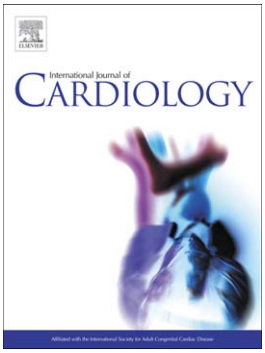

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PII: S0167-5273(16)33596-3
DOI: doi:10.1016/j.ijcard.2016.11.136
Reference: IJCA 23998

To appear in: *International Journal of Cardiology*

Received date: 23 August 2016
Accepted date: 6 November 2016

Please cite this article as: Kwok Chun Shing, Wong Chun Wai, Rushton Claire, Ahmed Fozia, Cunnington Colin, Davies Simon J., Patwala Ashish, Mamas Mamas A., Satchithananda Duwarakan, Ultrafiltration for acute decompensated cardiac failure: A systematic review and meta-analysis, *International Journal of Cardiology* (2016), doi:10.1016/j.ijcard.2016.11.136

Ultrafiltration For Acute Decompensated Cardiac Failure: A Systematic Review and Meta-analysis

Short running title: Ultrafiltration for cardiac failure

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Acknowledgements: None.

Conflicts of interest disclosures: The authors report no relationships that could be construed as a conflict of interest.

Word count: 4,493

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 which 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. 9 studies evaluated weight change following filtration and the pooled results suggest a decline in mean body weight -1.8 95%CI -4.68-0.97) 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 -3.39-10.80) 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.

Keywords: heart failure; meta-analysis; systematic review; ultrafiltration; diuretics

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.

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. Change 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 establishthe 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%).

Results

The process of study selection is shown in Figure 1. After removal of duplicates our search yielded 1,433 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 to 2014. There were a total of 857 participants (422 in filtration group and 435 in diuretic group). The average age was 68 years and 71% were male.

The quality assessment of 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 Table 3 and Table 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% (Figure 2). Exclusion of 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%) (Figure 3a). 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%) (Figure 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%) (Figure 4). Exclusion of Tabekiyrian 2010 study reduced heterogeneity to 0% and the results are non-significant (mean diference 0.55 95%CI -0.54 to 1.64).

In terms of rehospitalization, when compared to the diuretic group, there was a reduction with filtration for both heart failure hospitalization (RR 0.71 95%CI 0.51-1.00, 5 studies, 669 participants, I^2=38%) (Figure 5a) and all-cause rehospitalization (RR 0.89 95%CI 0.43-1.86, 3 studies, 260 participants, I^2=72%) (Figure 5b). Exclusion of Marenzi

2014 study reduced heterogeneity to 0% and the results are non-significant (mean difference 1.25 95% CI 0.91 to 1.71).

There were a total of 58 deaths out of 374 patients (15.5%) in the filtration group and 55 deaths out of 386 patients (14.2%) in the diuretic group which yielded a pooled risk that favoured diuretic use (RR 1.08 95% CI 0.77 to 1.52, 760 participants, I^2=0%) (Figure 6).

2 studies evaluated dialysis dependence and there was a non-significant greater risk of dialysis dependence in the filtration group (2 dialysis patients out of 37 total patients, 5.4%) compared to the diuretic group (2 dialysis patients out of 49 total patients, 4.1%) (RR 1.44 95% CI 0.03-59.72, 86 participants, I^2=68%)(Figure 7).

Discussion

Our analysis suggests that ultrafiltration appears to be as efficacious as diuretics in terms of fluid loss and weight reduction without significant decline in renal function. However, the usual care received in both treatment arms is poorly defined and the timing of the evaluation of outcomes is highly variable. It is unclear if other interventions are the same in the usual care group such as the dose of loop diuretics, other diuretics (e.g. thiazides, etc), implementation of fluid restriction, the aggressiveness of fluid restriction, use of continuous positive airway pressure, use of intravenous nitrates and use of inotropes. Furthermore, the timing of evaluation is important asthe amount of fluid loss, weight reduction and reduction in renal function after hospital stay or during follow up will depend on the aggressiveness of the usual care diuretic regime.

A number of reviews have been previous published evaluating the efficacy of filtration compared to diuretic therapy.[16-22] Jain et al published the most recent review on ultrafiltration in acute heart failure.[22] This review covered studies up until December 2015 and included 7 randomized trials and found that ultrafiltration was associated with greater weight loss and fluid removal with significant reduction in heart failure hospitalization rate but no difference in mortality. Our updated review with 3 additional studies found similar results except none of the results were statistically significant. The authors do raise the important point that it remains to be clarified whether higher upfront cost associated with ultrafiltration may be offset by reduction in rate of heart failure readmission and resource utilization. However, their study does not discuss important issues such as diuretic resistance which is an indication for ultrafiltration and the heterogeneity in methodology which is a limitation of included studies.

One challenge for this review was interpreting the findings in view of significant heterogeneity in study methodology. First, some studies have been non-specific regarding the diuretic regimes and definition of diuretic resistance. The prevalence of diuretic resistance will have a major effect on potential response in the control group. The duration of ultrafiltration is further not specified as using systems such as Aquadex have a longevity of 3 days. Consequently, it is likely that studies did not compare intravenous diuretics versus ultrafiltration but diuretics as part of usual care (control arm) compared with a period of ultrafiltration and subsequent usual care (intervention). The type of subsequent usual care is poorly specified and therefore deviations between the 'control' and 'intervention' groups after the period of ultrafiltration is not clear and potentially has major impact on overall patient outcomes. In the studies which evaluated length of stay in hospital it ranged from 6 to 17 days in the ultrafiltration group and 5 to 19 days in the diuretic group.[5,8,9,15] It is unclear why patients are admitted for a longer duration beyond the filtration period. Ongoing hospitalisation after ultrafiltration may relate to complications of ultrafiltration, any differential in standard treatment such as the use of vasodilators, a recurrence of congestion requiring continued parenteral diuretic therapy or difficultyin social discharge arrangements related to increased frailty or dependence which were not in the comparative patient demographics. High quality individual patient data would help clarify this issue further but is unavailable here. Furthermore, future studies should document the ongoing treatment of patients who remain in hospital after substantial fluid removal following ultrafiltration. This would then allow a true comparison of ultrafiltration (within a wider strategy of heart failure management) – the intervention – versus that of a usual strategy of ADHF management including diuretic use – the control arm.

In addition to efficacy endpoints, it is important to consider the safety impact of ultrafiltration compared to diuretics. Ultrafiltration is associated with potential vascular complications, pneumothorax and infections. Heparinization is required for aquadex which could lead to bleeding complications but we did not find any evidence of increased adverse bleeding events with ultrafiltration. In addition, ultrafiltration cannot be performed in all patient areas and may require a bed in a specialist unit with skilled nursing input. However, most of the studies failed to report events that may be related to heparinization and the studies also are underpowered to evaluate these relatively uncommon events. Nonetheless, it is important to consider the efficacy benefit as well as the risk of complications in selecting therapy for diuresis and many of the studies are underpowered to capture these complications.

Current evidence fails to identify any particular sub-groups that either benefit from or are harmed more by ultrafiltration in comparison to diuretics such as patients with cardiorenal syndrome. Congestion is believed to be one of the main drivers of cardiorenal syndrome. A potential benefit of ultrafiltration over diuretics is that there may be preserved renal function while fluid is removed with ultrafiltration while diuretics may cause renal hypoperfusion. In addition, theoretically, ultrafiltration may be more "gentle" in reducing congestion so that physiological compensatory mechanism can gradually compensate without sudden fluid shifts. Another potential benefit of ultrafiltration includes a greater reduction of sodium load and removal of potentially vasoactive substances below the filter clearance of the ultrafilter e.g. in terms of the Aquadex to remove <65 Kda molecules. While these these theoretical advantages are attractive they do not appear to translate into clear clinical benefit. Nevertheless, identification of sub-groups of patients who may benefit is important to help guide real world practice should be explored in future studies.

It has been suggested that ultrafiltration should be considered in diuretic resistance where there is persistent edema despite adequate diuretic therapy.[23] However, there is no definition of adequate diuretic therapy. Diuretic resistance is multifactorial in etiology and could include lower than efficacious duretic dose. This was demonstrated in the CARRESS trial using incremental diuretic doses and inotropes adjusted to maintain urine output of 3 to 5 litres per day.[4] We would therefore recommend ultrafiltration be considered for patients exhibiting diuretic resistance following a clinical diuretic regime similar to that used in CARRESS.

Based on the findings of the review we are in a position to propose a number of recommendations for future studies. We would suggest that future trials consider comparisons of intravenous diuretics alone versus ultrafiltration alone for resolution of congestive symptoms. Also, another question worth exploring is whether ultrafiltation in addition to maintenance diuretic therapy is superior to maintance diuretic therapy alone. Therefore clinical trials should be designed so the clearly state which question they wish to address. Specific patient groups which may benefit from ultrafiltration, such as those with hypokalemia, hyponatremia, profound hypotension and diuretic resistance should be explored. While it is clear that diuretics should be used cautiously in hypokalemia, it is less straight forward for cases of hyponatremia. In this situation hyponatremia often reflects reduced free water excretion that can be ameliorated with ultrafiltration. With respect to patients with decompensated heart failure who have significant hypotension, many studies have excluded patients whose systolic blood pressure measured below 100 mmHg. However,

hypotension is commonly encountered in clinical practice and in such instances inotropes can be used to facilitate the concomitant use of diuretics to relieve hypervolemia, as was done in the CARRESS-HF trial.[4] Future studies should also clearly define diuretic resistance within their study population as this is a stronger indication for ultrafiltration as well as the extent of cardiorenal syndrome in the cohort. In addition, the effectiveness of the ultrafiltration to cause diuresis and the extent of improvement in cardiac function will depend on the filtration settings. Important factors which need to be clarified include the system associated with best outcome, best types of filters, the optimal rate of filtration, duration of filtration procedure, the total extracorporeal blood volume and number of sessions. For diuretic protocol, there are a variety of factors which might influence dose and aggressiveness of diuresis such as fluid status, patient symptoms and electrolyte disturbance. In addition, the studies do not really talk about the cost implications of ultrafiltration compared to diuretics which is an important consideration.

This study has several strengths and limitations. We were able to perform an updated review with more trials than any of the previous review (10 studies). In addition, we were able to consider a variety of important outcomes such as change in body weight, renal function, length of stay as well as hard outcomes like mortality and rehospitalization. However, only 3 of the studies were adequately powered and the most recent high quality ultrafiltration trial, AVOID-HF, was terminated early by the sponsor. The termination took place because slower-than-projected study enrollment (study recruited 224 patients when 810 were planned) and termination was in no way related to signals of futility or safety concerns. While were were able to include the results of this trial it is clear it also lacks statistical power for the the primary endpoint. While the trial had be terminated early it remains the largest trial to date. The withdrawal of sponsors from the trial designed to answer some of these questions demonstrates the necessity for interventions and trials to be clinically independent of the providers of trial funding. In addition, the methodological quality of the smaller studies in general were poor and none of the studies blinded participants and personnel to the group which they were randomized to.

In conclusion, there is insufficient evidence to suggest routine use of ultrafiltration in any setting of acute decompensated heart failure. While we show evidence that it is superior to intravenous diuretics in terms of weight loss and heart failure admissions, as diuretics are inexpensive, there are a few arguments to consider routine ultrafiltration over diuretics. While ultrafiltration can remove 6-9 kilograms over a few days compared to parenteral diuretics can remove up to a few kilogram a day, ultrafiltration requires anticoagulation and

admission to specialist unit for close monitoring which is expensive.[4] Theoretically, ultrafiltration may require less time to achieve diuresis compared to diuretics, though current evidence suggests no difference in length of stay. More studies are needed to characterize whether certain cases of acute heart failure will benefit from ultrafiltration at an early stage and the best ultrafiltration protocol.

Author statement

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

Contributors

Kwok CS was responsible for the study design, concept, screening and data extraction, data analysis and text of the manuscript. CWW screened and extracted data in the review. All authors provided critical revision for important intellectual content.

Funding Sources

None.

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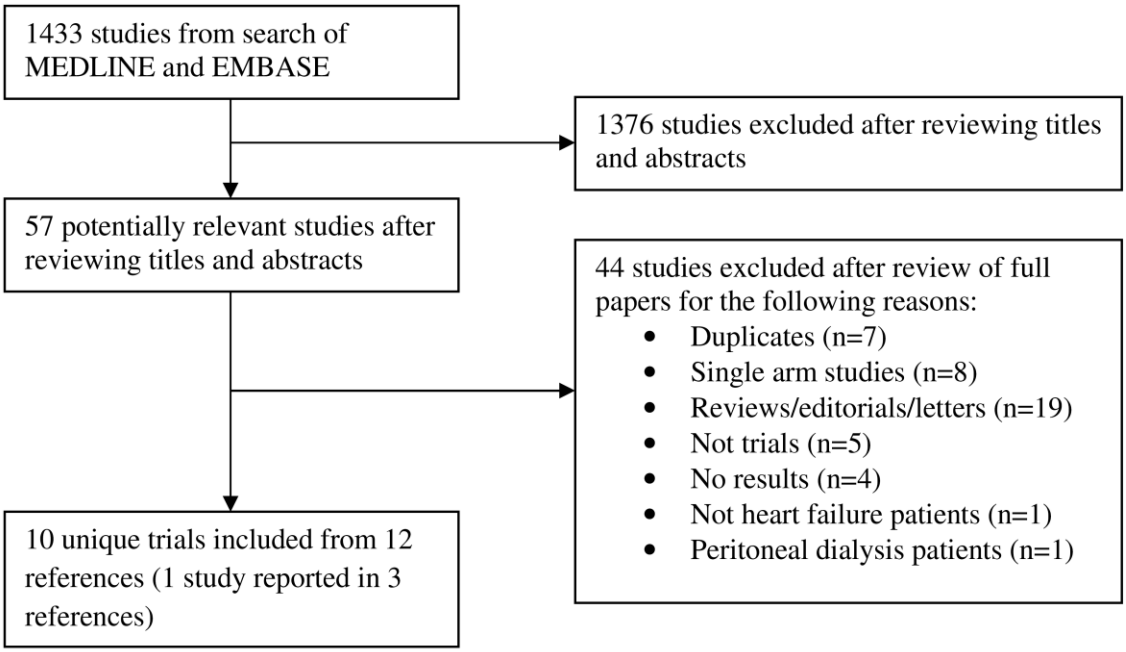
List of Tables and Figures



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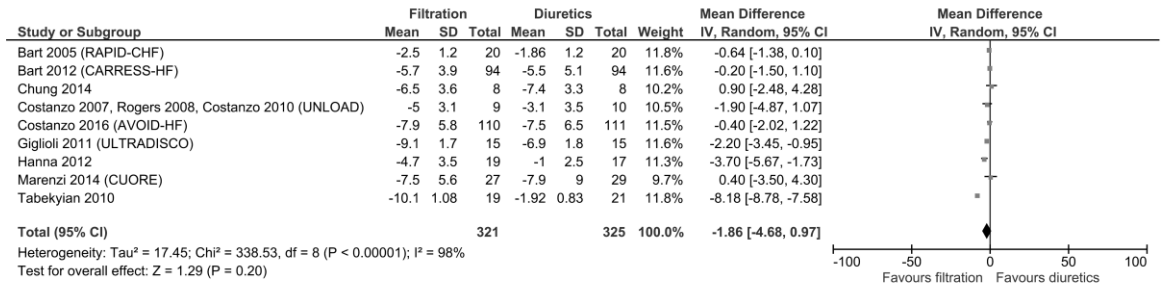

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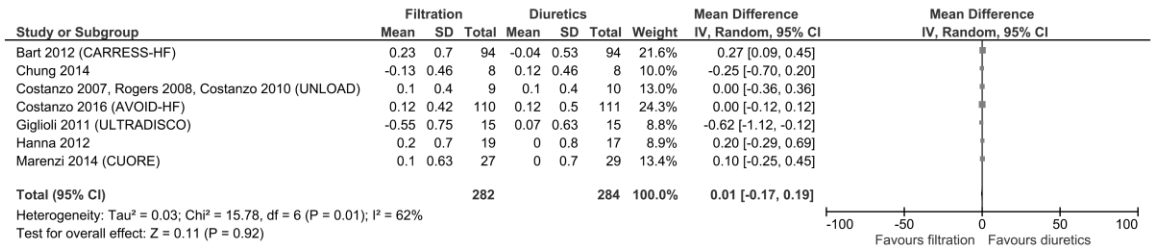

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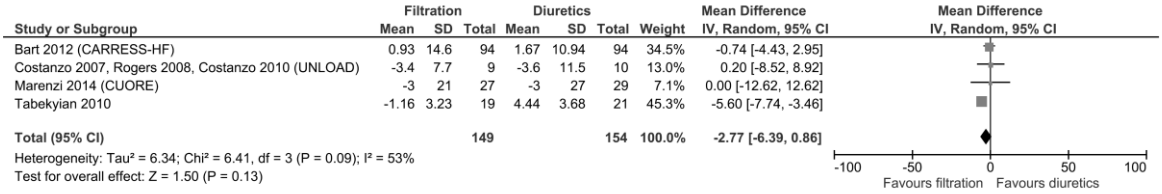

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Fig. 3

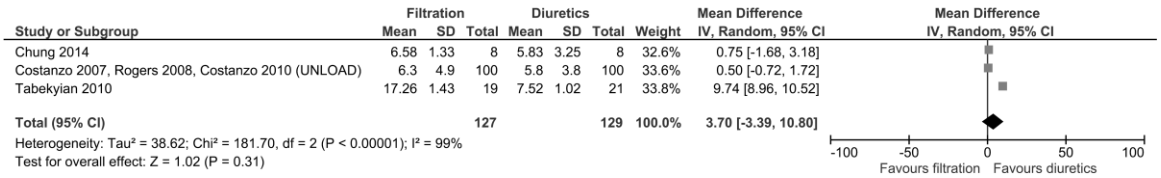
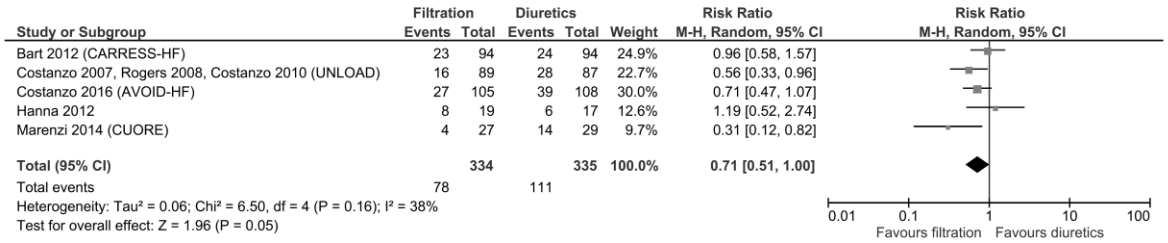


Fig. 4



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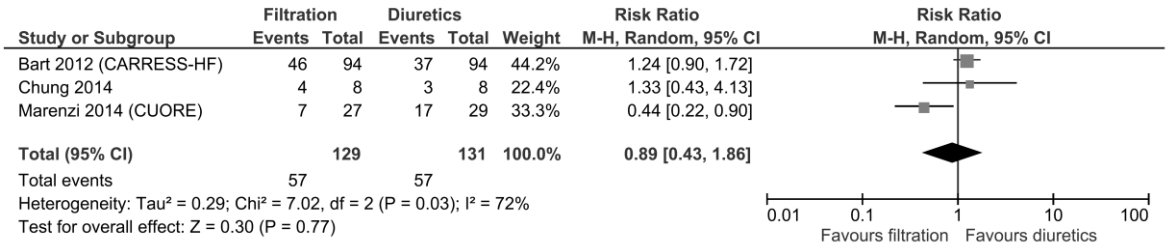

b

Fig. 5

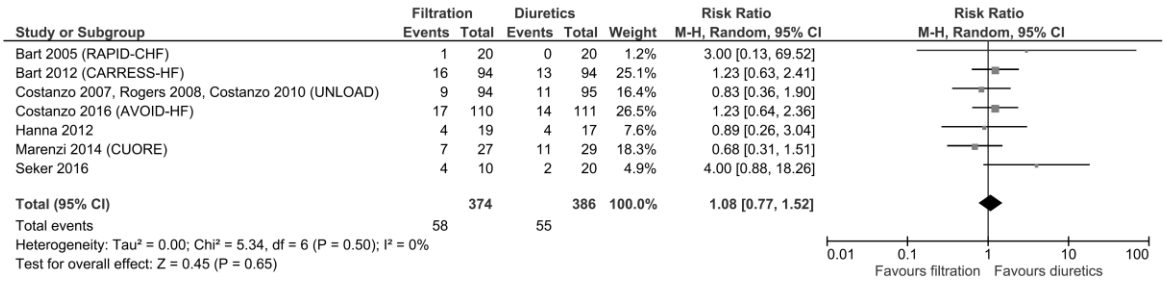

Fig. 6

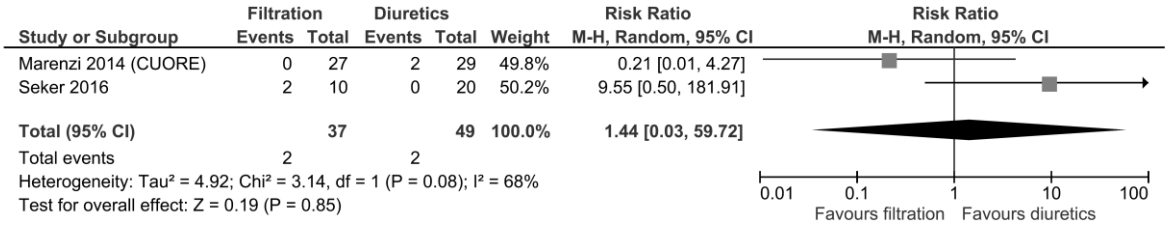

Fig. 7

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 & 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

Table 2: Quality assessment

Study ID	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome ascertainment	Complete outcome data
Bart 2005 (RAPID-CHF)	Unclear.	No, no allocation concealment.	No, unblinded.	No.	No, 2 patients did not undergo the ultrafiltration.
Bart 2012 (CARRESS-HF)	Web-based system.	No, no allocation concealment.	No, unblinded.	No.	No, 2 patients had missing data.
Chung 2014	Unclear.	No, no allocation concealment.	No, unblinded.	No.	Yes.
Costanzo 2007 & Rogers 2008 & Costanzo 2010 (UNLOAD)	Unclear.	No, no allocation concealment.	No, unblinded.	No.	Unclear.
Costanzo 2016 (AVOID-HF)	Central web-based system.	No, no allocation concealment.	No, unblinded.	Yes, an independent Study End-point Committee.	No, 9 patients lost to follow up and 10 patients withdrew participation.
Giglioli 2011 (ULTRADISCO)	Unclear.	No, no allocation concealment.	No, unblinded.	No.	Yes.
Hanna 2012	Randomized in blocks of 4 and 2 within 2 strata based on GFR.	Yes, random sealed envelope.	No, unblinded.	No.	No, 3 patients withdrew participation.
Marenzi 2014 (CUORE)	Computer-generated.	Yes, random sealed envelope.	No, unblinded.	Yes, blinded physicians.	No, 2 patients were not followed up.
Seker 2016	Unclear	No, no allocation concealment.	No, unblinded.	No.	Yes.
Tabakyian 2010	Unclear	No, no allocation concealment.	No, unblinded.	No.	Yes.

Table 3: Protocols for filtration and control group

Study ID	Protocol for filtration group:	Protocol for control group
Bart 2005 (RAPID-CHF)	System 100 for an 8h course with fluid removal rate determined by the attending physician (<500ml/h).	Not defined.
Bart 2012 (CARRESS-HF)	Aquadex System 100 performed at a fluid-removal rate of 200ml/h.	Doses of diuretics adjusted to maintain a urine output of 3 to 5L/day.
Chung 2014	Aquadex 100 system with a target weight to be removed established by the heart failure service with mean UF rate was 162ml/h.	IV furosemide with mean daily dose of 212 mg.
Costanzo 2007 & Rogers 2008 & Costanzo 2010 (UNLOAD)	Aquadex System 100 with flow between 10-40mL/min and total blood volume of 33mL. The duration and rate (<500ml/h) of fluid removal were decided by treating physician.	At least twice the pre-hospitalization dose of diuretics. 68 patients received IV diuretics as bolus injections and 32 as continuous infusion.
Costanzo 2016 (AVOID-HF)	Aquadex Flex Flow System with adjustment of therapy according to patient's response.	The diuretic protocol permit adjustment of therapy according to patient's response.
Giglioli 2011 (ULTRADISCO)	M 100 PRESET PRISMA filter and a blood flow rate of 150mL/h. Continuous UF technique with initial rate of 100-300mL/h. This was adjusted according to response.	Continuous IV furosemide at an initial dose of 250mg/24h. This was reduced or increased according to patient response to maximum dose of 500mg/24h.
Hanna 2012	NxStage System One with initial rate was 400mL/h for 6 hours then decreased to 200mL/h.	IV diuretics according to treating clinician.
Marenzi 2014 (CUORE)	Peristaltic pump/polysulphone filter and a blood flow from 40-100mL/min, and a blood volume of 100mL. Duration and filtration rate (100-500mL/h) varied with 1 or 2 sessions.	IV loop diuretics by experienced heart failure cardiologists according to guideline recommendations.
Seker 2016	UF with max rate of 500cc/h and duration determined by clinician. The rate of blood flow was set to 50-100mL/min. UF terminated if satisfactory clinical decongestion.	Maximum tolerable dose of IV diuretics as a bolus or continuous infusion.
Tabak'ian 2010	Dialyzer Diacap LO filter slow continuous filtration with 90 ml and rate 9.8 ml/h/mmHg. Diacap HI PS continuous veno-venous hemofiltration with 68 ml and rate 42 ml/h/mmHg.	Given furosemide doses ≥80mg/day and then furosemide or torasemide tablets.

Table 4: Study results

Study ID	Population	Results
Bart 2005 (RAPID-CHF)	CHF.	Change in weight (kg): -2.5±1.2 vs -1.86±1.2. Mortality at 30 days: 1/20 vs 0/20.
Bart 2012 (CARRESS-HF)	ADHF.	Change in weight (kg): -5.7±3.9 vs -5.5±5.1. Change in creatinine at 96 h (mg/dl): +0.23±0.70 vs -0.04±0.53. Change in GFR at 96 h: +0.93±14.60 vs +1.67±10.94. All-cause hospitalization: 46/94 vs 37/94. Heart failure hospitalization: 23/94 vs 24/94. Mortality: 16/94 vs 13/94.
Chung 2014	ADHF.	Change in weight (kg): -6.5±3.6 vs -7.4±3.3. Change in creatinine (mg/dl): -0.13±0.46 vs 0.12±0.46. Length of stay (days): 6.58±1.33 vs 5.83±3.25. All-cause hospitalization: 30-day 3/8 vs 3/8, 90-day 4/8 vs 3/8.
Costanzo 2007 & Rogers 2008 & Costanzo 2010 (UNLOAD)	ADHF.	Change in weight (kg): -5.0±3.1 vs -3.1±3.5. Change in creatinine (mg/dl): 0.1±0.4 vs 0.1±0.4. Change in GFR: -3.4±7.7 vs -3.6±11.5. Length of stay (days): 6.3±4.9 vs 5.8±3.8. Mortality: 9/94 vs 11/95. Heart failure hospitalization at 90 days: 16/89 vs 28/87.
Costanzo 2016 (AVOID-HF)	ADHF.	Change in weight (kg): -7.9±5.8 vs -7.5±6.5. Changes in serum creatinine at discharge (mg/dl): 0.12±0.42 vs 0.12±0.50. Heart failure hospitalization: 30 days 10/110 vs 22/111, p=0.034, 90 days 27/105 vs 39/108. Mortality at 90 days: 17/110 vs 14/111.
Giglioli 2011 (ULTRADISCO)	ADHF.	Change in weight (kg): -9.1±1.7 vs -6.9±1.8. Change in creatinine (mg/dl): -0.55±0.75 vs 0.07±0.63.
Hanna 2012	ADHF.	Change in weight (kg): -4.7±3.5 vs -1.0±2.5. Change in creatinine (mg/dl): 0.2±0.7 vs 0±0.8. Heart failure hospitalization at 90 days: 8/19 vs 6/17. Mortality: 4/19 (21.1%) vs 4/17 (23.5%).
Marenzi 2014 (CUORE)	CHF.	Change in weight (kg): -7.5±5.6 vs -7.9±9.0. Change in creatinine (mg/dl):0.1±0.63 vs 0±0.7. Change in GFR at discharge: -3±21 vs -3±27. CHF hospitalization: 1 year 4/27 vs 14/29. All-cause hospitalization: 1 year 7/27 vs 17/29. Mortality at 1 year: 7/27 vs 11/29. Chronic dialysis: 0/27 vs 2/29.
Seker 2016	CHF.	Mortality: 4/10 vs 2/20. Haemodialysis during follow up: 2/10 vs 0/20.
Tabak'ian 2010	CHF.	Change in weight (kg): -10.1±1.08 vs -1.92±0.83. Change in GFR -1.16±3.23 vs 4.44±3.68. Length of stay (days): 17.26±1.43 vs 7.52±1.02.

UF=ultrafiltration, HF=heart failure, CHF=congestive heart failure, IV=intravenous, GFR=glomerular filtration rate.

Highlights

- The role of ultrafiltration in acute decompensated heart failure is unclear.
- Ultrafiltration is as efficacious as diuretics for fluid loss via weight reduction.
- Ultrafiltration is not associated without significant decline in renal function.
- Ultrafiltration reduces heart failure hospitalization.
- Routine ultrafiltration in acute decompensated heart failure is not recommended.