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Passive Control of a Biventricular Assist Device with Compliant Inflow Cannulae

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Abstract

Rotary ventricular assist device (VAD) support of the cardiovascular system is susceptible to suction events due to the limited preload sensitivity of these devices. This may be of particular concern with rotary biventricular support (BiVAD) where the native, flow-balancing Starling response is diminished in both ventricles. The reliability of sensor and sensor-less based control systems which aim to control VAD flow based on preload have limitations and thus an alternative solution is desired. This study introduces a compliant inflow cannula (CIC) which could improve the preload sensitivity of a rotary VAD by passively altering VAD flow depending on preload. To evaluate the design, both the CIC and a standard rigid inflow cannula were inserted into a mock circulation loop to enable biventricular heart failure support using configurations of atrial and ventricular inflow, and arterial outflow cannulation. A range of left (LVAD) and right VAD (RVAD) rotational speeds were tested as well as step changes in systemic/pulmonary vascular resistance to alter relative preloads, with resulting flow rates recorded. Simulated suction events were observed, particularly at higher VAD speeds, during support with the rigid inflow cannula, while the CIC prevented suction events under all circumstances. The compliant section passively restricted its internal diameter as preload was reduced, which increased the VAD circuit resistance and thus reduced VAD flow. Therefore, a compliant inflow cannula could potentially be used as a passive control system to prevent suction events in rotary left, right and biventricular support.

Keywords

Compliant cannula, suction event, physiological control, biventricular assist device, heart failure.

Introduction

With a worldwide shortage of donor hearts, ventricular assist devices (VADs) are used as an alternative to heart transplantation to support end stage heart failure patients to recovery, future transplant or as a destination therapy [1]. VADs may be used to support the left (LVAD), right (RVAD) or both (BiVAD) sides of the heart. Ventricular dysfunction often occurs in the left ventricle, thus the many patients requiring mechanical circulatory support receive only an LVAD. However, the incidence of right heart dysfunction after LVAD insertion may be as high as 48% [2, 3] and is considered one of the most serious complications within the LVAD postoperative period [4]. Should pharmaceutical treatment strategies such as pulmonary vasodilators or inotropic agents fail, then there is little option but to use mechanical circulatory support to assist the right heart. The requirement for RVAD placement varies greatly between institutes, and has been reported between 5 and 48% of LVAD supported patients [2, 5, 6]. Several issues are apparent with BiVAD support, such as pump design, pump placement and flow balancing [7].

In healthy humans, flow balancing between the systemic and pulmonary circulations is regulated by several closed loop biological control systems such as the Frank-Starling and baroreceptor responses [8, 9]. Pulsatile VADs, when operated in a full-to-empty mode, have an inherent flow balancing capability which ensures the native circulations are not over- or under-loaded [10]. However, rotary VADs are relatively preload insensitive [11] and are prone to flow imbalances. Support by just one device (eg. LVAD support) may rely on having the native control mechanism of one functional ventricle (eg. Right ventricle) to balance flow. However, sudden changes in circulatory demands for which the rotary LVAD cannot account for may upset this balance, and thus LVAD support alone is still susceptible to flow imbalances. This situation is further exacerbated with the use of two rotary VADs for biventricular support, as any remnant native control mechanisms are absent due to the diminished left and right ventricular function. The few documented clinical studies of rotary biventricular support warn of haemodynamic instability [12-14] and report the importance of continued controller development to prevent pulmonary edema and suction events in the cannulated chambers. Suction events may result in harmful consequences such as full or partial / transient flow stoppages, endocardial damage and ventricular arrhythmias [15-18].

In order to balance flows with two Gyro pumps, Nosé et al. [19] incorporated inlet pressure sensors in each VAD to regulate flow, like the Frank-Starling mechanism. However, blood pump control systems like these may be limited by the low reliability of long term blood pressure and flow sensors [20]. Endo et al. [12] used VAD current to determine points of suction and full support in order to operate the VAD between these two points. While sensor-less systems such as this demonstrate promise, changes in the VAD circuit, such as the formation of thrombus, may give false estimations and lead to an inaccurate controller [21]. Reliability issues of sensor and sensor-less based control systems must be addressed before a reasonable solution can be found for clinical implementation.

Passive control systems which don't rely on sensors or inferred data to control the pump, have previously been used in the field of biventricular mechanical circulatory support. Gaddum et al. [22] used a two-sided, floating hub which was passively displaced by changes in LVAD and RVAD afterload which altered the clearance between the hub and the BiVAD impellers. The passively altered clearance aimed to alter LVAD/RVAD efficiency and thus balance the flow rates. However, this system resulted in hypersensitivity to afterload and insensitivity to preload, thus rendering it incapable of providing complete BiVAD control. Passive self-regulation is also used for the Cleveland Clinic continuous flow total artificial heart (TAH), which employs left and right supporting impellers on a single hub [23]. The position of the hub is dependent on the left / right atrial pressure difference and passively alters the right pump output through a change in outlet resistance, thus improving its preload sensitivity [24]. However, remnant ventricular contractility experienced in a BiVAD application may upset this ability for passive flow balance.

Our group has previously presented the use of a collapsible inflow cannula reservoir as a passive control system to prevent suction events during extracorporeal circulatory support of the left heart [25]. However, the additional volume of the reservoir removes the possibility for implantation whilst potentially promoting thrombus formation due to possible regions of stagnant flow. Therefore, the aim of this study was to investigate the use of a compliant, in-line inflow cannula (CIC) to improve the preload sensitivity of rotary VADs used in biventricular support, by passively controlling LVAD and RVAD outflow.

Methods

Mock Circulation Loop

A physical five element Windkessel mock circulation loop (MCL) including systemic and pulmonary circulations was used for this study [26, 27]. Atrial and ventricular chambers were represented by 40 mm and 50 mm respectively clear, vertical polyvinyl chloride (PVC) pipes with tee section connecting the inflow, outflow and heart chamber. Atrial volume was, therefore, directly related to the hydrostatic pressure in the chamber. In brief, ventricular systole was controlled through a series of electropneumatic regulators (ITV2030-012BS5, SMC Pneumatics, Brisbane, AUS) and 3/2 way solenoid valves (VT325-035DLS, SMC Pneumatics, Brisbane, AUS) 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 [28]. Mechanical check valves were used to simulate the mitral, aortic, tricuspid and pulmonary valves to ensure unidirectional flow throughout the circuit. Four independent Windkessel chambers were employed to simulate lumped systemic and pulmonary arterial and venous compliance. Proportional control valves (EPV-375B, HASS Manufacturing, NY, U.S.A.) allowed easy manipulation of systemic (SVR) and pulmonary (PVR) vascular resistance. Mechanical circulatory assistance was incorporated with cannulation through the atrium (AC) or ventricle (VC) for VAD inflow and the artery for VAD outflow. The working fluid throughout this study was a water/glycerol mixture (60/40% by mass) with similar viscosity and density to that of blood.

Cannula Construction and Evaluation

A smooth, 12 mm diameter rod was coated with two layers of 20 mL de-aired silicone (Silastomer P15, Dalchem, Cheltenham, Australia), with each layer allowed to set prior to adding the subsequent layer. The rod was removed, leaving a thin-walled CIC. The CIC had an average wall thickness of 2 mm, an inner diameter of 12 mm, a length of 100 mm, a priming volume of 22 mL and a compliance of approximately 0.125 mL/mmHg.

MCL parameters were manipulated to represent a medically treated, severe biventricular heart failure situation without VAD support. A VentrAssist (Ventracor Ltd., Sydney, Australia) rotary LVAD was connected to the MCL initially via the left atrium for LVAD

inflow and the aorta for LVAD outflow while a BP80 (Bio-Medicus, Inc., Eden Prairie, MN, USA) rotary RVAD was connected to the right atrium for RVAD inflow and the pulmonary artery for RVAD outflow (Figure 1). CICs were added to both the LVAD and RVAD inflow cannulae. VAD speeds were independently increased in increments of 100 RPM from 1800-3000 RPM for LVAD and 400-2000 RPM for RVAD to simulate a gradual change in preload. Step changes in PVR (100 to 400 Dynes.s.cm⁻⁵) and SVR (1500 to 2500 Dynes.s.cm⁻⁵) were independently made to induce sudden reductions in LVAD and RVAD preload respectively. All experiments were then repeated with the inflow cannulation site changed to the left and right ventricles. Finally, the study was repeated with the compliant inflow section replaced with rigid inflow cannula (RIC) made of PVC tubing for comparison. Suction events were defined as a left atrial pressure (LAP) or left ventricular volume equal to or less than zero. As this investigation focused on the haemodynamics leading to a suction event and preventing suction events occurring, no physical suction was represented in the system.

Data Acquisition

Haemodynamic and VAD parameters were captured at 100 Hz using a dSPACE acquisition system (DS1104, dSPACE, MI, USA). Systemic and pulmonary flow rates were recorded using magnetic flow meters (IFC010, KROHNE, Sweden) while LVAD and RVAD outlet flow rates were recorded with clamp on ultrasonic flow meters (TS410-10PXL, Transonic Systems, NY, USA). Circulatory and VAD pressures were recorded using silicon-based transducers (PX181B-015C5V, Omega Engineering, Connecticut, USA) while left and right ventricular volumes were recorded using a magnetostrictive level sensor (IK1A, GEFTRAN, Italy).

Results

Results were compared in AC and VC for LVAD and RVAD support to determine the effect of replacing the RIC with a CIC. An example comparison between RIC and CIC is shown in Figure 2. As the LVAD speed was incrementally increased from 1800 to 2400 RPM, the end systolic left ventricular volume (LVV_{sys}) gradually decreased, LVAD inflow cannula resistance (LVADR_{in}) stayed relatively constant, and the mean systemic flow rate (MSQ) gradually increased for both RIC and CIC. As the LVADR_{in} remained constant with VAD speeds between 2400 and 2900 RPM for the RIC, the LVV_{sys} gradually reduced to 0 mL, thus resulting in a suction event (predicted when LVV_{sys} < 0 mmHg). However, with the CIC, the LVADR_{in} steadily increased with VAD speeds higher than 2400 RPM, thus passively reducing the MSQ and maintaining positive LVV_{sys} and preventing a suction event.

As LVAD speed was increased from 1800 to 3000 RPM, LVADR_{in} remained relatively constant with the RIC (400 Dynes.s.cm⁻⁵), however increased from 400 to 3800 Dynes.s.cm⁻⁵ and 400 to 1600 Dynes.s.cm⁻⁵ (shown in Figure 2) with the CIC in AC and VC respectively. This gradual LVADR_{in} increase compensated for the LVAD speed increase, maintaining MSQ at approximately 4.8 L/min with both AC and VC whilst preserving positive LAP above 3 mmHg and/or LVV_{sys} above 70 mL (Figure 3). The onset profile of CIC restriction altered slightly when cannulation site was changed, with a rapid inflow restriction observed with AC at 2600 RPM compared to a gradual inflow restriction with VC. This can be attributed to the increased cannula inflow pressure caused by ventricular contractions that helped to cyclically stent the cannula open and prevent rapid collapse in VC. On the other hand, the constant LVADR_{in} of the RIC allowed for flow rates to increase to 5.5 L/min with increasing LVAD speed for both AC and VC before suction events (LAP / LVV_{sys} ≤ 0 mmHg / mL) were observed at 2800 RPM and 2900 RPM respectively.

Similar trends were noted with RVAD support with the RIC and CIC. The RVAD inflow cannula resistance (RVADR_{in}) remained relatively constant (1100 Dynes.s.cm⁻⁵) with the RIC when RVAD speed was incrementally increased from 400 to 1500 RPM, allowing mean pulmonary flow rates of approximately 5.3 L/min before suction events occurred in both AC and VC. As the RVAD speed was increased from 400 to 2000 RPM with the CIC, RVADR_{in} gradually increased from 1100 to 7000 Dynes.s.cm⁻⁵ and 1100 to 6000 Dynes.s.cm⁻⁵ for AC

and VC respectively. The increased RVAD_{Rin} served to maintain mean pulmonary flow rate at approximately 5.1 and 4.6 L/min for AC and VC respectively and prevent suction events by maintaining right atrial pressure above 3 mmHg and/or end systolic right ventricular volume above 50 mL (Figure 4). It should be noted that while these flow rates appear low for the reported suction events, changes in SVR or PVR were not incorporated in this test. Therefore, systemic and pulmonary arterial pressures were at high levels (MAP $\approx$ 110 mmHg and MPAP $\approx$ 25 mmHg) when flow rates were approximately 5 L/min.

Results were also taken to demonstrate the response of the RIC and CIC to a step change in SVR or PVR (Table 1). In left AC, a change in PVR from 100 to 400 Dynes.s.cm⁻⁵ resulted in a LAP reduction from 7.9 to 0 mmHg with the RIC, indicating a suction event, while the CIC maintained LAP at 5mmHg. The haemodynamics in Table 1 suggest that a mean aortic pressure (MAP) and MSQ of 95 mmHg and 4.65 L/min respectively were maintained when LAP reached 0 mmHg with the RIC. However, these results are an indication of the haemodynamics directly prior to the suction event occurring as no mechanical occlusion was included in our experimental apparatus. With the CIC, however, the MAP and MSQ dropped to 67 mmHg and 3.95 L/min respectively as the LVAD_{Rin} increased from 550 to 1800 Dynes.s.cm⁻⁵. Reductions in MSQ (AC: 4.65 L/min, VC: 4.4 L/min) were also noted with the RIC due to the increased PVR, however MAP was not reduced significantly. With CIC and LVAD VC however, the reduction in MAP (99 to 74 mmHg) and MSQ (5 to 4.1 L/min) was not as significant due to the remaining ventricular contractility opening the CIC with each pulse and reducing the change in LVAD_{Rin} (590 to 1100 Dynes.s.cm⁻⁵) compared to that seen in AC (550 – 1800 Dynes.s.cm⁻⁵). Positive LVV_{sys} was maintained with the CIC (31 mL), while a suction event occurred shortly after the PVR increase with the RIC.

Similar trends were noted for RVAD support, as suction events occurred with the RIC after the sudden increase in SVR, while the CIC maintained positive right ventricular systolic volume (27 mL) with VC and right atrial pressure (3.1 mmHg) with AC. In both cases with the CIC, mean pulmonary flow rate was reduced (AC: 3.65 L/min, VC: 3.75 L/min), however a similar (but slightly smaller) reduction was also noted with the RIC (AC: 3.84 L/min, VC: 3.92 L/min) due to the large increase in SVR.

Discussion

The use of rotary blood pumps to support patients with end stage heart failure continues to increase [24]. These devices, used for left, right or biventricular support, do not possess sufficient preload sensitivity to mimic the native Starling mechanism seen in healthy hearts and are susceptible to flow balancing issues and thus harmful suction events [11, 29]. This is particularly noticeable in biventricular support where both failing ventricles are lacking a normal Starling mechanism [29]. Previous attempts at BiVAD control have reported sensor drift [14], demonstrating the need for either a reliable sensor, reliable sensor-less controller, or a passive control mechanism. This paper details the use of a CIC which was capable of providing passive control of LVAD and / or RVAD flow based on preload in AC and VC.

Previous reports have demonstrated the ease with which suction events can occur with rotary VAD support [17, 30]. Our study revealed similar results with a RIC in AC and VC by simulating incremental changes in LVAD speed, RVAD speed, SVR or PVR. However, the addition of the CIC prevented suction events in all cases, even at VAD speeds far greater than those reached until suction with the RIC. The mechanism of suction prevention with the CIC is fairly simple, and relies on the passively increasing resistance of the VAD circuit (via a reduction in cannula volume and thus diameter) as preload is reduced. This resistance increase alters the flow, rather than completely restricting it, and therefore preserves positive atrial and ventricular pressures and volumes while maintaining sufficient cardiac output. The reduction in cardiac output was never more than 27% with the LVAD or RVAD CIC evaluated under increases in SVR and PVR in AC and VC. While the reduction in cardiac output could be considered significant, it prevented total occlusion of the inflow cannula by the ventricle walls and thus complete or intermittent cessation of flow which would be expected during a suction event. Meanwhile, the maximum reduction in cardiac output with the RIC was 23% prior to the suction event, and can be attributed to the reduction in ventricular contractility due to the MCL Starling response and the limited preload sensitivity of the of the rotary VAD.

The preload sensitivity of the VAD supported left ventricle, calculated by dividing the change in flow rate by the change in left atrial pressure from the step change in PVR test, averaged 0.0627 L/min/mmHg for AC and VC with the RIC. This compares closely with results reported by Salamonsen et al. [11], who reported rotary LVAD preload sensitivity to vary

between 0.03 and 0.31 L/min/mmHg. Addition of the CIC increased average preload sensitivity to 0.343 L/min/mmHg for AC and VC, which slightly exceeded values previously reported for the healthy human left ventricle (0.213 L/min/mmHg) [11]. However, increases in cardiac demand beyond that produced when the CIC is in its most expanded state may still require additional control strategies.

Passive restriction of the CIC is not only related to VAD preload. The cannulation site influenced the restriction of the compliant section as the remnant ventricular contractility served to keep the restricted section open, thus decreasing the VAD inflow cannula resistance. This was less noticeable, however, at lower ventricular volumes as the Starling mechanism implemented in the MCL ventricles decreased contractility as ventricular preload reduced. Distance and orientation of the compliant section from the cannulated chamber also altered the nature of restriction as the increased pressure head with lower placement (with respect to the cannulated chamber) of the compliant section delayed the passive restriction. In the clinical setting, the compliant section should be placed as close as possible to the cannulated chamber, thus rendering placement effects and changes in body position negligible. Meanwhile, the compliance and unstressed cannula dimensions influenced the performance of the compliant inflow cannula and may be used to improve the passive restriction mechanism.

While this study presented an in-vitro evaluation of the CIC concept, there are several features that must be addressed before clinical implementation. The compliance of the restricting segment must be optimized, while appropriate biomaterials must be investigated to ensure the degree of compliance can be met. Implantability issues, such as the potential for tissue growth around the compliant section and its implications on device compliance must be addressed. Potential for increased haemolysis due to the introduction of a stenosis and 'fluttering', as well as a reduction in cannula lifetime due to cyclic mechanical wear of the compliant section are also potential limitations that must be investigated. However the occurrences of significant changes in CIC diameter are not anticipated during normal VAD operation. Meanwhile, limitations existed with the experimental evaluation in this study, such as maintaining constant SVR and PVR while changing VAD speed. This, in turn, elevated arterial pressures to unreasonable levels while flow rates increased only mildly, thus causing a potential discrepancy between these results and what would be expected clinically. Auto-regulation of the vascular resistances (ie. through a baroreceptor response) would result in

larger flow rate changes and thus earlier induced suction events with the RIC and restriction of the CIC. Meanwhile, the high cannula resistance, even with the rigid design, was due to the long cannula length required for our experimental setup and should be addressed in future studies.

Conclusion

The limited preload sensitivity of rotary VADs gives rise to a need for control mechanisms to prevent harmful suction events, particularly in biventricular support when the left and right ventricular Starling response is severely reduced. While other research has focused on sensor and sensor-less based control systems, the reliability of these systems is presently insufficient for a destination therapy device. This study evaluated the use of a compliant section of tubing on the inflow cannula which passively increased the VAD circuit resistance and thus reduced VAD outflow when preload decreased. Compliant and rigid inflow cannulae were evaluated under various LVAD and RVAD speeds and severe step changes in SVR and PVR for comparison. The ease with which suction events can occur with the use of RIC and no physiological control mechanism (i.e. fixed speed) was clearly demonstrated, while the addition of the compliant section prevented suction events in all cases. This study revealed a CIC may be used as a passive control system to prevent harmful suction events in rotary left, right or biventricular support. However, further investigation into several key issues such as cannula compliance optimization, possible tissue integration and mechanical wear/deterioration must be addressed before clinical implementation.

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List of Figures

Figure 1 - Simplified schematic of the mock circulation loop (left) with the compliant inflow cannulae (right) on the LVAD and RVAD. LA - left atrium, LV - left ventricle, Ao - aorta, SVR - systemic vascular resistance, SV - systemic venous system, RA - right atrium, RV - right ventricle, PA - pulmonary artery, PVR - pulmonary vascular resistance, PV - pulmonary venous system.

Figure 2 - An example comparison between compliant and rigid LVAD ventricular inflow cannulae with increasing LVAD speed. LVVsys - end systolic left ventricular volume, LVADrin - LVAD inflow cannula resistance, MSQ - mean systemic flow rate.

Figure 3 - Comparison of compliant and rigid LVAD inflow cannulae for atrial (left) and ventricular (right) cannulation. LAP - left atrial pressure, LVVsys - end systolic left ventricular volume.

Figure 4 - Comparison of compliant and rigid RVAD inflow cannulae for atrial (left) and ventricular (right) cannulation. RAP - right atrial pressure, RVVsys - end systolic right ventricular volume.

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LVAD	Rigid Inflow				Compliant Inflow			
Inflow cannulation	LA	LA	LV	LV	LA	LA	LV	LV
PVR (Dynes.s.cm ⁻⁵)	100	400	100	400	100	400	100	400
LAP (mmHg)	7.9	0	8.8	1.4	7.2	5	8.3	4
LVVsys (mL)	212	147	132	0	202	112	117	31
MAP (mmHg)	100	95	100	87	100	67	99	74
MSQ (L/min)	5	4.65	5	4.4	5.0	3.95	5	4.1
LVADRin (Dynes.s.cm ⁻⁵)	490	460	520	490	550	1800	590	1100
RVAD	Rigid Inflow				Compliant Inflow			
Inflow cannulation	RA	RA	RV	RV	RA	RA	RV	RV
SVR (Dynes.s.cm ⁻⁵)	1500	2500	1500	2500	1500	2500	1500	2500
RAP (mmHg)	4.8	0	6.5	-2	4.9	3.1	7	3.2
RVVsys (mL)	108	71	78	0	110	76	89	27
MPAP (mmHg)	17.3	16.4	17.3	20	17.3	14	17.2	15
MPQ (L/min)	5	3.84	5	3.92	5	3.65	5.1	3.75
RVADRin (Dynes.s.cm ⁻⁵)	1070	1080	1110	1120	1080	1650	1140	1750

Table 1 - Haemodynamics for BiVAD support with rigid and compliant inflow cannulae in atrial and ventricular cannulation. LA - left atrium, LV - left ventricle, RA - right atrium, RV - right ventricle, SVR - systemic vascular resistance, PVR - pulmonary vascular resistance, LAP - left atrial pressure, RAP - right atrial pressure, LVVsys - end systolic left ventricular volume, RVVsys - end systolic right ventricular volume, MAP - mean aortic pressure, MPAP - mean pulmonary arterial pressure, MSQ - mean systemic flow rate, MPQ - mean pulmonary flow rate, LVADRin - LVAD inflow cannula resistance, RVADRin - RVAD inflow cannula resistance.

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