Distal thoracic aorta hemodynamics during exercise with continuous flow left ventricular assist system

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Abstract

Objectives: Continuous flow left ventricular assist systems (LVAS) are being discussed as a destination therapy. LVAS patients will have expanded activity of daily life, including exercise. In this study, we analyzed the effects of exercise on blood flow in the distal thoracic aorta of LVAD implanted animals.

Methods: Five calves with a continuous flow LVAS exercised on treadmill at two different pump flow rates (PFR), 60–80% (high PFR) and 25–30% (low PFR) of pulmonary artery flow rate. Pump, pulmonary artery and descending thoracic aorta flow waves were recorded before, during and after exercise. Systolic and diastolic flow volume in each cardiac cycle in pump and descending thoracic aorta flow was calculated.

Results: (1) Average flow rates – Pulmonary artery and descending thoracic aorta flow rates increased with heart rate during exercise and there was no difference between groups. (2) Pump flow wave – Pump regurgitation increased temporally during exercise at both PFRs, but sustained incidences of regurgitation after exercise were only observed at low PFR. Systolic and diastolic pump flow volume decreased during exercise at both PFRs, but systolic volume increased and diastolic volume decreased significantly after exercise at low PFR. (3) Descending thoracic aorta flow wave – At high PFR, systolic volume of descending thoracic aorta increased but diastolic flow volume decreased during exercise. At low PFR, both systolic and diastolic volume of the descending thoracic aorta decreased during exercise, but systolic volume increased and diastolic volume decreased after exercise. Systolic volume of the descending thoracic aorta in low PFR was significantly greater and diastolic volume was less than those in high PFR during and after exercise.

Conclusion: Exercise temporarily increases pump regurgitation with continuous flow LVAS support. Average flow rate of the descending thoracic aorta was maintained by compensation from increased heart rate, although the diastolic flow of the descending thoracic aorta decreased after exercise at the lower pump flow rate. Further study will be needed to evaluate whether or not this flow decrease causes hemodynamic and/or an oxygen delivery mismatch to peripheral tissue.

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1. Introduction

Long-term circulatory assist with clinically available pulsatile left ventricular assist systems (LVAS) is being increasingly considered. Concurrently, continuous flow LVAS are being thought of as a destination therapy [1]. This could result in increased numbers of out-of-hospital LVAS patients with expanded activity of daily life, likely including exercise [2,3]. We previously reported that there appeared to be correlation between pump regurgitation in continuous flow LVAS and decreased tissue perfusion distal to the outflow graft, possibly resulting in pathological changes of renal cortex arteries [4,5]. In this study, we analyzed the effects of pump regurgitant flow on aortic hemodynamics during exercise.
2. Materials and methods

2.1. Pump implantation

Five Jersey breed calves weighing 74.8 ± 8.1 kg (range 64.5–87.0) were implanted with a continuous flow LVAS (Evaheart, SunMedical Technology Research Corp., Nagano, Japan). This pump is a centrifugal LVAS with recirculating purge system as previously described [6]. At surgery, the animals were intubated endotracheally for mechanical ventilation and anesthesia was maintained with isoflurane and oxygen. The device was implanted in a left ventricle-descending thoracic aorta bypass configuration without cardiopulmonary bypass through a left thoracotomy. Ultrasonic flow probes (T206 series, Transonic Systems Inc., Ithaca, NY) were set on the pump outflow graft, descending thoracic aorta (2–3 cm distal to the outflow graft anastomosis), and pulmonary artery. Arterial pressure was obtained from a fluid-filled catheter implanted in the left carotid artery.

2.2. Study at rest

Data collection started 3–4 weeks after surgery, to eliminate any postsurgical effect. To determine the relationship between pump assist rate and regurgitant flow, arterial pressure, heart rate, pulmonary artery flow, pump flow and descending thoracic aorta flow wave were recorded at various pump flow rates by data acquisition system (WINDAQ: DATAQ Instruments Inc., Akron, OH).

2.3. Exercise protocol

Exercise tests were also performed beginning 3–4 weeks after surgery and then weekly thereafter for up to 27 weeks. All calves exercised on a treadmill at 4–5 km/h with an elevation of 1.5% for 10 min at two different pump flow rates (PFR) based upon percent pulmonary artery flow rate at rest (High PFR, pump flow rate 60–80% of pulmonary artery flow rate; low PFR, pump flow rate 25–30% of pulmonary artery flow rate) (Fig. 1). High pump flow rate was set at maximum rotational speed to prevent ventricular wall suction and lower pump flow rate was set at a point where pump regurgitant flow was present. Pump speed was not changed during exercise. The same hemodynamic and pump parameters as the study at rest were recorded before exercise, every 5 min during exercise and 5, 10 and 15 min after exercise.

2.4. Data analysis

All data were recorded by data acquisition system every 5 ms for 20 s. Pulsatility was quantified by pulse pressure and pulsatility index (pulse pressure/mean arterial pressure). The pump flow volume in systolic (Pump Vs) and diastolic phase (Pump Vd) in each cardiac cycle was calculated according to the method described in our previous report [7]. All data collected by data acquisition system were converted to fit Microsoft Excel (Microsoft, Redmond, WA) and StatView 4.5 (SAS Institute Inc., Cary, NC) files for statistical analysis. These parameters were expressed as mean value ± standard deviation. Student’s t-test was used for statistical analysis of significance of difference and P < 0.05 was regarded to be statistically significant.

2.5. Humane animal care

All animals received humane care in accordance with the Principles of Laboratory Animal Care formulated by the National Society for Medical Research as well as with the Guide for the Care and Use of Laboratory Animals, prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press (Revised in 1996), and the guidelines determined by the Institutional Animal Care and Use Committee of the University of Pittsburgh.

3. Results

3.1. Study at rest

A total number of 191 data collections representing 22 tests were analyzed. Pump and hemodynamic parameters at rest are shown in Fig. 2. Pulse pressure and pulsatility index decreased as pump flow increased. Pulmonary artery flow rate, descending thoracic aorta flow rate and heart rate were almost constant at pump assist rate > 0.3. At pump assist rate < 0.3 there was a gradual decrease in pulmonary artery flow, descending thoracic aorta flow and heart rate. Pump regurgitant flow was observed when the pump flow rate was decreased below 0.27 ± 0.07 of pulmonary artery flow rate with a mean arterial pressure of 103.9 ± 10.6 mmHg. Fig. 3 shows the results of flow wave analysis with descending
As pump flow increased, descending thoracic aorta flow volume in systole (DAVs) decreased while flow volume in diastole (DAVd) increased. Total descending thoracic aorta flow volume (DAVs + DAVd) in each cardiac cycle was almost constant at all pump flows. There were linear increases in PumpVs, PumpVd and total pump flow volume (PumpVs + Vd) in each cardiac cycle with pump flow rates (correlation coefficient = 0.83, 0.88 and 0.91, respectively). Systolic arterial pressure decreased and diastolic arterial pressure increased with increased pump flow rate, while there was no change in mean arterial pressure.

3.2. Exercise test

A total of 18 exercise tests were performed involving all animals. Pump flow rate, pulmonary artery flow rate and descending thoracic artery flow rate significantly increased along with the heart rate during exercise compared to at rest in both high and low pump flow rates (Fig. 4). At high PFR, maximum heart rate increased by 32.9%, maximum pulmonary artery flow rate by 32.6%, maximum pump flow rate by 27.3%, and maximum descending thoracic aorta flow rate by 30.5% compared to baseline. At low PFR, maximum heart rate increased by 36.6%, maximum pulmonary artery flow rate by 41.9%, maximum pump flow rate by 20.9%, and maximum descending thoracic aorta flow rate by 17.2% compared to baseline.

Fig. 5 shows the changes in systolic and diastolic pump flow volumes during exercise at both pump flow rates. In all cases, there was a significant increase in mean arterial pressure.
pressure during exercise ($P < 0.01$ compared to baseline). At high pump flow rate, Pump $V_s + V_d$, Pump $V_s$ and Pump $V_d$ were significantly decreased in the first 5 min of exercise, then increased back to baseline until the end of exercise although there was an increased mean arterial pressure ($P < 0.01$, compared to baseline). At low pump flow rate, Pump $V_s + V_d$ and Pump $V_s$ were slightly decreased in the first 5 min, then increased back to baseline until the end of exercise, but Pump $V_s$ increased ($P < 0.05$) and Pump $V_d$ decreased significantly ($P < 0.05$) after exercise.

Descending thoracic aorta flow characteristics for both assist rates were shown in Fig. 6 and Table 1. At high pump flow rate, DA $V_s + V_d$ and DA $V_s$ increased slightly but DA $V_d$ decreased during exercise (no significant difference compared to baseline), then increased back to baseline until the end of exercise.

Table 1

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DA $V_d$, descending thoracic aorta flow volume in diastole; DA $V_s$, descending thoracic aorta flow volume in systole; DA $V_s + V_d$, descending thoracic aorta flow volume/cardiac cycle; Ex., exercise; High, high pump flow rate; HR, heart rate (beats/min); Low, low pump flow rate; Post, post-exercise. All parameters except HR are expressed as milliliters each cardiac cycle. *$P < 0.05$ between groups; **$P < 0.05$ compared to baseline.

4. Discussion

Outpatient care of patients with an implantable pulsatile LVAS is becoming increasingly common [8,9]. Continuous flow LVAS may be a better choice for outpatient because of the inherent simplicity and size of the device. However, the potential for pump regurgitant flow could be one of the disadvantages of these pumps. There have been several reports about pump regurgitation and its effect to the cardiac function [10,11], but few reports focused on its effect to the extracardiac organs [4,5]. Certainly, there is less need to be concerned about pump regurgitant flow if the patient’s heart has extremely low cardiac function because the pump pressure head does not dramatically change throughout the cardiac cycle. However, if there is cardiac recovery there will be an increased pressure head against the pump as the heart starts to eject through the aortic valve. In this circumstance, regurgitant flow may become apparent due to increased pressure head during diastole.

4.1. Study at rest

At rest, descending thoracic aorta flow rate significantly decreased when pump flow rate was less than 27% of assist rate. This result supports the report by Litwak et al. [5] that lower pump flow is associated with decreased tissue perfusion distal to the outflow graft anastomosis with...
normal cardiac function. However, their data showed that the tissue perfusion decreased more linearly with pump flow than actual descending thoracic aorta flow rate, which suggests the cause of decreased descending thoracic aorta flow rate after exercise is maintained by increased heart rate; however, as average descending thoracic aorta flow rate after exercise is generally less than actual descending thoracic aorta flow rate, which is maintained by increased heart rate and pulmonary artery flow rate to compensate for decreased descending thoracic aorta flow rate. As Akimoto et al. reported [12], increased pump flow rate during exercise in rotary blood pump mainly depends on heart rate and there was almost no change in mean arterial pressure. Therefore, this apparent paradox can be explained by increased heart rate and pulmonary artery flow rate to compensate for decreased pump flow, which is the same physiologic mechanism seen in the patients with acute heart failure and aortic regurgitation [13].

At high pump flow rate, all pump flow volume parameters and DA Vd decreased in the first 5 min of exercise and then were almost constant after that, indicating that exercise does not significantly affect descending aortic hemodynamics, as shown in Fig. 1. At low pump flow rate, Pump Vs and DA Vs significantly increased, but Pump Vd and DA Vd decreased after exercise. We measured tissue perfusion in previous acute studies [5] but in this study, tissue perfusion was not measured because of a moving artifact during exercise. It seems that there is enough flow distribution for organs distal to the outflow graft because average descending thoracic aorta flow rate after exercise is still maintained by increased heart rate; however, as described in our previous report [5], blood distribution for tissues cannot be characterized only by average descending thoracic aorta flow rate but also by volume and time of perfusion in each cardiac cycle. As shown in Fig. 1, mean descending thoracic aorta antegrade flow is significantly decreased after exercise in the low-flow trial compared to that of high-flow.

4.2. Exercise test

Our hypothesis for the exercise test was that due to increased mean arterial pressure, there would be increased pump regurgitant flow (i.e. decreased pump diastolic flow) during exercise. In general, the increased ratio of maximum heart rate to maximum pulmonary artery flow rate in low pump flow rate were greater than those in high pump flow rate, although maximum pump flow rate and descending thoracic artery flow rate were less. As Akimoto et al. reported [12], increased pump flow rate during exercise in rotary blood pump mainly depends on heart rate and there was almost no change in mean arterial pressure. Therefore, this apparent paradox can be explained by increased heart rate and pulmonary artery flow rate to compensate for decreased pump flow, which is the same physiologic mechanism seen in the patients with acute heart failure and aortic regurgitation [13].

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4.3. Clinical application and study limitation

Although many methods for creating heart failure model in small animals have been reported [14–16], it is still difficult to make stable chronic heart failure model in large animals for long-term survival. This is the limitation of this study and is why we implanted LVAS in normal calves. Because of normal cardiac function, the responses to the regurgitant flow, especially increasing heart rate as compensation to the acute volume overload, are a normal physiological reaction [13]. Many reports indicate that pulsatile LVAS patients have good inotropic and chronotropic response to exercise [2,17–19]; however, this compensatory mechanism of increased heart rate may not be seen in some of the chronic heart failure patients with chronotropic impairment [20–22]. Furthermore, patients implanted with a continuous flow LVAS as destination therapy may receive β-blockade, anti-arrhythmic agents, and angiotensin-converting enzyme inhibitors [23–25]. These patients might have decreased chronotropic response to exercise under such an aggressive cardiac recovery program.

The situation we described in this article may be worst-case scenario for the heart failure patients who has received aggressive medical therapy (i.e. pump with regurgitation and cardiac recovery). However, given that these pumps are being considered for destination therapy, the number of candidates would increase thus the increased likelihood of encountering this problem. The other limitation is that this study was conducted with a specific pump and the pump regurgitation was intentionally produced with an unusually low pump speed. The incidence of pump regurgitation will likely vary according to the H-Q curve characteristics of the pump and this phenomenon needs to be included as a consideration for pump design [7], thus avoiding regurgitant flow within the normal operational pump flow range.

5. Conclusion

Exercise temporarily increases pump regurgitation with continuous flow LVAS during exercise. Average flow rate of the descending thoracic aorta was maintained by compensation with increased heart rate although the diastolic flow of the descending thoracic aorta decreased after exercise in lower pump flow rate. Further study will be needed to evaluate whether or not this flow decrease causes hemodynamic and oxygen delivery mismatch to peripheral tissue.

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References


