Hydrodynamic Analysis of the Miniaturized Hemofilter for a Wearable Ultrafiltration Device

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Key Words

Acute kidney injury • Artificial kidney • Computed tomography • Extracorporeal dialysis • Heart decompensation • Hemofiltration • Perfusion

ments of wearable medical devices and its structural design enables uniform blood flow distribution and stable hydrodynamics during operation.

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Abstract

Background/Aims: Using a small wearable hemofiltration device, heart failure (HF) patients may have the possibility of eliminating acute hemodynamic changes and the freedom from spending many hours attached to a large stationary treatment system. **Methods:** We developed a miniaturized hemofilter for a vest-type wearable ultrafiltration device for the treatment of overhydration and congestive HF. In this study, we investigated the feasibility of the newly developed hemofilter based on dynamic CT imaging and in vitro evaluation of hydrodynamic properties. **Results:** The dynamic CT imaging technique showed development of uniform flow distribution and effective bubble removal in the hemofilter. Hydrodynamic performance of the hemofilter was also acceptable with a stable pressure drop in the blood compartment and ultrafiltration profiles in the intended operating ranges for the treatment of congestive HF patients. **Conclusions:** The newly developed miniaturized hemofilter for a wearable ultrafiltration device meets the technical require-

Introduction

In the US, heart failure (HF) incidence approaches as much as 10 per 1,000 inhabitants >65 years of age [1]. Acute decompensated HF and fluid overload are the most common causes of hospitalization in HF patients [2]. Up to 75% of HF hospitalizations are caused by exacerbations of chronic disease. These are often triggered by nonadherence to sodium and fluid restriction, delayed recognition of signs and symptoms of congestion, worsening underlying renal insufficiency and diuretic resistance. Congestion hastens the progression of HF while its early resolution is associated with improved outcomes [3–5]. Patients with acute decompensated HF are generally treated with intravenous diuretics, which have limited efficacy especially in patients with chronic kidney disease [6], which has spurred an increased interest of the cardiology community in extracorporeal techniques of fluid removal. Conventional renal replacement therapy can be

a treatment option in case of fluid overload in patients refractory to diuretic therapy [7, 8]. However, current renal replacement therapy requires the use of stationary and bulky devices. Such acute hemofiltration treatments are time consuming (lasting >4–6 h) and they do not provide a steady removal of excess fluid and sodium.

A small wearable device that allows ambulatory hemofiltration to be performed in a slow and continuous fashion could offer patients the possibility of eliminating acute hemodynamic changes and the freedom from spending many hours attached to large stationary ultrafiltration machines, which are currently used for continuous renal replacement therapy. A wearable ultrafiltration device should facilitate prolonged frequent treatment at a low blood flow rate (<100 ml/min) for more than 12 h during the patient's daily activities. To be wearable, a hemofiltration unit should be simple and a blood pump control system should be combined with a hemofilter [9]. However, a lower blood flow rate increases membrane contact time, which accelerates blood-membrane interaction; consequently, membrane fouling or cake layers can develop on the surface of the dialysis membrane over long treatment times [10]. Therefore, blood flow distribution in a hemofilter for a wearable ultrafiltration device should be uniform to prevent clotting by hemoconcentration and stagnant flow.

CT imaging techniques are helpful to determine the adequacy of filter design and flow distribution. To analyze blood and dialysate flow distributions in hollow-fiber hemodialyzers, imaging techniques using a CT scanner have been used. Ronco et al. [11] suggested an imaging technique using a helical CT scanner and show effects of flow distributions on solute clearance in hemodialysis. Kim et al. [12] published three-dimensional flow perfusion maps in hollow-fiber hemodialyzers using perfusion CT and visualized flow mismatch between blood and dialysate flow that could lead to a reduction in solute clearance [13]. Additionally, hydraulic flow resistance, pressure drop in the blood compartment and hydraulic permeability are important parameters to decide specifications of hemofilters according to the clinical indication.

Recently, we developed a vest-type wearable ultrafiltration device for the treatment of overhydration and congestive HF, WAKMAN [14]: an easy-to-wear system compatible with daily activities of life, which allows a fully ambulatory treatment. It is equipped with an integrated pump-hemofilter unit, which is extremely compact and lightweight, a unit for the control/monitoring system utilizing wireless communication technology and a rechargeable battery placed in the back. In this study, we

Fig. 1. Integrated design of the miniaturized hemofilter with blood pump system. **a** Two rows of piezoelectric elements control the rates of blood flow and ultrafiltration. **b** A cassette-like hemofilter was designed to be integrated in the pump system; arrows show blood flow direction during the treatment. **c** The asymmetric structural design of the blood inlet port enhances uniform flow distribution.

evaluated blood flow distribution and hydrodynamic performances of the newly developed hemofilter for a wearable ultrafiltration device, WAKMAN, to investigate the feasibility of the miniaturized hemofilter for fluid-overloaded patients.

Materials and Methods

The hemofilter of WAKMAN was designed to meet the requirements of a wearable ultrafiltration device (fig. 1). It has a rectangular cuboid shape, to which a pump system can be integrated in a single unit and fitted in the vest pocket (fig. 1a, b). Technical data on the hemofilter are listed in table 1. Blood flows upward from the bottom to the top of the hemofilter to remove bubbles in the blood compartment of the hemofilter during the treatment. The asymmetric structure of the blood inlet port narrowing the gap from the left to the right side was designed to provide tangential and uniform blood flow distribution (fig. 1c). Operating ranges of blood and ultrafiltrate pump rates are 50–60 and 5–6 ml/min, respectively, and these pumps are driven by piezoelectric elements to avoid mechanical damage to blood cells.

Fig. 2. Cine scanning profiles of the miniaturized hemofilter. Uniform flow distribution develops in the hollow-fiber bundles after an initial phase of stabilization.

To analyze blood flow distribution in the hemofilter of WAKMAN, after priming blood and dialysate compartments with dialysate, the hemofilter was kept vertically by a support to generate upward blood flow. The dialysate compartment was hermetically closed so that transmembrane flux was not allowed. The scanning procedures were performed in two steps: the topogram for localization and cine scanning. The radiological parameters were as follows: 120 kVp, 200 mA, 512×512 matrix, 185-mm field of view, 0.5-s gantry rotation time and 10-mm scan coverage. Cine scanning was performed for 36 cycles supplying 30 ml/min of solution. The solution was composed of semi-skimmed bovine milk and Iomeron 200® (Bracco Diagnostics Inc., Princeton, N.J., USA) with a mixture ratio of 4.0:1.0 to simulate blood-like rheological properties, including a priming phase of the device with standard saline solution. We conducted two types of CT studies: the first was to analyze blood flow distribution under normal operating conditions and the second study was to observe the motion of air bubbles in the hemofilter. For the second study, we intentionally injected 2 ml of air using a 3-way stopcock and a syringe in the arterial line. Using an image processing program (ImageJ, version 1.43u; NIH), we analyzed blood flow distribution and bubble motion in the hemofilter. For quantitative analysis of perfusion profiles of contrast media with time, we normalized the intensity with the maximum value in the region of interest (ROI, $70 \times 30 \text{ mm}^2$) defined in figure 1b.

Hydrodynamic parameters of the hemofilter were measured using normal saline and semi-skimmed milk. Although normal saline and semi-skimmed milk are not able to mimic the non-Newtonian fluid behavior of blood, they are useful for the prediction of hydrodynamic performance and optimization of a hemofilter design in a preliminary step. A pressure drop in the blood compartment according to blood flow rate and effluent pressure was measured to calculate the transmembrane pressure (TMP). The ultrafiltration rate was directly calculated by measuring changes in the weight of the blood bag at 5-min intervals according to blood flow rate. The ultrafiltration coefficient of the hemofilter was calculated from the slope of the ultrafiltration rate – TMP curve.

Fig. 3. Normalized intensity profiles during contrast medium perfusion in ROIs of the miniaturized hemofilter.

Table 1. Technical specifications of the miniaturized hemofilter for WAKMAN

Internal fiber diameter	200 μm
Fiber wall thickness	30 μm
External fiber diameter	260 μm
Effective height	80 mm
Cut-to-cut height	100 mm
Number of hollow fibers	4,600
Effective surface area	0.3006 m^2
Priming volume in hollow-fiber bundle	14.5 ml
Total priming volume in the blood compartment	16.8 ml

Fig. 4. Cine scanning images of the miniaturized hemofilter after injection of air bubbles. Recovery of perfusion and removal of air bubbles are observed during the perfusion of contrast media.

Results

Figure 2 shows contrast medium perfusion profiles in the hemofilter with time. When contrast media arrived at the blood inlet port of the hemofilter, nonuniform flow distribution was observed for the first 3.0 s, with higher perfusion profiles in the right part of the fiber bundle. However, uniform flow distribution developed after 3.0 s as contrast media passed the whole hollow-fiber bundle and the perfusion profiles remained uniform until contrast media arrived at the blood outlet port of the hemofilter. Figure 3 shows normalized intensity profiles in ROI with time. At $t = 2.0$ s, there were some regions where contrast media were not properly perfused in the fiber bundle (A–C). However, as observed in figure 2, flow distributions in these regions recovered to normal values at $t = 4.0$ s.

When we intentionally injected air bubbles into the hemofilter, bubbles hindered blood stream flow into the hollow fibers for the first 5 s (fig. 4). However, as contrast media continued to flow through the fiber bundle, bubble size was reduced and uniform flow developed in the fiber bundle. From the movement of air bubbles from the right to the left part of the fiber bundle, it was possible to predict flow pathlines in the blood inlet indirectly.

Pressure drop in the blood compartment and TMP linearly increased with increasing blood flow rate for both normal saline and semi-skimmed bovine milk (fig. 5a, b) and the calculated ultrafiltration coefficients were 30.03 and 3.17 ml/h/mm Hg for normal saline and semi-skimmed bovine milk, respectively (fig. 5c), in the intended operating ranges of blood flow (50–60 ml/min) and ultrafiltration rate (5–6 ml/min) of the wearable ultrafiltration device (WAKMAN).

Discussion

In this study, we analyzed flow distribution and hydrodynamic performance of the newly developed hemofilter for a wearable ultrafiltration device. A dynamic CT imaging technique showed the development of uniform flow distribution and effective bubble removal in the hemofilter. Hydrodynamic performance of the hemofilter was also acceptable with a stable pressure drop in the blood compartment and ultrafiltration profiles in the intended operating ranges for the treatment of congestive HF patients. Development of uniform flow distribution and effective removal of air bubbles in hollow-fiber bundles of the newly developed hemofilter possibly were affected by the design of the blood inlet port (fig. 1c): tangential injection of the blood stream to the membrane potting and optimal asymmetry of the port enhanced flow distribution. In most hollow-fiber hemodialyzers, the arterial port (inlet cap) is designed to develop a normal blood stream to the surface of fiber potting. However, the modification in the arterial port design to tangential flow injection enhances flow distribution in peripheral regions of hollow-fiber bundles [11, 13].

The ultrafiltration coefficient of the newly developed hemofilter was overestimated in the hydrodynamic study with normal saline and underestimated for semi-skimmed milk. According to manufacturer's specifications, the selected membrane material of the hemofilter has an ultrafiltration coefficient of 42 ml/h/mm Hg/m². In our hydrodynamic study, this value was 9.51 ml/h/mm Hg/m². Theoretically, according to the international standard, a filtration test should be performed with anticoagulated bovine or human blood with a hematocrit of 32% and a protein content of 60 g/l [15]. The selection of a testing fluid influenced filtration performance of the hemofilter.

Fig. 5. In vitro test results on hydrodynamic performances of hemofilter with normal saline and semi-skimmed milk. **a** Experimental results with normal saline. **b** Experimental results with semi-skimmed milk. **c** Ultrafiltration rate and transmembrane pressure show a linear relationship for both normal saline and semi-skimmed milk.

In our study with semi-skimmed milk, milk fat and albumin possibly decreases effective membrane pore size despite the high water content compared to blood.

In conclusion, the newly developed miniaturized hemofilter for a wearable ultrafiltration device meets the technical requirements of wearable medical devices and its structural design enables uniform blood flow distribution and stable hydrodynamics during operation. A blood performance test is required to provide information on coagulation properties during the long treatment session for HF patients.

Acknowledgment

This study was supported by a Fondazione Cariverona grant (No. 2010.1087).

Disclosure Statement

Daniele Galavotti, Corrado Bellini and Matteo Brogli are employees of Rand S.r.l.; this study is partially supported by Rand S.r.l.

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