Original Article

# Intrinsic Investigations of Physiological Interaction for Pulsatile Rotary Blood Pumps

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**Abstract**

**Background:**
One of the major concerns with the use of circulatory assist devices (CADs) is their performance during the transition from supine to standing position. In standing position, vasodilatation of veins occurs in the legs, which decreases left ventricular end-diastolic pressure, and, in turn, the preload to the CAD. This research numerically studies the physiological interaction of pulse left ventricular assist devices (LVADs) in relation to cardiac output and stroke volume under systolic and diastolic situations.

**Methods:**
A cardiovascular system (CVS) model was used to configure the output of heart failure (HF) status by changing system parameters in one cardiac cycle, whereas LVAD pump was configured to change the fixed rotational speed. The terms of the pump cannulae model, real-time detection of aortic valve status, left ventricular stroke volume analysis, and LVAD control method were designed and analyzed.

**Results:**
The results showed that end-diastolic left and right ventricular volumes – pressures in heart failure condition were reduced from 183 mL to 164 mL with continuous fixed speed RBP support, Alongside with a corresponding increase in ejection fraction (16%).

**Conclusion:**
The results show that LVADs are more sensitive to preload than afterload when operating at a fixed speed.

**Keywords:**
Heart Failure; Rotary Blood Pumps; Cardiac Output; Cardiovascular System.

**الملخص**

**خلفية:**
أحد أهم المشاكل الرئيسية والمتعلقة بمضخات القلب (مضخات الدم الدوارة) هو ردة فعل المضخة عند رجوع الدم إلى القلب عن طريق الأوردة. عندما يتغير الوضع الجسماني للمريض من وضع الجلوس إلى وضع الوقوف، تتم زيادة حجم الدم في عروق الساق بسبب توسع الأوعية الدموية، وبالتالي رجوع الدم عن طريق الأوردة إلى الأذين الأيمن وبالتالي نقله إلى الأذين الأيسر. وينتج عن هذا انخفاض في الضغط الانبساطي البطيني الأيسر، وبالتالي التحميل (المسبق) لمضخة الدم الدوراة. في هذا البحث تمت دراسة التفاعل الفسيولوجي للنقاط التقييسية النبضية فيما يتعلق بحالات الانقباض والانبساط الناتج من القلب أثناء تدفق الدم.

**طريقة البحث:**
في هذا البحث سيتم استخدام النموذج الرياضي لنظام القلب والأوعية الدموية لتكوين إنتاج يماثل قصور القلب عن طريق تغيير معاملات النظام عند سرعة دوران ثابتة أثناء عمل المضخة.

**النتائج:**
أظهرت النتائج أن أحجام البطين الأيسر والأيمن الانبساطي بالنسبة لضغط الدم أثناء حالات القصور القلبي تقل من ١٨٣ مل إلى ١٦٤ مل مع دوران ثابت السرعة لمضخة القلب ومع زيادة مقابلة في جزء الطرد الطرد بنسبة (١٦ ٪).

**الخلاصة :**
وعليه نخلص إلى أن مضخات الدم الدوراة (مضخات القلب) هي أكثر حساسية للتحميل المسبق من التحميل اللاحق عند التشغيل بسرعة ثابتة.

## Introduction

Heart failure (HF) is a severe health condition that occurs when the heart does not pump enough blood to support the body organs. Over the last decade, this disease has been associated with a significant population worldwide [1, 2]. In the United States, there are approximately 5.3 million people with HF condition, yet less than 0.05% receive heart transplants annually [3]. Similarly, in Australia, the annual prevalence of heart failure is approximately 2% of the population [4]. The continuous intravenous inotropic support is used as a short-term treatment, and although this may improve symptoms, mortality may worsen. This sets the stopwatch for patients receiving inotropic therapy as survival rates after a year is only 10% to 30% [5]. Despite the small number of patients receiving an appropriate treatment through the health management of this disease, heart transplantation is becoming a useful option for affected individuals. However, the shortage of donor hearts has compelled mechanical circulatory assistance (MCS) to mitigate the severity of the heart failure situation [5].

MCS has proven to produce more favorable outcomes for the end-stage HF patients than for optimally medically treated HF patients [6]. For this reason, the use of MCS is expected to increase significantly, with the indications expanding to include both bridge to recovery (BTR) patients and destination therapy (DT) patients who were previously not considered transplant candidates. The location of the inflow cannula is a factor that may aid this treatment strategy, with atrial cannulation and ventricular cannulation favoring BTR and DT, respectively. These mechanical devices fall into two categories: constant flow rotary and pulsatile ventricular assist devices (VADs). Recent investigations on these two types of VADs indicate that patients have a higher chance of survival with rotary or constant flow support because they allow higher reliability, reduce sepsis, and decrease incidence of the right heart and end-organ failure [2]. These results are reflected in the U.S. Food and Drug Administration (FDA)'s recent approval of the rotary Heartmate II as a destination therapy [7]. The ability of constant flow support to provide optimal safety is likely to be due to the small size of devices, less implantation procedural time, and reduced device complexity, although the effect of the ventricles' interactions with either type of device is largely unknown [7]. There are many devices that support blood circulation in patients with HF condition, with the main distinguishing feature related to their mode of outflow, i.e., pulsatile or continuous [8, 9]. Although physiological pulsatility in the middle cerebral arteries was developed in patients with continuous axial ventricular support, the debate continues on the benefit of maintaining flow pulsatility [10]. In the cardiovascular system, the pulsatile rotary blood pumps (RBPs) have the benefit of generating physiological stress and flow. These devices can be useful in enhancing microcirculation and preventing gastrointestinal circulation complications [11]. However, the excessively large size and unreliable mechanical function of these devices far outweigh the advantages of pulsatile flow. The rotary pumps can overcome these problems by offering smaller and more reliable devices; however, the reduced operation of the pulse can be harmful to the vasculature and/or end-organ perfusion. For instance, Nishimura et al. discovered that extended non-pulsatile RBPs decreased the aortic wall thickness and smooth muscle cell size ratio [12]. Pulsing the velocity of an RBP to induce pulse pressure using a rotary pump is therefore an appealing control approach; however, the timing and operation advantages of this model are not clear [12].

The ability to regulate the velocity of continuous flow or RBP may allow the development of a simulated pulse, but until now, circulatory

assistance is traditionally provided at a steady mean rotational speed, which despite the sensitivity to left ventricular and aortic pressure, constantly decreases pulse pressure [13, 14]. In addition, the insensitivity of the device to the altering hemodynamic environment in which it operates can predispose the left ventricle (LV) to collapse [14] or regurgitate the pump flow [15]. Vandenberghe et al. conducted the simulation of synchronous and asynchronous ventricular assist with phase shifting. They found that the synchronous pulsing could maximize stroke volume and ventricular pressure, whereas asynchronous pulsing led to highly unphysiological hemodynamic [16]. However, the best timing of the pulses to favor interaction between heart and RBP was not decided until an accurate triggering of pulses was achieved. On the other hand, Rüschen et al. developed a simulation model to investigate the effect of pulsatility phase timing on the left ventricular stroke work (LVSW). However, this study was limited due to the computational environment in which it was conducted [17]. The purpose of this study was to investigate the physiological interaction of LVADs with cardiac output (CO) on both sides of the heart (left and right ventricular atria) in terms of volume and pressure during an HF. Furthermore, this work evaluated the systolic and diastolic reactions to find the most appropriate timing strategy to minimize the potential of a ventricular suck-down, enhance aortic pulse pressure, and improve the degree of ventricular washout or unloading.

## Methods

*Cardiovascular System Model Description*

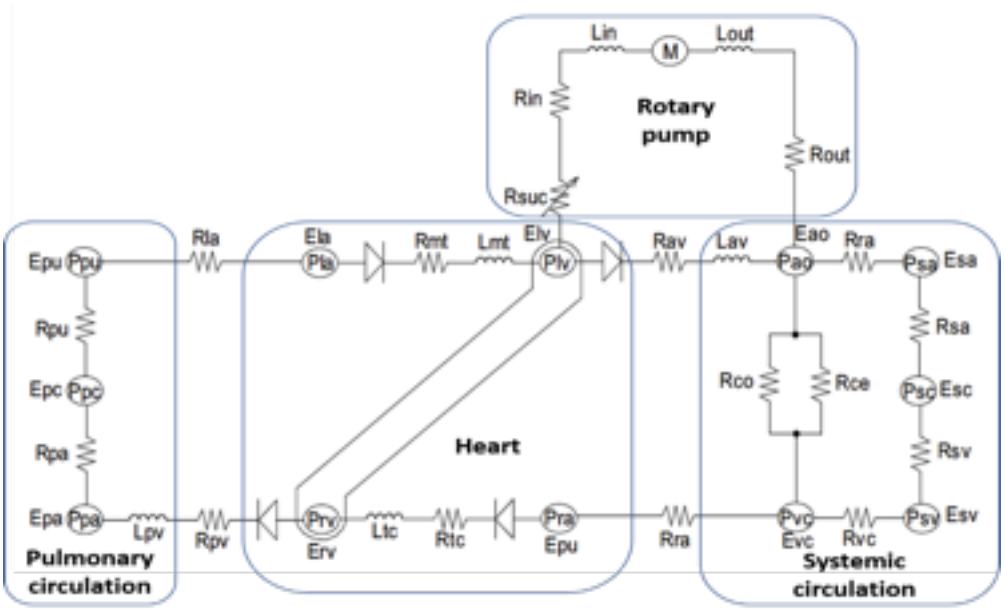
A cardiovascular system (CVS) software model was developed in conjunction with an LVAD to simulate a wide range of cardiovascular and pump operating conditions. The CVS model consists of 12 coronary, pulmonary, and systemic circulations on the left and right sides as shown in Fig. 1. The model also contains interventricular septum and pericardial interaction formulations. This model was validated using the literature data. A more detailed description of the model formulations is presented in [15, 18]. Three differing equations model the pump: an electric engine winding equation, an electric torque transfer, and a hydraulic pump equation. The input and output cannulae are also modeled on a constant flow resistance (in- and outlet), resulting in a decrease in pressure and inductive series of fluctuations (in- and outlet). A third resistance is included in the simulation of the suction events before cannula input. The amount of this variable force depends on the pressure of the LV.

*Pump control and parameters adjustment procedure*

To ensure that the LVAD flow was maintained at a safe level, a proportional–integral–derivative (PID) controller was introduced to vary the pump speed as required. The controller featured a negative feedback loop that compares the independent LVAD pump flow to the target flow. The error between the two signals is then fed into the PID controller that can then alter the pump speed to minimize the error signal. The gains of 1.2, 0.75, and 1 were initially used for the PID controller [19]. A saturation blow was used to ensure that the speed of the pump did not leave the safe operating region of 1800 rpm to 2800 rpm. The displacement of the hub was held constant at 0 mm.

During this analysis, the model parameters were carefully modified to ensure correct simulation of heart output, aortic pressure, and left aoric pressure. Table 1 shows the hemodynamic variables of the model for both healthy and heart failure patients. The model parameters were set as required to configure the simulation study. The pump rotational speed of LVAD was adjusted until the pump outlet flow was 5 L/min. The steady-state pilot

Fig.1. Electrical equivalent circuit analog of CVS - LVAD interaction. Rin: inlet cannulae resistances; Rout: outlet cannulae resistances; Lin: inlet cannulae instances; Lout: outlet cannulae instances; Rsuc: suction resistance; thor;1 & Pthor;2: intrathoracic pressures




simulations were performed to find the pressure head and flow of the LVAD at a particular speed. The inlet pressure was increased from 0 mmHg, and the resulting outlet pressure and pump outlet flow were recorded. The outlet resistance valve was then adjusted as per the cannulae response to maintain the outlet pressure at 100 mmHg, and the corresponding pump outlet flow was recorded. The pump was then configured with pulse peaks in systole or diastole to alter the rotational speed. The hemodynamic results were reported, such as left ventricular pressure/volume aortic pressure, pump outflow, and ventricular volumes.

## Results

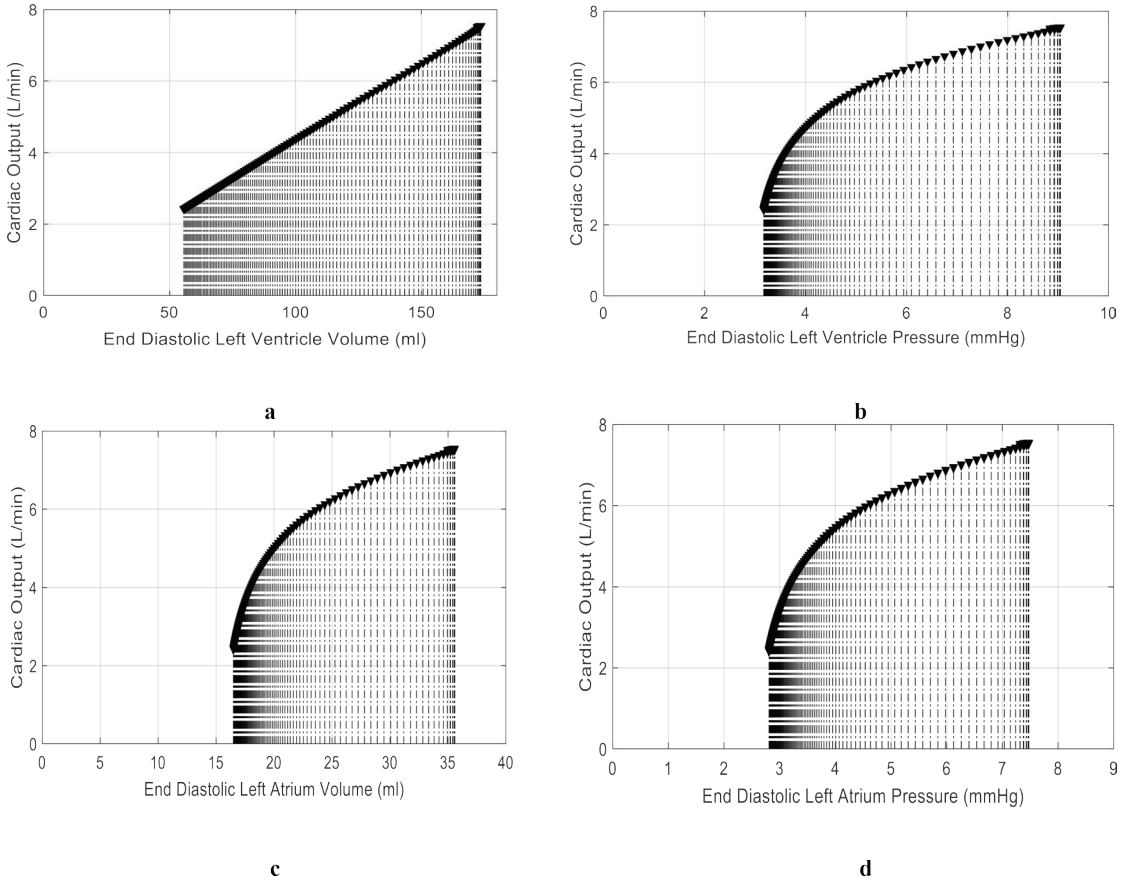
Under widely varying physiological conditions, the LVAD with the scheduled PID controller was tested using computer simulations.

Table 1. Hemodynamic variables of the model for both healthy and heart failure patients

| Model Parameter | Unit | Healthy | | Heart Failure | |
|---|---|---|---|---|---|
| | | Rest | Exercise | Rest | Exercise |
| Heart rate (HR) | bpm | 70 | 150 | 85 | 120 |
| Aortic resistance ($R_{ao}$) | mmHg/mL/s | 0.48 | 0.16 | 0.36 | 0.72 |
| Systemic arterial resistance ($R_{ar}$) | mmHg/mL/s | 0.5 | 0.17 | 0.25 | 0.5 |
| Systemic venous resistance ($R_{vr}$) | mmHg/mL/s | 0.22 | 0.07 | 0.11 | 0.22 |
| Vena cava resistance ($R_{vc}$) | mmHg/mL/s | 0.08 | 0.03 | 0.04 | 0.08 |

The simulation scenarios ranged in both rest and heavy practice from the healthy heart to HF where the heavier LVAD load. In the simulation the pulse rate was 60 beats per minute and the LVAD parameters were set as required. Fig. 2 illustrates the changes in CO for the left side. Fig. 2a indicates the relationship between CO and the end-diastolic left ventricular volume (LVEDV). The volume of CO with LVAD support was linearly changes from 2.5L/min to 4.5L/min. Fig. 2b shows that the variations in CO was non-linear changing in relation with the end-diastolic left ventricular pressure (LVEDP). For the left atrium, the CO was non-linearly changing in terms of both end-diastolic left atrium volume (LAEDV) and the end-diastolic left atrium pressure (LAEDP) (Fig. 2, a and b). In comparison to the right side of heart, the variation in CO has the same behavior in left side where the changes with the end-diastolic right ventricular volume (RVEDV) has linear relationship as shown in Fig. 3a. In the other hand, the end-diastolic right ventricular pressure (RVEDP), end-diastolic right atrium volume (RAEDV), and the end-diastolic right atrium pressure (RAEDP) have non-linear behavior with the CO (Fig. 3, b, c and d). The changes for end-systolic volume and stroke work (SW) are summarized in Table 2 in terms of systole, continuous and diastole.

Fig. 2. End-diastolic left ventricular volumes–pressures vs cardiac output: (a) End-diastolic (left ventricle volume vs cardiac output; (b) End-diastolic left ventricle pressure vs cardiac output; (c) End-diastolic left atrium volumes vs cardiac output; (d) End-diastolic left atrium pressure vs cardiac output.




## Discussion

The alteration of the speed of the pump to induce pulsatility in RBPs was found to in-

Fig. 3. End-diastolic right ventricular volumes–pressures vs cardiac output: (a) End-diastolic right ventricle volumes vs cardiac output; (b) End-diastolic right ventricle pressure vs cardiac output; (c) End-diastolic right atrium volumes vs cardiac output; (d) End-diastolic right atrium pressure vs cardiac output.

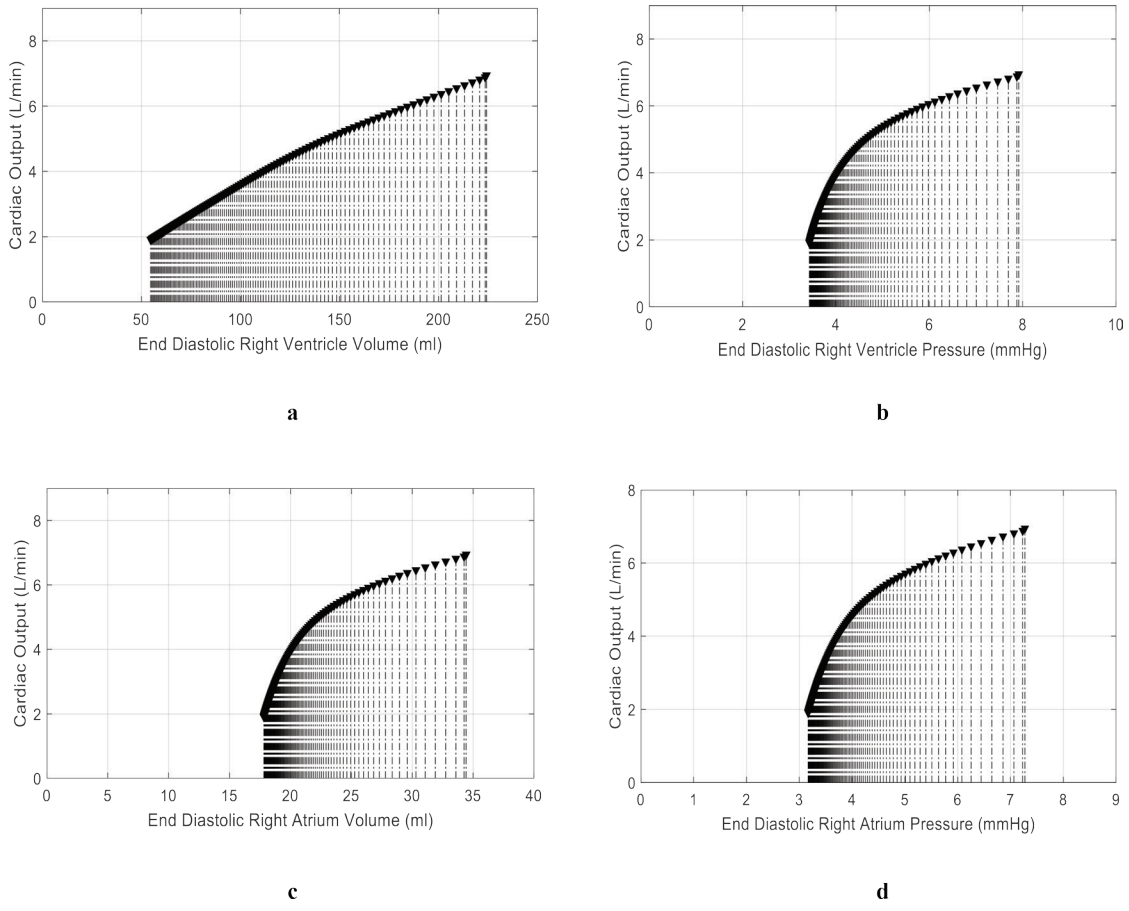



Table 2. Summary of results for hemodynamic variables.

| Parameters | In Systole | Continuous | In Diastole |
|---|---|---|---|
| **End-diastolic Left ventricle volume** | 163 mL | 144 mL | 147 |
| **end-diastolic Left ventricle pressure** | 22.5 mmHg | 10 mmHg | 8.2 mmHg |
| **Stroke Work** | 0.19 J | 0.18 J | 0.16 J |
| **Aortic Pulse Pressure** | 21 mmHg | 10mmHg | 7.5mmHg |
| **Ejection Fraction** | 19% | 16% | 14% |

fluence the end-diastolic left and right ventricular pressure and volume. Among three situations: constant speed, pulse peak in systole, and pulse peak in diastole, the pulse peak in diastole demonstrated the largest end-systolic volume (ESV) and the smallest SW and aortic pulse pressure, as shown in Table 2.

These findings suggest that pulsing the RBP in diastole can create a potentially ideal environment for myocardial recovery because the load on the heart is minimized. Furthermore, the reduced pulse pressure from the continuous operation mode, while not intuitively beneficial to the end-organ perfusion, may, in fact, benefit recovery. This is due to the maintenance of a higher diastolic aortic pressure,

and thus, the coronary blood flow is expected to increase as observed in other counter-pulsation devices [20, 21].

On the other hand, placing the pulse peak in systole created the largest pulse pressure by effectively amplifying the remnant ventricular pressure. This may be beneficial to improve the end-organ perfusion, particularly, under exercise conditions. The resulting reduction in the ESV, while predisposing the ventricle to the suck down events and thus the ventricular washout [22, 23].

The pulsatile output from an RBP might be beneficial for microcirculation, however, the effect on the coronary circulation should also be considered. With good aortic pressure autoregulation maintained between 60 to 200 mmHg, normal coronary blood flow is usually maintained despite changes to coronary perfusion pressure. However, due to the extravascular pressure, the endocardium is more susceptible to ischemia, especially at lower perfusion pressures [24, 25].

Therefore, the care should be taken to maintain a diastolic pressure of greater than 60 mmHg. In addition, the lowest trough of 'pulse peak in systole' could easily cause the diastolic aortic pressure to be lower than the minimum diastolic pressure for normal coronary blood flow (60 mmHg). Although the 'pulse peaks in diastole' maintained the largest diastolic aortic pressure, the timing of this pressure may not coincide with ventricular relaxation due to the phase delay caused by the cannula [26, 27].

## Conclusion

The physiological interaction of RBPs in terms of left ventricular/atrium volume–pressure and right ventricular/atrium volume–pressure with CO was investigated. The volume of the pump flow changed frequently in diastole, whereas it did not change in systole at varying blood pressures or pump speeds. This indicated that diastole would be more demanding for a high preload sensitivity compared to systole. Therefore, RBPs reduced outflow with a further small reduction in preload and thus left ventricular pressure (LVP) to prevent the abnormal reduction of ESV and even ventricular collapse so as not to suck much blood from the ventricle.

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