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## [Intervention Review]

## Ultrafiltration for acute heart failure

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## ABSTRACT

#### Background

Pharmacotherapies such as loop diuretics are the cornerstone treatment for acute heart failure (AHF), but resistance and poor response can occur. Ultrafiltration (UF) is an alternative therapy to reduce congestion, however its benefits, efficacy and safety are unclear.

#### Objectives

To assess the effects of UF compared to diuretic therapy on clinical outcomes such as mortality and rehospitalisation rates.

#### Search methods

We undertook a systematic search in June 2021 of the following databases: CENTRAL, MEDLINE, Embase, Web of Science CPCI-S and ClinicalTrials.gov. We also searched the WHO ICTRP platform in October 2020.

#### **Selection criteria**

We included randomised controlled trials (RCTs) that compared UF to diuretics in adults with AHF.

#### Data collection and analysis

Two review authors independently assessed trial quality and extracted data. We contacted study authors for any further information, and language interpreters to translate texts. We assessed risk of bias in included studies using Risk of Bias 2 (RoB2) tool and assessed the certainty of the evidence using GRADE.

#### **Main results**

We included 14 trials involving 1190 people. We included people who had clinical signs of acute hypervolaemia. We excluded critically unwell people such as those with ischaemia or haemodynamic instability. Mean age ranged from 57.5 to 75 years, and the setting was a mix of single and multi-centre. Two trials researched UF as a complimentary therapy to diuretics, while the remaining trials withheld diuretic use during UF. There was high risk of bias in some studies, particularly with deviations from the intended protocols from high cross-overs as well as missing outcome data for long-term follow-up.

We are uncertain about the effect of UF on all-cause mortality at 30 days or less (risk ratio (RR) 0.61, 95% confidence interval (CI) 0.13 to 2.85; 3 studies, 286 participants; very low-certainty evidence). UF may have little to no effect on all-cause mortality at the longest available follow-up (RR 1.00, 95% CI 0.73 to 1.36; 9 studies, 987 participants; low-certainty evidence).

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UF may reduce all-cause rehospitalisation at 30 days or less (RR 0.76, 95% CI 0.53 to 1.09; 3 studies, 337 participants; low-certainty evidence). UF may slightly reduce all-cause rehospitalisation at longest available follow-up (RR 0.91, 95% CI 0.79 to 1.05; 6 studies, 612 participants; low-certainty evidence).

UF may reduce heart failure-related rehospitalisation at 30 days or less (RR 0.62, 95% CI 0.37 to 1.04; 2 studies, 395 participants; low-certainty evidence). UF probably reduces heart failure-related rehospitalisation at longest available follow-up, with a number needed to treat for an additional beneficial effect (NNTB) of 10 (RR 0.69, 95% CI 0.53 to 0.90; 4 studies, 636 participants; moderate-certainty evidence).

No studies measured need for mechanical ventilation.

UF may have little or no effect on serum creatinine change at 30 days since discharge (mean difference (MD) 14%, 95% CI –12% to 40%; 1 study, 221 participants; low-certainty evidence). UF may increase the risk of new initiation of renal replacement therapy at longest available follow-up (RR 1.42, 95% CI 0.42 to 4.75; 4 studies, 332 participants; low-certainty evidence).

There is an uncertain effect of UF on the risk of complications from central line insertion in hospital (RR 4.16, 95% CI 1.30 to 13.30; 6 studies, 779 participants; very low-certainty evidence).

## **Authors' conclusions**

This review summarises the latest evidence on UF in AHF. Moderate-certainty evidence shows UF probably reduces heart failure-related rehospitalisation in the long term, with an NNTB of 10. UF may reduce all-cause rehospitalisation at 30 days or less and at longest available follow-up. The effect of UF on all-cause mortality at 30 days or less is unclear, and it may have little effect on all-cause mortality in the long-term.

While UF may have little or no effect on serum creatinine change at 30 days, it may increase the risk of new initiation of renal replacement therapy in the long term. The effect on complications from central line insertion is unclear.

There is insufficient evidence to determine the true impact of UF on AHF. Future research should evaluate UF as an adjunct therapy, focusing on outcomes such as heart failure-related rehospitalisation, cardiac mortality and renal outcomes at medium- to long-term follow-up.

## PLAIN LANGUAGE SUMMARY

## Fluid removal therapy in acute heart failure

## **Review question**

What are the effects of ultrafiltration (UF), a fluid removal therapy, in acute heart failure (AHF)?

## Background

AHF is a common condition where the heart does not pump effectively, causing fluid to accumulate in the lungs and body. This causes difficulty in breathing, damage to heart and kidneys, high readmission to hospital and high death rates. Usual care involves medications called diuretics to remove this excess fluid, but some people may become resistant to it. UF provides an alternative therapy to quickly remove fluid. A circuit removes blood from the patient, which is then filtered in a machine before going back to the patient. It requires monitoring, a large central line cannula (tube into a blood vessel) and a blood thinning medication. It is unclear whether UF is effective or safe in AHF.

## **Study characteristics**

We searched for studies comparing UF to usual care in people with AHF. We searched for all relevant studies up to June 2021 and found 14 studies with about 1200 people. People who were very sick and frail, such as those who have had heart attacks and infections, were often not studied.

## Certainty of the evidence

We used a validated tool (GRADE) to assess how certain we were of our results. Overall, there was low-certainty evidence from these studies because of variability in the study settings, conflicting results between studies and limitations in how the studies were designed.

## **Key results**

We are uncertain whether UF has an impact on death rates at a short-term follow-up, as there are not enough data. At the longest time of follow-up, UF may have little effect on death rates.

UF may reduce readmission to hospital rates within the short and long term. In particular, readmission rates from heart failure are probably reduced by 31% when followed up over a longer time frame (up to one year). The benefit of reducing heart failure-related rehospitalisation is seen in 1 of 10 people treated with UF.

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UF may increase the risk of needing long-term dialysis. It is not clear whether UF affects kidney function at 30 days since hospital discharge, or if the risk of central line complications are greater with UF. No studies researched the effect of UF on needing mechanical breathing support, or its effect on cost and health economics.

More robust studies looking at UF in conjunction with current therapy are needed. These should focus on outcomes that are important to patients, such as heart failure-related hospital readmission rates, cardiac death rates and kidney damage at medium to long term.