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Title:

A compliant, banded outflow cannula for decreased after-load sensitivity of rotary right ventricular assist devices

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Running Title

Decreased after-load sensitivity of a rotary RVAD

Abstract

Biventricular support with dual rotary ventricular assist devices (VADs) has been implemented clinically with restriction of the right VAD (RVAD) outflow cannula to artificially increase afterload and, therefore, operate within recommended design speed ranges. However, the low preload and high afterload sensitivity of these devices increases the susceptibility of suction events. Active control systems are prone to sensor drift or inaccurate inferred (sensor-less) data, therefore an alternative solution may be of benefit. This study presents the in-vitro evaluation of a compliant outflow cannula designed to passively decrease the afterload sensitivity of rotary RVADs and minimise left sided suction events. A one-way fluid-structure interaction model was initially used to produce a design with suitable flow dynamics and radial deformation. The resultant geometry was cast with different initial cross sectional restrictions and concentrations of a softening diluent before evaluation in a mock circulation loop. Pulmonary vascular resistance (PVR) was increased from 50 dyne.s.cm⁻⁵ until left sided suction events occurred with each compliant cannula and a rigid, 4.5 mm diameter outflow cannula for comparison. Early suction events (PVR ~ 300 dyne.s.cm⁻⁵) were observed with the rigid outflow cannula. Addition of the compliant section with an initial 3 mm diameter restriction and 10% diluent expanded the outflow restriction as PVR increased, thus increasing RVAD flow rate and preventing left sided suction events at PVR levels beyond 1000 dyne.s.cm⁻⁵. Therefore, the compliant, restricted outflow cannula provided a passive control system to assist in the prevention of suction events with rotary biventricular support while maintaining pump speeds within normal ranges of operation.

Keywords

Compliant cannula, suction event, physiological control, ventricular assist device, after-load sensitivity, heart failure.

Introduction

To address the worldwide shortage of donor hearts, ventricular assist devices (VADs) are used to support end stage heart failure patients to recovery, heart transplant or as a destination therapy. As the left ventricle is more susceptible to failure, most devices are implanted as a left VAD (LVAD). However, right heart dysfunction is considered one of the most serious complications following LVAD implantation [1]. While management of right heart failure may be achieved through administration of pharmaceutical treatment strategies, such as pulmonary vasodilators, inotropic agents and phosphodiesterase agents, placement of a right VAD (RVAD) has been reported in 5 to 48% of LVAD supported patients [2, 3]. While this indicates a large discrepancy between different reports on the requirement for RVAD support, it is clear that a treatment strategy for right ventricular failure is necessary.

As the majority of implanted devices are LVADs, device development and commercialization has followed a similar trend. In fact, the only devices currently approved for long-term right ventricular support by the Food and Drug Administration (FDA) are first generation, pulsatile blood pumps [4]. While these devices have supported a large number of patients, they are associated with a variety of negative attributes such as poor durability, haemolysis, thrombus formation and patient discomfort [5, 6]. The development of second and third generation rotary blood pumps (RBPs) has resolved many of these issues and resulted in improved survival and quality of life [6]. However, RBPs clinically approved for right heart assistance are limited by CE mark approval for only short term support [4].

To address the demand for long-term right heart support, some institutes have adapted clinically available LVADs to function as an RVAD. This has been achieved in humans with dual HeartWare HVAD (HeartWare Inc, Framingham, MA, USA), and Jarvik 2000 (Jarvik Heart Inc., New York, NY, USA) devices [7-9]. Various strategies have been employed to adapt these RBPs for right heart support. Some have attempted to reduce the pump speed to lower the outlet pressures [8]; however this may promote pump thrombus and impeller instability for hydrodynamically suspended devices [7]. Banding / restricting the RVAD outflow cannula diameter to approximately 5 mm has been shown to sufficiently reduce the RBP outlet pressure to match the pulmonary circulation [7], while allowing hydrodynamically suspended RBPs to operate about their rotational speed design point.

Unfortunately, RBPs lack the same level of preload sensitivity shown by the native heart or their pulsatile counterparts in fill-to-empty mode [10]. There are several clinical studies which warn of haemodynamic instability with rotary LVADs [11, 12]. The situation is further exacerbated with biventricular support, as the flow-balancing Starling response of the ventricles is diminished and thus can no longer be relied upon. Meanwhile, the afterload sensitivity of RBPs is overly high compared to the native heart [10], which results in reduced flow in cases of high outlet impedance, such as a sudden change in vascular resistance downstream of the RBP. This is particularly noteworthy for right heart support, as the right ventricle is more afterload sensitive than the left and systolic pulmonary artery pressures may rise above 60 mmHg in patients with severe pulmonary hypertension [13]. The importance of afterload sensitivity with rotary right ventricular support was highlighted by Hetzer et al. [7], who reported manually adjusting the banding diameter of the right-sided HeartWare HVAD to suit patients with different pulmonary vascular resistance (PVR).

Many reports have highlighted the importance of physiological controller development to prevent pulmonary oedema and suction events in the cannulated chamber [14, 15]. While some have described accurate control systems with rapid response times, most rely on sensor-based systems, which are prone to sensor drift or failure [16], or on sensor-less systems, which rely on potentially inaccurate inferred data [17]. Our group has presented the development of a passive control mechanism in the form of a compliant inflow cannula to increase the preload sensitivity of rotary LVADs and RVADs [18, 19]. However, this device is incapable of decreasing the inherently high afterload sensitivity of such devices. Therefore, the aim of this study was to develop, and evaluate in-vitro, a compliant outflow cannula to reduce the afterload sensitivity of rotary RVAD support by passively altering pump outflow.

Methods

Mock Circulation Loop

A physical five element Windkessel mock circulation loop (MCL) including systemic and pulmonary circulations was used for this study [20, 21]. Atrial and ventricular chambers were represented by clear, vertical polyvinyl chloride pipes with tee sections connecting the inflow, outflow and heart chambers. Ventricular systole was controlled through a series of electropneumatic regulators (ITV2030-012BS5, SMC Pneumatics, Brisbane, Queensland, Australia) and 3/2 way solenoid valves (VT325-035DLS, SMC Pneumatics) to provide passively filled heart chambers and variable contractility, heart rate and systolic time. A Starling response was implemented in both left and right ventricles which actively controlled ventricular contractility (through electropneumatic regulator supply current) based on ventricular preload [22]. Mechanical check valves were used to simulate the mitral, aortic, tricuspid and pulmonary valves. Four independent Windkessel chambers were employed to simulate lumped systemic and pulmonary arterial and venous compliance. Socket valves (VMP025.03X.71, Convair Engineering, Epping, Australia) allowed easy and repeatable manipulation of systemic and pulmonary vascular resistance. The working fluid throughout this study was a water/glycerol mixture (60/40% by mass) which, at a room temperature of 22°C, demonstrated similar viscosity (3.5 mPa.s) and density (1100 kg.m⁻³) to that of blood at 37°C.

Outflow Cannula Development

The MCL was initially used to assess the required RVAD outlet restriction diameter changes to balance circulatory flows during variations in PVR. MCL parameters were manipulated to represent a pharmaceutically treated severe biventricular heart failure condition, initially without RBP support (characterized in Table 1). Dual VentrAssist (Ventracor Ltd., Sydney, Australia) RBPs were connected to the left / right ventricles for inflow and the aorta / pulmonary artery for outflow (Figure 1). Both pumps were operated at the same rotational speed (2300 RPM), while the RVAD outflow cannula restriction diameter was increased from 3 mm to 6 mm, in 0.5 mm increments, using rapid prototyped tubing connectors. For each restriction diameter, PVR was manipulated until systemic and pulmonary flow rates balanced at 5.0 L/min.

Condition	MAP	MPAP	MSQ	MPQ	HR	SVR	PVR
	<i>mmHg</i>	<i>mmHg</i>	<i>L/min</i>	<i>L/min</i>	<i>BPM</i>	<i>dyne.s.cm⁻⁵</i>	<i>dyne.s.cm⁻⁵</i>
BHF	55	12	2.5	2.5	60	1300	100
BHF + RBP	100	18	5.0	5.0	60	1300	100

Table 1 – Haemodynamic parameters for steady state conditions of pharmaceutically treated severe biventricular heart failure (BHF) and severe BHF with dual rotary blood pump (RBP) support. MAP – mean aortic pressure, MPAP – mean pulmonary artery pressure, MSQ – mean systemic flow rate, MPQ – mean pulmonary flow rate, HR – heart rate, SVR – systemic vascular resistance, PVR – pulmonary vascular resistance.

Figure 1 - Schematic of the MCL setup for evaluation of the RVAD compliant outflow cannula. The final prototype is shown in the exploded image on the right. LA - left atrium, MV - mitral valve, LV - left ventricle, AoV - aortic valve, AoC - aortic compliance chamber, SQ – systemic flow meter, LVAD - left ventricular assist device, LVADQ – left ventricular assist device flow meter, SVR - systemic vascular resistance valve, SVC - systemic venous compliance chamber, RA - right atrium, TV - tricuspid valve, RV - right ventricle, PV - pulmonary valve, PAC - pulmonary arterial compliance chamber, PQ – pulmonary flow meter, RVAD - right ventricular assist device, RVADQ – right ventricular assist device flow meter, PVR - pulmonary vascular resistance valve, PVC - pulmonary venous compliance chamber. Arrows indicate direction of flow.

To determine the outflow cannula profile for suitable deformation, the resultant pressures on both sides of the restricted section at each level of PVR were used as boundary conditions in a one way fluid-structure interaction (FSI) model in ANSYS (Canonsburg, PA, USA). Using ANSYS WorkBench, CFX was used to solve the fluid component of the model, while Mechanical ANSYS Parametric Design Language (APDL) was used to solve the structural component. The one way FSI model allowed wall pressure generated by the fluid component to be exported to the structural component, while external wall pressure remained atmospheric. Flow was assumed to be laminar, Newtonian, viscous and incompressible while the fluid was modelled as the same water and glycerol mixture (60/40% by mass) used in-

vitro. All simulations were completed in the flow condition defined during the preliminary in-vitro testing at 5 L/min. The cannula wall was assumed to be hyperelastic, isotropic, incompressible and homogenous, while large deflections were allowed. The compliant outflow cannula was modelled as a soft translucent silicone rubber (RTV-2, Barnes, Brisbane, Australia) with the two parameter Mooney-Rivlin coefficients, C_{10} and C_{01} , of 0.0444 and 0.0083 MPa respectively [23].

Various cannula profiles were evaluated by altering the length of the restricted section (15mm, 20mm and 25mm) and the fillet applied to the restriction entrance (0mm, 2mm and 5mm). The symmetrical profile was also offset to reduce the divergence angle and limit outlet flow separation (symmetrical, 1:2 axial offset) according to Figure 2. Fixed supports were defined at each end. The radial deformation for each profile was determined through simulation of the corresponding inlet (LVAD outlet pressure) and outlet pressures (mean pulmonary artery pressure) from the in-vitro results at each level of PVR. Fluid velocity profiles were also recorded to identify regions of stagnant or recirculating flow.

Figure 2 – Example cross-sectional geometry of the compliant outflow cannula modelled in ANSYS including fillet radius (0, 2, 5 mm), length ($a+b$ – 15, 20, 25 mm) and offset symmetry ($a:b$ – 1:1, 1:2). Direction of flow is from left to right.

Construction and In-Vitro Evaluation

The selected cannula profile was cast with soft translucent silicone rubber (RTV-2, Barnes, Brisbane, Australia) with varying degrees of a softening diluent (0%, 10%, 20% and 30% by mass) (Silicone Diluent, Barnes, Brisbane, Australia) to achieve greater radial deformation during PVR changes. Unstressed restrictions of 3 and 4 mm with 1 mm wall thickness were cast with each concentration of diluent. Each silicone outflow cannula was cast in a rapid prototyped (Objet Alaris 24, Stratasys, Eden Prairie, MN, USA) mould and allowed to set.

The compliant section was then attached to the MCL in the same configuration as shown in Figure 1. LVAD speed was set to 2300 RPM for all experiments, while RVAD speed was manually adjusted to balance systemic and pulmonary flow rates at the lowest degree of PVR ($50 \text{ dyne.s.cm}^{-5}$) (Table 2). PVR was then increased from 50 to $1000 \text{ dyne.s.cm}^{-5}$, in increments of $50 \text{ dyne.s.cm}^{-5}$, or until left ventricular suction was observed (left ventricular volume $\leq 0 \text{ mL}$). Finally, the experiment was repeated with a 4.5 mm diameter rigid outflow cannula to compare the afterload sensitivity of each device.

Restriction diameter (mm)	4				3	Rigid
Diluent concentration (%)	0	10	20	30	10	-
Initial RVAD speed (RPM)	2300	2025	1900	1700	2625	2350

Table 2 – Right ventricular assist device (RVAD) speed for each cannula required to balance systemic and pulmonary flow rates at the lowest degree of pulmonary vascular resistance. RPM – revolutions per minute.

Data Acquisition

Haemodynamic and VAD parameters were captured at 100 Hz using a dSPACE acquisition system (DS1104, dSPACE, Wixom, MI, USA). Systemic and pulmonary flow rates were recorded using magnetic flow meters (IFC010, KROHNE, Duisburg, Germany) while LVAD and RVAD outlet flow rates were recorded with clamp-on ultrasonic flow meters (TS410-10PXL, Transonic Systems, Ithaca, NY, USA). Circulatory and VAD pressures were recorded using silicone-based transducers (PX181B-015C5V, Omega Engineering, Stamford, CT, USA) while left and right ventricular volumes were recorded using magnetostrictive level sensors (IK1A, GEFTRAN, Provaglio d'Iseo, Italy).

Results

Results were initially obtained to determine the required RVAD outflow diameter deformation during PVR changes to be used as boundary conditions in the FSI simulation. As expected, an increase in outflow cannula diameter resulted in higher pulmonary flow rates. The subsequent increase in PVR, required to balance systemic and pulmonary flow rates, resulted in increased pulmonary pressure with larger outflow diameters (Figure 3). This was particularly noticeable with RVAD outflow diameters above 4.5 mm, with the 6 mm diameter cannula requiring a PVR of 1000 dyne.s.cm⁻⁵ to maintain balanced flow rates of 5.0 L/min. In this condition, the mean pulmonary artery pressure reached a maximum of 71 mmHg, compared to just 12 mmHg with the 3 mm diameter cannula (PVR of 50 dyne.s.cm⁻⁵). These results were then used as the inlet and outlet boundary conditions for the FSI simulation.

Figure 3 –Result showing the RVAD outflow cannula diameter (ie. restriction diameter) required to balance systemic and pulmonary flow rates with increasing pulmonary vascular resistance (PVR) and the resultant increased mean pulmonary artery pressure (MPAP).

Results from the FSI simulation were obtained to determine an outflow cannula profile which would produce suitable deformation to balance systemic and pulmonary flow rates during changes in PVR. The radial deformation (Table 3), defined as the total change in restriction diameter due a simulated increase in mean pulmonary artery pressure from 12 mmHg to 71 mmHg, varied with restriction length, profile (symmetrical / offset) and fillet radius. Changes in profile resulted in large changes to radial deformation with the simulated increase in mean pulmonary artery pressure. For instance, the 15 mm long symmetrical cannula with 2 mm fillet experienced a change of diameter of only 0.10 mm compared with 0.51 mm with the 15 mm long offset cannula with 5 mm fillet. Similarly large deformation (0.49 mm) occurred

with the 20 mm long offset cannula with 5 mm fillet; however the two profiles produced varied results in the flow dynamics simulation (Figure 4). Although it exhibited slightly increased deformation, the shorter profile cannula appeared to result in regions of stagnation and recirculation at the entrance to the restriction, which was not observed with the longer profile version. Therefore, the 20 mm long offset cannula with 5 mm fillet was selected for in-vitro validation.

Length (mm)	15		20		25	
Profile	Symmetrical	Offset	Symmetrical	Offset	Symmetrical	Offset
No fillet	0.13	0.14	0.21	0.20	0.22	0.20
2mm fillet	0.10	0.26	0.16	0.21	0.18	0.20
5mm fillet	0.25	0.51	0.15	0.49	0.18	0.27

Table 3 – Simulation results of the total change in diameter (mm) for each profile when mean pulmonary artery pressure was increased from 12 to 71 mmHg. Geometrical features correspond to Figure 2 with fillets, lengths (a + b), symmetrical profiles (a = b) and offset profiles (a:b = 1:2). This simulation was completed using the soft translucent silicone rubber (RTV-2) model with no diluent and a flow rate of 5 L/min.

Figure 4 –Fluid velocity vectors for (a) the 20 mm long offset cannula with 5mm fillet and (b) the 15 mm long offset cannula with 5mm fillet. This simulation was completed using the soft translucent silicone rubber (RTV-2) model with no diluent and a flow rate of 5 L/min. Direction of flow is from left to right. Potential regions of recirculating and stagnant flow can be seen at the restriction entrance for the shorter profile.

Comparisons between a rigid outflow cannula and compliant outflow cannulae of varying diluent concentrations and restriction diameters during in-vitro simulations of PVR changes are shown in Figure 5. As PVR was increased from 50 to 300 dyne.s.cm⁻⁵ with the rigid outflow cannula, mean pulmonary flow rate reduced from 5.0 L/min to 4.4 L/min. This reduction in venous return to the left ventricle resulted in left ventricular volume decreasing from an initial 120 mL to 0 mL, thus demonstrating the potential for a left ventricular suction event. The compliant cannulae with 4 mm initial restriction and 0, 10 and 20% diluent concentrations resulted in only slightly higher levels of PVR (350 – 400 dyne.s.cm⁻⁵) before left ventricular suction. However, addition of more diluent (i.e. 30%) resulted in a lower reduction of pulmonary flow rate with increased PVR and maintained left ventricular volume

above 0 mL until PVR was increased beyond 600 dyne.s.cm⁻⁵. Reduction of the unstressed restriction diameter to 3 mm and a diluent concentration of 10% resulted in mean pulmonary flow rate being maintained at approximately 4.6 L/min with no suction events as PVR increased to the maximum value of 1000 dyne.s.cm⁻⁵. Greater diluent concentrations (20 and 30%) with the 3 mm restriction resulted in an overly compliant device which expanded excessively, while the 0% diluent was not suitably compliant to expand under the initial setup conditions and, therefore, significantly restricted flow through the RVAD.

Figure 5 – Resultant haemodynamic results during pulmonary vascular resistance (PVR) increases with a rigid outflow cannula and compliant cannulae of various diluent concentrations (0, 10, 20 and 30%) and unstressed restriction diameters (3 and 4 mm). MPQ – mean pulmonary flow rate, LVVsys – end systolic left ventricular volume.

Discussion

Biventricular support with dual RBPs has been reported clinically [7, 8, 24], and the stated success of this strategy may result in a long-term therapy for patients experiencing total heart failure. However with both ventricles possessing a reduced Starling capacity to alter cardiac output during changes in patient state, this approach is susceptible to flow imbalances and potentially harmful suction events. Many have reported the complexities of balancing systemic and pulmonary flow rates with dual rotary support, particularly in the early postoperative phase [7, 8, 14, 24]. Saito et al. [14] reported difficulties weaning from CPB due to requirements for delicate adjustment of BiVAD flow rate. Severe pulmonary congestion was also reported due to a sudden reduction of PVR following extubation, which was resolved through setting the Jarvik 2000 device (RVAD) to its minimum speed and adjusting the DuraHeart (Terumo Heart Inc, Ann Arbor, MI) LVAD speed to balance flow rates. However, this technique may result in a delay between the PVR reduction and the LVAD-induced increase in venous return to the right atrium, potentially causing intermittent suction events.

Restricting the RVAD outflow cannula allows both devices to operate at similar pump speeds near the middle of their suggested operating ranges, and thus provides a greater capability to increase or decrease either pump's rotational speed during changes in vascular resistance. This strategy has been evaluated extensively in-vitro [25] and reported clinically [7], with both highlighting the benefits which variable restrictions or automatic speed changes would have to better cope with changes in PVR. Our study demonstrated that a compliant, restricted RVAD outflow cannula can passively alter right sided support during changes in PVR. This strategy also maintained both LVAD and RVAD pump speeds within the recommended ranges, thus reducing the risk of impeller instability and pump thrombus [26, 27].

While each compliant outflow cannula maintained higher left ventricular volume with increased levels of PVR compared with the rigid outflow cannula, there were large differences between designs. As expected, increasing the softening diluent concentration to 30% resulted in a more compliant system and maintained left ventricular volume above 0 mL at PVR levels beyond 600 dyne.s.cm⁻⁵ with the 4 mm restriction. However, reduction of the restriction diameter to 3 mm and only 10% diluent maintained left ventricular volume above 0 mL at PVR levels beyond 1000 dyne.s.cm⁻⁵. This can be attributed to the initial RVAD

speeds required to balance systemic and pulmonary flow rates with low PVR. For instance, while the 4 mm restriction (30% diluent) was able to expand significantly under increasing pressure, the necessary low pump speed of 1700 RPM hindered the capacity to maintain pulmonary flow rates when PVR was significantly increased. Much higher RVAD speeds (2625 RPM) were required to overcome the initial restriction of the 3 mm cannula (10% diluent), which provided the capacity for suitable pulmonary flow rates as the restriction expanded with increasing PVR. The minor increase in left ventricular volume as PVR was increased beyond $400 \text{ dyne.s.cm}^{-5}$ with the 3 mm cannula (10% diluent) can be attributed to the increased RVAD speed and the non-linear elastic behaviour of the silicone restriction.

The capacity to maintain left ventricular volume above 0 mL with the compliant cannula was due to a decrease in afterload sensitivity, calculated by dividing the change in mean pulmonary flow rate per change in mean pulmonary artery pressure over the entire duration of the PVR increase. Salamonsen et al. [10] defined the afterload sensitivity of the DuraHeart and HeartWare centrifugal RBPs to be between 0.10 and 0.12 L/min/mmHg at various afterloads. These values are similar to those observed in our study, with an afterload sensitivity of 0.083 L/min/mmHg for the VentrAssist device with a rigid outflow cannula. Addition of the compliant outflow cannula decreased afterload sensitivities to 0.021 and 0.008 L/min/mmHg for the 4 mm (30% diluent) and 3 mm (10%) compliant cannulae respectively. These values compare closely to the healthy left ventricle, reported to be between 0.02 and 0.05 L/min/mmHg [10], thus demonstrating a more physiologic response to afterload changes compared to standard RBP therapy.

While dual RBP control strategies have been implemented in-vivo with some success, most rely on flow or pressure sensors which are prone to drift and may require recalibration [28, 29]. Passive control systems have also been reported which are hypersensitive to afterload [30] or specific to a single device [31]. Our system, which employs a compliant, restricted outflow section on the RVAD, passively deforms under changing PVR and, therefore, prevents left sided suction events without the requirement for sensors. A similar device could be used to reduce LVAD afterload sensitivity; however the initial pump speed would need to be sufficiently high to overcome the restriction. Nevertheless, there are also limitations associated with such a device including issues with implantability and durability, such as preventing tissue ingrowth and maintaining long term compliance, which must be addressed before progressing to the clinical setting. This study would benefit from improved

representation of ventricular suction through the addition of realistic ventricular wall dynamics, and characterization of the hyperelastic material characteristics with various concentrations of softening diluent. Meanwhile, further investigation and validation of the flow dynamics within the compliant outflow cannulas of various diluent concentrations is required to prevent flow separation and regions of stasis which may promote thrombus formation [32, 33].

Conclusion

This in-vitro study demonstrated the capacity of a compliant outflow cannula to passively alter RBP flow rate during changes in PVR. The ease with which left sided suction events can occur during increases in PVR with a RBP was demonstrated with a rigid, restricted outflow cannula. Addition of a compliant restricted section resulted in the capacity to prevent left sided suction events with increased PVR, and was dependent on the original restriction diameter and material properties (diluent concentration). Addition of the softening diluent and a smaller initial restriction diameter resulted in the lowest afterload sensitivity and, therefore, prevented suction events at the highest levels of PVR. Best results were achieved with a 3 mm diameter restriction with 10% diluent concentration which prevented left ventricular volume reducing below 0 mL at PVR beyond 1000 dyne.s.cm⁻⁵. This study revealed a compliant, restricted outflow cannula may be used as a passive control system to reduced afterload sensitivity and thus minimise harmful suction events with rotary biventricular support, while maintaining both pump speeds within normal ranges of operation.

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