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Ultrafiltration for acute decompensated cardiac failure: A systematic review and meta-analysis☆

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ABSTRACT

Background: Ultrafiltration is a method used to achieve diuresis in acute decompensated heart failure (ADHF) when there is diuretic resistance, but its efficacy in other settings is unclear. We therefore conducted a systematic review and meta-analysis to evaluate the use of ultrafiltration in ADHF.
Methods: We searched MEDLINE and EMBASE for studies that evaluated outcomes following filtration compared to diuretic therapy in ADHF. The outcomes of interest were body weight change, change in renal function, length of stay, frequency of rehospitalization, mortality and dependence on dialysis. We performed random effects meta-analyses to pool studies that evaluated the desired outcomes and assessed statistical heterogeneity using the I^2 statistic.
Results: A total of 10 trials with 857 participants (mean age 68 years, 71% male) compared filtration to usual diuretic care in ADHF. Nine studies evaluated weight change following filtration and the pooled results suggest a decline in mean body weight −1.8; 95% CI, −4.68 to 0.97 kg. Pooled results showed no difference between the filtration and diuretic group in change in creatinine or estimated glomerular filtration rate. The pooled results suggest longer hospital stay with filtration (mean difference, 3.70; 95% CI, −3.39 to 10.80 days) and a reduction in heart failure hospitalization (RR, 0.71; 95% CI, 0.51–1.00) and all-cause rehospitalization (RR, 0.89; 95% CI, 0.43–1.86) compared to the diuretic group. Filtration was associated with a non-significant greater risk of death compared to diuretic use (RR, 1.08; 95% CI, 0.77–1.52).
Conclusions: There is insufficient evidence supporting routine use of ultrafiltration in acute decompensated heart failure.

1. Introduction

Acute decompensated heart failure (ADHF) accounts for nearly 1 million hospitalizations worldwide [1]. ADHF is a blanket term covering a heterogeneous group of patients sharing a common clinical presentation of symptoms and signs of congestion or ‘fluid overload.’ Diuretics have been the treatment option of choice for congestion for decades—irrespective of any clinical differences in presentation of ADHF. Diuretic prescriptions are thought to reduce severe congestion slowly and therefore contribute to prolonged hospitalizations in these patients. In addition, their use may also be complicated by electrolyte disturbances and some patients may become refractory to their use.

Ultrafiltration, using either extracorporeal hemodialysis circuits or peritoneal dialysis [2], is a recognized method for mechanical fluid management in patients with renal failure and has also been proposed as a therapeutic intervention to optimise fluid management in patients with decompensated heart failure. Several studies have evaluated the efficacy of extracorporeal ultrafiltration compared to intravenous diuretics among decompensated patients without diuretic resistance and the results are inconsistent [3–6].

In view of the inconsistent evidence and the emergence of new studies we conducted a systematic review and meta-analysis to determine whether reported trials compared the efficacy of ultrafiltration with diuretics alone and if any patient groups more likely to benefit or be harmed by ultrafiltration compared to diuretics.

☆ The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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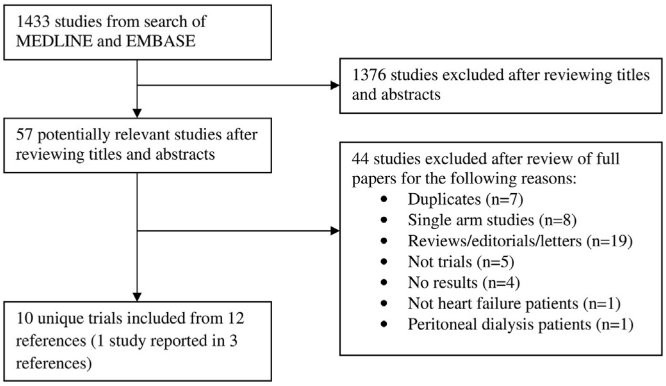

Fig. 1. Flow diagram of study selection.

2. Methods

We selected studies that investigated outcomes among patients with ADHF who were treated with either ultrafiltration or intravenous diuretics. There was no restriction on whether patients had diuretic resistance but where available, information about the definition and prevalence of diuretic resistance was collected from each included study. The outcomes of interest were weight change, change in creatinine and/or change in estimated glomerular filtration rate, length of stay, hospitalization, mortality and dialysis dependence. Included studies had to evaluate a group managed with ultrafiltration compared to an intravenous/oral diuretics group. There was no restriction based on phenotype or definition of heart failure, or language of study report but we only included randomized trials.

We searched MEDLINE and EMBASE using OVID SP with no date or language restriction in March 2016. The exact free search terms were: (furosemide or bumetanide or diuretic or diuresis) AND (hemodialysis or haemodialysis or dialysis or hemofiltration or haemofiltration or ultrafiltration or aquapheresis) AND (heart failure or cardiac failure or left ventricular impairment or cardiac insufficiency or cardiac decompensation). We checked the bibliography of relevant studies and reviews for additional studies that met the inclusion criteria.

Two reviewers (CSK and CWW) screened all titles and abstracts retrieved from the search for studies that met the inclusion criteria. The full manuscript of studies that potentially met the inclusion criteria was reviewed and the final decision to include or exclude studies was made with the other reviewers. Independent double extractions were performed by two reviewers (CSK and CWW) and data were collected on study design, year, country, number of participants, mean age, % male, participant inclusion criteria, protocol for filtration group, protocol for control group and results.

Quality assessment of the studies was conducted with consideration of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome ascertainment and complete outcome data.

We used RevMan V.5.3.5 (Nordic Cochrane Centre) to conduct random effects meta-analysis using the inverse variance method for pooling log risk ratios (RRs). We used random effects because the studies were conducted in a wide range of settings in different populations, hence the need to take heterogeneity into account for the pooled effect estimate. Where possible, we chose to pool adjusted risk estimates from primary studies and when these data were not available, raw data were used to calculate unadjusted risk estimates. Changes in creatinine were converted to mg/dl so that studies could be pooled using common units. Where there were outcomes evaluated at multiple time points we chose to pool the results with the longest follow up because we wanted to establish the longer term benefits of ultrafiltration compared to intravenous diuretics. We used the I^2 statistic to assess statistical heterogeneity. I^2 Values of 30%–60% represent moderate levels of heterogeneity [7]. We performed sensitivity analysis where there was significant heterogeneity in an analysis (I^2 > 60%).

3. Results

The process of study selection is shown in Fig. 1. After removal of duplicates, our search yielded 1433 titles and abstracts. After independent screening for study inclusion, the full manuscripts or conference abstracts of 57 studies were reviewed and 10 were retained for final inclusion in the review [3–6,8–15].

The description of the included studies is shown in Table 1. There were 10 randomized trials which took place in USA, Canada, Italy, Turkey and Russia between 2003 and 2014. There were a total of 857 participants (422 in the filtration group and 435 in the diuretic group). The average age was 68 years and 71% were male.

The quality assessment of the included studies is shown in Table 2. Random sequence generation was unclear in 6 studies. Allocation concealment was upheld in 2 studies and none of the studies were blinded to participants and personnel. The outcome assessment was blinded in 2 studies and 5 studies had complete outcome data.

The description of the population, filtration and diuretic protocol and results are shown in Tables 3 and 4. Most studies reported patients who had ADHF in NYHA class III to IV. A variety of filtration methods and protocols were used and the diuretic regimen was not consistent across the studies. None of the studies recorded any definition for diuretic resistance nor evaluate its prevalence in the study cohort.

A total of 9 studies evaluated weight change and the pooled results suggest a decline in body weight following filtration compared to diuretics: mean difference, −1.86; 95% CI, −4.68 to 0.97 kg; 646 participants, $I^2 = 98\%$ (Fig. 2). Exclusion of the Tabekiyrian 2010 study reduced the heterogeneity from 98% to 55%. After exclusion of this study, the results suggested a significant decrease in body weight with ultrafiltration (mean difference, −1.12; 95% CI, −2.01 to −0.22).

Change in creatinine was reported in 8 studies and the pooled results showed no difference between the filtration and diuretic group (mean difference, 0.01; 95% CI, −0.17 to 0.19 mg/dl; 566 participants, $I^2 = 62\%$) (Fig. 3). However, for estimated glomerular filtration rate, there was a decline with filtration compared to diuretics but this was not significant (mean difference, −2.77; 95% CI, −6.39 to 0.86 ml/min/m^2; 4 studies, 303 participants, $I^2 = 53\%$) (Fig. 3b).

Length of stay was reported in 3 studies and the pooled results suggest longer hospital stay with filtration compared to diuretics (mean difference, 3.70; 95% CI, −3.39 to 10.80; 256 participants, $I^2 = 99\%$) (Fig. 4). Exclusion of the Tabekiyrian 2010 study reduced heterogeneity

Table 1
Study design and participant characteristics.

Study ID	Study design; country; year	Sample size; filtration group; diuretic group	Mean age	% Male	Participants
Bart 2005 (RAPID-CHF)	RCT; USA; 2003–2004	40; 20; 20	68.5	70	Congestive heart failure
Bart 2012 (CARRESS-HF)	RCT; USA/Canada; 2008–2012	188; 94; 94	67.5	75	Acute decompensated heart failure with worsened renal function
Chung 2014	RCT; USA; Unclear	16; 8; 8	71.5	94	Acute decompensated heart failure
Costanzo 2007, Rogers 2008 and Costanzo 2010 (UNLOAD)	RCT; USA; 2004–2005	200; 100; 100	63	69	Acute decompensated heart failure
Costanzo 2016 (AVOID-HF)	RCT; USA; 2013–2014	221; 110; 111	67	71	Acute decompensated heart failure
Giglioli 2011 (ULTRDISCO)	RCT; Italy; Unclear	30; 15; 15	69	87	Decompensated heart failure
Hanna 2012	RCT; USA; 2003–2006	36; 19; 17	60	80.6	Acute decompensated heart failure admitted to intensive care unit
Marenzi 2014 (CUORE)	RCT; Italy; 2006–2010	56; 27; 29	74	23	Congestive heart failure
Seker 2016	RCT; Turkey; Unclear	30; 10; 20	67	63	Heart failure with evidence of right ventricular failure
Tabakyian 2010	RCT; Russia; Unclear	40; 19; 21	30–82 years	78	Congestive heart failure

RCT = randomized controlled trials.