#### LABORATORY STUDY



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# Effect of peritoneal dialysis versus hemodialysis on renal anemia in renal in end-stage disease patients: a meta-analysis

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#### ABSTRACT

The aim of this meta-analysis was to evaluate the effect of peritoneal dialysis (PD) and hemodialysis (HD) on renal anemia (RA) in renal disease patients by a meta-analysis. Relevant studies published before June 2015 were searched. Pooled odds ratio (OR) with 95% confidence interval (CI) was used to evaluate the effect of HD and PD on RA based on five indexes: hemoglobin, ferritin, transferrin saturation index, serum albumin, and parathyroid hormone. Sensitivity analysis and publication bias assessment were conducted to evaluate the stability and reliability of our results. A total of fourteen eligible studies with 1103 cases underwent HD and 625 cases underwent PD were used for this meta-analysis. There were no significant difference for levels of hemoglobin (SMD = -0.23, 95% CI: -0.74 to 0.28), ferritin (SMD = 0.01, 95% CI: -0.59 to 0.62), parathyroid hormone (SMD = 0.11, 95% CI: -1.53 to 1.75) and transferrin saturation index (SMD = -0.06, 95% CI: -0.67 to 0.56) between HD and PD group. However, the content of serum albumin in HD group was much more than that in PD group (SMD = 1.58, 95% CI: 0.35 to 2.81). Neither of the included studies could reverse the pooled side effect and Egger's test demonstrated no publication bias. Both of the two dialysis strategies have a similar effect on RA in renal disease patients.

#### **ARTICLE HISTORY**

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## KEYWORDS

Peritoneal dialysis; hemodialysis; renal anemia; meta-analysis; renal in endstage

## Introduction

Anemia is a clinical manifestation that commonly happened in patients with renal disease.<sup>1</sup> Untreated anemia is associated with several physiological abnormalities which will significantly reduce patients' life quality.<sup>2,3</sup> The management of anemia with erythropoiesis-stimulating agents (ESAs) is an important treatment for chronic kidney disease (CKD) patients with anemia (namely renal anemia [RA]) who receiving dialysis programs.<sup>4</sup>

Recently, a number of factors were recognized to be associated with dialysis modes, such as the iron deficiency, severe hyperparathyroidism, vitamin deficiency, aluminum toxicity, inflammation, as well as inadequate dialysis.<sup>5,6</sup> However, little evidence has been made with regard to the contribution of inflammation to RA observed in different dialysis patients. Inflammatory stimuli will cause the release of several cytokines and results in a series of systemic changes. The serum albumin, hemoglobin, ferritin, and transferrin saturation index were reported to be involved in the presence of inflammation.<sup>7</sup> In secondary hyperparathyroidism of

CKD patients, the high level of parathyroid hormone is suggested to be of multiple biological effects, including a negative influence on the RA patients.<sup>8,9</sup>

The most common treatment modalities for CKD are HD (hemodialysis) and PD (peritoneal dialysis). However, the function and outcomes between these two dialysis techniques are controversial. A recent clinical study has demonstrated that the serum albumin could predict the mortality of both PD and HD patients while the mortality was different in different dialysis modalities.<sup>10,11</sup> However, the most recent cohort studies suggested that patients treated with either PD or HD in end-stage renal disease showed remarkably similar outcomes.<sup>12,13</sup>

Therefore, in the present work, we performed a meta-analysis to compare the effect of PD and HD on RA in patients with renal disease. The data of hemoglobin, ferritin, transferrin saturation index, serum albumin, and parathyroid hormone indexes between HD and PD groups were pooled respectively. Our study aimed at finding the effect of dialysis modalities on RA and provide a basis for clinical application.

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Supplemental data for this article can be accessed <u>here</u>.

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## **Materials and methods**

#### Search strategy

Related clinical studies about the effect of PD and HD on RA were systematically searched from Pubmed (http://www.ncbi.nlm.nih.gov/pubmed) and Embase (http://www.embase.com) databases, with the retrieval deadline of June 2015. Keywords for all searches were ("renal anemia" or "renal anemia" or "anemia of renal failure") in combination with ("hemodialysis" or "hemodialysis") and ("peritoneal dialysis").

#### Inclusion and exclusion criteria

Studies included in this meta-analysis should meet the following criteria: (1) they reported clinical research about the effects of PD and HD on RA; (2) the number of patients in both PD and HD groups should be provided; (3) at least one of the following indexes should be provided, including hemoglobin (g/dL), ferritin (ng/mL), transferrin saturation index (%), serum albumin (g/dL), and parathyroid hormone.

Studies should be excluded if they (1) were reviews, reports, letters, and comments; (2) had not available data to be extracted.

## Data extraction and quality evaluation

Wan-ning Wang and Wen-long Zhang reviewed and screened the articles, respectively based on the inclusion and exclusion criteria. Afterward, information about the publications and the patients from the included studies were extracted, including the first author's name, year of publication, country, demographic information of patients in both PD and HD groups (age, gender, weight/BMI, time on dialysis, and the levels of hemoglobin, ferritin, transferrin saturation index, serum albumin, and parathyroid hormone). Any discrepancies during data extraction were resolved by discussion with Tao Sun.

The quality assessment of included trials was conducted by Wan-ning Wang and Wen-long Zhang independently according to the evaluation criterion tool proposed by AHRQ (Agency for Healthcare Research and Quality).<sup>14</sup> Any disagreement was resolved by inviting Zhong-gao Xu for discussion. The tool evaluates the study quality through eleven items, each of which was responded with "yes" or "no" or "not clear".

## **Statistical analysis**

Meta-analysis was conducted by the R 3.12 software (R Foundation for Statistical Computing, Vienna, Austria).

The effect size was assessed by standardized mean difference (SMD) and 95% confidence interval (CI). A random-effects model was used for heterogeneous outcomes (p < .05 and  $l^2 > 50\%$ ), and a fixed-effect model was used for the homogeneous outcomes (p > .05 and  $l^2 < 50\%$ ).<sup>15</sup> Publication bias was evaluated by Egger's test.<sup>16</sup> Finally, the sensitivity analysis was also conducted to calculate the results by omitting one study at one time to measure its effect on the pooled SMD.

## Results

## **Trail flow**

The flow chart of the literature search and study selection was presented in Figure 1. A total of 1636 potentially relevant studies were searched from PubMed (n = 1020) and Embase (n = 616). Afterward, 528 duplicates and 987 obvious irrelevant articles were removed. After title and abstract evaluation, 41 were excluded because they were letters (n = 8), case series (n = 7), and literature reviews (n = 26). The left 80 publications underwent further review while 66 of them (23 were unable to be data-extracted and 43 were not reported RA disease) were removed. Finally, a total of fourteen studies were included in this meta-analysis.<sup>17–30</sup>

## **Characteristics of included studies**

The characteristics of the fourteen studies and basic information of the subjects were listed in Table 1. These studies distributed from Europe (Spain, UK, Portugal, Ireland, and Germany), Africa (South Africa), America (Canada and USA) and Asia (Turkey and Kuwait) were published from 1991 to 2014. Among them, 11 studies reported the comparison of hemoglobin between HD



Figure 1. Literature search and study selection.

Image: constant with the section in the sectin in the section in the section in the section in the sec	Table 1. Chi	aracteristics of	14 inclu	papr	studies	in this meta	a-analysis.							
F. Concore         203         Spain         HD         6         40:20         Si=15         M         Si=64:5         M         Si=64:5         M         Si=64:5         M         Si=64:5         M         Si=74:90         M         Si=74:90         Romenonia           GK Subus         Did         12         7/5         S(17-10)         7/7-109         T         1/4:12         N         3/2:40         3/2:14.90         M         Secondinal study           MK Practuoso         Dil         Pin         2/2         S(17-10)         7/7-109         T         1/4:1         2/2:40         2/2:40         Secondinal study         Consortional study           MK Practuoso         Dil         Pin         S(17-10)         7/7-109         T         1/4:1         2/2:40         2/2:40         2/2:40         2/2:40         Discretional study         Consortional study         Discretional Study <t< th=""><th>Author</th><th>Study Year location</th><th>Type</th><th>Z</th><th>Gender (M/F)</th><th>Age (years)</th><th>Weight (kg)/BMI</th><th>Time on dialysis</th><th>Hemoglobin (g/dL)</th><th>Ferritin (ng/mL)</th><th>Transferrin saturation index (%)</th><th>Serum albumin (g/dL)</th><th>Parathyroid hormone</th><th>Study types</th></t<>	Author	Study Year location	Type	Z	Gender (M/F)	Age (years)	Weight (kg)/BMI	Time on dialysis	Hemoglobin (g/dL)	Ferritin (ng/mL)	Transferrin saturation index (%)	Serum albumin (g/dL)	Parathyroid hormone	Study types
KL         Clic         323         Signal         Signa         Signa	F. Coronel	2003 Spain	모	69	40/29	<b>65±15</b>	NA	64±69 m	11.6±1.3	338 ± 167	23.1 ± 7.7	<b>4.1</b> ±0.3	412 ± 438 pg/mL	A comparative mul-
GK Sides         Dot         UK         HD         12         10.2         C (50-30)         T (-1) (-1)         D (-1)         D (-1)         C (50-sectional)         D (50-sectional) <thd (50-sectional)<="" th=""> <thd (50-sectional)<="" th=""></thd></thd>			DD	63	32/31	56±15	NA	26±26 m	$11.4 \pm 1.4$	218 ± 214	$26.2 \pm 10.8$	$3.7 \pm 0.4$	272 ± 290 pg/mL	ucenter study
R. Function         Total	G.K. Sakkas	2004 UK	Ð	12	10/2	62 (35–76)	75 (60–90)	47 (6–192) m	$11.3 \pm 0.9$	NA	NA	$3.9 \pm 0.4$	8.4 ± 10 pmol/L	Cross-sectional observational study
M.K. Functionoo         Distribution         Total         S1         Total         S1         Total         S1         Total         S1         Total         S1         S1         Generational Study           A Vega         D1         Ho         37         10/6         63-11         53.15.5         NA         NA         605-0000103 Study         Descriptional Study           Low         D1         Holand         D0         16         NA         53.15.5         NA         NA         Descriptional Study           Low         D3         South Minda         D0         32         Total         33.5.0.03         NA         Descriptional Study           Low         D3         South Minda         D3         South Minda         NA         D37.5.000         S14.7.7         D05         Descriptional Study           A Veux         D0         10         D21         South N         NA         D37.5.000         S14.7.7         NA         Descriptional Study           A Veux         D0         D22         South N         NA         D37.5.000         <			PD*	12	7/5	55 (37–70)	79 (51–105)	47 (7–196) m	$12.6 \pm 1.3$	NA	NA	$3.9 \pm 0.5$	22 ± 20 pmol/L	
W Gue         Total         PD         14         86         38 + 13         M         15 + 13<         M	M.R. Fructuoso	2011 Portugal	ÐH	37	21/16	$67.3 \pm 14.9$	NA	$6.1 \pm 6.5$ y	$11.9 \pm 1.2$	NA	NA	$3.36 \pm 0.44$	NA	<b>Cross-sectional</b>
A Vaga         2014 Ieland         10         17         M.         66:15         23:3:5:         M.         M.         IG:0:5:5:         M.         Coss-sectional           16. Otpoch         2013 South Mitra         10         70         M.         56:1:13         M.         M.         2043:17:33         39:1:13         39:1:10         39:1:13         M.         Coss-sectional           A Vaux         2041 Lively         10         3         11/1         59:1:13         39:1:10         39:1:10         39:1:10         Sectional         Observational study           A Vaux         2041 Lively         10         3         11/1         59:1:13         39:1:10         39:1:1         39:1:1         39:1:10         39:1:13         39:1:10         39:1:13         10:0:1:10 <t< td=""><td></td><td></td><td>Ua</td><td>14</td><td>8/6</td><td>38 0 + 13 3</td><td>NA</td><td>10+13 v</td><td>115+18</td><td>NA</td><td>۸A</td><td>3 35 + 0 33</td><td>NA</td><td>observational study</td></t<>			Ua	14	8/6	38 0 + 13 3	NA	10+13 v	115+18	NA	۸A	3 35 + 0 33	NA	observational study
	A. Vega	2014 Ireland	2	176	NA	66±15	$26.3 \pm 5.5$	NA	NA	$165.0 \pm 55.2$	34 ± 9.8	$4.0 \pm 0.5$	NA	Cross-sectional
	n													observational study
I.G. Opechi         2013         Subtractioned			Ы	42	NA	$58 \pm 17$	$26.1 \pm 3.9$	NA	NA	$204.2 \pm 78.9$	$36 \pm 10.1$	$3.8 \pm 0.4$	NA	
X varx         2004         Turky         PD         56         1/17         50.61.2.1         MA         143.E116m MA         233.E11         337.11         337.10         80.65.E18.1 pmol/L         coss-sectional           AA. Huuse         1998         Ganada         HD         157         50.41.3         34.4.305.m         10.3.1.16         37.6.1.83.500.pm/L         coss-sectional         berrational study           AA. Huuse         1999         USA         HD         157         54.4.15         MA         13.2.4.12         332.4.100         805.4.183.0pg/mL         coss-sectional           J. Gunnel         1999         USA         HD         29         97/1         54.4.15         MA         10.7.1.6.1         356.4.3.12         332.4.100         MB         253.8.4.3.2.00         MM         coss-sectional           J. Gunnel         1999         USA         HD         29         17/1         37.4.30         MA         MA         738.8.4.5.5         281.4.10.2         368.4.4.10         MM         coss-sectional         beservational study         coss-sectional         beservational study         coss-sectional         coss-sectional         coss-sectional         coss-sectional         coss-sectional         coss-sectional         cos-sectional <t< td=""><td>I.G. Okpechi</td><td>2013 South Afr</td><td>ica HD</td><td>56</td><td>26/30</td><td><b>38.6±1.4</b></td><td>NA</td><td>49.8 ± 71.5 m</td><td><math>8.5 \pm 0.3</math></td><td><math>549.4 \pm 54.3</math></td><td><b>24.7 ± 1.4</b></td><td><math>3.97 \pm 0.09</math></td><td>52.1 ± 7.3 pmol/L</td><td>Cross-sectional observational study</td></t<>	I.G. Okpechi	2013 South Afr	ica HD	56	26/30	<b>38.6±1.4</b>	NA	49.8 ± 71.5 m	$8.5 \pm 0.3$	$549.4 \pm 54.3$	<b>24.7 ± 1.4</b>	$3.97 \pm 0.09$	52.1 ± 7.3 pmol/L	Cross-sectional observational study
A. Yauz         2004 Turkey         HD         38         21/1         50:11         50:11:1         50:11:1         50:11:1         Conssectional constrained constr			DD	26	17/9	$36.0 \pm 2.2$	NA	14.5 ± 11.6m	$8.2 \pm 0.4$	$457.8 \pm 81.6$	$21.2 \pm 1.2$	$3.87 \pm 0.10$	80.6 ± 18.1 pmol/L	
A. House         198         Canada         PD         5         304         5732+183.0 pym         Constrained         2323+46.0         2323+183.0 pym         Constrained         Constraine         Constrained         Con	A. Yavuz	2004 Turkey	몃	38	21/17	50±19	63 ± 19	27 ± 32 m	9.9±1.4	$404 \pm 243$	30 ± 11	NA	170.8 ± 180.1 pg/mL	Cross-sectional observational study
A.A. House         198         Canada         Ho         157         36/4         57.22.11.46         NA         14.21.10.68         10.47.12.012         233.45.05         235.11.12         392.40.06         187.41.93         Conserctional           J. Gunnell         1999         USA         HD         25         2143         53.41.12         NA         37.41.0         NA         37.41.00         187.41.93         OM         OM         78.44.1.05         34.44.006         187.41.93         OM         OM         36.41.1.2         33.44.006         187.41.93         OM         OM         78.44.1.05         34.44.006         187.41.93         OM         OM         A			PD*	40	19/21	$50 \pm 13$	70 ± 13	34.6 ± 30.5 m	$10.8 \pm 1.6$	376.0 ± 336.7	$40.8 \pm 18.7$	NA	275.9 ± 183.0 pa/mL	
$ \  \  \  \  \  \  \  \  \  \  \  \  \ $	A.A. House	1998 Canada	모	157	93/64	57.22 ± 1.46	NA	14.21 ± 0.68 m	$10.47 \pm 0.12$	258.7 ± 42.66	$28.5 \pm 1.12$	$3.92 \pm 0.04$	282.8 ± 29.2 pg/mL	Cross-sectional
1. Gumeli       199       US       10       20       54.33       53.41.13       M       37.41.10       M       756 (2110-342       38 (35-4.4.2)       M       Gae-ontrol study         MA. Gões       2010       US       190       26       201/16       51.4.17       M       41.4.1 V       M       73 (88-34)       256 (210-342       38 (35-4.2)       M       M       Gae-ontrol study         MA. Gões       2010       US       190       27       14/1       27.5.4.20       N       M       73 (88-34)       N       M       M       Gae-ontrol study       Gae-ontro			G	176	77/57	57 A6 + 1 51	NA	15 77 + 0.60 m	10 71 + 0 1 4	<b>753 8 + 56 75</b>	28.1 + 1.02	3 11 + 0 06	187 / + 10 3 nd/ml	observational study
A. Goes         Z010         S1         Z010         S1         Z1         MA         Z1         Z1         MA         Z1         Z1         MA         Z1         Z1         MA         Z1         Z1 <thz1< th="">         Z1         Z1</thz1<>	Gunnell	1999 1154	달	6	54/38	10:1 - 0/c 53 + 18		111 60.0 7 17.0 1 2 2 + 3 0 v		(001-07) 82	20.1 ± 1.02 22 4 (17 1–28 2)	3 8 (3 5-4 0)	10/.1 - 12/.2 pg/111L	Cace-control study
			<u> </u>	3.6	00/16 90/16	51 + 17	AN	4 4 + 4 1 v	AN	173 (88–334)	256 (21 0-34 2	(0. <u>7</u> -0.0) 0.0 3 8 (3 5-4 7)	AN	case-collicion siding
Z Aydin       Z014       Turkey       PD       29       1/17       54 ± 14       277 ± 740       NA	M A Góas		Ē	000	19/10	47 + 14	73 5 + 3 20	NA NA	NA	406 + 200	32 + 12	NA NA	NA	Croce-certional
Z         Model         S01         Turkey         PD         29         12/17         54±14         36±214         37±17         NA         NA         Coss-sectional coss-sectional doservational study           J. Fadrowski         2014         Turkey         HD         20         8/12         493±12.0         35.6±4.1         NA         10.7±1.2         769±389         24.7±9.7         41±0.4         NA         Coss-sectional observational study           J. Fadrowski         2004         US         31/16         16.5±1.7         NA         NA         11.1±1.4         NA         NA         NA         NA         Coss-sectional observational study           J. Fadrowski         2004         US         37/29         0.7±5.6         NA         NA         NA         NA         NA         NA         Coss-sectional observational study           J. Hilali         2005         Suwait         HD         S3         10.7±15.6         NA         11.1±1.4         NA         NA         NA         Coss-sectional observational study           J. Hilali         2005         Kuwait         HD         S3         10.2±15.6         NA         11.1±1.1         NA         NA         NA         NA         S3         S3.79.6.4.0			2	ì		-				1	4			observational study
Z. Aydin       2014       Turkey       HD       20       8/12       49.8±12.0       35.6±4.1       NA       11.7±1.2       769±389       24.7±9.7       4.1±0.4       NA       Cross-sectional observational study observational stud			D	29	12/17	$54 \pm 14$	$27.7 \pm 7.40$	NA	NA	$364 \pm 214$	37 ± 17	NA	NA	(
	Z. Aydin	2014 Turkey	무	20	8/12	$49.8 \pm 12.0$	$23.6 \pm 4.1$	NA	$11.7 \pm 1.2$	$769 \pm 389$	$24.7 \pm 9.7$	$4.1 \pm 0.4$	NA	Cross-sectional
J. Fadrowski       PD       21       14/7       47.7 ± 12.1       28.4 ± 7.7       NA       10.7 ± 1.7       269 ± 135       29.4 ± 14.8       3.6 ± 0.3       NA       Cross-sectional         J. Fadrowski       2004       USA       HD       33       17/16       16.5 ± 1.7       NA       11.1 ± 1.4       NA       NA       NA       NA       Observational study         N. Al-Hilali       2005       Kuwait       HD       83       30/33       51.5 ± 15.2       NA       NA       11.1 ± 1.4       NA       NA       NA       NA       Observational study       Observational study         N. Al-Hilali       2005       Kuwait       HD       83       30/33       51.5 ± 15.2       NA       32.1 ± 2.4       11.(10.1-12.0)       194 (123 - 279)       NA       2.8 (2.3 - 3.3)       29/mL       Cross-sectional         U. Frei       2009       Germany       HD       83       105/113       60.7 ± 15.6       NA       11.2 ± 1.1       NA       2.8 (2.3 - 3.3)       29/mL       Cross-sectional       Observational study         U. Frei       2009       Germany       HD       88       155/113       60.7 ± 15.6       NA       11.2 ± 1.21       NA       2.8 (2.3 - 3.3)       24 (8.5 - 53.4)														observational study
JJ. Fadrowski       2004       US       31       17/16       16.5±1.7       NA       NA       NA       NA       NA       NA       NA       NA       NA       Coss-sectional observational study observat			6	21	14/7	47.7±12.1	$28.4 \pm 7.7$	NA	$10.7 \pm 1.7$	$269 \pm 135$	$29.4 \pm 14.8$	$3.6 \pm 0.3$	NA	
N. Al-Hilali         2005 Kuwait         PD         66         37/29         10.7 ± 5.6         NA	J.J. Fadrowski	2004 USA	Ð	33	17/16	$16.5 \pm 1.7$	NA	NA	$11.1 \pm 1.4$	NA	NA	NA	NA	Cross-sectional
N. Al-Hilali 2005 Kuwait HD 83 30/53 51.5 $\pm 15.2$ NA NA 11.3 $\pm 1.4$ 11 (10.30 $\pm 1.30$ (71 $\pm 2.36$ ) NA 3.2 (3.0 $\pm 3.3$ (3.7 $\pm 6.40$ ) pg/mL Cross-sectional observational study PD* 35 20/15 55.8 \pm 13.3 NA 19.2 $\pm 2.4$ 11 (10.30 $\pm 1.30$ (71 $\pm 2.36$ ) NA 3.2 (3.0 $\pm 3.3$ (3.7 $\pm 6.40$ ) pg/mL Cross-sectional observational study ND 88 175/113 60.7 \pm 15.6 NA 19.2 $\pm 2.4$ 11.2 $\pm 1.1$ NA			2	č			414	A I A	· · · · · · · · · · · · · · · · · · ·		V 1 V		V I V	observational study
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	ileliHJA N	2005 Kuwait	5 5	8 8	30/53	515+157	NA NA	37 1 + 7 4	11 (10 30–11 8) 11 (10 30–11 8)	130 (71_736)	NA	3 7 (3 0–3 4)	33 (17 9–64 0) na/ml	Croce-cartional
U. Frei 2009 Germany HD 288 175/113 60.7±15.6 NA 19.2±2.1 11 (10.1-12.0) 194 (123-279) NA 2.8 (2.3-3.3) 24 (8.5-534) pg/mL Multicentre, open- label uncontrolled study A. Férnandez 1991 Spain HD 13 NA 44.23±15.36 NA 52.46±42.32m 8.76±1.99 436.59±528.53 NA NA NA NA NA Cass-sectional study D* 24 NA 51.81±13.87 NA 36.63±25.73m 9.61±1.84 459.32±557.75 NA NA NA NA NA NA NA Cass-sectional study			2	3		10.0								observational study
U. Frei 2009 Germany HD 288 175/113 60.7±15.6 NA 12-24 w 11.2±1.1 NA NA NA NA Multicentre, open-label uncontrolled study A férnandez 1991 Spain HD 13 NA 44.23±15.36 NA 52.46±42.32m 8.76±1.99 436.59±528.53 NA NA NA NA NA Cross-sectional study D* 24 NA 51.81±13.87 NA 36.63±25.73m 9.61±1.84 459.32±557.75 NA NA NA NA NA NA Cross-sectional study			PD*	35	20/15	$55.8 \pm 13.3$	NA	19.2 ± 2.1	11 (10.1–12.0)	194 (123- 279)	NA	2.8 (2.3–3.3)	24 (8.5–53.4) pg/mL	
A. Férnandez       1991       91       45/46       52.4±14.0       NA       11.6±1.1       NA       NA       NA       study         A. Férnandez       1991       Spain       HD       13       NA       44.23±15.36       NA       52.46±42.32m       8.76±1.99       436.59±528.53       NA       NA       NA       NA       Cross-sectional         D*       24       Na       53.46±42.32m       9.61±1.84       459.32±557.75       NA       NA       Observational study	U. Frei	2009 Germany	모	288	175/113	$60.7 \pm 15.6$	NA	12-24 w	$11.2 \pm 1.1$	NA	NA	NA	NA	Multicentre, open-
PD       91       45/46       52.4±14.0       NA       12.24 w       11.6±1.1       NA       NA       NA       NA       NA         A. Férnandez       1991       5pain       HD       13       NA       44.23±15.36       NA       52.46±42.32m       8.76±1.99       436.59±528.53       NA       NA       NA       Cross-sectional         A. Férnandez       1991       5pain       HD       13       NA       44.23±15.36       NA       52.46±42.32m       8.76±1.99       436.59±528.53       NA       NA       Cross-sectional       observational study         PD*       24       NA       51.81±13.87       NA       36.63±25.73m       9.61±1.84       459.32±557.75       NA       NA       NA       observational study														label uncontrolled
A. Férnandez       1991       Spain       HD       13       NA       44.23±15.36       NA       52.46±42.32m       8.76±1.99       436.59±528.53       NA       NA       NA       Cross-sectional         PD*       24       NA       51.61±1.84       459.32±557.75       NA       NA       NA       Observational study			Ud	91	45/46	57 4 + 14 0	NA	12-24 w	116+11	NA	NA	NA	NA	study
PD* 24 NA 51.81±13.87 NA 36.63±25.73m 9.61±1.84 459.32±557.75 NA NA NA NA Observational study	A Eárnandaz	nien 7001	Ē		VIV	11 73 ± 15 36	VIN	57 16 ± 17 3.7m	8 76 ± 1 00	136 50 + 578 53	VN	VN		Croce-cortional
PD* 24 NA 51.81±13.87 NA 36.63±25.73m 9.61±1.84 459.32±557.75 NA NA NA NA	A. Fernanuez	mede reer	2	2		0C.CI ± C2.44	<b>K</b> NI	1112C.24 ± 04.2C	٥./٥ ± 0/.0	CC.02C I &C.0C4	EN .	<b>N</b>	AN	observational study
			PD*	24	NA	$51.81 \pm 13.87$	NA	36.63 ± 25.73m	$9.61 \pm 1.84$	$459.32 \pm 557.75$	NA	NA	NA	

and PD, ten reported the comparison of ferritin between HD and PD, eight reported the transferrin saturation index in both HD and PD groups, nine reported the serum albumin in both HD and PD groups, and six studies reported the parathyroid hormone in both HD and PD groups. A total of 1103 cases underwent HD and 625 cases underwent PD were used for this metaanalysis. There were more males than females in these patients. There was no significant difference in weight or BMI between the patients who underwent HD and PD.

#### **Quality evaluation**

As shown in Supplementary Table 1, the quality of all the studies was relatively high. Almost all the included studies described more than four items according to AHRQ.

#### **Meta-analysis**

Comparison of hemoglobin, ferritin, transferrin saturation index, serum albumin, and parathyroid hormone indexes between HD and PD groups were shown in Figure 2(a)–(e).

There were eleven studies reported the content of hemoglobin between the HD and PD groups (Figure 2(a)). The random-effect model was used to evaluate the effect because a significant heterogeneity existed among these studies ( $l^2 = 93.9\%$ , p < .0001). Meta-analysis showed no significant difference in the hemoglobin content between patients suffered from HD and PD (SMD = -0.23, 95% CI: -0.74 to 0.28).

Totally ten studies reported the comparison of ferritin between HD and PD (Figure 2(b)). There was significant heterogeneity among these studies ( $l^2 = 95.2\%$ , p < .0001), therefore, the random-effect model was used to evaluate the effect size. No significant difference of ferritin was found between the HD and PD groups (SMD = 0.01, 95% CI: -0.59 to 0.62).

Eight publications reported the transferrin saturation index in both HD and PD groups (Figure 2(c)). As well, significant heterogeneity was detected ( $l^2 = 94.7\%$ , p < .0001) and the random-effect model was used for meta-analysis. As a result, the transferrin saturation index in both HD and PD groups showed no significant difference (SMD = -0.06, 95% CI: -0.67 to 0.56).

With regard to the serum albumin, nine studies were included in the meta-analysis (Figure 2(d)). The randomeffect model was chosen because of the high heterogeneity ( $l^2 = 98.3\%$ , p < .0001). The content of serum albumin in HD group was much more than that in PD group (SMD = 1.58, 95% CI: 0.35 to 2.81), indicating that the HD dialysis may be superior to PD dialysis. There were six studies reported the compassion of parathyroid hormone in HD and PD groups (Figure 2(e)). High heterogeneity was found among these studies ( $l^2 = 98.7\%$ , p < .0001). Therefore, the random-effect model was used to evaluate the effect. However, no significant difference was found for parathyroid hormone between the two dialysis strategies (SMD = 0.11, 95% Cl: -1.53 to 1.75).

#### Sensitivity analysis and publication bias

In order to evaluate the effect of each study on the pooled SMD value, the sensitivity analysis was performed (Figure 3). Neither of the included studies could reverse the pooled side effect in each meta-analysis of the five indexes, indicating the stable results of our meta-analysis.

The results of the Egger's test were presented in Supplementary Table 2. The studies included in all the meta-analyses demonstrated no publication bias, suggesting that our results were reliable.

#### Discussion

Recently, both PD and HD are the most comment methods for clinical treatment of nephropathy. RA is one of the most common complications of CKD that mainly caused by nephropathy. In the present study, we evaluated the effect of PD and HD on RA, and the results demonstrated that there was no significant difference in hemoglobin, ferritin, transferrin saturation index, and parathyroid hormone between HD and PD groups. However, the content of serum albumin in HD group was much more than that in PD group.

During dialysis, several factors were recognized to be associated with postoperative outcomes of RA patients, such as hemoglobin, ferritin, transferrin saturation index, and parathyroid hormone. ESAs are recommended to correct RA, as maintenance of hemoglobin within a suitable range can play an important role in patients outcomes.<sup>31</sup> However, the issue remains controversial, because recent prospective randomized trials have suggested that maintaining hemoglobin to normal or near normal levels in CKD patients dose not confer any survival benefit.<sup>31,32</sup> In our study, the hemoglobin levels showed no significant difference in both PD and HD groups, indicating that the impact of hemoglobin variability may produce a similar clinical outcome between patients treated with PD and HD. One of the factors involved in dialysis is the blood loss, which makes patients prone to develop iron deficiency.<sup>19</sup> However, there was no statically significant difference for ferritin and transferrin saturation index between PD

(a) Study	Experimental	Control Sta	ndardised mean difference	SMD 95%-CL	N(fixed) W(random)
Study	Total Mean 3D	Total mean 3D		3WD 95%-CI	W(IIXed) W(Iandoni)
Coronel F 2003 Sakkas G K 2004	69 11.60 1.30 12 11 30 0.90	63 11.40 1.40 12 12 60 1 30 —		0.15 [-0.19; 0.49]	12.4% 9.6% 1.9% 7.8%
Fructuoso M 2011	37 11.90 1.20	14 11.50 1.80		0.28 [-0.33; 0.90]	3.8% 8.7%
Okpechi I G 2013	56 8.50 0.30	26 8.20 0.40		0.89 [0.40; 1.37]	6.2% 9.2%
House A A 1998	157 10.47 0.12	126 10.71 0.14	-	-1.85 [-2.13; -1.57]	18.5% 9.7%
Aydin Z 2014	20 11.70 1.20	21 10.70 1.70		0.66 [0.03; 1.29]	3.6% 8.7%
Fadrowski J J 2004 Al-Hilali N 2005	33 11.10 1.40 83 11.00 1.11	66 11.30 1.40 35 11.00 1.41		-0.14 [-0.56; 0.28]	8.3% 9.4% 9.3% 9.4%
Frei_U 2009	288 11.20 1.10	91 11.60 1.10	÷.	-0.36 [-0.60; -0.13]	25.8% 9.8%
Férnandez A 1991	13 8.76 1.99	24 9.61 1.84		-0.44 [-1.12; 0.24]	3.1% 8.5%
Fixed effect model	806	518	\$	-0.42 [-0.54; -0.30]	100%
Random effects mode	el =93.9% tau-squared=0.1	682, p<0.0001		-0.23 [-0.74; 0.28]	100%
neterogeneny. r squarea-	-00.070, tau "Squarea-0.	1002, p 10.0001			
		-2	-1 0 1 2		
(b)	Experimental	Control	Standardised mean differen	ice	Million d) Million dama)
Study	Total Mean SD	lotal Mean SD	1	SMD 95%-CI	w(fixed) w(random)
Coronel F 2003	69 338.00 167.00	63 218.00 214.00		0.63 [0.28; 0.98]	13.2% 10.3%
Okpechi I G 2013	56 549.40 54.30	26 457.80 81.60	-*	1.42 [ 0.90; 1.93]	6.1% 9.9%
Yavuz A 2004	38 404.00 243.00	40 376.00 336.70	+	0.09 [-0.35; 0.54]	8.2% 10.1%
Gunnell J 1999	92 78.00 17.50	36 173.00 61.50	- 1	-2.65 [-3.15; -2.14]	6.3% 9.9%
Goes M A 2010 Avdin Z 2014	29 406.00 209.00	29 364.00 214.00		0.20 [-0.32; 0.71]	6.1% 9.9%
Al-Hilali N 2005	83 130.00 122.22	35 194.00 115.56		-0.53 [-0.93; -0.13]	10.1% 10.2%
Férnandez A 1991	13 436.59 528.53	24 459.32 557.75		-0.04 [-0.72; 0.63]	3.6% 9.4%
Fixed effect model	733	442		-0.04 [-0.17; 0.09]	100%
Random effects model	5 2% tau-squared=0 89	62 p<0.0001	$\Rightarrow$	0.01 [-0.59; 0.62]	100%
neterogeneny. r oquarea a		oz, p -0.000 i			
			-3 -2 -1 0 1 2	3	
(c)	Experimental	Control St	andardised mean differend	e	
Study	Total Mean SD	Total Mean SD	3	SMD 95%-CI	W(fixed) W(random)
Coronel F 2003	69 23.1 7.70	63 26.2 10.80		-0.33 [-0.68; 0.01]	15.5% 12.9%
Vega A 2014	176 34.0 9.80	42 36.0 10.10	-	-0.20 [-0.54; 0.13]	16.1% 12.9%
Yavuz A 2004	38 30.0 11.00	40 40.8 18.70		-0.69 [-1.15; -0.23]	4.8% 11.8% 8.8% 12.5%
House A A 1998	157 28.5 1.12	126 28.1 1.02		0.37 [0.13; 0.61]	32.8% 13.2%
Gunnell J 1999 Goes M A 2010	92 22.4 1.85 29 32 0 12 00	36 25.6 3.30 29 37 0 17 00		-1.36 [-1.78; -0.94] -0.34 [-0.85: 0.18]	10.4% 12.6% 6.8% 12.3%
Aydin Z 2014	20 24.7 9.70	21 29.4 14.80		-0.37 [-0.98; 0.25]	4.8% 11.8%
Fixed effect model	637	383		-0.08 [-0.21: 0.06]	100%
Random effects model				-0.06 [-0.67; 0.56]	100%
Heterogeneity: I-squared=	94.7%, tau–squared=0.7	/338, p<0.0001 □		1	
		-3	-2 -1 0 1 2	3	
(d)	Experimental	Control Sta	andardised mean differend	e	
Study	Total Mean SD	Total Mean SD	1.9	SMD 95%-CI V	V(fixed) W(random)
Coronel F 2003	69 4.10 0.30	63 3.70 0.40		1.13 [0.76; 1.50]	18.1% 11.3%
Sakkas G K 2004	12 3.90 0.40	12 3.90 0.50	±:	0.00 [-0.80; 0.80]	3.8% 10.9%
Vega A 2014	176 4.00 0.50	42 3.80 0.40		0.02 [-0.59; 0.64]	21.4% 11.3%
Okpechi I G 2013	56 3.97 0.09	26 3.87 0.10	<b>三</b>	1.06 [0.57; 1.56]	10.1% 11.2%
House A A 1998 Gunnell J 1999	157 3.92 0.04	126 3.44 0.06 36 3.80 0.18		9.59 [8.76; 10.42] 0.00 [-0.39 0.39]	3.6% 10.8% 16.6% 11.3%
Aydin Z 2014	20 4.10 0.40	21 3.60 0.30	-	1.39 [0.70; 2.08]	5.2% 11.0%
Al-Hilali N 2005	83 3.20 0.30	35 2.80 0.74		0.84 [0.43; 1.25]	14.7% 11.2%
Fixed effect model	702	375	4	0.94 [0.78; 1.10]	100%
Random effects mode	el 🛛		$\diamond$	1.58 [0.35; 2.81]	100%
Heterogeneity: I-squared	=98.3%, tau–squared=3.	.451, p<0.0001		٦	
		-10	-5 0 5	10	
(e)	Experimental	Control S	Standardised mean differen	ce	
Study	Total Mean SD	Total Mean SD	E 2	SMD 95%-CI	W(fixed) W(random)
Coronel F 2003	69 412.0 438.00	63 272.0 290.00	-	0.37 [ 0.03; 0.72]	27.7% 16.8%
Sakkas G K 2004	12 8.4 10.00	12 22.0 20.00		-0.83 [-1.67; 0.01]	4.7% 16.2%
Yavuz A 2004	38 170.8 180.10	40 275.9 183.00		-2.39 [-2.99; -1.80] -0.57 [-1.03; -0.12]	9.2% 16.6% 16.0% 16.7%
House A A 1998	157 282.8 29.20	126 187.4 19.30	-	3.76 [3.37; 4.15]	21.6% 16.8%
AI-Hilali, N 2005	83 33.0 34.15	35 24.0 33.26		0.26 [-0.13; 0.66]	20.9% 16.8%
Fixed effect model	415	302	\$	0.62 [0.44; 0.80]	100%
Random effects model Heterogeneity: I-squared=9	98.7%, tau-squared=4.13	32, p<0.0001		0.11 [-1.53; 1.75]	100%
				7	
			4 -2 0 2	4	

**Figure 2.** Forest plot. (a) Forest plot for the comparison of hemoglobin between HD and PD groups. (b) Forest plot for the comparison of ferritin between HD and PD groups. (c) Forest plot for the comparison of transferrin saturation index between HD and PD groups. (d) Forest plot for the comparison of serum albumin between HD and PD groups. (e) Forest plot for the comparison of parathyroid hormone between HD and PD groups.



Figure 3. Sensitivity analysis of the included studies. (a) hemoglobin; (b) ferritin; (c) transferrin saturation index; (d) serum albumin; (e) parathyroid hormone.

and HD groups, which suggested that these two dialysis methods might present similar results for iron supply in patients with RA. The role of parathyroid hormone as a uremic toxin on erythropoiesis has been discussed in several studies. It was reported that high levels of serum parathyroid hormone are involved in decreasing survival of red blood cells and their progenitor number.<sup>33</sup> Middle-molecular-weight solutes were suggested to be responsible for the toxic effect of red blood cells.<sup>34</sup> Previous evidence has proved that ambulatory PD is more efficient in eliminating middle-molecular-weight substances and results in less anemia than HD.<sup>35</sup> However, a recent study indicated that no significant difference was found in red blood cell survival between HD and PD.<sup>36</sup> In our study, there was no significant difference in parathyroid hormone levels between HD and PD dialysis strategies, thus, the beneficial effect of PD and HD on anemia may be related to elevated erythropoiesis other than improved red blood cells survival.

Severe RA tended to be associated with manifestations of fluid overload and other risk factors. In our study, the content of serum albumin in HD group was much more than that in PD group, which may in part be explained by fluid overload resulting in dilution of albumin in PD group. Besides, the PD itself, using peritoneum as the semipermeable membrane, can lead to albumin loss. The serum proteins in PD patients averages 5 g per 24 h, of which, 4 g is albumin.<sup>17</sup> However, we cannot get the conclusion from the serum albumin level in the two-dialysis ways that HD was more efficient than PD in the treatment of RA. For one thing, we did not know if the difference in serum albumin level causes by ESAs treatment or dialysis strategies. For the other, it is unclear that if the reduced serum albumin level in PD group leads to anemia-related inflammatory conditions. Therefore, the association between albumin and dialysis strategies needs further clinical studies to clarify.

In our meta-analysis, high levels of heterogeneity were detected in hemoglobin, ferritin, transferrin saturation index, parathyroid hormone, and albumin between HD and PD groups, thus, the random-effected model was used for effect size. The reason for the high heterogeneity may be explained by different detection methods of these indexes, ethnic and lifestyle differences. Other confounding factors such as gender and age may also contribute to the heterogeneity. In order to detect if the time span or changing guidelines the hemoglobin targets, we performed a cumulative metaanalysis, and the results showed that during 1991 and 2014, the results were not changed significantly. Therefore, neither the time span nor the changing guidelines attributed to the heterogeneity of this study.

Our meta-analysis is the first one to evaluate the effect of PD and HD on RA. Both the sensitivity analysis and the publication bias analysis suggested that our results were stable and reliable. However, several limitations should be pointed out in this study. Firstly, there were significant heterogeneities across the included studies in the meta-analysis of the five indexes. As discussed above, the heterogeneities may associate with many factors. We did not perform the subgroup metaanalysis because of the inconsistency caused by unavailable or incomplete data of some studies. For instance, the treatment of ESAs should be considered as an important factor that is associated with the five indexes analyzed in our study. However, some of the included patients received ESAs before dialysis<sup>25,26</sup> and others were not.<sup>23,24</sup> So the effects ESAs were not analyzed in our study. Besides, we did not correct the concomitant variables such as age, gender and other confounding factors that may affect the results of this analysis. Therefore, it is necessary to develop more studies with larger sample size to assess the commonality of our results.

In conclusion, in our study, though the albumin in HD group was much more than in PD group, the hemoglobin, ferritin, transferrin saturation index, and parathyroid hormone were similar in the two groups. These results suggest that both of the two-dialysis strategies have a similar effect on RA in patients with renal diseases.

## **Disclosure statement**

All authors declare that they have no conflict of interests to state.

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