, cellulose acetate, polymethyl methacrylate, and polyacrylonitrile membranes[3]. It is generally believed that the dialysis membranes affect the quality of dialysis in patients undergoing maintenance hemodialysis, but recent evidence-based studies have failed to provide strong evidence[4,5]. This meta-analysis was undertaken to evaluate the efficacy and safety between PES dialyzers and dialyzers with a different membrane material by collecting clinical data from randomized clinical trials (RCTs).

METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[6] statement for conducting a high-quality meta-analysis.

Data sources and searches

The Cochrane Library, EMBASE, PubMed, and ClinicalTrials.gov databases were searched for RCTs. The search period was set from January 1990 to February 2021. The following keywords were used in search strategies and a sensitive filter for RCTs was also used: "hemodialysis," "hollow fiber dialyzer," "polyether sulfone," "kidney disease," and "dialysis." In addition, the references listed in the selected trials were also reviewed for additional trials and information.

Study selection

Studies from the literature independently searched were screened by two investigators (CCM and YML); a third investigator will be consulted when encountering disagreements. We included studies that met the following inclusion criteria: (1) RCTs conducted in humans; (2) patients with kidney disease underwent randomly one study week of three consecutive hemodialysis treatments; (3) full-text articles of controlled trials examining PES hollow fiber dialyzer versus other member dialyzers, including polysulfone dialyzer, cellulose acetate dialyzer, and polymethyl methacrylate dialyzer; and (4) the change of blood urea nitrogen, creatinine, β2-microglobulin, hemoglobin, albumin, phosphoric acid, or myoglobin was examined. If there were duplicate studies or reports of similar results from the same trial, the literature with the most comprehensive data will be included. Reviews, meta-analyses, editorials, observational studies, and studies without results or a control group will be excluded.

Data extraction and quality assessment

A standardized data extraction form was used to extract clinical data independently by two different authors, and a third investigator was consulted to resolve conflicting opinions. The following information was extracted from the included studies: authors' names, year of publication, baseline characteristics of the participants, total number of individuals per arm, mean age, primary disease or condition, and the device used per arm. The change in value before and after hemodialysis of the following endpoints was extracted: urea nitrogen, creatinine, β2-microglobulin, hemoglobin, albumin, phosphoric acid, and myoglobin. In addition, information regarding blinding, random sequence generation, allocation concealment, indications

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for incomplete outcome data, indications for selective reporting, and other biases were also collected to evaluate the quality of the included investigations.

Statistical analysis

Data analysis was based on the intention-to-treat principle. Dichotomous outcomes were reported by risk ratio and 95% confidence interval (CI). Differences in continuous outcomes were reported by standard mean differences (SMDs) including the 95%CI. Heterogeneity was assessed through the Cochran's Q test and I^2 statistic; a Cochran's $p<0.10$ and an $I^2>50$ were considered significant heterogeneity. Pooled analyses were conducted using a fixed effect model, whereas a random effect model was used if there was significant heterogeneity.

RESULTS

Search results

A total of 527 potentially relevant publications were identified according to the search strategy. Among which, 72 publications were reviewed through full-text reading and 6 studies that met the selection criteria were finally included, as shown in Supplementary Figure S1[7-12]. The baseline characteristics of the included studies were shown in Supplementary Table S1. We included 232 participants in our meta-analysis, including 116 treated with PES dialyzer and 116 with other dialyzers. The quality assessment of the included studies was detailed in Supplementary Table S2 and Supplementary Figures S2 and S3.

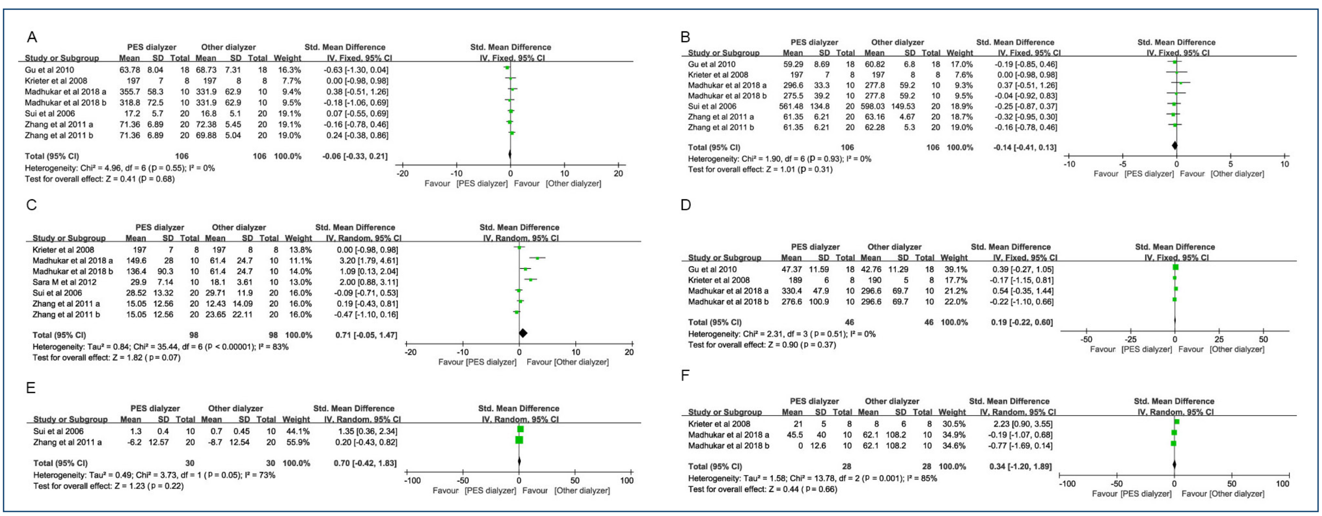

Figure 1. (A) Forest plot of urea nitrogen clearance. (B) Forest plot of creatinine clearance. (C) Forest plot of β2-microglobulin clearance. (D) Forest plot of phosphoric acid clearance. (E) Forest plot of hemoglobin removal rate. (F) Forest plot of myoglobin removal rate.

Table 1. Different dialyzers with various manufacturers based on the included membrane materials.

Member material	Manufacturer	Dialyzer	Country
Polyether sulfone	Nipro	PES series, ELISIO series	Japan
	Peony	PES series	China
	OCI	HD series	China
Polysulfone	Fresenius	HF series, F series, FX series, Hemoflow series, Optiflux series, Revaclear, and Revaclear Max	USA/Japan
	Toray industries	TS series	Japan
Cellulose acetate	NISSHO Corporation	FB series	Japan
	KAWASUMI	CTA series	Japan
	Nipro	SUREFLUX series, FB series	Japan
Polymethyl methacrylate	Toray industries	B series	Japan

Clinical results

The efficacy endpoints included the clearance of urea nitrogen, creatinine, β2-microglobulin, and phosphoric acid, while the safety endpoint was the change of hemoglobin and myoglobin.

Clearance of urea nitrogen

Five RCTs involving 212 patients reported the clearance of urea nitrogen, with 106 patients randomized to PES dialyzer group and 106 randomized to other dialyzer groups. No differences existed in the clearance of urea nitrogen (SMD -0.06; 95%CI -0.33 to 0.21; p=0.68; I^2=0%; Figure 1A).

Clearance of creatinine

Five RCTs involving 212 patients reported the clearance of creatinine, with 106 in each of the PES dialyzer and other dialyzer groups. No differences existed in the clearance of creatinine (SMD, -0.14; 95%CI -0.41 to 0.13; p=0.31; I^2=0%; Figure 1B).

Clearance of β2-microglobulin

Five RCTs involving 196 patients reported the clearance of β2-microglobulin, with 98 patients in PES dialyzer group and 98 in other dialyzer groups. No differences existed in the clearance of β2-microglobulin (SMD 0.71; 95%CI -0.05 to 1.47; p=0.07; I^2=83%; Figure 1C).

Clearance of phosphoric acid

Three RCTs involving 98 patients reported the clearance of phosphoric acid, with 46 patients in PES dialyzer group and other dialyzer groups. No differences existed in the clearance of phosphoric acid (SMD 0.19; 95%CI -0.22 to 0.60; p=0.37; I^2=0%; Figure 1D).

Change of hemoglobin

Two RCTs involving 60 patients (30 in PES dialyzer group and 30 in other dialyzer groups) reported the change of hemoglobin. No differences existed in the change of hemoglobin (SMD 0.34; 95%CI -1.20 to 1.89; p=0.66; I^2=85%; Figure 1E).

Change of myoglobin

Two RCTs involving 56 patients reported the change of myoglobin, with 28 patients in each group. No differences existed in the change of myoglobin (SMD 0.34; 95%CI -1.20 to 1.89; p=0.66; I^2=85%; Figure 1F).

Sensitivity and publication bias analysis

The meta-analysis results of the clearance of urea nitrogen were as follows: SMD -0.06; 95%CI -0.33 to 0.21; p=0.68; I^2=0%. For sensitivity analysis, the results were consistent after excluding each individual study, which demonstrated that the heterogeneity among the studies did not affect the combined results as shown in Supplementary Figure S4. The results of Egger's test showed no significant evidence of publication bias, as shown in Supplementary Figure S5.

DISCUSSION

This meta-analysis included 232 patients with kidney disease, who were randomized to PES dialyzer or other dialyzer groups during maintenance hemodialysis in six RCTs. Based on this meta-analysis, the small solute clearance (urea, creatinine, and phosphate) in PES dialyzer was comparable and not significantly different from other dialyzers. In addition, the clearances and removal rates of low-molecular-weight proteins (β2-microglobulin and myoglobin) were not significantly different.

The basic principle of dialysis treatment is that blood and dialysate exchange solutes through the dialysis membrane. Electrolytes and excess water in the blood enter the dialysate to be removed, and some bicarbonate and electrolytes in the dialysate enter the blood to remove toxins and water, maintaining acid-base balance and internal environmental stability. At present, several kinds of dialyzer membrane materials are commonly used in clinical practice, including PES, polysulfone, cellulose acetate, polymethyl methacrylate, and polyacrylonitrile membranes. Dialyzers were developed by various manufacturers based on the above membrane materials, as shown in Table 1. Studies have shown that PES has good heat resistance, corrosion resistance, and hydrophilicity. Furthermore, clinical trials have reported the efficacy and safety of using PES dialyzer in clinical practice[13-15]. However, there was no comprehensive analysis about PES dialyzer, compared with other dialyzers. As the first meta-analysis included RCTs to compare PES dialyzer with other dialyzers, quality assessment, sensitivity analysis, and publication bias analysis were addressed to obtain high-quality evidence. No clinically meaningful difference was found among the PES dialyzer and other dialyzers when small solute clearance and low-molecular-weight protein parameters were studied. These results had less difference from the previous published literature in that the clearance of β2-microglobulin was higher in PES dialyzer group than in other dialyzer groups[9,10]. Based on the sensitivity analysis, the results of this meta-analysis were stable, which was consistent in each heterogeneity analysis. No significant publication bias was revealed in the meta-analysis.

This meta-analysis included all the available RCTs that met the inclusion criteria. In addition, the quality of included clinical trials was all middle-to-excellent, and the results of our meta-analysis were reliable based on the sensitivity and publication bias analyses.

However, the study also had several limitations. First, the included clinical trials had a relatively small sample size, which caused to a restricted power with the results. Second, different PES dialyzers used in each clinical trial, including PES series (Nipro), ELISIO series (Nipro), and HD series (OCI), may cause the heterogeneity of the results. However, no strong heterogeneity was found among the trials. Third, the different calculation method for clearance used in different clinical trials and various substances used, especially the drugs, may have an influence on the results. Furthermore, polyacrylonitrile-derived filter was not included in this meta-analysis. Further RCTs with large sample sizes are needed to explore the efficacy and safety profile of PES dialyzer in clinical practice. In addition, detailed subgroup analysis can be conducted when enough clinical trials are published in the future.

CONCLUSION

No differences were demonstrated between PES dialyzer and other dialyzer groups with respect to the clearance of urea, creatinine, phosphate, and β2-microglobulin. In addition, the removal rates of microglobulin and myoglobin were not significantly different between PES dialyzer and other dialyzer groups.

AUTHORS' CONTRIBUTIONS

CM: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **YL:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing.

AVAILABILITY OF DATA AND MATERIAL

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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