Meta-Analysis

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Effect of bioimpedance-defined overhydration parameters on mortality and cardiovascular events in patients undergoing dialysis: a systematic review and meta-analysis

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Abstract

Objective: To evaluate the role of bioimpedance-defined overhydration (BI-OH) parameters in predicting the risk of mortality and cardiovascular (CV) events in patients undergoing dialysis.

Methods: We searched multiple electronic databases for studies investigating BI-OH indicators in the prediction of mortality and CV events through 23 May 2020. We assessed the effect of BI-OH indexes using unadjusted hazard ratios (HRs) and 95% confidence intervals (CIs). Sensitivity analysis was used for each outcome.

Results: We included 55 studies with 104,758 patients in the meta-analysis. Extracellular water/total body water (ECW/TBW) >0.4 (HR 5.912, 95% CI: 2.016–17.342), ECW/intracellular water (ICW) for every 0.01 increase (HR 1.041, 95% CI: 1.031–1.051), and OH/ECW >15% (HR 2.722, 95% CI: 2.005–3.439) increased the risk of mortality in patients receiving dialysis. ECW/TBW >0.4 (HR 2.679, 95% CI: 1.345–5.339) and ECW/ICW per increment of 10% (HR 1.032, 95% CI: 1.017–1.047) were associated with an increased risk of CV events in patients undergoing dialysis. A 1-degree increase in phase angle was a protective factor for both mortality (HR 0.676, 95% CI: 0.474–0.879) and CV events (HR 0.736, 95% CI: 0.589–0.920).

Conclusions: BI-OH parameters might be independent predictors for mortality and CV events in patients undergoing dialysis.

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Introduction

As a renal replacement therapy, renal dialysis is, in principle, a selective treatment for renal dysfunction or renal diseases that includes peritoneal dialysis (PD) or hemodialysis (HD).[1] Following a rapid increase in dialysis use over a period of approximately two decades, the incidence of dialysis initiation in most high-income countries reached a peak in the early 2000s and has remained stable or has decreased slightly since then.[2] However, mortality remains unacceptably high among patients on dialysis, especially in the first 3 months following initiation of HD treatment. According to the 2019 Annual Data Report from the U.S. Renal Data System, the annual mortality was 156 per 1000 patient-years for patients undergoing PD and 167 patients for those receiving HD in the United States.[3]

Overhydration (OH) is relatively common among patients receiving dialysis, with an incidence of 56.5% to 73.1%.[4–6] Observational studies have shown an association between OH and mortality in patients receiving dialysis.[7,8] Therefore, it is essential to objectively measure patients' hydration status to obtain a more clearly defined assessment of prognosis in patients on dialysis. Common clinical approaches, such as measuring weight changes and the isotope dilution method, have certain limitations, which have led to the development of bioimpedance analysis (BIA).[9–11] Bioimpedance-defined overhydration (BI-OH) indicators have been suggested to predict mortality risk and cardiovascular (CV) events in patients receiving dialysis.[9,12] Previous studies have indicated that phase angle (PA) level is linked to a decreased risk of death among patients undergoing PD or HD.[13,14] Other evidence suggests that a higher extracellular water (ECW)/intracellular water (ICW) ratio, ECW/total body water (TBW) ratio >0.4, and overhydration (OH)/ECW ratio >15% are independent risk factors for mortality and CV events in patients undergoing HD or PD treatment.[15–18] However, Rhee et al. and Shin et al. demonstrated that a 1-degree increase in PA was not associated with increased risk of mortality and CV events in patients undergoing dialysis, without statistical significance.[14,19] A post-hoc study from a cross-sectional survey by Guo et al. found that ECW/TBW >0.4 had no effect on CV events, with $P>0.05$.[20]

A newly published meta-analysis predicted the risk of death in patients with renal and heart failure using a 1-degree decrease in PA and OH/ECW >15%.[12] Nevertheless, the role of specific OH parameters in predicting the risk of death and CV events in patients receiving dialysis remains unclear. To further clarify the correlation between OH parameters measured using BIA and the above clinical outcomes in patients on dialysis, we conducted a meta-analysis adding measures such as ECW/TBW >0.4 and ECW/ICW per every 0.01 increase, as well as subgroup analysis of dialysis methods and literature quality.

Methods

In this meta-analysis, approval of the Institutional Review Board and informed consent were not required. Our study was performed and documented according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines (Supplementary Material). The supplementary material describes the methods of this study in detail. The present study was approved by the Open Science Framework Registries (https://osf.io/registries), registration number 10.17605/OSF.IO/H2KJ4.

Literature search strategy

We performed a search of the published literature in the PubMed, Embase, Cochrane Library, and Web of Science databases up to 23 May 2020. The keywords in the search strategy were as follows: dialysis, renal dialysis, renal insufficiency, chronic kidney failure, and electric impedance. The search strategy is presented in Supplementary Table 1.

Inclusion and exclusion criteria

The inclusion criteria were as follows. i) Patients with renal diseases including chronic renal insufficiency, end-stage renal disease, renal failure, and other renal diseases, and were undergoing PD or HD. ii) BIA and its parameter indexes were ECW/TBW >0.4,[9] ECW/ICW, OH/ECW$>15\%$,[21] and PA. iii) The outcomes were unadjusted hazard ratio (HR) of mortality (main outcome) and unadjusted HR of CV events (secondary outcome). When multiple follow-up time points of the outcome event were reported, the final follow-up time point at which the outcome event occurred was included in the analysis. iv) Cohort studies.

Exclusion criteria were: i) animal studies; ii) non-English language international publications; iii) studies with unavailable data; and iv) case reports, meeting abstracts, meta-analyses, reviews, or editorials.

Data extraction and quality assessment

The literature was reviewed and the research data were extracted by two researchers (Yajie Wang and Zejuan Gu) according to the inclusion and exclusion criteria. In the case of a conflict, the point of disagreement was discussed between the two parties until agreement was reached. The following information was collected from the studies: first author, year of publication, country, method of renal replacement therapy, number of patients, age, body mass index, sex, follow-up, primary outcome, secondary outcome, mortality, BIA method, Newcastle–Ottawa scale (NOS) score, and quality assessment score. The quality of the articles was evaluated using the NOS, with scores ranging from 0 to 10. "Low quality" studies were defined as those with scores <5 and those with scores ≥ 5 were considered "high quality" studies.

Statistical analysis

The data were evaluated using unadjusted HRs and 95% confidence intervals (CIs) to determine effect sizes. To evaluate heterogeneity for each outcome, random-effects ($I^2 \geq 50\%$) and fixed-effects ($I^2 < 50\%$) models were used. When $I^2 \geq 50\%$ and $P < 0.05$, subgroup analysis was carried out for the dialysis method and literature quality. We performed sensitivity analysis for all outcomes. $P < 0.05$ was considered statistically significant. All analyses were conducted using R studio 4.0.3 (www.r-project.org; The R Foundation for Statistical Computing, Vienna, Austria).

Results

Literature search and study characteristics

In a search of the selected electronic databases, 12,076 studies were initially identified in total. After removing duplicates, 7839 studies for subsequently screened. Finally, 55 studies were included.[5,7,13–65] A flow diagram of the complete search strategy, article screening, and exclusion and inclusion processes in this review are shown in Figure 1.

There was a total of 104,758 participants in the 55 studies, with follow-up times ranging from 1 to 15 years. A total of 14,624 patients died, with up to 15 years of follow-up. Among the 55 studies, 32 were assessed as high quality and 23 as low quality. The baseline characteristics of the study participants are summarized in Table 1.

Qualitative analysis of included studies

Regarding dialysis methods, HD treatment was used in 31 of 55 studies and PD treatment in 16 studies; 4 studies used a combination of these two treatments. For the bioimpedance method, 18 of 55 studies reported the overhydration index (OHI) method, 16 studies the PA method, 11 studies the extracellular water expressed as a ratio (ECWR) method, 2 studies the bioimpedance vector analysis method, and 2 studies reported the OHI+ECWR method;

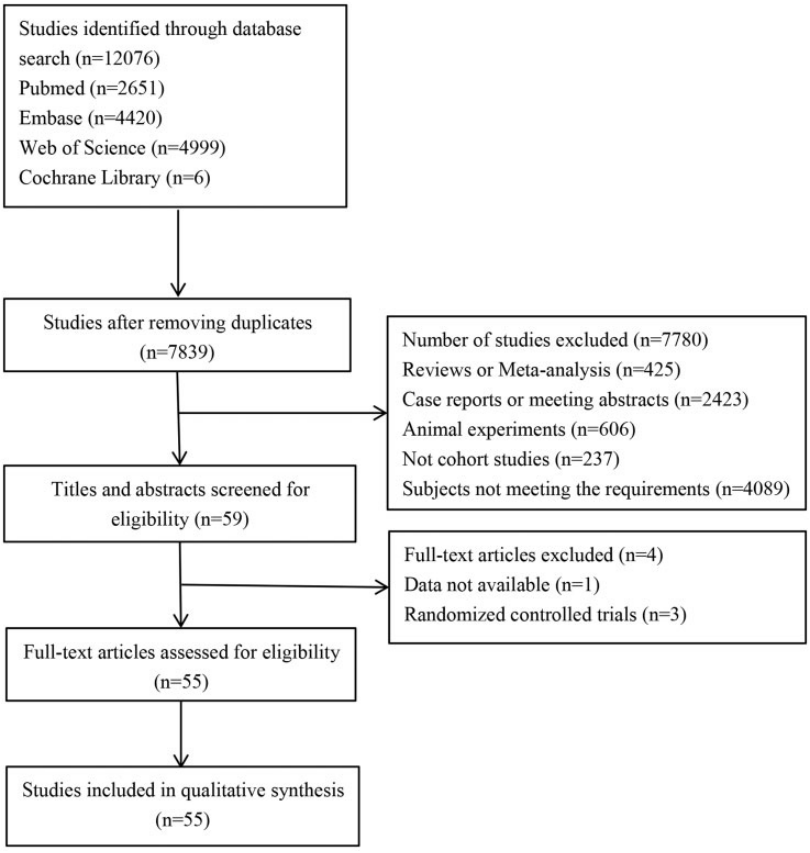

Figure 1. Flow chart of the literature search.

Table 1. Baseline characteristics of included studies.

Author	Year	Country	Dialysis method	N	Age, years	BMI, kg/m^2	Male/ Female	Follow-up (years)	Primary outcome	Secondary outcome	Mortality	BIA method	NOS score	Quality
Abad[22]	2011	Spain	127 HD, 37 PD	164	61.1±14.5	25.3±5.0	99/65	6	Mortality	NA	100	PA	5	HQ
Avram[23]	2006	USA	PD	177	54±16	25.4±4.94	73/104	15	Mortality	NA	89	PA	2	LQ
Beberashvili[24]	2014	Israel	HD	91	64.0±11.5	28.1±5.5	57/34	3	Mortality	NA	38	PA	6	HQ
Beberashvili (1)[25]	2014	Israel	HD	250	68.7±13.6	26.6± 4.5	158/92	1.4	Mortality	NA	64	PA	5	HQ
Caetano[26]	2016	Portugal	HD	697	67 (55.5–76)*	(25–29.9)*	394/303	1	Mortality	NA	66	OHI	5	HQ
Chazot[7]	2012	France	HD	158	64.7±13.8	26.9±5.1	78/80	6.5	Mortality	Hypertension	unclear	OHI	4	LQ
Chen[27]	2007	China	PD	227	59.53±14.37	23.27±3.57	100/127	3	Mortality	NA	58	ECWR	5	HQ
de Araujo[28]	2012	Brazil	109 HD, 36 PD	145	54.9±15.4	24.7 (21.9–28.7)*	72/73	1.3	CV events	Mortality	13	PA	5	HQ
Dekker[29]	2017	International	HD	8883	63±14.8	NA	5081/3802	1	Mortality	NA	unclear	OHI	4	LQ
Demirci[30]	2016	Turkey	HD	493	57.7±13.9	26.1±4.8	253/240	2.3	Mortality	CV mortality	93	BIVA	5	HQ
Di Iorio[52]	2004	Italy	HD	515	63.62±15.35	24.56±4.45	316/199	1.25	Mortality	NA	75	PA	4	LQ
Fan[31]	2015	UK	PD	183	54.9±15.6	NA	95/88	1.7	Mortality	Technique failure	37	ECWR	4	LQ
Fein[53]	2002	USA	PD	53	53	NA	17/36	8	Mortality	NA	21	ECWR	3	LQ
Fiedler[32]	2009	Germany	HD	90	61±14	NA	53/37	3	Mortality	Hospital admission events	36	PA	4	LQ
Guo[5]	2015	China	PD	307	47.8±15.3	22.7±3.9	132/175	3.2	Mortality	CV mortality	52	ECWR	6	HQ
Hoppe[33]	2015	Poland	HD	241	61.9±12.5	26.1±3.9	160/81	2.5	Mortality	NA	42	OHI	1	LQ
Jotterand Drepper[34]	2016	Germany	PD	54	56.1± 15.5	25.5±3.6	33/21	6.5	Mortality	NA	19	OHI	4	LQ
Kim[36]	2015	South Korea	HD	240	65.6±12.8	NA	147/93	2	Mortality	Hospital admission events	50	OHI	4	LQ
Kim[35]	2017	South Korea	HD	77	52.6±12.5	NA	40/37	5	Mortality	CV events	24	ECWR	4	LQ
Koh[37]	2011	Malaysia	PD	128	48.0±1.2	24.3±0.4	59/69	2.2-2.3	Mortality	NA	35	PA	5	HQ
Maggiore[54]	1996	Italy	HD	131	62.5±13.6	NA	66/65	2.2	Mortality	NA	23	PA	4	LQ
Mathew[38]	2015	India	85 HD, 14 PD	99	55.26±12.5	22.23±4.2	78/21	2	Mortality	NA	33	OHI	5	HQ
O'Lone[40]	2014	UK	PD	529	57.0 (46.7–68.8)*	NA	329/200	4	Mortality	NA	95	OHI+ECWR	4	LQ
Oei[39]	2016	UK	PD	336	57.9 (48.1–69.0)*	NA	207/129	2	Mortality	NA	48	OHI	4	LQ
Onofriescu[41]	2015	Romania	HD	221	53.8±13.9	25.5±5.0	116/105	5.5	Mortality	CV events	66	OHI	6	HQ
Paniagua[42]	2010	Mexico	388 HD, 365 PD	753	48.64±17.55	25.22±5.15	415/338	1.4	Mortality	CV mortality	182	ECWR	5	HQ

(continued)

Table 1. Continued.

Author	Year	Country	Dialysis method	N	Age, years	BMI, kg/m^2	Male/ Female	Follow-up (years)	Primary outcome	Secondary outcome	Mortality	BIA method	NOS score	Quality
Paudel[43]	2015	UK	PD	455	56.1± 0.7	26.8±0.3	278/177	2	Mortality	NA	72	OHI	3	LQ
Pillon[55]	2004	USA	HD	3009	60.5±15.4	NA	1589/1420	1.5	Mortality	NA	361	BIVA	4	LQ
Pupim[56]	2004	USA	HD	194	55.7±15.4	NA	102/92	3	Mortality	CV mortality	50	PA	4	LQ
Rhee[64]	2015	South Korea	PD	129	49.74±10.01	23.59±3.31	80/49	2.1	residual renal function	Mortality	15	ECWR	3	LQ
Segall[45]	2014	Romania	HD	149	53.9±13.7	22.8±8.1	82/67	1.1	Mortality	NA	43	PA	5	HQ
Shin[14]	2017	South Korea	HD	142	64±13	22.5 (20.4, 24.9)*	75/67	2.4	Mortality	CV mortality	15	PA	3	LQ
Siriopol[47]	2015	Romania	HD	173	57.9±14.0	NA	85/88	1.8	Mortality	NA	31	OHI	3	LQ
Siriopol (1)[48]	2017	Romania	HD	285	58.9 ±14.1	NA	136/149	3.4	Mortality	NA	89	OHI	5	HQ
Tangvoraphonchai[49]	2016	UK	HD	362	63 (50–76)*	NA	216/146	4.1	Mortality	NA	110	OHI	6	HQ
Tian[50]	2016	China	PD	152	60.5±12.8	24.0±3.8	62/90	5	Mortality	NA	44	ECWR	4	LQ
Wizemann[21]	2009	Poland	HD	269	65±15	25.6±4.7	NA	3.5	Mortality	NA	86	OHI	5	HQ
Zoccali[18]	2017	International	HD	39,566	60.9±15.7	27.1±18.5	23593/15973	1.4	Mortality	NA	5866	OHI	5	HQ
Arrigo[57]	2018	Switzerland	HD	144	73 (59–81)*	NA	88/56	1	Mortality	NA	27	OHI	5	HQ
Avram[58]	2010	USA	PD	62	54±16	NA	28/34	8	Mortality	NA	21	ECWR	6	HQ
Bansal[59]	2018	USA	HD	3751	58.1±11.6	29.0±5.9	2047/1704	7	Mortality	CV events	776	PA	5	HQ
Beberashvili[60]	2010	Israel	HD	81	64.3±11.9	28.3±5.6	53/28	2.2	Mortality	NA	22	PA	5	HQ
Ng[15]	2018	China	PD	311	58.8±12.2	24.9±4.3	172/139	2.2	Mortality	CV events	81	OHI+ECWR	4	LQ
Hecking[61]	2018	Germany	HD	38,614	60.9±15.7	25.9±5.3	23011/15603	1	Mortality	NA	5640	OHI	7	HQ
Huang[62]	2018	China	HD	178	60.9±11.6	23.9±3.8	87/91	2.7	Mortality	CV mortality	24	OHI	5	HQ
Huang[13]	2019	China	PD	760	45.2±14.5	22.5±3.2	465/295	2	Mortality	CV events	125	PA	5	HQ
Kim[17]	2018	South Korea	HD	142	64±13	23.4±8.5	75/67	2.4	Mortality	CV events	15	ECWR	6	HQ
Mushbick[63]	2003	USA	PD	48	51±15	25.7±5.0	25/23	2	Mortality	NA	8	PA	3	LQ
Rhee[19]	2018	South Korea	HD	208	65.19±12.9	22.62±3.21	208/0	1	Mortality	NA	84	ECWR+PA	6	HQ
Voroneanu[65]	2014	Romania	HD	98	55.4±13.2	NA	49/49	2	Mortality	CV mortality	16	N- proBNP and hs–cTnT	5	HQ
Yajima[16]	2019	Japan	HD	234	65.1±12.6	22.0±3.8	162/72	2.8	Mortality	CV mortality	72	ECWR	6	HQ

*Indicates extreme value.

Notes: References[5] and[20] had the same study population, but the follow-up time was different; thus the basic data in reference[20] were not included in Table 1. This was similar for references[44] and[45], and references[47,48,] and[46].

Values are mean±standard deviation or (range).

PD, peritoneal dialysis; HD, hemodialysis; N, number of samples; BMI, body mass index; CV, cardiovascular; BIA, bioelectrical impedance analysis; BIVA, bioelectrical impedance vector analysis; ECWR: extracellular water ratio; PA, phase angle; hs-cTnT, high-sensitivity cardiac T troponin; NT–pro-BNP, N-terminal pro–B-type natriuretic peptide; OHI, overhydration index; NOS, Newcastle–Ottawa scale; LQ: low quality; HQ, high quality; TBW, total body water; ICW, intracellular water; ECW, extracellular water; NA, not available.

only 1 study reported the PA+ECWR method and 1 study the N-terminal pro–B-type natriuretic peptide+high-sensitivity cardiac T troponin method.

Studies were divided into primary outcomes and secondary outcomes. Death was the primary outcome in 49 studies, CV events was the primary outcome in 1 study, and residual renal function was the primary outcome in 1 study. Secondary outcome events were reported in 20 articles, mainly CV death (8 articles), CV disease (6 articles), hospitalization events (2 articles), death (2 articles), hypertension (1 article), and technical failure (1 article).

Risk of mortality

There was no heterogeneity among two included studies;[5,17] therefore, we used a fixed-effects model for the analysis (I^2=0.0%). We found that an ECW/TBW ratio >0.4 was a significant risk factor for mortality, with HR (95% CI) 5.912 (2.016–17.342), P=0.001 (Table 2).

Two studies[16,35] on ECW/ICW (per increment of 0.01) showed no remarkable heterogeneity (I^2=45.7%). The result indicated that each 0.1-unit increase in the ECW/ICW ratio could independently predict the mortality risk: HR (95% CI) 1.041 (1.031–1.051), P<0.001 (Table 2).

Considerable heterogeneity was present after combining six studies[13,14,19,24,25,37] (I^2=73.6%); therefore, a random-effects model was used for the analysis. A 1-degree increase in PA was found to be a protective factor against death: HR (95% CI) 0.676 (0.474–0.879), P<0.01 (Table 2; Figure 2a). However, owing to the significant heterogeneity among the six studies, subgroup analysis was conducted for the dialysis method and quality assessment. In terms of dialysis method, a 1-degree increase in PA was associated with a reduced risk of death in patients receiving PD (HR 0.488, 95% CI: 0.225–0.751, P<0.05) and HD (HR 0.749, 95% CI: 0.511–0.986, P<0.05) treatment (Table 2; Figure 2b). The same result was observed in both the high-quality articles (HR 0.686, 95% CI: 0.467–0.905, P<0.05) and low-quality articles (HR 0.560, 95% CI: 0.021–1.099) (Table 2; Figure 2c).

In eight studies,[7,18,21,26,29,34,36,41] OH/ECW >15% was an independent risk factor for death: HR (95% CI): 2.722 (2.005–3.439), P<0.001 (Table 2; Figure 3a). A subgroup analysis was conducted for the dialysis method and quality assessment with large heterogeneity (I^2=97.3%). Results of the subgroup analysis showed that OH/ECW >15% was closely related to the risk of death in patients undergoing HD (HR 2.265, 95% CI: 1.602–2.929, P<0.01) and PD (HR 7.820, 95% CI: 6.183–9.457, P<0.05) treatment (Table 2; Figure 3b). The same result was found for high-quality studies (HR 1.833, 95% CI: 1.259–2.407, P<0.05) and low-quality studies (HR 3.835, 95% CI: 2.548–5.122, P<0.05) (Table 2; Figure 3c).

Risk of CV events

There were two studies on ECW/TBW ratio >0.4,[5,17] two studies on ECW/ICW (per increment of 0.01),[16,35] and three studies on PA.[13,14,31] Among them, ECW/TBW >0.4 (HR 2.679, 95% CI: 1.345–5.339, P=0.005) and every 0.01 unit increment in ECW/ICW ratio (HR 1.032, 95% CI: 1.017–1.047, P<0.001) were considered risk factors for CV events whereas a 1-degree increase in PA (HR 0.736, 95% CI: 0.589–0.920, P=0.007) emerged as a protective factor against CV events (Table 2).

Sensitivity analysis and publication bias assessment

To determine the effect of individual studies on HRs, we carried out sensitivity analysis for each outcome. The results revealed that

Table 2. Results of overall meta-analysis.

Characteristics	HR (95% CI)	*P*	I^2
Mortality			
ECW/TBW >0.4			
Overall	5.912 (2.016–17.342)	0.001	0.0
Sensitivity analysis	5.912 (2.016–17.342)		
ECW/ICW for every increase by 0.01			
Overall	1.041 (1.031–1.051)	<0.001	45.7
Sensitivity analysis	1.041 (1.031–1.051)		
1-degree increase in PA			
Overall	0.676 (0.474–0.879)	<0.01	73.6
Sensitivity analysis	0.676 (0.474–0.879)		
Dialysis method			
HD	0.749 (0.511–0.986)	<0.05	78.5
PD	0.488 (0.225–0.751)	<0.05	0.0
Quality assessment			
High quality	0.686 (0.467–0.905)	<0.05	78.3
Low quality	0.560 (0.021–1.099)	>0.05	NA
OH/ECW >15%			
Overall	2.722 (2.005–3.439)	<0.001	97.3
Sensitivity analysis	2.722 (2.005–3.439)		
Dialysis method			
HD	2.265 (1.602–2.929)	<0.05	96.9
PD	7.820 (6.183–9.457)	<0.05	NA
Quality assessment			
High quality	1.833 (1.259–2.407)	<0.05	90.7
Low quality	3.835 (2.548–5.122)	<0.05	92.7
Cardiovascular events			
ECW/TBW >0.4			
Overall	2.679 (1.345–5.339)	0.005	0.0
Sensitivity analysis	2.679 (1.345–5.339)		
ECW/ICW for every increase by 0.01			
Overall	1.032 (1.017–1.047)	<0.001	49.2
Sensitivity analysis	1.032 (1.017–1.047)		
1-degree increase in PA			
Overall	0.736 (0.589–0.920)	0.007	0.0
Sensitivity analysis	0.736 (0.589–0.920)		

OH, overhydration; TBW, total body water; ICW, intracellular water; ECW, extracellular water; PA, phase angle; PD, peritoneal dialysis; HD, hemodialysis; HR, hazard ratio; NA, not applicable; CI, confidence interval.

removing each study did not remarkably affect the overall HR, and the results of this meta-analysis were reliable and robust (Table 2). Additionally, there were fewer than nine studies included for each indicator in our study, which did not conform to the standard of publication bias.

Discussion

Recently, there has been increasing evidence that fluid overload is frequently present in a substantial number of patients receiving dialysis.[6] More than one-third of incident patients undergoing dialysis, who

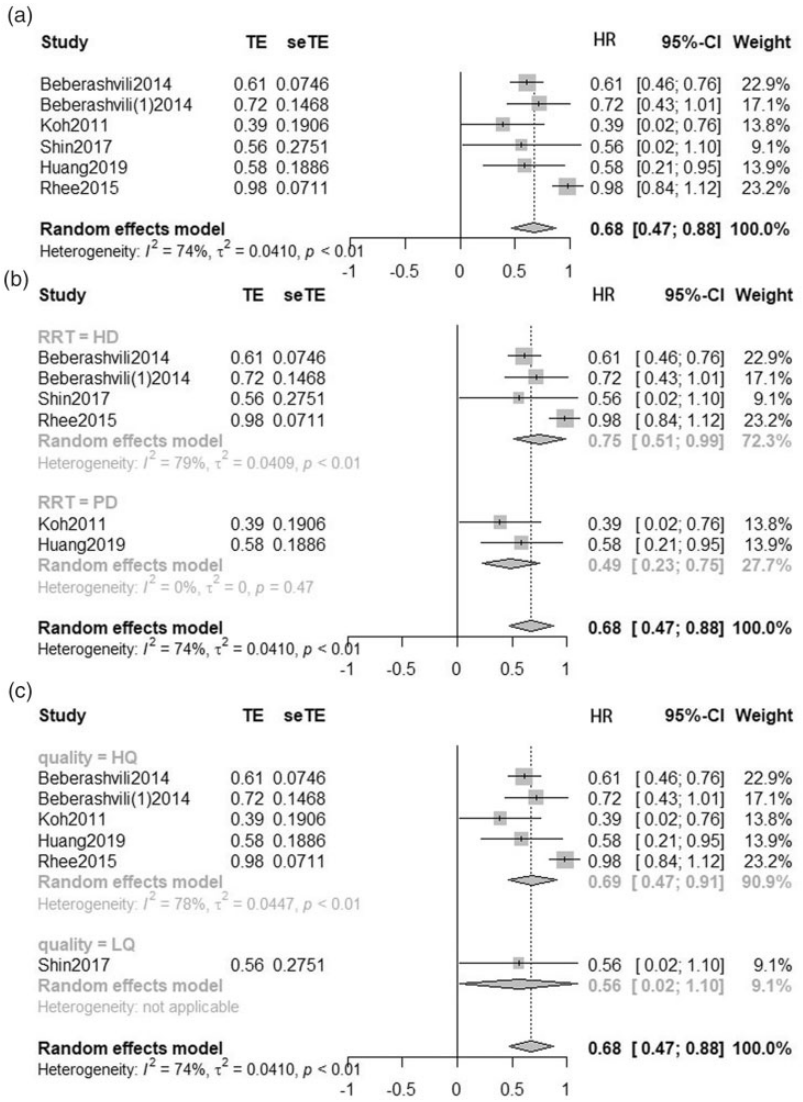

Figure 2. Forest plots of mortality among patients receiving dialysis with a 1-degree increase in phase angle. (a) Overall analysis; (b) subgroup analysis for dialysis method; (c) subgroup analysis for quality assessment.

TE, hazard ratio; seTE, standard error; HR, hazard ratio; CI, confidence interval; RRT, dialysis method; PD, peritoneal dialysis; HD, hemodialysis; HQ, high quality; LQ, low quality.

are considered euvolemic or dehydrated on clinical assessment, have fluid overload using BIA measurement.[4] Therefore, it is critical to make an accurate assessment of hydration status in this patient population. In our meta-analysis, four electronic databases were comprehensively searched to clarify the role of BI-OH markers in predicting the risk of mortality and CV events for patients receiving HD and PD. A total of 55 studies including 104,758 participants were identified. Among the BI-OH indices,

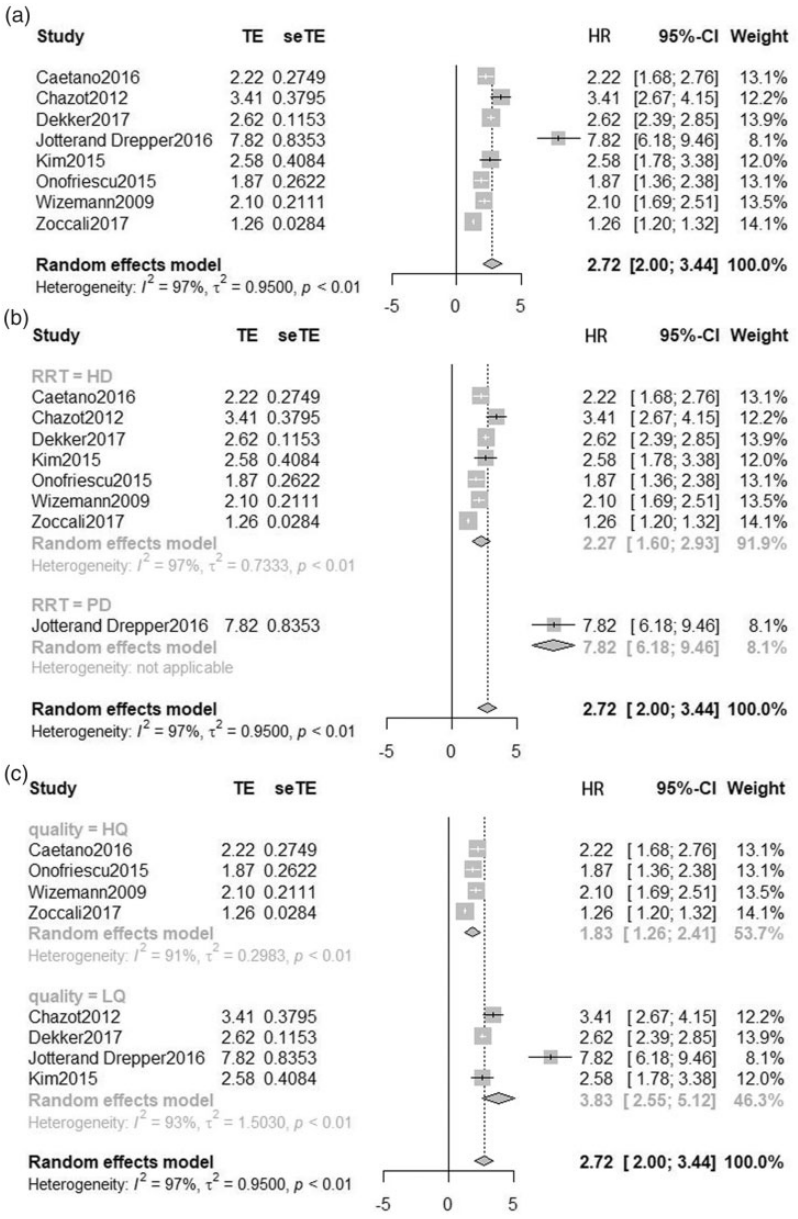

Figure 3. Forest plots of mortality among patients receiving dialysis with overhydration/extracellular water ratio >15% (a) overall analysis; (b) subgroup analysis for dialysis method; (c) subgroup analysis for quality assessment.
TE, hazard ratio; seTE, standard error; HR, hazard ratio; CI, confidence interval; RRT, dialysis method; PD, peritoneal dialysis; HD, hemodialysis; HQ, high quality; LQ, low quality.

ECW/TBW >0.4 and ECW/ICW (per increment of 10%) were found to be risk factors for mortality and CV events. Moreover, OH/ECW >15% was related to a reduced risk of death. Additionally, a 1-degree increase in PA emerged as a protective factor against mortality and CV events. All results suggested that multiple BI-OH parameters are associated with the risk of mortality and CV events, which may provide practical information to predict clinical outcomes among patients receiving dialysis.

Of note, there were various indices used to evaluate hydration status when using BIA to measure the risk of mortality. The ECW/TBW ratio was frequently used whereas OH/ECW and ECW/ICW were less frequently adopted. ECW/TBW ratios among patients were consistent, although the absolute values of ECW and TBW were different,[9] thus leading to the wide use of ECW/TBW. Multiple studies showed that the ECW/TBW ratio as a risk factor independently predicted mortality.[5,15,17] In 529 patients undergoing PD, O'Lone et al. found that this ratio as a continuous variable was not associated with increased mortality.[40] Kang et al. conducted a retrospective study of 631 unselected incident patients on PD and concluded that a higher overload index (ECW/TBW >0.37) was associated with an increase in mortality;[66] the ECW/TBW ratio showed a slightly significant difference. According to deviations from the normal value, a possible explanation may be patients' nutritional status (including age and sex). The study by Shu et al.[67] showed that ECW/ICW (per increment of 10%) remained a risk factor after adjusting obesity, age, sex, ethnicity, and other confounders, which would make the results more reliable and consistent with our results. PA level is calculated using BIA measurements as the arc tangent of the reactance-to-resistance ratio. Our results have been further confirmed in a previous study.[12] A meta-analysis also indicated that a 1-degree decrease in PA level is considered a risk factor of mortality,[12] indirectly suggesting results that are consistent with our results. In a single-center, retrospective study by Rhee et al. including 208 patients with acute kidney injury, a 1-degree increase in PA did not show any statistical significance in the prediction of in-hospital mortality ($P>0.05$).[64] The reason may be related to the large number of studies included in our study and different study populations.

Another clinical outcome, CV events, can also occur in patients on dialysis. BI-OH indices are important predictors of their occurrence and development, which can serve to predict the risk of CV events. Prior studies have confirmed that every 0.1-unit increase in the ECW/ICW ratio and ECW/TBW >0.4 are risk factors for CV events, which is supported by Ng et al.[15] In contrast to our results, CV events were found to be associated with PA in one study, mainly owing to a small number of patients and other confounding factors.[14] PA cutoff values should be obtained for routine assessment and improving outcomes in patients receiving dialysis, but these outcomes were rarely determined in the included studies.

Our study has several strengths as follows. First, this meta-analysis included a considerable number of studies with large sample sizes (from 48 to 39,566), which may make our results more generalizable and reliable. Second, identical criteria were applied between studies in classifying BI-OH methods, which did not limit further meta-analyses and subgroup analyses for each hydration indicator. The main limitation of our meta-analysis was the absence of publication bias. The reason may be the inclusion of fewer than 9 studies for each indicator in our study, which does not conform to the standard of publication bias.

Unadjusted HRs were used in our cohort studies, which may be a source of bias.

Conclusions

Our results showed that ECW/TBW >0.4, ECW/ICW (per each 0.1-unit increase), and OH/ECW >15% were risk factors for mortality in patients receiving dialysis. ECW/TBW >0.4 and ECW/ICW (per increment of 10%) were associated with an increased risk of CV events; a 1-degree increase in PA was a protective factor against mortality and CV events.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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