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Original article

The influence of mortality rate from membrane flux for end-stage renal disease: A meta-analysis

Feng Zhao [a], Zhipeng Wang [b], Lin Liu [c,d], Sheng Wang [e,*]

[a] Department of blood transfusion medicine and nephrology, Linzi District People's Hospital, Binzhou Medical University, No. 139, Huangong Road, Linzi District, Zibo City 255400, Shandong Province, China
[b] Department of urinary surgery, Linzi District People's Hospital, Binzhou Medical University, No. 139, Huangong Road, Linzi District, Zibo City 255400, Shandong Province, China
[c] Linzi District People's Hospital, Binzhou Medical University, No. 139, Huangong Road, Linzi District, Zibo City 255400, Shandong Province, China
[d] Medical intensive care unit, PKUCare Luzhong Hospital, No. 65, Taigong Road, Linzi District, Zibo City 255400, Shandong Province, China
[e] Department of biotherapy, Linzi District People's Hospital, Binzhou Medical University, No. 139, Huangong Road, Linzi District, Zibo City 255400, Shandong Province, China

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ABSTRACT

To evaluate the influence of the high-flux hemodialysis (HFHD) and the low-flux hemodialysis (LFHD) on mortality rate for end-stage renal disease (ESRD). Four electronic databases including *PubMed*, *EMBASE*, the *Cochrane Library*, and *ClinicalTrails* were searched to identify relevant randomized clinical trials up to 31 August 2015. Seven studies enrolling a total of 4412 patients were included in this meta-analysis. For all-cause mortality comparing with LFHD, the result showed that there were significant difference (RR = 0.75; 95% CI [0.60–0.94]; I^2 = 84%; $P < 0.00001$). For death due to infection comparing with LFHD, the result showed that there was no significant difference (RR = 0.92; 95% CI [0.75–1.13]; I^2 = 0%; P = 0.86). For cardiovascular mortality, the overall meta-analysis result showed that there was a significant difference between the HFHD versus the LFHD (RR = 0.75; 95% CI [0.60–0.94]; I^2 = 55%; P = 0.11). Publication bias was not detected by funnel plot. Based on these results, our study suggests that the HFHD has superior effectiveness over LFHD for long-term survival in ESRD.

Maintenance hemodialysis (MHD) accounts for most dialysis treatments, and is the main renal replacement therapy technology in end-stage renal disease (ESRD) [1]. With gradual maturation and diversification of hemodialysis technology, the life expectancy of patients undergoing MHD has greatly improved, but there is still a high mortality rate; the annual fatality rate is 14–26% in European countries and the USA [1,2]. Large and medium molecular weight substances retained in the blood may be an important cause of high mortality in MHD [3]. Recently, pathologic and retrospective observational studies demonstrated retention of medium molecular weight substances, such as β2-microglobulin (β2-MG) [4,5], which led to a variety of pathologic abnormalities and was strongly correlated with death, cardiovascular disease, infections, etc. [3,6]. High-flux hemodialysis [7] (HFHD) can more effectively clear β2-MG [8,9], but relevant original researches showed that HFHD was no more effective than low-flux hemodialysis (LFHD) [10] for long-term effects of treatment [4]. A previous meta-analysis conducted by Palmer and colleague in 2012 included studies with sample size less than 30, that may lead to inaccuracy without additional analysis [11]. The focuses from the review of the KDOQI group [12] were not on the membrane flux for ESRD, and the number of included studies was insufficient. In order to improve the prognosis and life expectancy of ESRD patients based on the different membrane flux, we conducted a meta-analysis to comprehensively assess the efficacy of HFHD and LFHD for ESRD.

1. Materials and methods

1.1. Search strategy

We searched potential literatures in *PubMed*, *EMBASE*, the *Cochrane Library* and *ClinicalTrails.gov* up to 31 August 2015 to identify eligible randomized clinical trials investigating the HFHD and LFHD for ESRD. Medical Subject Headings (MeSH) and text words were both used as follows: dialysis, hemodialysis, haemodialysis, "kidney failure", "renal failure", "end-stage kidney", ESRD, high-flux, low-flux, membrane.

* Corresponding author.
E-mail address: shengwangemail@163.com (S. Wang).

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1.2. Literature selection and exclusion

All studies were selected in accordance with the following inclusion criteria:

- all studies in our meta-analysis were randomized clinical trials;
- eligible studies included the ESRD patients older than 18 years;
- the intervention was HFHD which was defined as the ultrafiltration coefficient of greater than 20 mL/h/mmHg or β2-MG clearance greater than 20 mL/min;
- the control group was LFHD which was defined as the ultrafiltration coefficient of less than 10 mL/h/mmHg or β2-MG clearance less than 10 mL/min;
- eligible studies should include at least one of the following outcomes: all-cause mortality, death due to infection, cardiovascular mortality during the treatment.

Studies were excluded in accordance with following criteria:

- study including patients with malignant tumor or acute infectious diseases;
- follow-up less than 24 months;
- study's arm sample size less than 30;
- duplicates;
- data were insufficient or cannot be obtained by contacting the correspondent author.

1.3. Data extraction and quality assessment

The relevant information including patients' characteristics, underlying illnesses, mean time on dialysis, interventions, controls, outcomes (all-cause mortality, death due to infection, or cardiovascular mortality), follow-up time were independently extracted and entered into a database by two investigators. For missing data, we contacted the correspondent authors of original studies to obtain it if possible. Intention-to-treat (ITT) datasets were used to analyze all outcomes wherever available [13].

Disagreements between two authors on data extraction and quality assessment were resolved by discussion or by consulting the lead investigator.

1.4. Statistical analysis

RevMan 5.3 software (Cochrane collaboration, London, UK) was used to perform all data analyses. For dichotomous data [14,15], we used relative risk (RR) with its 95% confidence interval (CI) as effect estimator. We performed a statistical test for heterogeneity and adopted I^2 of greater than 40 as evidence for heterogeneity according to *Cochrane handbook* [16]. If heterogeneity was presented, we would use a random-effects model to synthesize effect size [17]. Visual inspection of funnel plot was used to potential publication bias as qualitative method [18]. In a funnel plot, studies with larger sample size that provide a more precise estimate of an intervention's effect form the spout of the funnel, whereas studies with smaller sample size with less precision form the cone end of the funnel. Asymmetry in the funnel plot indicates potential publication bias.

2. Result

2.1. Study selection and data collection

We initially identified 2359 records obtained from 4 electronic databases (Fig. 1). Based on the inclusion and exclusion criteria, retrieved titles and abstracts were independently screened by two reviewers and full text copies of eligible studies were downloaded

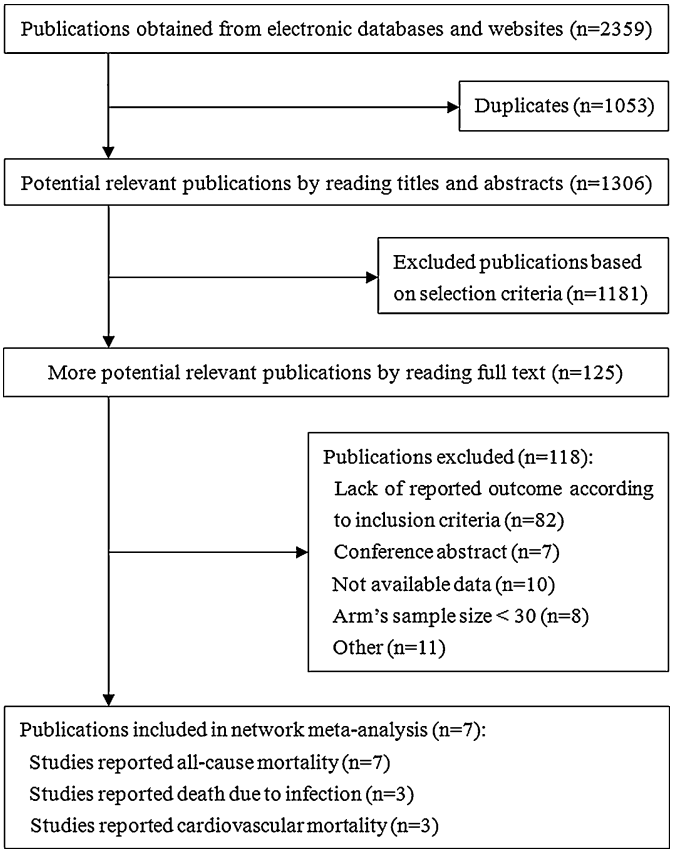

Fig. 1. Summary of trial identification and selection.