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NEPHROLOGY – ORIGINAL PAPER

Value of bioimpedance analysis estimated "dry weight" in maintenance dialysis patients: a systematic review and meta-analysis

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Abstract

Background Volume overload is a common complication in patients with end-stage kidney disease who undergo maintenance dialysis therapy and associated with hypertension, left ventricular hypertrophy and mortality in this population. Although bioimpedance analysis (BIA), an objective method to assess overhydration, is associated with poor outcomes in observational studies, in randomized controlled trials (RCTs) the results were conflicting. We have examined the role of BIA for assessing the "dry weight" and fluid status in order to improve fluid overload in comparison with a control or clinical-based prescription in patients with ESKD receiving haemodialysis or peritoneal dialysis.

Methods All RCTs and quasi-RCTs in which BIA was used to improve fluid overload and assess the effect on all-cause mortality, cardiovascular morbidity, systolic blood pressure and volume control and arterial stiffness were included.

Results Seven RCTs with 1312 patients could be included in this review. In low-to-medium quality of the evidence, the use of BIA did not reduce all-cause mortality (relative risk 0.87, 95% CI 0.54–1.39) and had small to no effect on body change, but it improved systolic blood pressure control (mean difference (MD) −2.73 mmHg, 95% CI −5.00 to −0.46 mmHg) and reduce overhydration, as measured by BIA, with 0.43 L [(MD), 95% CI 0.71–0.15 L].

Conclusion In ESKD patients, BIA-based interventions for correction of overhydration have little to no effect on all-cause mortality, whereas BIA improved systolic blood pressure control. Our results should be interpreted with caution as the size and power of the included studies are low. Further studies, larger or with a longer follow-up period, should be performed to better describe the effect of BIA-based strategies on survival.

Keywords Volume control · Bioimpedance analysis · Haemodialysis · Cardiovascular disease · Mortality · Blood pressure · Hypertension

Adrian Covic and Adi-Ionut Ciumanghel have equally contributed to the paper.

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Introduction

It is estimated that there are approximately 3 million patients with end-stage kidney disease (ESKD) in the world [1]. Although a decline in mortality has been observed in recent years, the mortality in patients starting dialysis is more than eight fold higher than in the general population [2] with more than 40% of deaths due to the cardiovascular causes [3].

Volume overload is the most common complication in ESKD ranging from 10 to 60% in previous studies [1, 4, 5] and is dependent on several factors, including sodium and fluid intake, cardiac function, residual kidney function,

dialysate composition and ultrafiltration volume [1]. It is associated with hypertension, left ventricular (LV) hypertrophy and mortality in the dialysis population [6–9].

Clinical evaluation of fluid overload can be difficult in ESKD populations and prone to underestimation or overestimation. Objective methods have been proposed for defining fluid overload: inferior vena cava collapse index, left atrial volume on echocardiography, flat slopes on plasma volume slope monitoring, evaluation of NT-proBNP, lung ultrasonography or bioimpedance. The most utilized and increasingly validated approach to objectively assess (over) hydration is the use of bioimpedance. This technique has been used in different forms (single/multiple frequency, segmental/whole body) and is validated by isotope dilution methods, by accepted reference body composition methods and by techniques that measure relative changes in fluid volumes [10]. Bioelectrical impedance analysis (BIA) was also successfully used to guide HD patients towards normohydration and better blood pressure (BP) control [11].

Although initial observational studies have found an independent association between fluid overload and increased mortality in ESKD patients [12], the results from randomized trials are conflicting [13, 14]. Therefore, this review aims to critically analyse the benefits and harms of bioelectrical impedance analysis (BIA) measurements to guide fluid management in patients with ESKD receiving haemodialysis (HD) or peritoneal dialysis (PD).

Methods

We have conducted a systematic review and meta-analysis according to a previously published protocol (http://www.crd.york.ac.uk/PROSPERO/CRD42017067964). Also a Cochrane-based methodology [15] and previously published protocol was used as an example [16].

All randomized controlled trials (RCTs) and quasi-RCTs looking at BIA-based intervention to improve fluid status in people with ESKD will be eligible for inclusion.

Types of participants

Adults aged 18 years with ESKD and on chronic dialysis (>3 months).

Types of interventions

Studies assessing BIA-based strategies to improve fluid overload in comparison with a control or clinical-based prescription of a target weight were included.

Examples of interventions include BIA-based versus clinical-based prescription of target “dry weight” or BIA-based versus standard care prescription of target “dry weight”.

Types of outcome measures

Primary outcomes

1. All-cause mortality.
2. Cardiovascular morbidity [both fatal (myocardial infarction (MI), stroke, sudden death, congestive heart failure, arrhythmia) and non-fatal cardiovascular events (MI, stroke, congestive heart failure, arrhythmia)].

Secondary outcomes

1. Measures of volume status or changes in body volume, including interdialytic weight gain (IDWG) or daily weight gain and bioimpedance measurements of extracellular water (ECW).
2. Side effects, e.g. any symptomatic intradialytic hypotension (number of events and number of patients with events), nausea, vomiting, muscle cramps, restlessness, dizziness, fainting or anxiety [17] or any major adverse events as reported by the authors.
3. BP control SBP, MAP, DBP in mm Hg, at end of intervention, or change between beginning and end of intervention; or number of patients achieving BP target. In HD studies, pre-HD SBP measurements will be used.
4. Arterial stiffness, as assessed by pulse wave velocity, in m/s, at end of intervention, or change between beginning and end of intervention.

Search methods for identification of studies

We searched MEDLINE (to 1st of February 2017), clinicaltrials.gov website, the Cochrane Controlled Clinical Trials Register Database (through Issue 2 of 12, February2017), and hand-searched reference lists for relevant articles (Supplementary Table S1). We also wrote letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies. There was no language restriction.

The titles and abstracts were screened independently by two authors. Two authors independently assessed retrieved abstracts and, if necessary the full text, of these studies to determine which studies satisfy the inclusion criteria.

Data extraction was carried out independently by two authors using standard data extraction forms. Studies reported in non-English language journals were translated before assessment. When more than one publication of one study exists, reports were grouped together and the publication with the most complete data was used in the analyses. Any discrepancy between published versions was highlighted.

Assessment of risk of bias in included studies was independently assessed by two authors using the Cochrane risk of bias assessment tool [15].

Measures of treatment effect

For dichotomous outcomes (e.g. death, cardiovascular events), results were expressed as risk ratio (RR) with 95% confidence interval (CI). Where continuous scales of measurement are used to assess the effects of treatment (IDWG, SBP), the mean difference (MD) was used, or the standardized mean difference (SMD) if different scales have been used. For continuous data, the preferred data were the end of treatment data. If data were reported at more than one time point during the study, all data were extracted. If outcome data for a study were reported for more than one period of follow-up, we performed subgroup analyses for different periods of follow-up (≤6 weeks, >6 weeks to 12 weeks, >12 weeks). If a study had more than two intervention arms, the control group sample size was split by the number of subgroup comparisons for that study [15].

Heterogeneity was analysed using a Chi-square test on N − 1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I^2 test [18]. I^2 values of 25, 50 and 75 correspond to low, medium and high levels of heterogeneity. If possible, funnel plots were used to assess for the potential existence of small study bias [15]. Data were pooled using the random-effects model, but the fixed-effect model was used to ensure robustness of the model chosen and susceptibility to outliers.

If a sufficient number of studies are identified, subgroup analysis was used to explore possible sources of heterogeneity. The following subgroups were explored: dialysis modality: HD and PD, type of BIAs (type of device), endpoint measurement at different time points: ≤6 weeks, >6–12 weeks, >12 weeks, time on dialysis (dialysis vintage): <6 months versus >6 months, studies with high versus low risk of bias and geographical area: North America, Latin America, Asia, Europe.

We aimed to perform sensitivity analyses in order to explore the influence of the following factors on effect size: unpublished studies, taking account of risk of bias, excluding any very long or large studies.

Results

Description of studies

Results of the literature search

The systematic review yielded 171 references, 62 of which were considered potentially eligible after initial screening of titles and abstracts, and 12 relevant review articles were obtained for reference lists. Of the full-text articles screened, seven RCTs were included and six ongoing RCTs have been identified (Fig. 1).

Included studies

Seven studies were included in this systematic review, with five studies in HD ($n = 844$ patients) [13, 14, 19–21] and two in PD ($n = 468$ patients) [22, 23]. Six studies were published in English, and one study was in Portuguese. The overall mean age varied from 48.56 [19] to 62.7 years [20]. Mean dialysis vintage varied from 18 [23] to 107 months [13], and the study duration ranged from 12 [22] to 42 weeks [13]. All studies reported proportion of patients with hypertension or diabetes. BCM (multi-frequency impedance) was used in five out of seven studies [13, 14, 19, 20, 22]. Single-frequency bioimpedance methods were used in two studies [19, 23]. For one study, we found two reports, but only the most recent publication was included [13, 14]. The detailed baseline studies characteristics are presented in Tables 1 and 2.

Excluded studies

All the other studies were excluded due to study design (not a RCT), or due to interventions/populations that were not eligible (Fig. 1).

Risk of bias in included studies

Risks of bias in individual studies are shown in "Supplementary Figure 1"; a summary of the overall risks of bias is provided in Fig. 2. Trials generally had very serious limitations due to risks of bias in most domains leading to downgrading of overall evidence quality. The selection bias was unclear in five studies. Blinding of the participants was of high risk in three studies [21–23] since the access to measurements was not blinded and we considered that this might influence the clinical practice irrespective of the study arm or protocol. A high rate of dropout (>10%) and not using intention to treat analysis was considered of high risk of bias for four studies under attrition bias [20–23].

Serious adverse events were generally not reported with one exception [20].

Effects of interventions

All-cause mortality

For all-cause mortality, we included data from six studies [13, 14, 19–21, 23], with 1152 patients in total. BIA-based interventions had no significant effect on all-cause mortality

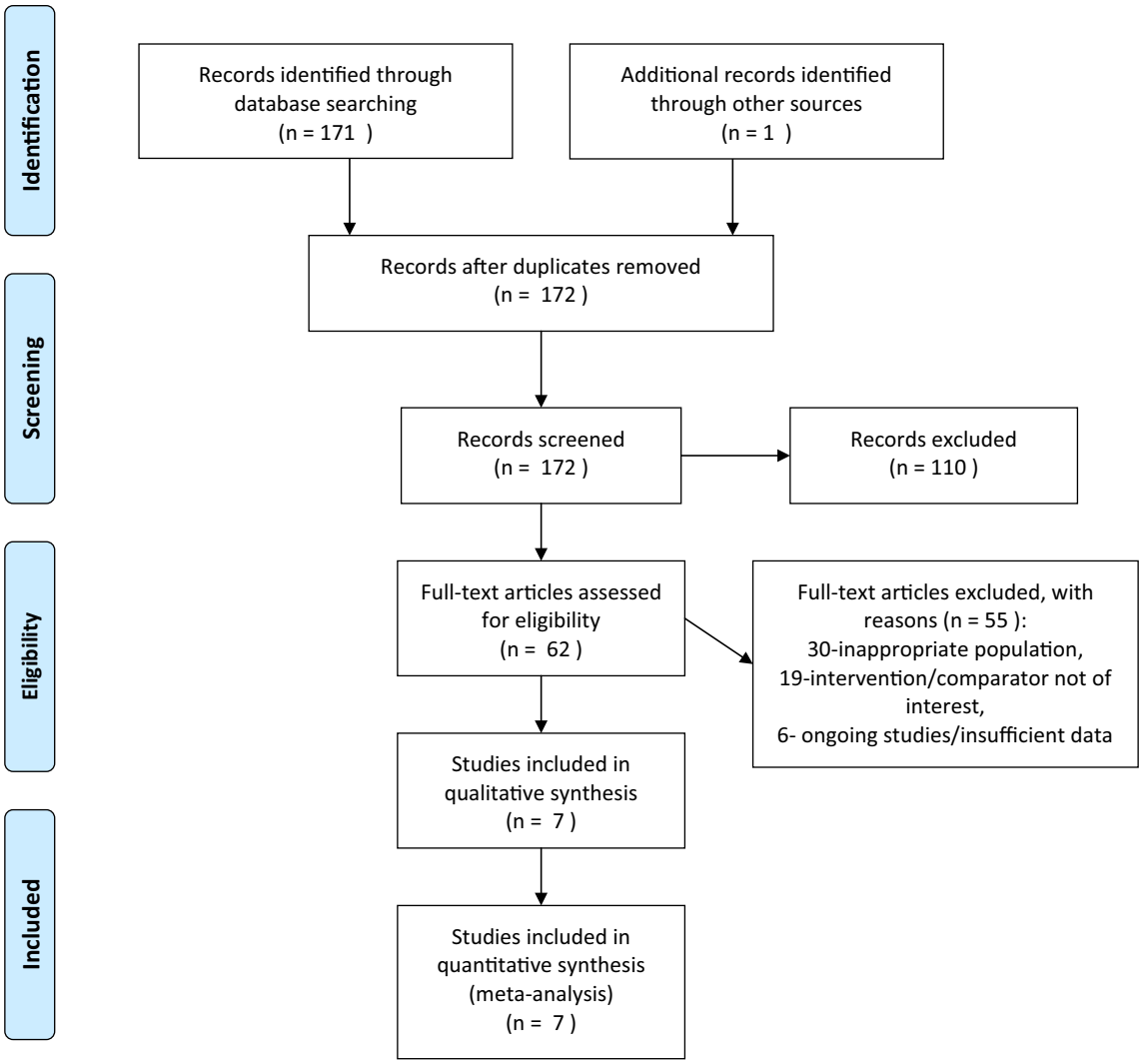

Fig. 1 Flow chart showing the number of citations retrieved by individual searches and number of trials included in the systematic review

(relative risk (RR) 0.87, 95% CI 0.54–1.39). Heterogeneity was low ($I^2 = 0$) (Fig. 3).

Cardiovascular mortality/morbidity

Insufficient data were reported/available in order to perform a cumulative meta-analysis on this outcome. Hur et al. [24] reported that six patients in the intervention group and four patients in the control group were hospitalized because of new cardiovascular events during the study period. Onofriescu et al. [13] reported one death from acute myocardial infarction and one death as sudden cardiac death in the clinical-methods group. For the bioimpedance group, no death was reported due to cardiovascular cause. Ponce et al. [21] reported that three patients died of acute myocardial infarction in the control group but do not report the number of events in the active group.

Measures of volume status or changes in body volume

Different ways of reporting this outcome were found: overhydration (L), ECW, ICW, E/I, relative fluid overload (RFO), percentage of patients overhydrated, etc. Using different methods to report changes in hydration status, all the included studies described a significant reduction in the overhydration status in the interventional arm (bioimpedance arm). For example, Onofriescu et al. [13] reported a significant decrease in relative fluid overload in the bioimpedance group, from 9.52 to 7.46% (mean difference, 2.05; 95% confidence interval [CI], 1.10–5.70%; $p < 0.03$). The cumulative analysis of the end of treatment level of overhydration showed a statistically significant 0.43 L less OH in the intervention arm (Fig. 4).

Table 1 Baseline characteristics of the studies

Authors	Type of study	Population	Type BIA	Study group	Control group	Follow-up (months) (m)	Intervention	Inclusion criteria	Exclusion criteria	Outcomes
Luo [22]	RCT	160 CAPD	BCM	78	82	3	Patients and nurses were informed about the overhydration as measured by BCM every 6 weeks	Stable PD patients (CAPD), >18 years, on PD for at least 3 months, no acute infection or new cardiovascular event	–	Changes in overhydration, changes in BP control and BP medication
Ponce [21]	RCT	189 HD	BCM	101	88	12	One monthly BCM measurements were available and used as targets to improve overhydration	HD patients, older than 18, with a relative predialytic overhydration (OH) at baseline of >15% (on average >2.5 L) as assessed by the (BCM©). All patients were treated by three times weekly online HDF treatment of ≥4 h per session	Any kind of metal implants or metal prosthetic joints, e.g. implanted defibrillators, cardiac pacemakers, with major amputations, pregnant women, and patients with symptomatic aortic valve stenosis	Correction of overhydration, hypotensive events, blood pressure control, mortality, hospitalizations and side effects
Onofriescu [13]	RCT	131 HD	BCM	62	69	42	Dry weight prescription using results derived from repeated 3-month bioimpedance measurements to guide ultrafiltration for strict volume control compared with clinical judgement without bioimpedance measures	All adult patients (aged >18 years), on maintenance HD therapy for more than 3 months	Limb amputations, metallic joint prostheses, absence of a permanent vascular access, decompensated cirrhosis, pregnancy, or a cardiac stent or pacemaker	The primary outcome was all-cause mortality over 2.5 years (the duration of the intervention) secondary outcomes were change in relative arterial stiffness, fluid overload, and blood pressure (BP)

Table 1 (continued)

Authors	Type of study	Population	Type BIA	Study group	Control group	Follow-up (months) (m)	Intervention	Inclusion criteria	Exclusion criteria	Outcomes
Hur [14]	RCT	156 HD	BCM	78	78	12	In the intervention group (n 78), fluid overload information was provided to treating physicians and used to adjust fluid removal during dialysis. In the control group (n 78), fluid overload information was not provided to treating physicians and fluid removal during dialysis was adjusted according to usual clinical practice	Patients willing to participate in the study with written informed consent, older than 18 years, and on maintenance HD therapy scheduled thrice weekly (12 h weekly) for 3 months or longer	pacemaker or defibrillator, artificial joints or pins, amputation, permanent or temporary catheters, being scheduled for living donor kidney transplantation, presence of serious life-limiting comorbid situations (e.g. malignancy, uncontrollable infection, and end-stage cardiac, pulmonary, or hepatic disease), being pregnant, or lactating	The primary outcome was regression of left ventricular mass index during a 1-year follow-up improvement in blood pressure and left atrial volume were the main secondary outcomes changes in arterial stiffness parameters were additional outcomes
Darlan [19]	RCT	70 HD	BIA	34	36	4	Patients were submitted to a baseline interdialytic 24 h-ABPM and were randomized to one of two different strategies to establish the dry weight: clinical evaluation only or clinical evaluation plus bioimpedance	Chronic renal failure patients on programme of renal replacement therapy by haemodialysis for more than three [3] months, clinically stable, undergoing treatment in dialysis units in the cities of Carazinho and Paved, inside the Rio Grande do Sul, aged between 18 and 80 years	Infectious, decompensation (requiring hospitalization for infectious cause), heart disease (myocardial infarction less than three months or hospitalization for heart failure) or respiratory disease (requiring treatment for asthma or chronic bronchitis)	Systolic and diastolic blood pressure measured by 24 h-ABPM, before and after the intervention and the occurrence of intradialytic symptoms related to extracellular depletion, as muscle cramps and hypotension

Table 1 (continued)

Authors	Type of study	Population	Type BIA	Study group	Control group	Follow-up (months) (m)	Intervention	Inclusion criteria	Exclusion criteria	Outcomes
Huan-Sheng [20]	RCT	298 HD	BCM	148	150	12	The participants were randomized into study group (dry weight (DW) determined by BCM-BIS) and control group (dry weight determined by clinical symptoms) with stratification by diabetes mellitus and centres	MHD patients with age ≥18 and dialysis vintage ≥3 months	Coronary stents or pacemaker implantation Metallic devices in body, such as artificial joints or pins Contralateral or bilateral amputations Pregnancy	All-cause Hospitalization, Complications During DW Adjustment; intradialysis morbidities
Tan [23]	RCT	308 CAPD	BI 101 ASE	149	158	12	To determine whether availability of longitudinal BI measures as vector plots helped clinicians maintain stable fluid status	Sequential patients attending clinic who were willing to be enrolled, only excluding patients unlikely be on PD for more than 6 months for whatever reason		Fluid volumes, ECW, TBW, and their ratio (ECW/TBW) secondary clinical outcomes—blood pressure, residual kidney function, membrane function, and dialysis dose

Table 2 Baseline studies characteristics and reported outcomes

Study	*N*	Intervention versus comparison	Follow-up duration (months)	Age (years)	Male sex *N* (%)	Diabetes *N* (%)	Cardiovascular disease history %	Diuretics	Body mass index (kg/m^2)	Anuria (%)	Dialysis vintage (months)	Residual kidney function %	Dialysis vascular access primary	Outcome
Luo 2011 [22]	160 PD	BCM versus Clinic	3	59.63 ± 13.9 60.28 ± 16.0	43.6% 48.8%	26.9% 28.0%	N/A	N/A	N/A	N/A	35.2 ± 32.34 33.2 ± 30.97	100	PD	1. Changes in overhydration 2. Changes in blood pressure
Darlan M. L. 2010 *NCT01104909 [19]*	70 HD	BIA versus Clinic	4	48.56 ± 13.7 49.11 ± 16.4	50% 52.8%	20.6% 19.4%	N/A	N/A	24.1 ± 5.6 24.33 ± 4.2	N/A	54.91 ± 55.1 42.53 ± 36.2	N/A	N/A	The reduction of dry weight and of blood pressure
Hur E 2013 *NCT00974857 [14]*	156 HD	BCM versus Clinic	12	50.9 ± 13.2 52.4 ± 11.4	44 (68.8) 43 (69.4)	15 (19.2) 12 (15.4)	24% 22%	N/A	26.1 ± 4.4 26.3 ± 4.5	76% 77%	63.8 ± 45.7 59.9 ± 43.9	N/A	100% AVF	1. Regression of left ventricular mass index 2. Improvement in blood pressure and left atrial volume
Ponce 2014 [21]	189 HD	BCM versus Clinic	12	65.82 ± 14.5 66.7 ± 15.1	72 (71.3) 72 (81.8)	39 (38.6) 35 (39.8)	72.3% 73.9%	N/A	24.15 ± 3.68 24.45 ± 3.49	N/A	N/A	N/A	N/A	1. Changes in hydration status 2. Hypotensive events 3. Blood pressure 4. Death/hospitalization

Table 2 (continued)

Study	*N*	Intervention versus comparison	Follow-up duration (months)	Age (years)	Male sex *N* (%)	Diabetes *N* (%)	Cardiovascular disease history %	Diuretics	Body mass index (kg/m^2)	Anuria (%)	Dialysis vintage (months)	Residual kidney function %	Dialysis vascular access primary	Outcome
Huan-Sheng 2016 [20] *NCT02325856*	298 HD	BCM versus Clinic	12	62.7 ± 12.1 62.1 ± 11.5	65 (43.9) 80 (53.3)	56 (37.84) 56 (37.33)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1. All-cause hospitalization 2. Complications during DW adjustment
Onofriescu 2014 [13] *NCT01828658*	131 HD	BCM versus Clinic	42	52 ± 13 54 ± 13	54% 52%	10% 9%	65% 73%	N/A	24 ± 3 25 ± 5	N/A	107 ± 60 104 ± 57	N/A	N/A	1. All-cause mortality 2. Change in relative arterial stiffness, fluid overload, and blood pressure (BP)
Tan B. K. 2016 [23] *NCT00801112*	131 DP	BI 101 ASE versus Clinic	12	58.3 ± 15.3 56.9 ± 14.7	38 (65.5) 44 (60.3)	N/A	N/A	54.3 54.8	N/A	0	18 (7–32) 22 (8–34)	100	PD	1. Change in ECW and body composition 2. Blood pressure, residual kidney function, membrane function, and dialysis dose.

Table 2 (continued)

Study	*N*	Intervention versus comparison	Follow-up duration (months)	Age (years)	Male sex *N* (%)	Diabetes *N* (%)	Cardiovascular disease history %	Diuretics	Body mass index (kg/m^2)	Anuria (%)	Dialysis vintage (months)	Residual kidney function %	Dialysis vascular access primary	Outcome
Tan B.K. 2016 [23] *NCT00801112*	SH non-anuric 84	BI 101 ASE versus Clinic	12	56.6 ± 11.2 52.5 ± 14.4	16 (38.1) 11 (26.2)	N/A	N/A	29.3 28.6	N/A	0	17 (7–37) 24 (11–41)	100	PD	1. Change in ECW and body composition 2. Blood pressure, residual kidney function, membrane function, and dialysis dose.
Tan B.K. 2016 [23] *NCT00801112*	SH anuric 75	BI 101 ASE versus Clinic	12	51.1 ± 13.1 55.5 ± 13.5	19 (50) 23 (62.2)	N/A	N/A	0 2.6	N/A	100	52 (22–86) 65 (31–105)	0	PD	1. Change in ECW and body composition 2. Blood pressure, residual kidney function, membrane function, and dialysis dose.

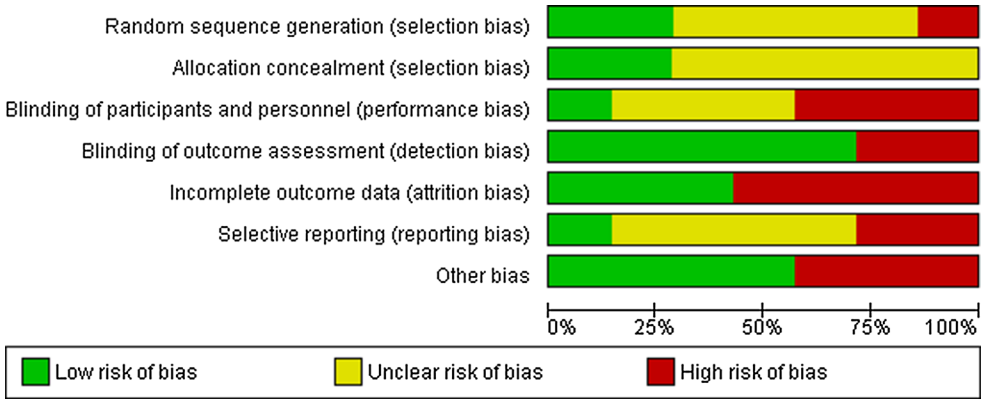

Fig. 2 Risk of bias graph review authors' judgements about each risk of bias item presented as percentages across all included studies

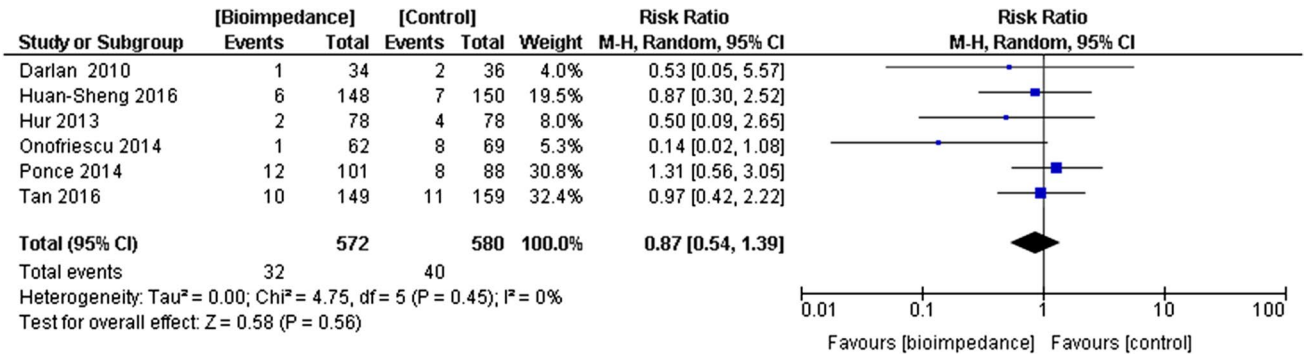

Fig. 3 Forest plot for all-cause mortality

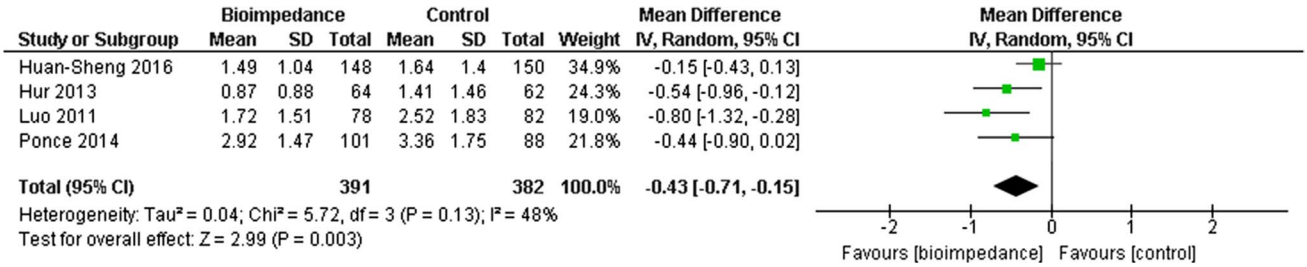

Fig. 4 Forest plot for change in overhydration (L)

Effect on end of treatment body weight and change in body weight

Data regarding body weight, end of treatment value or changes during the follow-up were reported by five studies [14, 19, 20, 22, 23]. In the cumulative analysis, we found no significant difference between the standard care group and the BIA group (Fig. 5a for end of treatment body weight and Fig. 5b for change in body weight).

Blood pressure control

BIA-based interventions were associated with a 2.73 mmHg lower mean blood pressure in comparison with the control arm. The results were reported by all studies with 1197 patients in total (Fig. 6).

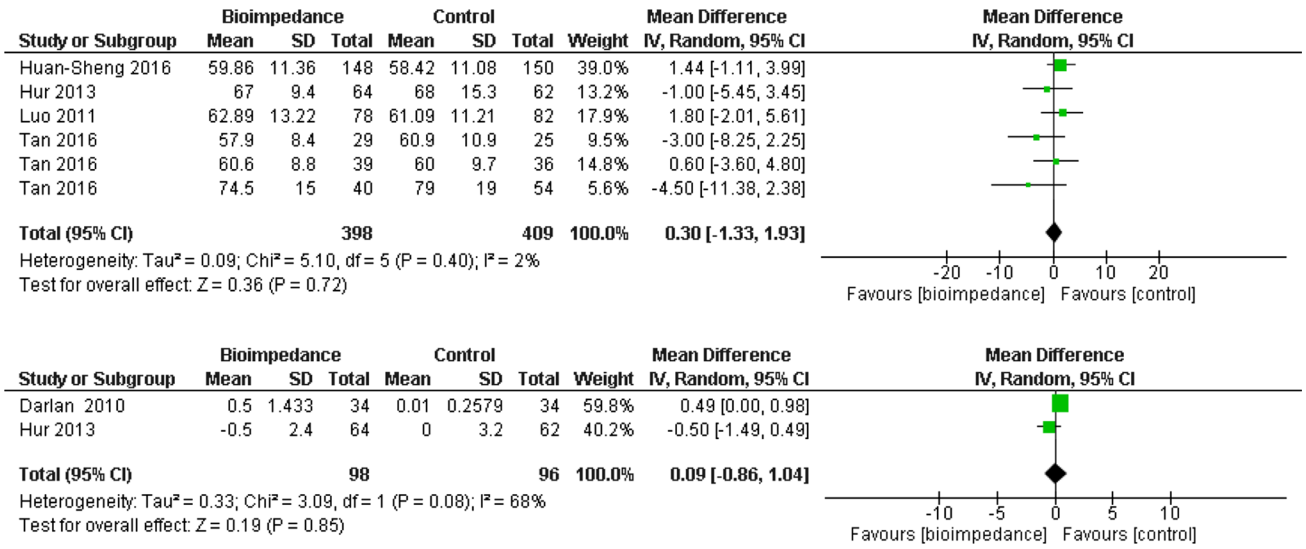

Fig. 5 Forest plot for end of treatment body weight (**a**) and change in body weight during follow-up (**b**)

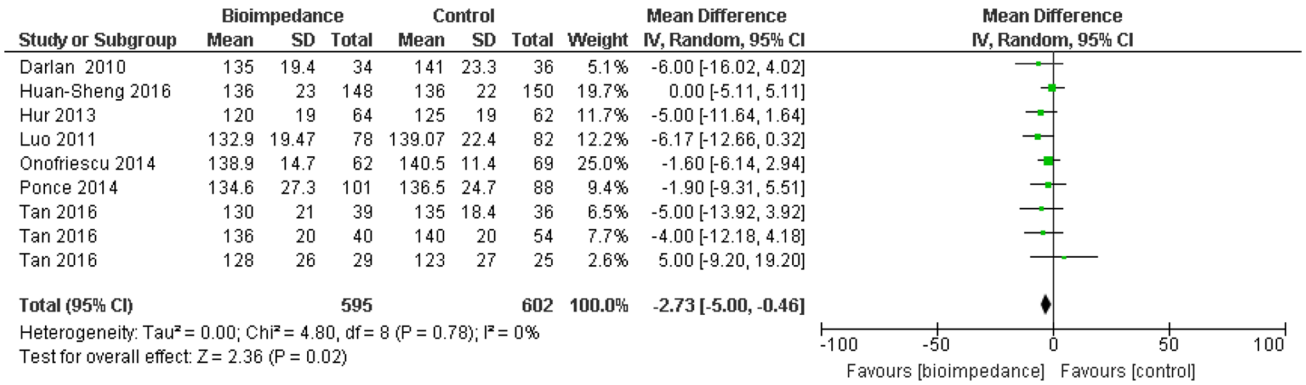

Fig. 6 Forest plot for systolic blood pressure control

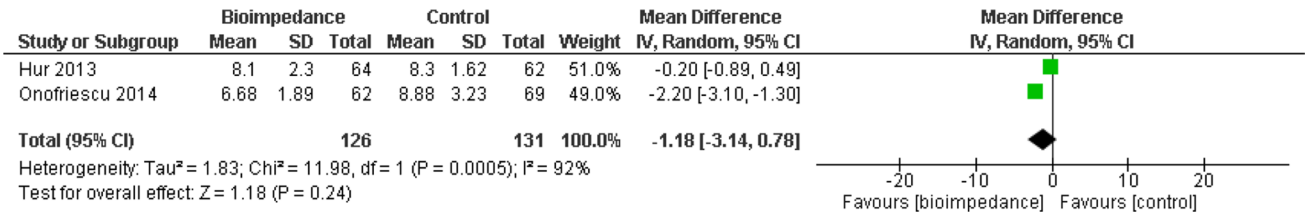

Fig. 7 Forest plot the effect on arterial stiffness (pulse wave velocity in m/s)

Effect on arterial stiffness

Hur et al. [14] and Onofriescu et al. [13] reported data on the end of treatment values of the arterial stiffness. The cumulative analysis showed a lower value in the intervention group, mean differences 1.18 m/s (95% CI −3.14, 0.78 m/s) (Fig. 7).

Side effects

Serious adverse events were not reported in any study. Darlan 2010 [19] reported no differences in terms of number of side effects between the two groups. The same results are reported by Sheng 2016 [20], Onofriescu 2014 [13] and Hur 2014 [14]. However, Luo 2011 [22] terminated their study early due to compelling benefits in the bioimpedance group

regarding adverse effects and overall mortality although no data are presented to support this information). Sheng 2016 reported systematically intradialytic complications and found that no difference was found when comparing the incidence of hypotension events and cramping events [20].

Investigation for sources of heterogeneity and publication bias

The tests for heterogeneity were not found significant when considering all-cause mortality, SBP control and end of treatment body weight. However, supplemental analysis could not be performed due to insufficient data in the following domains: heterogeneity by length of follow-up, type of compounds or quality of trials. Importantly, detection of small study (either small sample size or low number of censored events) was limited by a paucity of data in this regard throughout the sampled literature.

Discussion

In this meta-analysis, we found that in ESKD patients, BIA-based interventions for correction of overhydration have little to no effect on all-cause mortality. Bioimpedance-based dry weight assessment was associated with lower blood pressure, lower end of treatment overhydration and reduced arterial stiffness, but did not significantly impact all-cause mortality, body weight or change in body weight in this systematic review and meta-analysis of seven studies with 1312 patients.

The topic of dry weight calculation is important because it guides treatment in dialysis populations. Fluid overload contributes heavily to mortality risk in ESKD patients. Classic clinical signs of overhydration such as peripheral oedema, hypertension or pulmonary congestion lack accuracy. Hence, BIA has emerged as an objective tool to assess fluid overload. BIA provides individualized fluid status/overload assessment on the basis of normal extracellular volume, taking into account their own body composition. It is highly reproducible, relatively inexpensive, easy to use and, importantly, has already been validated clinically [25]. Despite these favourable traits, there is still a paucity of robust evidence to guide implementation of this technology clinically (as seen by the current systematic review).

In observational studies, BIA-detected overhydration was associated with all-cause mortality [6, 9, 25, 26]. In their influential paper, Wizemann et al. showed that fluid overload, as assessed by BIA, is an important and independent predictor of mortality, secondary only to diabetes [9]. Onofriescu et al. indicated that this relationship is maintained even when adjustments for echocardiographic parameters are considered [25].

Unfortunately, the results of the current study seem to go against these initial positive findings. It is possible that the existing studies are underpowered to show the effect of BIA on all-cause mortality. Even the study by Onofriescu et al. [13], the only study that showed a beneficial effect of BIA use on survival was not powered enough to properly analyse this outcome.

Another possible explanation is related to the interpretation of BIA results. Although the CLIMB study showed that aggressive dry weight reduction can have deleterious effects [27] and BIA is the only method that provides data to avoid both overhydration as well as underhydration, it has been suggested that trends rather than absolute BIA measurements may be more meaningful [28].

Our analysis showed a beneficial effect of BIA related to a better control of blood pressure and possibly to a reduction in arterial stiffness estimates. Although BIA use was not associated with a reduction or change in total body weight in our analysis, the positive effect of this technique on the assessed vascular parameters could be secondary to changes in total body compartmental composition as showed by the reduction in the overall overhydration level. BIA does not differentiate between intravascular and interstitial extracellular water excess, and these beneficial effects could be associated with a better intravascular fluid control.

Potential limitations and sources of bias in the review process

To our knowledge, this is the first systematic review that assesses the benefits and harms of bioimpedance, when compared to standard care in adult population with ESKD. The main strengths of this review include the comprehensive searches of multiple databases and application of Cochrane methodology. Core outcome domains are reported as suggested by the recent international SONG-HD initiative [29]. We managed to include data from seven studies (one unpublished studies) with more than 1300 participants. Also, all the ongoing studies and observational data are presented in detail. Nevertheless, our review has some important limitations. We acknowledge that between studies, it is difficult to quantify how different these studies may have truly been with regard to the standard of care arms since practices may have varied widely. We acknowledge that the devices have not been cross-validated and estimation algorithms are proprietary but all of devices do present validation studies, previously published [30, 31]. Also, the included studies did not standardize BP measurements. The blood pressure comparison in the HD patients included pre-HD BP. It is arguable whether this is a useful metric of overall BP burden, chronic volume overload or even overall prognosis. Also, loss or residual kidney function was not included under outcomes

and this might underestimate the medium to long-term risks related to reduction in overhydration.

The included studies had small sample sizes with short follow-up and variability of follow-up period. The amount of data available on patient-relevant outcomes (e.g. mortality, cardiovascular events, side effects) is limited and reported incompletely when available. Also, the quality of the included studies is low to medium level when looking at the risk of bias scale.

Conclusion

Bioimpedance-based dry weight assessment does not have a statistically significant effect on all-cause mortality in patients with end-stage kidney disease. However, this method can improve blood pressure control, overall overhydration and arterial stiffness measurements. Due to the small sample size of existing studies, larger studies with longer follow-up, possibly in combination with other promising methods such as lung ultrasonography, will likely shape the next generation of dry weight assessment in guiding fluid management for ESKD patients.

Compliance with ethical standards

Conflict of interest Adrian Covic received speaker honoraria from Amgen, Roche, Fresenius Medical Care and Abbott and is a member of the European Renal Best Practices Board. All the other authors have nothing to declare.

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