Systematic Review and Meta-Analysis

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Ultrafiltration for patients with acute decompensated heart failure

A systematic review and meta-analysis

Meng-jun Wang, MM[a,b], Yan-mei Zheng, BM[a], Hong-xu Jin, MD[a,*]

Abstract

Background: Ultrafiltration plays an indispensable role in relieving congestion and fluid retention in patients with acute decompensated heart failure (ADHF) in recent years. So far, there is no consistent agreement about whether early ultrafiltration (UF) is a first-line treatment for patients with ADHF. We, therefore, conducted a meta-analysis to assess the efficacy and safety of UF.

Methods: PubMed, Embase, and Cochrane Library databases were searched for randomized controlled trials (RCTs) that compared UF with diuretics in patients with ADHF and included our interested outcomes. The primary outcomes are heart failure rehospitalization, all-cause rehospitalization, and mortality. The second outcomes are fluid loss, weight loss, and adverse events. RevMan Version 5.4.1 was used to analyze the data of included studies.

Results: A total of 12 studies with 1197 patients were included. Our results showed a reduction in heart failure rehospitalization (risk ratio [RR] 0.67, 95% confidence interval [CI]: 0.52–0.87, $P = .003$) and all-cause rehospitalization (RR 0.62, 95% CI: 0.42–0.92; $P = .02$), an increase in fluid loss (1.47 L, 95% CI: 0.95–1.99 L, $P < .001$) and weight loss (1.65 kg, 95% CI: 0.90–2.41 kg; $P < .001$). There was no difference in mortality (RR 1.09, 95% CI: 0.78–1.51; $P = .62$). There were inconsistent agreements about which group have more total adverse events. Subgroup analysis showed that UF with larger mean fluid-remove rate (≥200 mL/h) could significantly remove more fluid, lose more weight, and decrease heart failure rehospitalization. Less weight loss for patients with ADHF may correlated to higher percent of ischemic etiology (ischemic etiology ≥50%).

Conclusion: Although UF is more effective in removing fluid than diuretics and decrease rehospitalization of heart failure and all causes, there is not enough evidence to prove that UF is superior because of adverse events and mortality in the UF group. The mean fluid-removal rates should be set to ≥200 mL/h. Patient with different etiology may have different effects when treated with UF and it is a weak conclusion.

Trial registration: The systematic review was registered with the International Prospective Registry of Systematic Reviews. (https://www.crd.york.ac.uk/prospero/, registration number CRD42021245049).

Abbreviations: ADHF = acute decompensated heart failure, CI = confidence interval, MD = mean difference, RCTs = randomized controlled trials, RR = risk ratio, UF = ultrafiltration.

Keywords: acute decompensated heart failure, diuretics, meta-analysis, ultrafiltration

1. Introduction

Acute decompensated heart failure (ADHF) is a type of acute heart failure, which refers to patients with a previous history of chronic heart failure. Most of these patients are due to fluid retention, which causes a poor prognosis.[1] Loop diuretics have been recognized as a cornerstone in relieving severe fluid accumulation.[2] However, it remains some shortcomings, such as diuretic resistance and renal dysfunction.[2,3]

Ultrafiltration (UF) is a distinctive way to selectively remove excessive fluid without affecting circulating volume and activating neuro-humoral reaction.[4] The recommendations of ultrafiltration in the ACC/AHA guidelines indicate that UF should be considered for patients with obvious volume overload (Class IIb, Level of Evidence: B) and intractable congestion not responding to medical therapy (Class IIb, Level of Evidence: C).[5] The 2016 ESC guidelines do not recommend the routine use of UF.[6]

So far, there is no consistent agreement about whether early UF is the first-line treatment for patients with ADHF. Therefore, the aim of this meta-analysis is to compare UF with diuretics about efficacy and safety for ADHF patients.

Editor: Neil Patel.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Wang Mj, Zheng Ym, Jin Hx. Ultrafiltration for patients with acute decompensated heart failure: a systematic review and meta-analysis. Medicine 2021;100:50(e28029).

Received: 2 June 2021 / Received in final form: 1 November 2021 / Accepted: 10 November 2021

http://dx.doi.org/10.1097/MD.0000000000028029

2. Methods

Ethical approval was not necessary. As a systematic review, our study is a secondary study of the published literature.

2.1. Search strategy

We searched PubMed, Embase, and Cochrane Library databases using the search terms: "ultrafiltration," "heart failure," "cardiac failure," "randomized controlled trial" for all articles till January 18, 2021. A supplementary search of PubMed was made on May 23, 2021. Reference lists of related studies were screened to identify other articles that did not be found online search.

2.2. Study selection

Inclusion criteria: RCTs; the age of patients ≥18 years old and the patients meet the criteria of diagnosis for acute heart failure; the intervention group was ultrafiltration; the comparison group was diuretics; these studies must include one or more designated outcomes. Exclusion criteria: ultrafiltration was performed by continue renal replacement therapy; studies were published over 20 years.

Two reviewers (WMJ and ZYM) independently screened all articles' titles and abstracts to exclude studies that are unrelated. Second, full-text articles were critically assessed for eligibility, according to inclusion and exclusion criteria. Disagreements were resolved by discussion.

2.3. Assessment of included study and data extraction

Two authors (WMJ and JHX) assessed the quality of the RCTs independently. The risks of bias were assessed by the Cochrane Collaboration's assessment tool for RCTs.[7] Two authors (WMJ and ZYM) extracted the following data independently. The data of studies included basic information of studies such as county, patients' age, the male sex, comorbidities, medication, protocols for ultrafiltration and diuretics, and results of studies. The primary outcomes were heart failure rehospitalization, all-cause rehospitalization, mortality. Secondary outcomes were fluid loss and weight loss, adverse events.

2.4. Statistical analysis

RevMan Version 5.4.1 (The Cochrane Collaboration, 2020) was used to analyze the data of included studies. Dichotomous data and continuous data were calculated with Mantel–Haenszel risk ratio (RR) and mean difference (MD), respectively. All outcomes except adverse events were used for meta-analysis. The outcomes of adverse events were list in the table of results of studies. If not providing standard deviation, we used the method of Cochrane handbook to estimate the value. A measure of statistical significance was $P = .05$, and 95% confidence interval (CI) was used. Heterogeneity with Chi-square Q and I^2, funnel plots, and Egger P-value were used in this article. Fixed effect model was applied in the process of analysis. If $I^2 > 50\%$, the fixed effect model will be changed to a random model.

3. Results

3.1. Literature search

The study flow diagram was shown in Fig. 1. Six hundred thirty four records were searched online, and 1 record was identified through references. After preliminary screening, 41 full-text articles were assessed by inclusion and exclusion criteria and a total of 12 studies[8–19] were included.

3.2. Study characteristics and data

In the 12 RCTs,[8–19] 1197 patients were involved, 584 in the UF group, 613 in the diuretics group. The patients' characteristics were listed in Table 1, protocols for UF and diuretics in Table 2, results of studies in Table 3. Six studies were conducted in the USA,[8–12,14] 3 studies in China,[15,18–19] 2 studies in Italy,[13,16] 1 study in Turkey.[17] The age of patients of included studies ranged from 50.8 to 86.5. The percent of the male sex ranged from 55 to 100. UF was performed by Aquadex system 100 in 4 studies[8–11] and by FQ-16 in 3 studies.[15,18–19] The intervention groups in 3 studies combined UF with diuretics.[8,16,19] One study included patients with diuretic resistance determined by which the patients were given furosemide 160 mg/d for 48 hours and 24 hours urine output <0.5 mL/kg h before randomization.[18]

3.3. Assessment for the risk of bias

The assessment of risks of bias was shown in Fig. 2. The RCTs about UF were open-label trials, so the risk of performance bias was high. Attrition bias existed in 2 studies,[9,14] because more patients withdrew in the UF group. Other bias existed in Costanzo et al,[12] because of the early termination of the study.

3.4. Publication bias

The Funnel plot of weight loss was shown in Fig. 3. Despite the heterogeneity of studies, there may be publication bias among the included studies.

3.5. Outcomes of meta-analysis

3.5.1. Heart failure rehospitalization and all-cause rehospitalization. Four studies reported the rehospitalization for heart failure, and 628 patients were involved: 311 for UF, 317 for diuretics. There are 4 studies for all-cause rehospitalization which included 208 patients: 94 for UF, 114 for diuretics. The follow-up period ranged from 1 month to 1 year. The rate of heart failure rehospitalization and all-cause rehospitalization in UF group were significantly lower than that in the diuretics group: RR 0.67 [95% CI: 0.52–0.87; $P = .003$; $I^2 = 53\%$] (Fig. 4A), RR 0.62 [95% CI: 0.42–0.92; $P = .02$; $I^2 = 14\%$] (Fig. 4B), respectively. Marenzi et al[16] in heart failure rehospitalization was removed: RR 0.74 [95% CI: 0.56–0.97; $P = .03$; $I^2 = 17\%$]. The sensitivity analysis for the comparison of all-cause rehospitalization between groups did not change the overall result.

3.5.2. Mortality. Eight studies reported mortality involving 860 patients, 414 in the UF group, and 446 in the diuretics group. Follow-up time ranged from 1 month to 1 year. There was no statistical significance in mortality between UF group and diuretics group: RR 1.09 [95% CI: 0.78–1.51; $P = .62$; $I^2 = 0\%$] (Fig. 4C). The sensitivity analysis for the comparison of mortality between groups did not change the overall result.

3.5.3. Fluid loss and weight loss. Data on fluid loss was available for 7 studies including 748 patients, 368 in UF, and 377 in the diuretics group. Eleven studies involving 1165 patients provided data on weight loss, 574 patients in UF group, 591

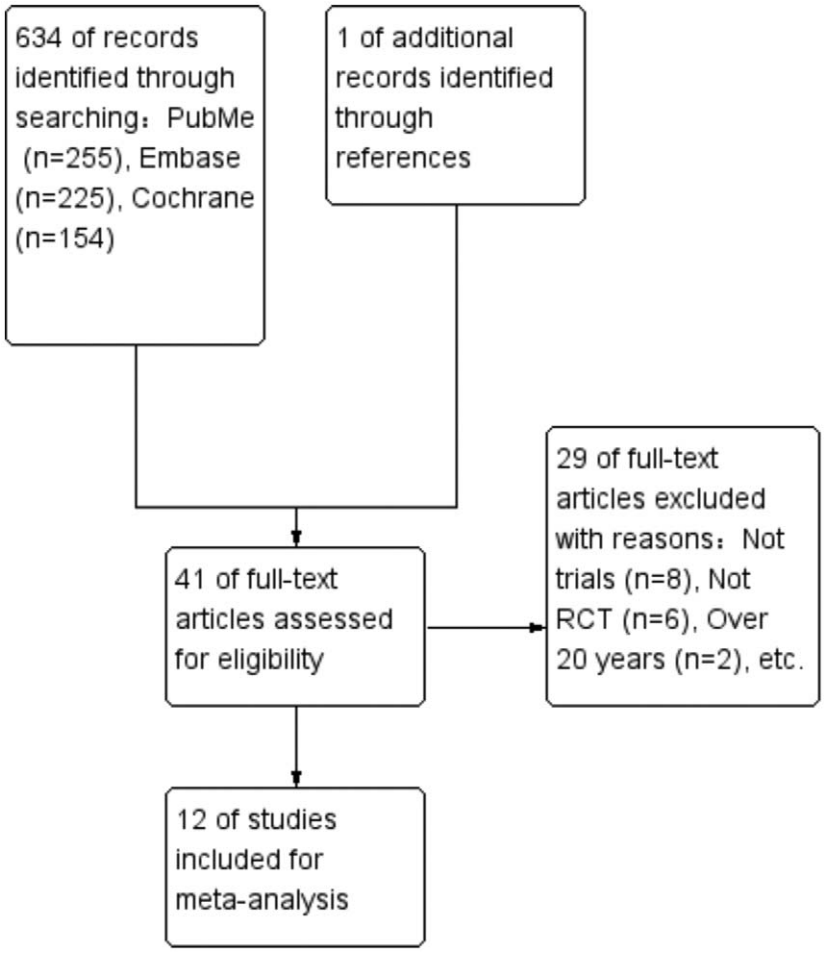

Figure 1. Study flow diagram.

patients in the diuretics group. The data's recording time ranged from 24 to 96 hours, except for Şeker et al[17] at discharge, Hanna et al,[14] Shen et al[18,19] during the intervention period, Hu et al[15] on the 8th day and Marenzi et al[16] at discharge. Fluid loss and weight loss in the UF group were significantly more than that in the diuretics group: MD (fluid loss): 1.47 [95% CI: 0.95–

Table 1

Characteristics of studies.

Study	Bart 2005	Bart 2012	Chung 2014	Costanzo 2007	Costanzo 2016	Giglioli 2011	Hanna 2012	Hu 2020	Marenzi 2014	Seker 2016	Shen 2017	Shen 2021
Multicenter trial	Yes	Yes	No	Yes	Yes	No	No	No	Yes	No	No	No
Country	USA	USA	USA	USA	USA	Italy	USA	China	Italy	Turkey	China	China
Patients	40	188	16	200	221	30	36	100	56	30	134	148
Age, y	70/70	69/66	69/74	62/63	67/67	72.4/65.8	60/59	70.6/73.52	73/75	66.5/66.8	58.4/57.5	67.4/67.3
Male (%)	67.5/69.5	78/72	87.5/100	70/68	69.1/73	87/87	84.2/76	55/55	83/81	60/65	70.2/67.7	60.8/63.9
LVEF (%)		30/35	22/26		36.3/36.6	34/30	19/18		<40%	32.1/31.7		
Ischemic (%)		70/51	50/50		40/34	60/60	21/29.4		55/59			35.1/34.7
Hypertension (%)	60/65			74/74	88.2/83	20/60	78.9/82.4	80/80	66/48	100/85		29.7/26.4
DM (%)	35/53	65/67		50/50	61.8/64	40/60	36.8/29.4	65/63.3	45/59	60/50		
Cr (pg/ml)		1.9/2.09	1.9/1.4		1.5/1.6			1.7/1.5	1.9/1.7	1.56/1.36	1.0/1.0	1.4/1.3
ACEI/ARB (%)	70/70	55/52		63/68	38.2/43.2	86.7/80		100/98.3	66/74			95.9/94.4
Diuretics (%)	65/95	91/96	50/75		55.4/55.9			100/100	97/100			
BB (%)	75/65	79/78	75/87.5		52.7/57.7	66.7/80		100/98.3	76/74			97.3/95.8

A/B = ultrafiltration/diuretics, ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin II receptor blocker, BB = beta-blockers, Cr = creatinine, DM = diabetes mellitus, LVEF = left ventricular ejection fraction.

Table 2

Protocols for ultrafiltration and diuretics.

Study	Ultrafiltration	Diuretics
Bart 2005	System 100, with fluid removal to a maximum of 500 mL/h for median 8 h per session. The dose of furosemide received during the first 24 h was 80 mg.	The median cumulative dose of furosemide received during the first 24 h was 160 mg.
Bart 2012	Aquadex System 100. The median duration of the treatment was 40 h.	Doses of diuretics as necessary to maintain a urine output of 3–5 L per day. The median duration was 92 h.
Chung 2014	Aquadex system 100 at mean fluid-removal rate was 162 mL/h.	A mean daily furosemide dose of 212 mg per day.
Costanzo 2007	Aquadex System 100 at an average rate of 241 mL/h for 12.3 ± 12 h.	Average daily furosemide dose during the 48 h after randomization was 181 ± 121 mg.
Costanzo 2016	Aquadex FlexFlow System at an average rate of 138 ± 47 mL/h for 80 ± 53 h.	Average daily furosemide dose was 271.26 ± 263.06 mg for an average of 100 ± 78 h.
Giglioli 2011	PRISMATM System with a rate of fluid removal ranging from 100–300 mL/h for 46 h.	The dose at an initial 250 mg/24 h, and was gradually decrease according to patients' clinical situation.
Hanna 2012	NxStage System One with a UF rate set at 400 mL/h for 6 h and then decreased to 200 mL/h.	Doses and frequencies designated by the treating clinician.
Hu 2020	FQ-16 type HF ultrafiltration dehydration device with a UF rate set at 200–300 mL/h for 10.8 h/d	Mean torasemide dose: 20 mg/d, mean torvaptan dose: 10 mg/d
Marenzi 2014	A simplified device consisting of a peristaltic pump, a polysulphone filter. The average daily intravenous furosemide dose was 194 ± 175 mg/d.	Average daily furosemide dose was 153 ± 115 mg/d.
Seker 2016	The ultrafiltration rate was 150–400 mL/h. Mean duration was 20.5 ± 4.6 h.	Average daily furosemide dose was 164.1 ± 51.3 mg.
Shen 2017	FQ-16 with a rate of fluid removal ranging from 300 to 500 mL/h	Furosemide dose was 1 mg/kg
Shen 2021	FQ-16 with a rate of fluid removal ranging from 300 to 500 mL/h. Furosemide dose was 140 mg/d before randomization. 40 mg furosemide injection was given after ultrafiltration and 24 h after ultrafiltration.	Furosemide dose was 140 mg/d

1.99; $P < .001$; $I^2 = 47\%$] (Fig. 5A), MD (weight loss): 1.65 [95% CI: 0.90–2.41; $P < .001$; $I^2 = 62\%$] (Fig. 5B). The sensitivity analysis for the comparison of fluid loss and weight loss between groups did not change the overall result.

3.6. Adverse events

We have listed total adverse events in Table 3. We did not perform a meta-analysis for adverse events because of the heterogeneity of the kinds of adverse events in all studies.

Two primary studies have reported that adverse events in the UF group significantly increased compared with the diuretics group: a serious adverse event over the 60 days of follow-up in Bart et al[9] (UF vs diuretics: 68 vs 54, $P = .03$); an adverse event of special interest in Costanzo et al[12]: (UF vs diuretics: 34 vs 19, $P = .018$). In Bart et al,[9] serious adverse events included cardiovascular disorder, renal failure, bleeding complications, catheter-related complications, etc. In Costanzo et al,[12]adverse events of special interest included infection, bleeding, symptomatic hypotension, anemia, acute coronary syndrome, and most of the events need medical intervention. In Şeker et al,[17] there were more adverse events in the UF group: (UF vs diuretics: 8 vs 4). The adverse events included hematoma, infection and bleeding complications, hemodialysis, hypotension, cardiac arrest, and death. In Hanna et al,[14] adverse events per patient week were greater in the UF group (2.68 for UF vs 2.47 for diuretics, $P = .41$).

In Costanzo et al,[11] the total number of adverse events in the diuretics group was more than that in the UF group. The adverse events included catheter/needle site, filter, infection, bleeding,

Table 3

Results of studies.

	Heart failure rehospitalization		All-cause rehospitalization		Adverse events		Mortality		Fluid loss		Weight loss	
Study	UF	UC	UF	UC	UF	UC	UF	UC	UF	UC	UF	UC
Bart 2005					2		1/20	0/20	8.41 ± 3.64	5.38 ± 3.64	2.5 ± 1.2	1.86 ± 1.2
Bart 2012	23/90	24/93			68	54	16/94	13/94	7.44 ± 4.33	7.08 ± 4.18	5.7 ± 3.9	5.5 ± 5.1
Chung 2014			3/8	4/8	4	4					6.5 ± 3.6	7.4 ± 3.3
Costanzo 2007	16/89	28/87			101	119	9/94	11/95	4.6 ± 2.6	3.3 ± 2.6	5 ± 3.1	3.1 ± 3.5
Costanzo 2016	27/105	39/108			34	19	17/110	14/111	12.9 ± 10.78	8.9 ± 10.78	10.7 ± 7.2	10.3 ± 9.2
Giglioli 2011									9.7 ± 2.9	7.8 ± 2	9.1 ± 1.7	6.9 ± 1.8
Hanna 2012			8/19	6/17	2.68	2.47	4/19	4/17	5.22 ± 3.41	2.17 ± 2.39	4.7 ± 3.5	1 ± 2.5
Hu 2020			8/40	22/60	2		0/40	1/60			3.72 ± 3.81	1.34 ± 1.32
Marenzi 2014	3/27	14/29	7/27	17/29			7/27	11/29			7.5 ± 5.6	7.9 ± 9
Seker 2016					8	4	4/10	2/20	7.89 ± 1.83	6.89 ± 4.41		
Shen 2017											4 ± 8.35	0.6 ± 9.53
Shen 2021					0	2					4.1 ± 5.3	1.1 ± 3.4

UF = ultrafiltration, UC = usual care.

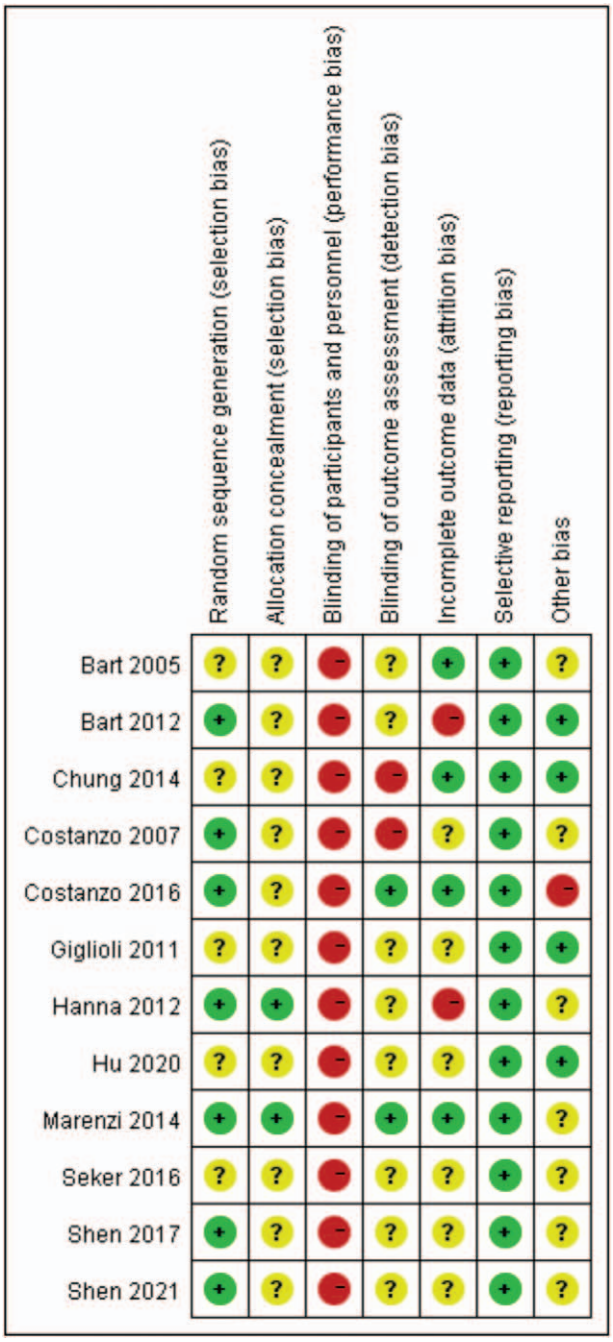

Figure 2. Risk of bias: low risk of bias (+), unclear risk of bias (?), high risk of bias (–).

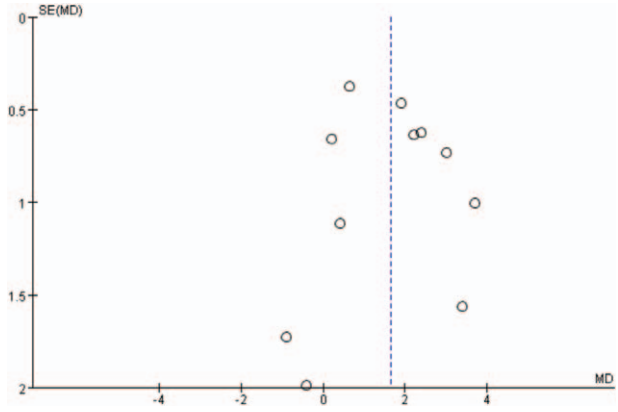

Figure 3. Funnel plot of weight loss.

hypotension, worsening heart failure, arrhythmias, cardiac arrest, dialysis, anemia, myocardial infarction, and neurologic. Among these kinds of adverse events, the number of hypotension, arrhythmias, anemia, and dialysis in the UF group were more than that in the diuretics group. In Yancy et al,[5] there was 1 death in the UF group during the 30-day follow-up period and one catheter site infection that required treatment. In the UF group of Hu et al,[15] two patients had subcutaneous congestion at the puncture site and no patient had an infection or major bleeding. In Shen et al,[19] there was 2 died during treatment in the diuretics group, due to worsening heart failure. There was no death in the ultrafiltration group, and no obvious adverse events occurred during and after ultrafiltration. In Chung et al,[10] 4 patients in each group developed a transient rise in Cr >0.3 mg/dL above the baseline line.

3.7. Subgroup analysis

3.7.1. Mean fluid-removal rate. According to mean fluid-removal rate, we identified 2 groups: mean fluid-removal rate ≥200 mL/h; mean fluid-removal rate <200 mL/h. Three studies[10–12] have reported mean fluid-removal rate. The mean fluid-removal rates in the 6 studies[8,14–16,18–19] were identified as ≥200 mL/h by the information provided by these RCTs. The mean fluid-removal rate in 1 RCT[9] was identified as <200 mL/h by the information provided by one article.[22] Subgroup analyses found a different magnitude of effect in the following aspects: weight loss, fluid loss, and heart failure rehospitalization. The MD of weight loss (≥200 mL/h) was 2.06 [95% CI: 0.92–3.2] compared with 0.14 (95% CI: −0.92–1.20) for lower fluid-removal rate (Fig. 6); the MD of fluid loss (≥200 mL/h) was 2.45 [95% CI: 1.80–3.09] compared with 0.14 (95% CI: –0.19–2.04) for lower fluid-removal rate (Fig. 7); the RR of heart failure rehospitalization (≥200 mL/h) was 0.45 [95% CI: 0.28–0.73] compared with 0.82 (95% CI: 0.60–1.12) for lower fluid-removal rate (Fig. 8).

3.7.2. Ischemic etiology. Seven RCTs[9–10,12–14,16,19] have shown the percentage of ischemic etiology for included patients. Ischemic etiology in 3 studies[9–10,13] was ≥50%, and the percentage in 4 studies[12,14,16,19] was <50%. The MD of weight loss (≥50%) was 0.72 [95% CI: −0.78–2.23] compared with 2.46 (95% CI: 0.71–4.22) for lower percentage of ischemic etiology (Fig. 9).

4. Discussion

Our analysis revealed that UF is a more effective way of removing fluid than diuretics. Rehospitalization for heart failure and all-cause, meanwhile, is lower than diuretics. Our results were partly consistent with Wobbe meta-analysis.[20] Moreover, we updated the review by adding 4 more studies, and heterogeneity was lower in our analysis. Heterogeneity still existed in weight loss regardless of sensitivity analysis, but not in fluid loss. The

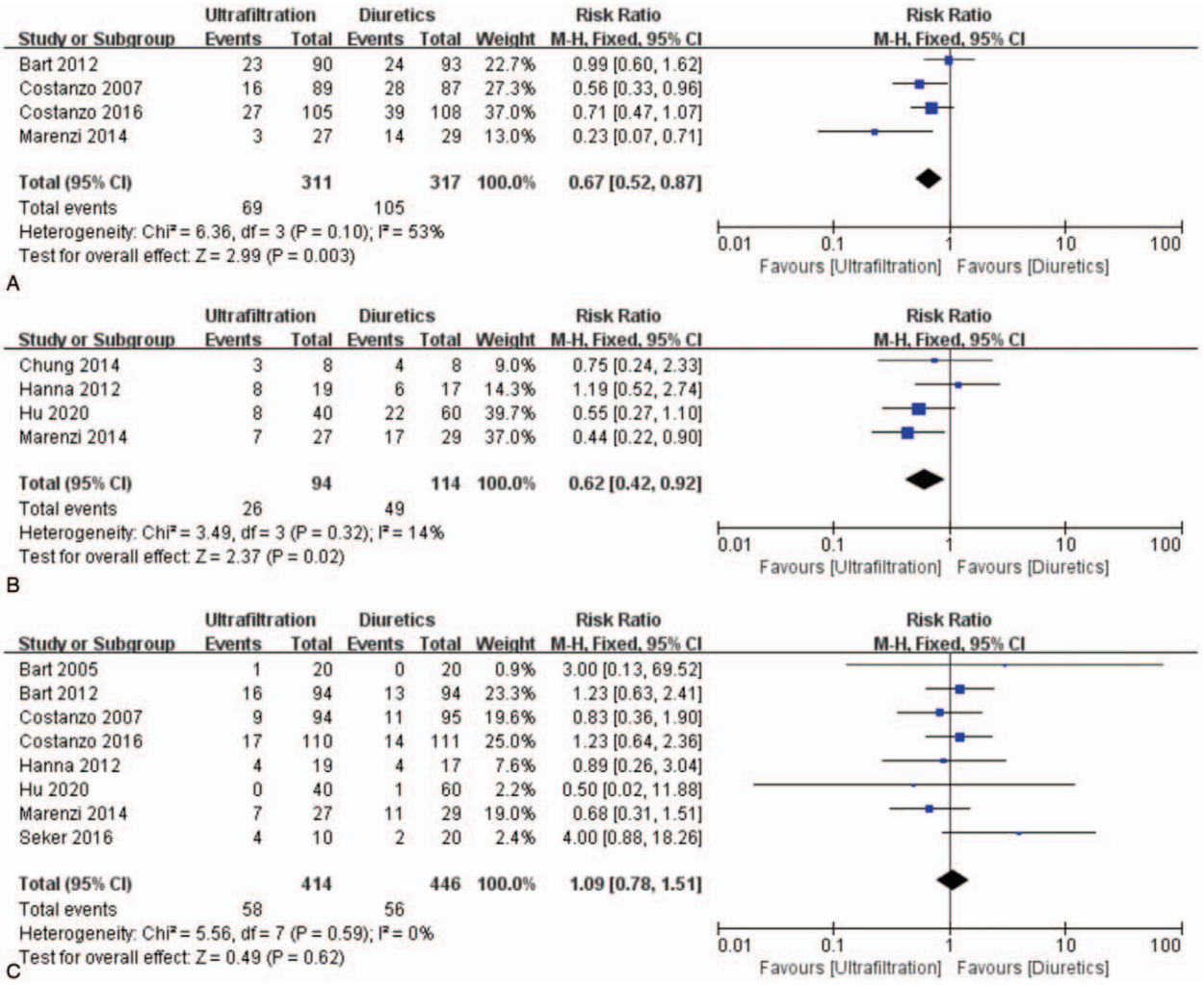

Figure 4. A, Heart failure rehospitalization. B, All-cause rehospitalization. C, Mortality.

probable reasons were variations in the protocols of both groups such as differences in water and sodium intake.

It is not surprising that ultrafiltration's ability in removing fluid is better than diuretics. There are 2 reasons that we supposed. Firstly, we can adjust the speed fluid loss and duration of UF according to patients' situations. However, when using diuretics, it's not so easy to control it, because every patient responds differently to diuretics. Secondly, we must pay attention to the fact that the majority of people in most of the included studies have been exposed to diuretics, which may decrease the efficiency of diuretics. Diuretic resistance may exist among some patients, this term, however, does not have a well-accepted definition so far.[2]

The readmission rate for heart failure, as we considered, was lower than diuretics due to the improvement of diuretic resistance. The dose of diuretics could be decreased after performing UF,[9] and sensitivity to diuretics can be restored in the process. Another reason may be related to removing more extra fluid. On the other hand, UF do not activate neuro-humoral activity, which was proved by Giglioli et al.[13] All-cause rehospitalization was significantly lower than the diuretic group. Indeed, heart failure readmission was involved. The result implies that UF, directly or indirectly, exerts a good effect on some of the disease that related heart failure.

A meta-analysis of Wobbe et al[20] suggested that UF is a safe and effective treatment without a difference in renal impairment, and lower incidences of worsening heart failure. Shi et al[21] concluded that UF did not have a difference in worsening heart failure, cardiovascular outcome, hemorrhage, the change of serum creatinine and infection, but not in hypotension. However, we cannot deny the fact that central venous catheter and heparin are used during the process of UF, and it must increase the risks of infection and hemorrhage. On the other hand, UF has, as we proved, the ability to removing more fluid, which may have the chance of causing renal dysfunction, although the meta-analysis of BW and XS did not reveal renal impairment. In our experience, patients with vascular and structural diseases of the kidney are more prone to renal impairment.

Subgroup analysis showed that UF with larger mean fluid-remove rate (≥200 mL/h) could significantly remove more fluid and lose more weight, most importantly, decrease heart failure

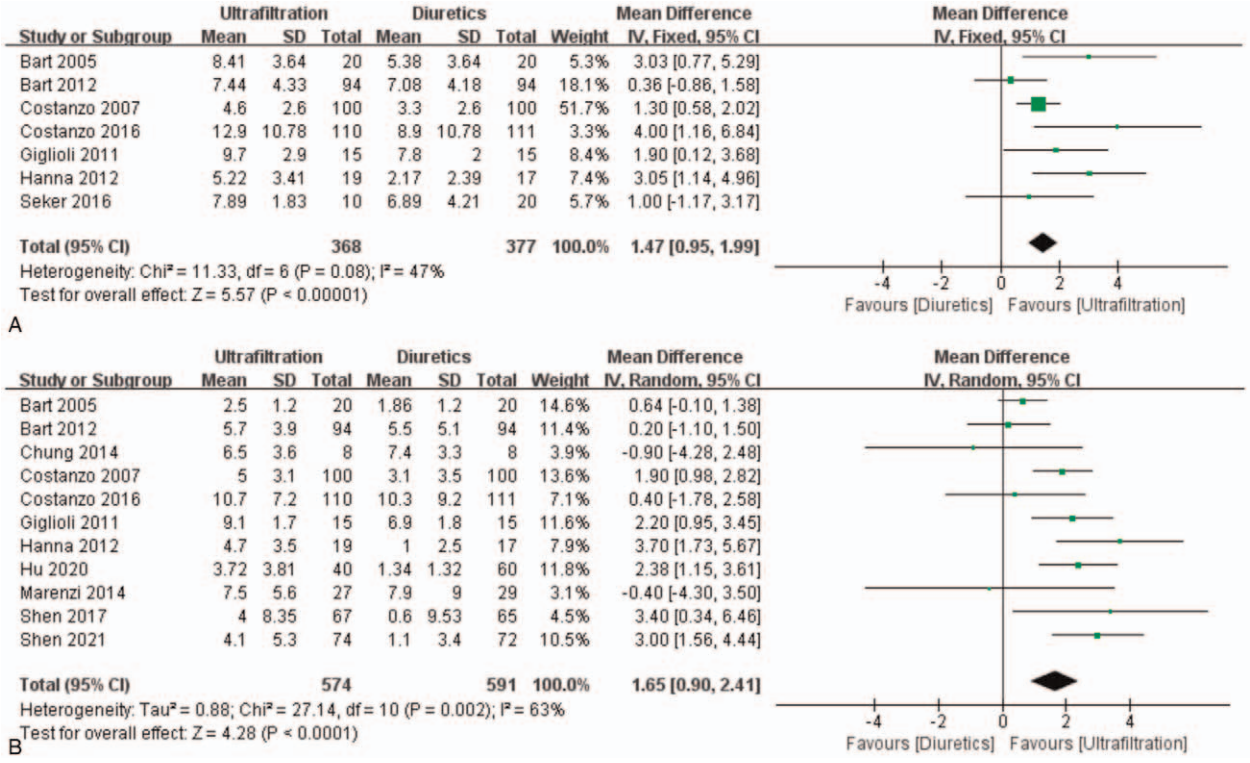

Figure 5. A, Fluid loss. B, Weight loss.

rehospitalization when compared with lower mean fluid-remove rate (<200 mL/h). Consequently, fluid-remove rate of UF is important for patients with ADHF. Larger fluid-remove rate may result in more fluid remove. Enough reduction of fluid excess will have a good effect on relieving decongestion and other good outcomes. In addition, suitable fluid-remove rate could reduce the risk of filter clogging. Subgroup analysis also implied that less weight loss for patients with ADHF in the process of UF correlated to higher percent of ischemic etiology (ischemic etiology ≥50%) and it is a weak conclusion.

More high-quality RCTs should be designed and implemented to enhance the level of evidence of the benefit of UF in the future.

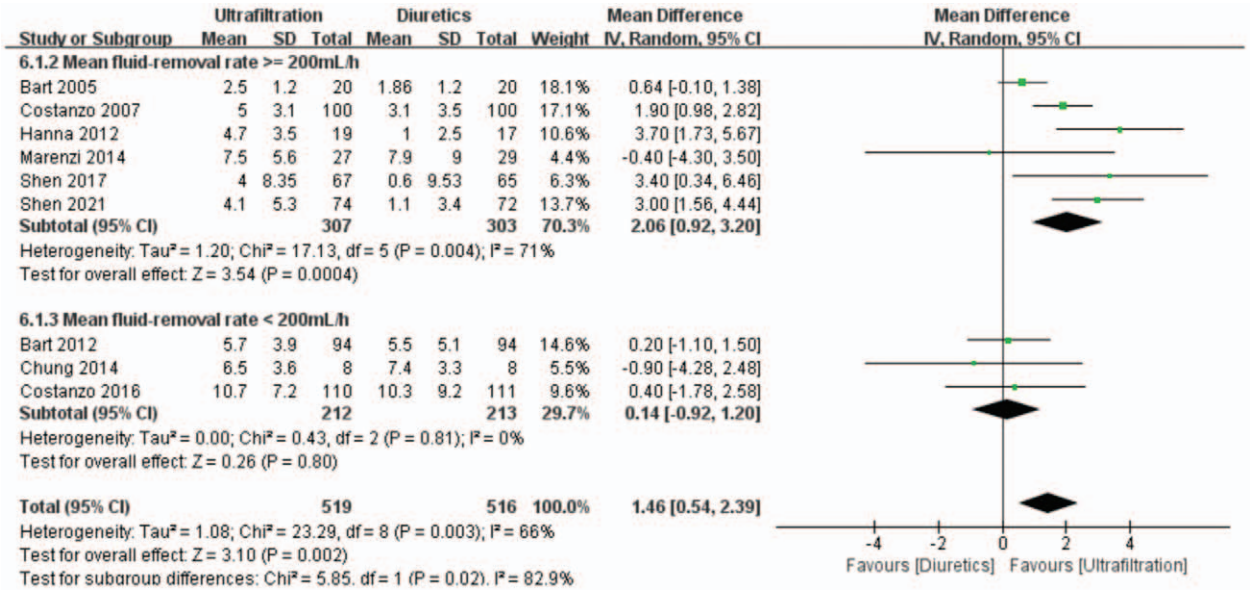

Figure 6. Subgroup analysis of weight loss for mean fluid-remove rate.

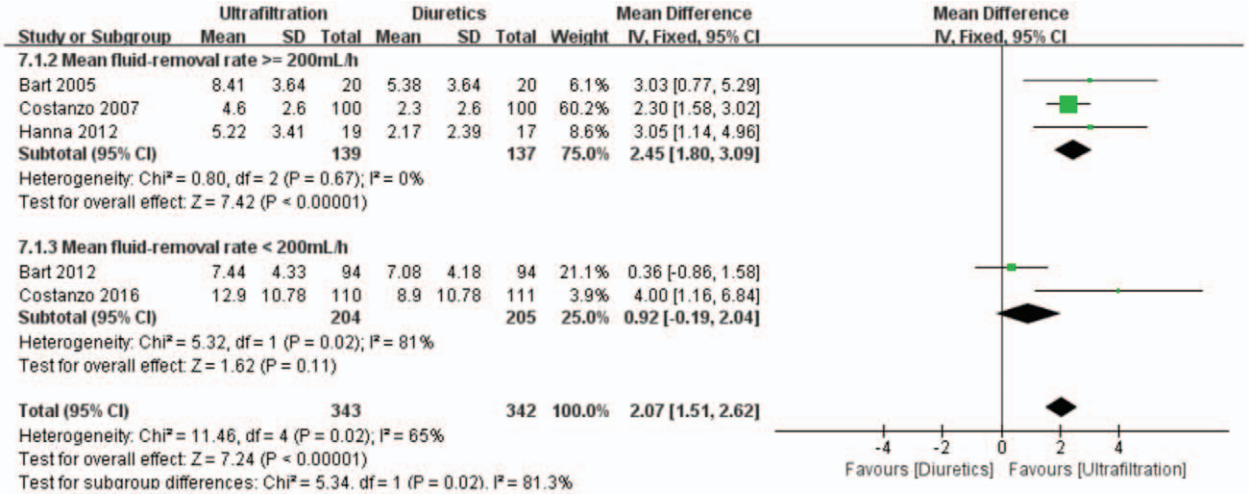

Figure 7. Subgroup analysis of fluid loss for mean fluid-remove rate.

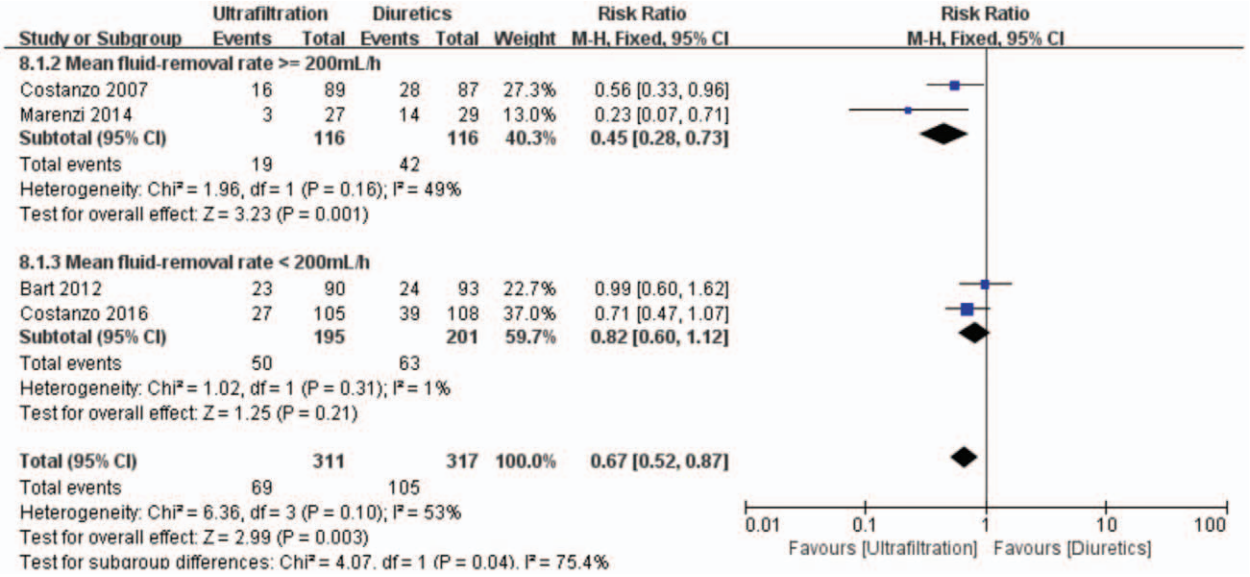

Figure 8. Subgroup analysis of rehospitalization for heart failure for mean fluid-remove rate.

As a treatment of ADHF, UF must be more suitable for some kinds of patients. Our study showed that patients with ischemic etiology may suffer from less weight loss. Therefore, future studies should figure out what kinds of patients are suitable for UF. How to use UF more safely and effectively should be focused on in future studies. Firstly, the fluid-removal rate is important. It is not suitable that the rate is too fast or slow. Besides, the fluid-removal rate could be adjusted by patients' conditions. Secondly, UF therapy should be precisely monitored to avoid hypoperfusion. Avoiding other adverse events such as bleeding and infection is also crucial. Lastly, more patients should be included in future studies to explore adverse events. Meanwhile, total adverse events are not an ideal end point, because diuretics and UF have different characteristics with respect to adverse events. For example, bleeding and infection are more likely to occur during ultrafiltration.

5. Conclusion

UF is more effective in removing fluid than diuretics and can decrease rehospitalization of heart failure and all causes. UF have a better function in solving "water problems" and improving diuretic resistance. However, there were inconsistent agreements about which group have more total adverse events and UF do not improve mortality in patients with ADHF. Therefore, we can't draw a conclusion that UF is superior than diuretics. UF with larger mean fluid-remove rate (≥200 mL/h) could significantly remove more fluid, lose more weight, and decrease heart failure

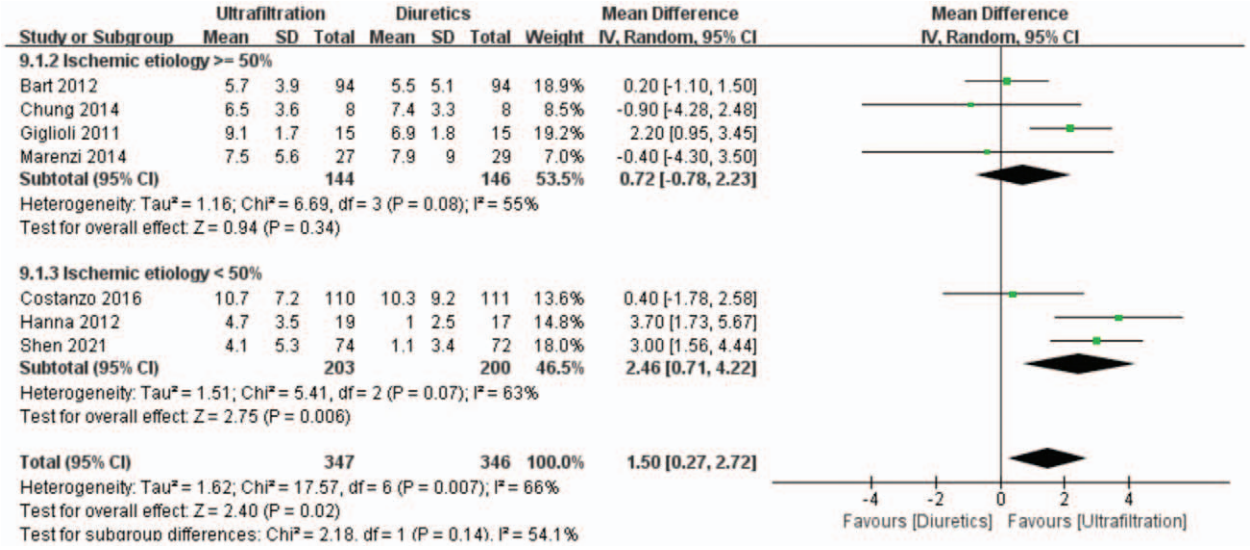

Figure 9. Subgroup analysis of weight loss for ischemic etiology.

rehospitalization. We can hold a clue that less weight loss for patients with ADHF may associated to higher percent of ischemic etiology. However, our study still had limitations. There was a high heterogeneity about weight loss and most RCTs did not provide enough information to assess the bias of RCTs. Due to the heterogeneity of the kinds of adverse events in all studies, we cannot make a consistent conclusion about the safety of UF.

Acknowledgments

The authors thank Xing-shun Qi, MD, for giving consultations about the work

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