

## Ultrafiltration in the management of refractory congestive heart failure

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**SUMMARY** Ultrafiltration was performed in nine patients with congestive cardiac failure that was refractory to conventional medical treatment. A mean of 12.7 litres of fluid was removed, and there was a sustained symptomatic improvement in all patients. Weight loss continued after ultrafiltration and a sustained increase in serum sodium concentration was also noted. A transient fall in right atrial pressure was seen only at four hours after ultrafiltration. No adverse haemodynamic effects were seen four and eighteen hours after fluid removal. Intracardiac dimensions measured by echocardiography remained unchanged. Ultrafiltration can be used to relieve symptoms in patients with refractory congestive heart failure and gross oedema.

Some patients with severe heart failure and gross peripheral oedema are resistant to conventional forms of medical treatment including vasodilators. In addition some patients become unresponsive to treatment because of the development of pharmacological tolerance or because of a further deterioration in cardiac function. Management of patients with refractory congestive heart failure is difficult because they have a poor prognosis and distressing symptoms of dyspnoea and gross peripheral oedema. The removal of large volumes of extracellular fluid by venesection, haemodialysis, and peritoneal dialysis is likely to provide such patients with symptomatic relief<sup>1</sup> but is limited by the tendency for adverse haemodynamic effects, such as hypotension and tachycardia, to develop.

Ultrafiltration, however, is a rapid method of selectively removing body water in which controlled fluid removal can prevent sustained haemodynamic upset.<sup>2,3</sup> In addition ultrafiltration can be performed by a venous technique and is less likely than haemodialysis to cause adverse haemodynamic effects.<sup>4,5</sup> Though symptomatic improvement has been demonstrated after ultrafiltration in individual patients with refractory congestive heart failure,<sup>6-8</sup>

there are no data on its haemodynamic effects. The aim of this study was to assess the symptomatic and haemodynamic response to ultrafiltration of patients who had severe congestive heart failure that was resistant to conventional forms of medical treatment.

### Patients and methods

All patients admitted with chronic congestive heart failure over a three year period were considered for ultrafiltration. In order to maintain an haemodynamically stable study population patients with valvar heart disease were excluded. Only nine patients remained in congestive heart failure with gross peripheral oedema after they had been treated with diuretics, vasodilators, and inotropic agents. These were the patients in whom we tried ultrafiltration (Table). Their ages ranged from 47 years to 65 years (mean 53 years). Fluid intake was restricted to 1 litre per day. The mean dose of frusemide was 600 mg/day (range 160-1000 mg/day) either orally or by intravenous infusion. Vasodilator treatment was continued in six patients. All patients had New York Heart Association class IV symptoms and all had gross peripheral oedema. Informed consent was obtained from all patients.

The following were measured daily—weight (kg); fluid balance; heart rate; systemic blood pressure (standard cuff sphygmomanometry); and serum

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Table Data on nine patients with congestive heart failure who were treated by ultrafiltration

Patient	Sex	Age	Aetiology	Daily drug treatment
1	M	49	Coronary artery disease	Frusemide 1000 mg, spironolactone 100 mg, digoxin 0.25 mg
2	M	47	Congestive cardiomyopathy	Frusemide 160 mg, spironolactone 100 mg, captopril 75 mg
3	M	51	Restrictive cardiomyopathy	Frusemide 500 mg, spironolactone 100 mg, isosorbide dinitrate 40 mg, nifedipine 40 mg
4	M	49	Coronary artery disease	Frusemide 240 mg, spironolactone 100 mg, digoxin 0.125 mg, captopril 75 mg
5	F	65	Congestive cardiomyopathy	Frusemide 1000 mg, spironolactone 200 mg, prazosin 4 mg
6	M	49	Restrictive cardiomyopathy	Frusemide 250 mg, spironolactone 100 mg, digoxin 0.25 mg, captopril 37.5 mg
7	M	56	Coronary artery disease	Frusemide 1000 mg, spironolactone 200 mg, digoxin 0.25 mg,
8	M	59	Congestive cardiomyopathy	Frusemide 320 mg, spironolactone 200 mg, digoxin 0.125 mg, prazosin 9 mg
9	F	47	Congestive cardiomyopathy	Frusemide 1000 mg, spironolactone 200 mg

urea, creatinine, and electrolytes. In six patients invasive haemodynamic monitoring and simultaneous M mode echocardiography were performed before and four hours and eighteen hours after the completion of each ultrafiltration procedure.

#### HAEMODYNAMICS

A Swan-Ganz catheter was inserted by internal jugular venous cannulation and manipulated into the right main pulmonary artery. The right atrial, pulmonary artery, and pulmonary capillary wedge pressures were measured and cardiac output was evaluated by the thermodilution technique by means of an IL 720 cardiac output computer. All measurements were made in triplicate and the mean of these results was taken.

#### ECHOCARDIOGRAPHY

M mode echocardiograms were obtained with an SKI Ekoline echocardiograph and left atrial, right ventricular, left ventricular end diastolic, and left ventricular end systolic dimensions were measured.

#### ULTRAFILTRATION

Ultrafiltration was performed by venous cannulation through a double lumen dialysis cannula in two patients, via the femoral approach in eight patients, and by the internal jugular approach in one. In seven patients a Gambro AK10 machine was used with a Cordis-Dow 1.5 m<sup>2</sup> cellulosic based membrane. In two patients a Fresenius A2008C machine was used with a new highly permeable polysulphone membrane (F60). The latter has the advantage of providing improved permeability and biocompatibility.<sup>9,10</sup> Ultrafiltration was continued until the development of either distressing muscle cramps or sustained hypotension. If peripheral oedema persisted the procedure was repeated on subsequent days depending on patient tolerance.

#### STATISTICAL METHODS

We used the paired Wilcoxon test for statistical analysis.

#### Results

The overall fluid loss ranged from 3.7 litres to 23 litres (mean 12.7). Ultrafiltration was performed 2–5 times per patient (mean 2.9) and lasted 45 minutes to 12 hours (mean 3.8 hours). The amount of fluid removed at each procedure was 1.7–6.0 litres (mean 3.0 litres) with the standard cellulosic membrane and 20 and 23 litres on the two occasions on which the polysulphone membrane was used. Each individual treatment was stopped because of muscle cramps or sustained hypotension. Transient

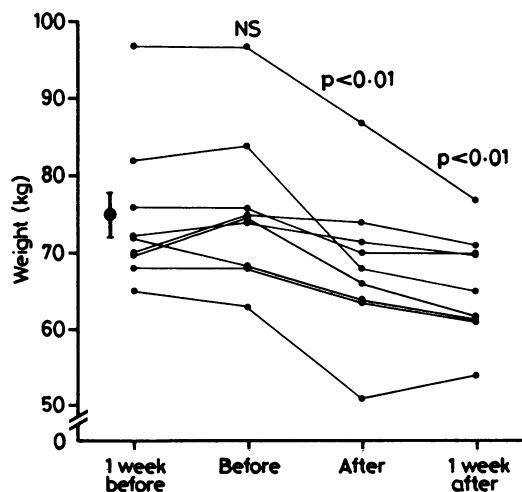


Fig. 1 Weights (kg) of individual patients and mean (SEM) measured one week before ultrafiltration, after the completion of ultrafiltration, and at one week after fluid removal.

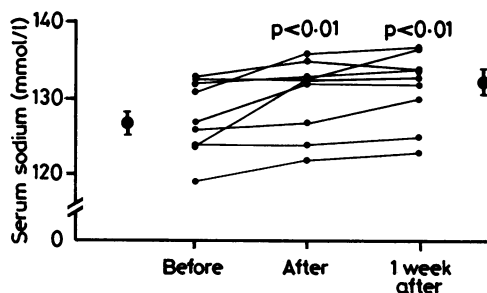


Fig. 2 Serum sodium concentrations for individual patients and mean (SEM) shown immediately before, after the completion of ultrafiltration, and at one week after ultrafiltration.

hypotension developed in all patients during the procedure; this responded rapidly to temporary discontinuation of fluid removal or, in four patients, to intravenous infusion of 20 g of albumin. Ultrafiltration was discontinued when it was considered clinically that the maximum benefit had been obtained.

Figure 1 shows patients' weights over the study period. No significant change in weight was seen during the week before ultrafiltration, indicating both a stable clinical state and a lack of response to drug treatment. Significant weight reduction occurred after ultrafiltration and continued in the week after the completion of ultrafiltration, indicating an improved response to diuretic treatment. Figure 2 shows the serum sodium concentrations. There was a significant increase in the serum sodium concentration after ultrafiltration and this increase was sustained over the subsequent week. No significant change occurred in either the serum urea or creatinine concentrations over the study period. Mean (SD) albumin concentration was unchanged (33 (4) g/l vs 35 (5) g/l) after ultrafiltration, despite the infusion of intravenous albumin during the procedure in four patients.

#### HAEMODYNAMICS

Right atrial pressure was significantly reduced four hours after the completion of ultrafiltration, though by 18 hours it had returned towards the value before ultrafiltration. No change was seen in the heart rate, mean systemic blood pressure, or mean pulmonary artery pressure. Pulmonary capillary wedge pressure (mean (SD)) which was 26 (6) mm Hg before ultrafiltration was unchanged four hours (27 (6) mm Hg) and 18 hours (31 (9) mm Hg) after completion of each ultrafiltration period. Similarly cardiac output (mean (SD)) which was 3.2 (0.7) l/min before ultrafiltration remained unchanged four hours (3.3

(0.6) l/min) and 18 hours (3.3 (0.4) l/min) after each procedure. Echocardiographic measurement of intracardiac dimensions remained unchanged throughout.

#### PROGRESS AFTER ULTRAFILTRATION

Symptoms improved and all patients became considerably less distressed immediately after ultrafiltration. Two patients who were non-insulin dependent diabetics developed systemic infection after ultrafiltration; the one with cellulitis had been treated for staphylococcal septicaemia before ultrafiltration. The source of infection in both cases was related to the indwelling Swan-Ganz catheter used for haemodynamic monitoring and not to the ultrafiltration procedure itself. In both cases staphylococci were isolated from blood culture within one week of ultrafiltration. Antibiotic treatment was successful in one, but the other patient died of ventricular fibrillation five days after the start of antibiotic treatment. Two patients were readmitted within three months of ultrafiltration with recurrence of peripheral oedema. Both these patients responded quickly to increased diuretic treatment and were able to be discharged home free of oedema after a short hospital admission. The remaining patients were free of oedema during subsequent follow up and one patient improved to New York Heart Association class III.

There were two hospital deaths after ultrafiltration. One patient with congestive cardiomyopathy and staphylococcal septicaemia died of documented ventricular fibrillation and the other, a patient with restrictive cardiomyopathy, of progressive deterioration in heart failure. A further five patients died during subsequent follow up (mean time to death 3.4 months, range 1–9 months). Sudden cardiac death was the presumed cause of all deaths and all the patients had remained free of oedema since ultrafiltration. The two surviving patients were oedema free throughout the subsequent year of follow up.

#### Discussion

This study has demonstrated that ultrafiltration is a safe, effective, and relatively simple method for producing symptomatic improvement in patients with refractory congestive heart failure.

The ultrafiltration procedure used in this study has several advantages in the management of these patients. First, the rate at which fluid is removed can be accurately controlled by altering the transmembrane hydrostatic pressure. This fine control of fluid removal is of considerable importance in preventing sustained haemodynamic upset in patients

who are already haemodynamically compromised. Towards the end of the study a new highly permeable, biocompatible filter became available and was used in two patients. In both of them over 20 litres of fluid was removed during a single ultrafiltration procedure. Use of this type of membrane may make it possible to render patients oedema free without the need for repeated intervention. The other major advantage is that vascular access is simple and necessitates only percutaneous central venous cannulation.

In our patients there was a significant improvement in serum sodium concentration, which was of similar magnitude to that found after ultrafiltration in fluid overloaded patients with renal failure.<sup>11</sup> All patients experienced transient hypotension when fluid was removed too rapidly during ultrafiltration. This was confirmed by pulmonary capillary wedge pressure measurement made in one patient during the procedure. When fluid was removed too rapidly from the intravascular compartment the wedge pressure fell from 30 mm Hg to 12 mm Hg with consequent fall in cardiac output and blood pressure. When ultrafiltration was transiently discontinued and intravenous albumin was infused, there was a rapid return to a stable haemodynamic state as the wedge pressure increased to 28 mm Hg. We therefore advise that the ultrafiltrate should be removed at a rate of less than 400 ml per hour and that intravenous albumin should be infused in hypoalbuminaemic patients in order to redistribute fluid from the interstitium into the intravascular compartment and promote removal by ultrafiltration.

As expected the reduction in weight found immediately after ultrafiltration reflected the amount of fluid removed during the procedure. Weight reduction continued over the week after ultrafiltration, however, and since fluid intake was restricted to one litre daily before and after ultrafiltration this indicates an improved response to diuretic treatment. This finding has been reported in fluid overloaded patients without pump failure<sup>11</sup> but its mechanism remains unclear. Though improved absorption of diuretic due to improvement of intestinal oedema may play a part in some patients, the continued weight reduction was also seen in those patients on intravenous therapy. In the absence of improved haemodynamics, an effect on the renin angiotensin

system or a resetting of baroreceptors must be postulated as a possible underlying mechanism.

Though sustained symptomatic relief from gross oedema was achieved in these patients there was no improvement in haemodynamic variables, except for a transient fall in right atrial pressure. This finding is not surprising in patients in whom the underlying pathophysiological mechanism is primary myocardial failure, since ultrafiltration is dealing only with the secondary effects. Nor can it be expected to improve outcome in a group of patients with such a poor prognosis.

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