

Continuous Renal Replacement Therapy for Congestive Heart Failure: The Wearable Continuous Ultrafiltration System

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Ultrafiltration is effective in the treatment of fluid and sodium overload in congestive heart failure. There is no available device to provide this therapy to ambulatory patients. We built and tested *in vivo* a wearable belt that can provide continuous ultrafiltration, 168 hours a week. Nine pigs underwent ureteral ligation and subsequently were allowed fluids *ad lib*, producing fluid overload. Next day, ultrafiltration was performed for 8 hours. The device consists of a hollow-fiber filter, a 9 V battery-operated pulsatile blood pump, a micro pump for heparin infusion, and another micro pump to control ultrafiltration rate. Blood flow was 65 ml/min and the weight of the device is less than 2.5 lb. Fluid removal rate ranged from 0 to 700 ml/h and averaged 106 ml/h. Salt removed was 7.6 g. No complications were observed. The potential impact on the quality of life of these patients by reducing the shortness of breath, leg swelling, and returning their ability to enjoy salt in their food might be significant, and a reduction in morbidity could be expected. The economic impact in reducing hospital admissions and length of stay, intensive care unit utilization, and drug consumption could be significant. Further studies are needed to compare this innovative approach with traditional drug-based therapy. ASAIO Journal 2006; 52:59–61.

The incidence of class III and IV congestive heart failure (CHF) continues to expand with the growing incidence of other conditions such as diabetes, obesity, coronary heart disease, and diastolic dysfunction.¹ In addition, the improved outcomes in ischemic heart disease and myocardial infarction fuel further increments in this population. The treatment of patients with this condition is one of the major expenses in the health care bill of any western nation, represents a most significant financial burden to US hospitals and the Medicare program.^{2,3}

The morbidity and mortality of this condition have been somewhat improved with numerous pharmacological agents such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, Nesiritide, diuretics, and β -blockers, as well as the use of pacemakers and implantable defibrillators.^{4–6}

However, not enough progress has been made in the treatment of fluid overload and sodium retention that are the

hallmarks of decompensated CHF and the main reasons for its increased morbidity and hospitalization requirements. These two complications are further aggravated by several endocrine derangements⁷ and release of noxious cytokines.⁸

There is a growing body of literature supporting the notion that the physical removal of fluid, cytokines and a myocardial depressant factor^{9,10} by convection (*i.e.*, blood ultrafiltration) can significantly improve outcomes and shorten hospital stays and intensive care unit utilization.^{11,12}

However, all present ultrafiltration methods depend on the use of stationary and bulky devices attached to wall electrical outlets and do not allow prolonged or continuous ultrafiltration. In addition, acute treatments performed over 4 to 6 hours of hemofiltration, although efficient and capable of removing up to 23 liters of fluid excess in one session, are not physiological and can be conducive to blunt shifts in fluid content in different compartments, hypotension, and hemodynamic instability. Furthermore, they do not provide for a steady removal of excess fluids and sodium.

We report the development and initial animal trials of a wearable continuous ultrafiltration device that can be used 24 hours a day, 7 days a week. This device can effectively remove the excess fluid and sodium overload in patients with class III and IV CHF.

Materials and Methods

This study was reviewed and approved by the Institutional Animal Care and Use Committee at Cedars Sinai Medical Center, Los Angeles, CA. Nine pigs, weighing 126 lb on average, underwent surgical ligation of both ureters and, subsequently, were allowed fluids *ad lib* to produce acute renal failure and fluid overload.

After 24 to 48 hours, the animals were anesthetized and a double-lumen catheter was inserted in the jugular vein. The carotid artery was cannulated as well for blood sampling. The double lumen catheter was connected to the continuous ultrafiltration device and the blood ultrafiltered for 8 hours. The device consisted of a hollow-fiber filter, a pulsatile blood pump, a heparin reservoir and a micro pump for heparin infusion, and another micro pump to control the amount of ultrafiltrate removed. Heparin was infused into the blood circuit regularly to prevent the clotting of blood in the device. The pulsatile pump used a 9 V energy source, and it propelled the blood through the device. The average blood flow was 65 ml/min. The total weight of the device is less than 2.5 lb.

The design of the device is shown in **Figure 1**. The proposed ergonomic adaptation to the human body is shown in **Figure 2**, and the proposed blood access is a double lumen and double cuffed central venous catheter, tunneled under the skin and

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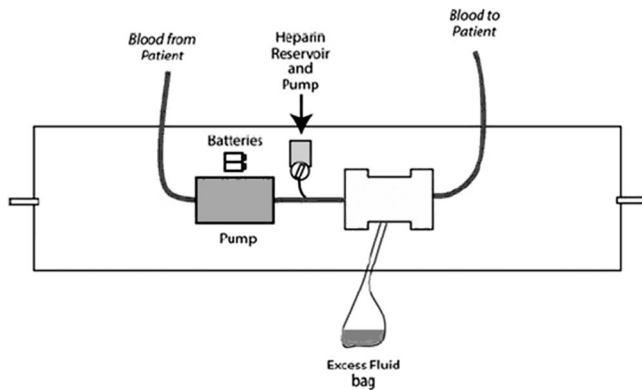


Figure 1. The design of the wearable continuous ultrafiltration system.

exiting at the level of the waist (**Figure 3**). The animals were euthanized at the end of the procedure, while still under general anesthesia, using a commercially available solution.

Results

The amounts of fluid removed from each animal by the device are shown in **Table 1**. The amount of fluid removal was controlled by a volumetric pump or manually adjusted by partially or completely occluding the exit of the ultrafiltrate to the collection bag. The hourly amount of fluid removed ranged from 0 to 700 ml/h. The average blood flow was 65 ml/min and the average fluid removal was 106 ml/h. The average amount of salt removed was 7.6 g per 8 hours. No complications were observed. There were no complications or untoward effects on the animals attributable to the ultrafiltration during the experiments.

Discussion

There is a growing body of literature supporting the notion that blood ultrafiltration is an effective tool in the treatment of class III and IV CHF patients.^{13–16} It has been shown to have significant effects on the electrolyte and endocrine derangements associated with this condition. Also, it allows for the

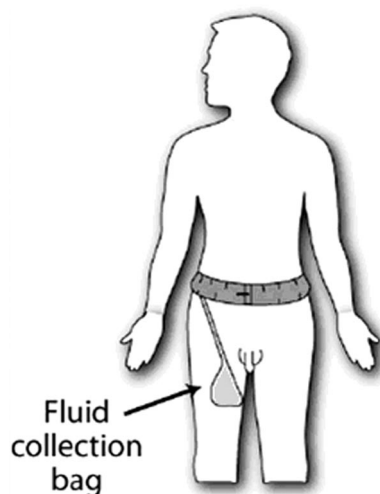


Figure 2. The proposed ergonomic adaptation to the human body.

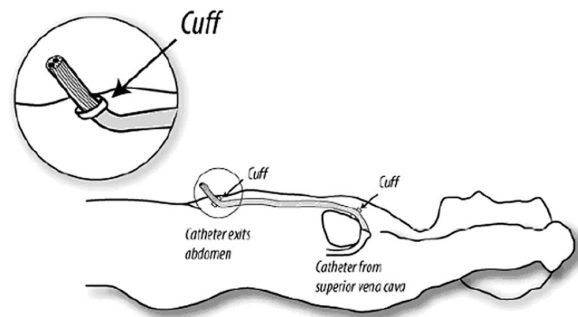


Figure 3. Proposed blood access is a double-lumen and double-cuffed central venous catheter, tunneled under the skin and exiting at the level of the waist.

avoidance of diuretics that are so often conducive to renal failure, hypotension, and further metabolic complications. However, this can only be accomplished by using stationary dialysis machines or ultrafiltration devices that are not amenable to be worn on the patient's body and used continuously while the patient is ambulatory.

The aim of the present experiments was to evaluate the safety and efficiency of ultrafiltration with a novel miniaturized device that can be worn on the patient's body while performing slow continuous ultrafiltration, 24 hours a day, 7 days a week. In this study, the device performed flawlessly in terms of ultrafiltrated fluid removal at a wide range of volumes, from 0 to 700 ml/h. The noise level was negligible, and there were no operating difficulties, except for a decrease in blood flow through the device as the ultrafiltration rate exceeded 700 ml/h. This is attributable to the marked hemoconcentration inside the hollow fibers of the device because of the removal of too much water. A decrease in the rate of ultrafiltration resulted in the normalization of the blood flow.

The effective removal of such large quantities of water from a patient at virtually any long-term ultrafiltration rate, that a treating physician might prescribe, points to the fact that this device may be a valuable tool for the treatment of fluid overload, especially in CHF patients. The use of a very low blood flow of only 65 ml/min makes it very unlikely that these very ill patients may experience blunt compartment shifts or hemodynamic compromise.

To our knowledge, there is no other device available in our therapeutic arsenal to treat ambulatory patients with ultrafiltration 24 hours a day and 7 days a week continuously. The device described here would reduce the incidence of acute pulmonary edema, ascites, and other stigmata of class III and IV CHF. Also, ultrafiltration has been shown to spare and even improve renal function in CHF patients, in contrast to the deleterious effects of diuretics on glomerular filtration rate.^{17,18} Worsening of renal function has been recently associated with a markedly increased mortality.^{19,20} Thus, a significant reduction in the use of diuretics and other drugs by these patients would hopefully be beneficial in preventing worsening azotemia as a result of massive diuretic use.

The device is a very effective tool for the removal of sodium. Because sodium retention is one of the cardinal problems of CHF, these unfortunate patients are usually condemned to draconian restrictions of salt intake, commonly 2 to 3 grams per day. However, the salt concentration in the ultrafiltrate is equal to that of the plasma, *i.e.*, 0.9 grams of salt per 100 ml. Thus, a steady removal of 1.5 to 2 liters per day would result

Table 1. Average Blood Flow (Qb) and Cumulative and Average Ultrafiltration Rate (UF, in milliliters) from Each Animal

Pig No.	1	2	3	4	5	6	7	8	9	Average
Qb, ml/min	38.6	44.2	54.2	69.5	62.2	81.7	78.2	79.1	75.4	64.8
UF, 1 h	100	150	180	160	390	50	190	90	225	170.5
UF, 2 h	200	220	200	370	500	85	370	190	260	266.1
UF, 3 h	300	380	350	560	540	95	440	360	355	375.6
UF, 4 h	500	500	700	725	540	95	545	520	390	501.7
UF, 5 h	800	600	700	810	540	160	545	520	435	568.9
UF, 6 h	1000	680	1400	880	600	445	545	520	525	732.8
UF, 7 h	1100	700	1400	960	640	625	620	580	615	804.4
UF, 8 h	1150	800	1400	1000	645	685	645	640	680	849.4
UF, average	144	100	175	125	81	87	81	80	85	106

in the removal of 13.5 to 18 grams of salt per day from a patient. We would hope that this would result in somehow alleviating some salt intake restrictions.

Because intermittent blood ultrafiltration has already been shown to improve outcomes in these patients, we have some reason to believe that the impact in outcomes with this ultrafiltration device will be as beneficial to CHF patients. The impact on their quality of life by reducing the shortness of breath, leg swelling, and returning to them some ability to relax salt intake restrictions in their food might be significant but difficult to quantitate. Furthermore, we would expect improved outcomes in the treatment of CHF patients, namely, a reduction in morbidity. Further clinical studies as well as widespread adoption and patient satisfaction studies would be needed to quantitate these results.

The risk of infection with this device is no different from any other implanted or extra corporeal device. However, we believe this risk can be greatly mitigated by using strict sterile conditions such as in an operating room environment whenever the blood circuit is manipulated. Currently, many indwelling catheters inserted in large vessels are opened and closed by a nurse or a technician who is not scrubbed, masked, and gowned and does not wear sterile gloves. Also the patient is neither gowned nor masked. We believe that observing simple sterility measures will greatly mitigate the risk of infection. Furthermore, in many cases, catheters are flushed and capped after use. Then, until the next use, sometimes 2 or 3 days later, a stagnant column of fluid remains in the lumen of the catheter and any bacteria in that column of fluid is not exposed to antibodies or white cells until the catheter is used again, allowing it to fester and multiply. The continued flow in our device would not allow such a thing to occur, and any bacteria that penetrated the blood circuit would be immediately washed out by the continued blood flow and dealt with by antibodies and white cells, further mitigating the risk of infection. Under no circumstances do we make the claim that infection will be completely avoided, but rather that the risk can be significantly mitigated.

The economic impact in the reduction of hospital length of stay, intensive care unit utilization, drug consumption, and number of hospital admissions may be considerable, and its actual value remains to be studied.

References

- Lewis CE, Jacobs DR Jr, McCreath H, *et al*: Weight gain continues in the 1990s: 10-year trends in weight and overweight from the CARDIA Study. *Coronary Artery Risk Development in Young Adults. Am J Epidemiol* 151: 1172–1181, 2000.
- American Heart Association. *Heart Disease and Stroke Statistics — 2005 Update*. Dallas, TX: American Heart Association, 2005.
- Krumholz HM, Parent EM, Tu N, *et al*: Readmission after hospitalization for congestive heart failure among Medicare beneficiaries. *Arch Intern Med* 157: 99–104, 1997.
- Stevenson LW: Tailored therapy to hemodynamic goals for advanced heart failure. *Eur J Heart Fail* 1: 251–257, 1999.
- Nohria A, Lewis E, Stevenson LW: Medical management of advanced heart failure. *JAMA* 287: 628–640, 2002.
- Fonarow GC: Pharmacologic therapies for acutely decompensated heart failure. *Rev Cardiovasc Med* 3 Suppl 4: S18–27, 2002.
- Schrier RW, Abraham WT: Hormones and hemodynamics in heart failure. *N Engl J Med* 341: 577–585, 1999.
- Levine B, Kalman J, Mayer L, *et al*: Elevated circulating levels of tumor necrosis factor in severe chronic heart failure. *N Engl J Med* 323: 236–241, 1990.
- Blake P, Hasegawa Y, Khosla MC, *et al*: Isolation of “myocardial depressant factor(s)” from the ultrafiltrate of heart failure patients with acute renal failure. *ASAIO J* 42: M911–915, 1996.
- Blake P, Paganini EP: Refractory congestive heart failure: Overview and application of extracorporeal ultrafiltration. *Adv Ren Replace Ther* 3: 166–173, 1996.
- Coraim FI, Wolner E: Continuous hemofiltration for the failing heart. *New Horiz* 3: 725–731, 1995.
- Agostoni PG, Marenzi GC, Pepi M, *et al*: Isolated ultrafiltration in moderate congestive heart failure. *J Am Coll Cardiol* 21: 424–431, 1993.
- Kramer P, Wigger W, Rieger J, *et al*: Arteriovenous haemofiltration: A new and simple method for treatment of over-hydrated patients resistant to diuretics (in German). *Klin Wochenschr* 55: 1121–1122, 1977.
- Silverstein ME, Ford CA, Lysaght MJ, *et al*: Treatment of severe fluid overload by ultrafiltration. *N Engl J Med* 291: 747–751, 1974.
- Donato L, Biagini A, Contini C, *et al*: Treatment of end-stage congestive heart failure by extracorporeal ultrafiltration. *Am J Cardiol* 59: 379–380, 1987.
- Sheppard R, Panyon J, Pohwani AL, *et al*: Intermittent outpatient ultrafiltration for the treatment of severe refractory congestive heart failure. *J Card Fail* 10: 380–383, 2004.
- Francis GS, Siegel RM, Goldsmith SR, *et al*: Acute vasoconstrictor response to intravenous furosemide in patients with chronic congestive heart failure; activation of the neurohumoral axis. *Ann Intern Med* 103: 000–6, 1985.
- Gottlieb SS, Brater DC, Thomas I, *et al*: BG9719 (CVT-124), an A1 adenosine receptor antagonist, protects against the decline in renal function observed with diuretic therapy. *Circulation* 105: 1348–1353, 2002.
- Hillege HL, Girbes ARJ, de Kam PJ, *et al*: Renal function, neurohormonal activation, and survival in patients with chronic heart failure. *Circulation* 102: 203–210, 2000.
- Weinfeld MS, Chertow GM, Stevenson LW: Aggravated renal dysfunction during intensive therapy for advanced chronic heart failure. *Am Heart J* 138: 285–290, 1999.