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Title:

EVALUATION OF INFLOW CANNULATION SITE FOR IMPLANTATION OF RIGHT SIDED ROTARY VENTRICULAR ASSIST DEVICE

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Abstract

Right heart dysfunction is one of the most serious complications following implantation of a left ventricular assist device (LVAD), often leading to the requirement for short or long term right ventricular support (RVAD). The inflow cannulation site induces major haemodynamic changes and so there is a need to optimize the site used depending on the patient's condition. Therefore, this study evaluated and compared the haemodynamic influence of right atrial (RAC) and right ventricular (RVC) inflow cannulation sites. An in-vitro, variable heart failure, mock circulation loop was used to compare RAC and RVC in mild and severe biventricular heart failure (BHF) conditions. In the severe BHF condition, higher ventricular ejection fraction (RAC: 13.6%, RVC: 32.7%) and thus improved heart chamber and RVAD washout was observed with RVC, which suggested this strategy might be preferable for long term support (ie. bridge to transplant or destination therapy) to reduce the risk of thrombus formation. In the mild BHF condition, higher pulmonary valve flow (RAC: 3.33 L/min, RVC: 1.97 L/min) and lower right ventricular stroke work (RAC: 0.10 W, RVC: 0.13 W) and volumes were recorded with RAC. These results indicate an improved potential for myocardial recovery, thus RAC should be chosen in this condition. This in-vitro study suggests that RVAD inflow cannulation site should be chosen on a patient-specific basis with a view to the support strategy to promote myocardial recovery or reduce the risk of long-term complications.

Keywords

Cannula, right ventricular assist device, rotary blood pump, heart failure.

Introduction

The ongoing international shortage of donor hearts necessitates the use of ventricular assist devices (VADs) to support end stage heart failure patients to recovery, future transplant or as a destination therapy [1]. The majority of clinically apparent ventricular dysfunction is seen in the left ventricle, thus the requirement for left ventricular support with a left VAD (LVAD) is the more common therapy. However, right ventricular dysfunction is being increasingly recognized as one of the most common and serious complications both before and after LVAD insertion [2]. Should right heart dysfunction fail to resolve with short term pharmaceutical treatment strategies such as pulmonary vasodilators or inotropic agents, reoperation and insertion of a short or long term right VAD (RVAD) may be required. The requirement for RVAD placement varies greatly between institutes, and has been reported between 5 and 48% of LVAD supported patients [3-5].

VADs are connected to the heart and great vessels via inflow and outflow cannulae respectively. Outflow cannulation is generally achieved through the ascending aorta (LVAD) and the anterior aspect of the pulmonary artery (RVAD). The VAD inflow cannulation site represents the primary interface between patient and device, and position of the cannula in either the atrium or ventricle induces major haemodynamic changes. The choice of inflow cannulation site is often dependant on the cannula design or preference of the surgeon and can be limited by anatomical constraints or the presence of thrombus within the heart chambers [6, 7].

The choice of inflow cannulation site should also be based on the treatment strategy and addressed on a patient-by-patient basis. For instance, if myocardial recovery is anticipated, efforts should be made to unload the heart by reducing ventricular stroke work and end systolic pressure and volume [8, 9]. This is becoming increasingly familiar when using VAD therapy to treat cardiogenic shock, which has shown relatively high rates of patient recovery and subsequent device removal [10, 11]. In cases where long-term support is predicted, such as those implanted for destination therapy, treatment should focus on reducing the risk of postoperative complications such as the formation of thrombus. Regions of static flow within the heart may predispose the patient to thromboembolic events and can be related to the ventricular ejection fraction (EF) and end-diastolic ventricular volume [12-16]. This is witnessed in the increasing risk of stroke with a reduction in EF [17, 18]. Therefore, the haemodynamic effect of each inflow cannulation site should be considered prior to implantation of VAD support.

The haemodynamic effect of LVAD inflow cannulation site has been researched extensively through numerical simulations [19], in-vitro evaluation [8] and in-vivo animal models [20-22]. Most agree that left ventricular cannulation is the preferred interface site for implantable LVADs [15, 23]. This is due

to improved LVAD inflow conditions resulting from remnant heart activity, which in turn increases pump flow rate and support efficiency [15]. Meanwhile, the improved chamber washout due to ventricular contraction combined with the smaller, unloaded left ventricle reduces the risk of thromboembolism [24]. However left atrial cannulation allows for easier surgical insertion and also promotes the potential for cardiac ventricular recovery by alleviating ventricular workload and preserving remaining cardio-myocytes [23, 25].

While inflow to the RVAD is usually delivered via right atrial cannulation (RAC), some institutions are now considering right ventricular cannulation (RVC) [26-29]. However, the haemodynamic influence of the RVAD inflow site has not been evaluated to the same degree as the LVAD inflow cannulation site. Schlensak et al. (2011) [30], did however investigate the effect of RVAD inflow cannulation site in 31 patients supported with dual Thoratec PVAD devices to provide biventricular support. The 15 patients with RVC demonstrated higher RVAD flow rates compared to those with RAC due to higher RVAD inflow pressures promoting rapid RVAD filling. The increased flow rate resulted in improved perfusion of the end organs and subsequently improved kidney and liver function. However, RAC was the chosen technique prior to implementation of RVC. Hence, even though survival was relatively similar between the two groups, the improved clinical experience with VAD support may have promoted the improved results noted in the RVC group. Even though this study was published recently, it was completed with the pulsatile first generation devices which are rapidly being replaced by the more durable rotary blood pumps (RBPs), particularly with the implementation of dual LVADs for biventricular support [28, 31]. A similar study which characterizes the effect of RVAD inflow cannulation site for RBPs would serve to enhance future biventricular support with continuous flow devices.

Therefore, this study employed an in-vitro mock circulation loop (MCL) to characterize the haemodynamic difference between RAC and RVC with continuous flow, biventricular support in mild and severe heart failure simulations. The results of this study provide insights into the hemodynamic effect of atrial or ventricular RVAD inflow cannulation site, which may guide inflow site selection so as to promote recovery of the right heart and reduce the risk of long-term, postoperative complications.

Methods

Mock Circulation Loop

A physical five element Windkessel MCL including systemic and pulmonary circulations was used for this study [32, 33]. Atrial and ventricular chambers were represented by 40 and 50 mm clear, vertical polyvinyl chloride pipes with tee sections connecting the inflow, outflow and heart 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. Heart rate and systolic time were maintained at 60 beats per minute and 40% respectively throughout this study. 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 [34]. 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.) and socket valves (VMP025.03X.71, Convair Engineering, Epping, Australia) allowed easy manipulation of systemic and pulmonary vascular resistance respectively.

RVAD Inflow Cannulation

A BP80 (Bio-Medicus, Inc., Eden Prairie, MN, USA) RBP was initially attached to the MCL through the right atrium for RVAD inflow and the pulmonary artery for RVAD outflow. A VentrAssist (Ventracor Ltd., Sydney, Australia) rotary LVAD was connected to the MCL via the left ventricle and aorta for inflow and outflow cannulation respectively for all tests. A detailed schematic of the MCL and VAD connections is shown in Figure 1. 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.

MCL parameters were manipulated to simulate a mild degree of biventricular heart failure (BHF), defined in Table I. LVAD and RVAD support was then initiated where LVAD speed was set at a constant 2300 RPM in the mild BHF condition. To characterise the haemodynamic effect of RVAD inflow cannulation site at various pump speeds, an RVAD speed ramp test was completed. For this test, RVAD speed was increased from 400 to 1500 RPM in increments of 100 RPM or until a suction event occurred. A suction event was defined as the right ventricular volume / right atrial pressure (RAP) being equal to or less than 0 mL / mmHg. The RVAD inflow cannulation site was then changed to the right ventricle before the speed ramp test was repeated. LVAD and RVAD cannulae were then clamped and MCL parameters manipulated to represent a severe BHF condition (Table I)

before the speed ramp tests were repeated. In this severe BHF condition, LVAD speed was set at 2400 RPM.

To add an additional clinical relevance to the study, LVAD and RVAD speeds were manipulated to restore MCL haemodynamics to a pre-defined restored condition (mean aortic pressure: 100 mmHg, mean pulmonary arterial pressure (MPAP): 18 mmHg, mean systemic flow rate: 5.0 L/min). This was completed in mild and severe BHF conditions to compare the restoring effect of RAC and RVC.

	LAP (mmHg)	MAP (mmHg)	MSQ (L/min)	LV _{EDV} (mL)	RAP (mmHg)	MPAP (mmHg)	MPQ (L/min)	RV _{EDV} (mL)
Mild BHF	10	79	4.0	210	10	19	4.0	190
Severe BHF	12	55	2.3	288	12	16	2.3	253

Table I - Mock circulation loop haemodynamic parameters used to simulate conditions of mild and severe biventricular heart failure (BHF). LAP - left atrial pressure, MAP - mean aortic pressure, MSQ - mean systemic flow rate, LV_{EDV} - left ventricular end diastolic volume, RAP - right atrial pressure, MPAP - mean pulmonary arterial pressure, MPQ - mean pulmonary flow rate, RV_{EDV} - right ventricular end diastolic volume.

Figure 1 - Schematic of the MCL setup for evaluation of RVAD inflow cannulation site. LA - left atrium, MV - mitral valve, LV - left ventricle, AoV - aortic valve, AoC - aortic compliance chamber, SQ - systemic 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, PVR - pulmonary vascular resistance valve, PVC - pulmonary venous compliance chamber, RVAD - right ventricular assist device, LVAD - left ventricular assist device, x denotes a valve.

Data Acquisition

Haemodynamic and VAD parameters were captured at 100 Hz using a dSPACE acquisition system (DS1103, 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 for RAC and RVC in mild and severe BHF conditions at various VAD rotational speeds and restored conditions to determine the haemodynamic influence of cannulation site. All results presented in this section refer to the right side of the heart and pulmonary circulation unless stated otherwise. Results from the speed ramp test for mild and severe BHF in RAC and RVC are presented in Figure 2. In the mild BHF condition (Figure 2a) RVAD flow rate (RVADQ) was higher in RVC compared with RAC for all RVAD speeds other than when the two had converged at a RVAD speed of 1500 RPM (5.1 L/min). This was not translated into total mean pulmonary flow rate (MPQ), as RAC consistently had equal-to or higher MPQ than RVC. This can be attributed to the ventricular Starling response increasing ventricular contractility due to the higher ventricular end diastolic volume (EDV) with RAC. This resulted in increased pulmonary valve flow in RAC compared to RVC and indicated that although higher RVADQ is experienced with RVC, the ventricular Starling response was able to compensate and result in increased cardiac output with RAC. Ventricular ejection fraction (EF) was consistently higher in RVC compared to RAC at RVAD speeds above 600 RPM due to the decreased EDV combined with a relatively consistent ventricular stroke volume. At low RVAD speeds (ie. 400 - 700 RPM), ventricular stroke work (SW) was relatively similar between the two cannulation sites. However as RVAD speed was increased in RAC, the weakened ventricle was unable to overcome the high pulmonary arterial pressures, thus decreasing stroke volume and SW. In RVC, SW decreased to a lesser degree as the ventricle maintained some ejection through the pump as RVAD speed increased.

Similar trends from the mild BHF condition were observed in the severe BHF condition in the RVAD speed ramp test. However, a maximum RVAD speed of only 1100 RPM, compared to 1500 RPM in mild BHF, was reached due to the reduced Starling response in both left and right ventricles being unable assist in balancing flow rates, and hence volumes, between the systemic and pulmonary circulations. RVADQ was consistently higher with RVC compared to RAC at lower RVAD speeds. However, the diminished ventricular contractility at higher RVAD speeds (due to reduced ventricular volume and hence contractility through the ventricular Starling response) resulted in similar RVAD preload between the two cannulation sites and therefore comparable RVADQ. MPQ was similar between the two cannulation sites, indicating that flow through the pulmonary valve was again higher with RAC. MPAP was also comparable between the cannulation sites which, combined with similar MPQ, indicated that neither RAC nor RVC is more hydraulically efficient in severe BHF. EF was consistently higher in RVC compared to RAC as ventricular ejection occurred through the ventricular inflow cannula. SW was generally lower with RAC except at the lowest (400 RPM) and highest (1100 RPM) RVAD speeds evaluated, thus demonstrating a decreased work load on the ventricle in RAC.

Figure 2 - Haemodynamics for right atrial (RAC) and right ventricular (RVC) inflow cannulation in the (a) mild and (b) severe biventricular heart failure condition during the speed ramp test. RVADQ – RVAD flow rate, MPQ – mean pulmonary flow rate, MPAP – mean pulmonary arterial pressure, RVEF – right ventricular ejection fraction, RVSW – right ventricular stroke work (Watts), RPM – revolutions per minute.

To provide a higher degree of clinical relevance to the study, results were taken from the restored haemodynamics test for mild and severe BHF in RAC and RVC. The haemodynamics for each cannulation site in mild and severe BHF are presented in Table II while ventricular PV loops are shown in Figure 3. In mild BHF, a RVAD speed of 900 RPM was required for RAC and RVC to maintain restored haemodynamics (MPAP: 18 mmHg, MPQ: 5 L/min), indicating similar efficiency between the cannulation sites. However, in severe BHF, a higher RVAD speed was required in RVC (1300 RPM) compared to RAC (1100 RPM), indicating that RAC was actually more efficient than RVC in severe BHF. This could be due to the high EDV in RAC increasing ventricular contractility through the ventricular Starling response, even with its diminished sensitivity in severe BHF. As expected, right atrial pressure (RAP) was lower in RAC compared to RVC as the RVAD pumped fluid from the cannulated chamber. RVAD flow rate was higher in RVC (mild BHF: 3.03 L/min, severe BHF: 4.8 L/min) compared to RAC (mild BHF: 2.67 L/min, severe BHF: 3.9 L/min) due to the increase preload from ventricular systole in RVC. Evaluation of the ventricular PV loops revealed increased EF in RVC (mild BHF: 31.8%, severe BHF: 32.7%) compared to RAC (mild BHF: 27.6%, severe BHF: 13.6%) in both conditions, indicating increased ventricular washout with RVC. While

values were both low in comparison with a healthy right ventricle, SW was increased with RVC compared to RAC in mild and severe BHF.

Condition	Mild BHF		Severe BHF	
Cannulation Site	RAC	RVC	RAC	RVC
RVADS (RPM)	900	900	1100	1300
RAP (mmHg)	6.5	9.0	4.8	6.5
MPAP (mmHg)	18	18	18	18
RVPsys (mmHg)	28	27	23	20
MPQ (L/min)	5.0	5.0	5.0	5.0
RVADQ (L/min)	2.67	3.03	3.9	4.8
RVVsys (mL)	110	120	108	78
RVVdias (mL)	152	176	125	116
EF (%)	27.6	31.8	13.6	32.7
SW (Watts)	0.10	0.13	0.03	0.05

Table II – Haemodynamics for the restored test with right atrial (RAC) and right ventricular (RVC) inflow cannulation in mild and severe biventricular heart failure (BHF) conditions. RVADS – RVAD speed, RAP – right atrial pressure, MPAP – mean pulmonary arterial pressure, RVPsys – right ventricular systolic pressure, MPQ – mean pulmonary flow rate, RVADQ – RVAD flow rate, RVVsys – systolic right ventricular volume, RVVdias – diastolic right ventricular volume, EF – right ventricular ejection fraction, SW – right ventricular stroke work (Watts), RPM – revolutions per minute.

Figure 3 – Pressure-volume loops for right atrial (RAC) and right ventricular (RVC) inflow cannulation shown for conditions of mild (a) and severe (b) right heart failure. RVP – right ventricular pressure, RVV – right ventricular volume.

Discussion

First generation RVADs are being phased out in favor of the more durable RBPs, particularly as the adaptation of a rotary LVAD for right ventricular support gains clinical acceptance [28, 35]. The primary interface between RBPs and the patient is the inflow cannula, with inflow cannula placement in either the atrium or ventricle potentially inducing major haemodynamic changes. Whilst rotary LVAD inflow cannula placement has been evaluated extensively [8, 19-22], the haemodynamic influence of rotary RVAD inflow cannula placement has not been previously characterized. There is, therefore, a need to find the most appropriate inflow cannulation site to improve the performance of the cardiac-RVAD interaction to suit the support strategy selected for each patient.

Although the results of LVAD inflow cannulation site cannot be directly translated to RVAD inflow cannulation site due to different ventricular function (eg. sensitivity of the Starling response) and vascular parameters, our study showed that some similar trends exist. For instance, previous in-vitro [8] and in-vivo [20] studies have shown that left atrial cannulation reduced left ventricular stroke work compared to left ventricular cannulation which may encourage myocardial recovery [36]. In our study, RAC reduced SW in almost all cases with exceptions at the lowest RVAD speeds, when RVAD support was not significant enough to alter right ventricular function, and at the highest RVAD speeds, when over-pumping resulted in diminished right ventricular contractility due to the Starling response. Reduced right ventricular volumes were also noted with RAC in the mild BHF condition, thus reducing the stress on the ventricular wall. Ventricular unloading by reducing SW and EDV is vital for patients identified for bridge to recovery treatment, as the aim of this strategy is to reduce the workload of the heart until it recovers [37].

Another advantage when aiming for bridge-to-recovery therapy is maintaining flow through the pulmonary valve. In our mild BHF condition, right ventricular systolic pressure was higher in RAC as ventricular ejection could not occur through the RVAD inflow cannula. This resulted in increased pulmonary valve flow with RAC which may prevent the valve from becoming stenotic and reduce the risk of thrombus formation around the valve [20]. Meanwhile, RAC allows for easier surgical insertion off bypass, particularly for the extracorporeal placed devices, and promotes potential for myocardial recovery through preservation of the remaining cardio-myocytes by eliminating the need to core the apex. Therefore, RAC presents several advantages over RVC in a mild BHF condition with a view to myocardial recovery and should be selected to treat this patient population.

With a view to long term LVAD support, the efficiency of the pump becomes important to reduce power consumption, thus increasing battery life and reducing mechanical wear. McGee (2008) [37] suggested that RVC provides better draining and higher flows compared to RAC, and similar

conclusions have been made for LVAD inflow cannulation site [8, 20, 21]. Schlensak (2011) [30] reported higher RVAD flow with RVC, however this study was completed with first generation devices which have different operating characteristics to RBPs. In our study, RVADQ was higher with RVC in almost all conditions. This was particularly noticeable at low RVAD speeds when the right ventricle was severely dilated and the right ventricular Starling response increased RVAD preload with RVC. However, the higher RVADQ did not translate to a higher MPQ as the larger EDV in RAC increased right ventricular contractility through the Starling response, thus preserving ejection through the pulmonary valve. This was less noticeable in the severe BHF condition due to the diminished Starling sensitivity; however these results indicate that neither RAC or RVC significantly increases RBP support efficiency.

Neurologic complications remain one of the most serious adverse events while receiving mechanical circulatory support [38], thus there is a need to promote heart chamber and RBP washout to reduce the risk of thrombus formation, stroke and pulmonary embolism [16, 39, 40]. As is the case with LVAD support, the higher and more pulsatile RVADQ with RVC may improve the washout of the rotary RVAD and reduce the risk of thrombus forming in the pump [23]. Improved washout (ie. higher EF) was also noted in the right ventricle in our study with RVC, thus potentially reducing the risk of thrombus formation in the heart chamber. The increased EF in RVC can be attributed to the remnant ventricular contractility forcing ejection through the RBP. This is, however, not possible in RAC and right ventricular ejection is confined solely through the pulmonary valve. Therefore, the lower EF recorded with RAC, particularly in the severe BHF case, may predispose the right ventricle to thrombus formation [18, 41]. It is for this reason that RVC should be chosen for long-term RVAD support with a view to transplant or destination therapy. This choice, however, is often dependant on the preference of the surgeon, and can be limited by anatomical constraints or the pre-operative presence of thrombus within a vessel [6, 7].

Conclusion

In-vitro investigation of right VAD inflow cannula site in a MCL revealed improved heart chamber washout with cannulation of the right ventricle in the severe BHF case. This may be translated clinically to a reduced potential for thrombus formation, which is particularly vital with a view to long term RVAD support such as bridge to transplant or destination therapy. RAC should be preferred in a mild BHF condition with a view to myocardial recovery to increase flow through the pulmonary valve, reduce right ventricular work and preserve the myocardium. However, the conclusions drawn from this study can only be taken as a guide and, ultimately, inflow cannula placement will be chosen based on patient constraints, device availability and the preference of the surgeon. Future work would benefit from a review of performance in-vivo for confirmation of the recommendations made from this in-vitro study.

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