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Rotary pump speed modulation for generating pulsatile flow and phasic left ventricular volume unloading in a bovine model of chronic ischemic heart failure

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BACKGROUND: Rotary blood pumps operate at a constant speed (rpm) that diminishes vascular pulsatility and variation in ventricular end-systolic and end-diastolic volumes, which may contribute to adverse events, including aortic insufficiency and gastrointestinal bleeding. In this study, pump speed modulation algorithms for generating pulsatility and variation in ventricular end-systolic and end-diastolic volumes were investigated in an ischemic heart failure (IHF) bovine model ($n = 10$) using a clinically implanted centrifugal-flow left ventricular assist device (LVAD).

METHODS: Hemodynamic and hematologic measurements were recorded during IHF baseline, constant pumps speeds, and asynchronous (19–60 cycles/min) and synchronous (copulse and counterpulse) pump speed modulation profiles using low relative pulse speed (±25%) of 3,200 ± 800 rpm and high relative pulse speed (±38%) of 2,900 ± 1,100 rpm. End-organ perfusion, hemodynamics, and pump parameters were measured to characterize pulsatility, myocardial workload, and LVAD performance for each speed modulation profile.

RESULTS: Speed modulation profiles augmented aortic pulse pressure, surplus hemodynamic energy, and end-organ perfusion ($p < 0.01$) compared with operation at constant speed. Left ventricular external work and myocardial oxygen consumption were significantly reduced compared with IHF baseline ($p < 0.01$) but at the expense of higher LVAD power consumption.

CONCLUSIONS: Pump speed modulation increases pulsatility and improves cardiac function and end-organ perfusion, but the asynchronous mode provides the technologic advantage of sensorless control. Investigation of asynchronous pump speed modulation during long-term support is warranted to test the hypothesis that operating an LVAD with speed modulation will minimize adverse events in patients supported by an LVAD that may be associated with long-term operation at a constant pump speed.

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The technical advantages and improved outcomes with continuous-flow (CF) left ventricular assist devices (LVADs) have led to their nearly exclusive use as mechanical circulatory support therapy in patients with heart failure (HF), but there are also concerns over potential risks of non-pulsatile

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(or diminished pulsatility) blood flow. Arterial pulse pressure (ΔP) and flow are significantly diminished during CF LVAD support at constant pump speed (rpm).[1] Adverse cardiovascular events, such as aortic insufficiency, gastrointestinal bleeding, and right HF have been reported with CF LVAD support, which were not observed as often with pulsatile flow (PF) LVADs.[2,3] Other reported effects of CF LVAD support include reduced coronary blood flow,[4] increased pulmonary vascular resistance,[5] elevated inflammatory markers,[6] and cardiac disuse atrophy.[7] It has also been suggested that there is a lower rate of myocardial recovery in patients supported by CF LVADs than by PF LVADs.[8] Subsequently, there is a renewed interest in the potential physiologic benefits of PF.

Pump speed modulation with CF LVADs is being developed using a variety of control strategies and experimental systems to generate physiologic pressures, flows, and ventricular volume unloading. Pump speed can be modulated at a rate independent of the native heart rate (asynchronous) or at a rate equal to native heart rate (synchronous), with the latter requiring an integrated "timing" sensor. Synchronous modulation can also be timed to deliver maximum LVAD outflow precisely during LV systole (copulse) or during diastole (counterpulse). Early LVAD pump speed modulation strategies favored asynchronous control,[9,10] whereas later work implemented sinusoidal and synchronous flow modulation.[11–13] Other PF variables, such as pulse timing, width, and amplitude, have been investigated with computer simulation and mock flow loop models.[14,15] Clinically, pump speed modulation has also been used for anti-thrombotic cycling.[16] The understanding of potential physiologic responses to pump speed modulation with CF LVAD support is limited. This study used a HF bovine model to investigate acute hemodynamic responses, end-organ perfusion, and pump performance during CF LVAD support with pump speed modulation.

Methods

Animals

CF LVADs with pump speed modulation were tested in 10 male Jersey calves (weight, 70–175 kg). The animals used in this study received humane care and were handled in accordance with National Institutes of Health and the University of Louisville Animal Care Committee guidelines. All experimental procedures were approved by the University of Louisville Institutional Animal Care and Use Committee.

Induction of HF

Chronic ischemic HF (IHF) was induced in calves as previously reported.[7,17] Briefly, general anesthesia was achieved with intravenous diazepam (0.4 mg/kg) and ketamine (4 mg/kg) and maintained with isoflurane (1%–3%) and oxygen (100%). A 6F diagnostic catheter was advanced from the carotid artery to selectively engage the left main coronary artery. To induce chronic IHF, a suspension of 90-μm polystyrene microspheres (Polysciences Inc, Warrington, PA) was injected into the left main coronary artery. Real-time observation of hemodynamic and electrocardiographic changes demonstrated severe and irreversible myocardial ischemia.

After the procedure, animals were recovered and treated for progressive IHF.[18] The development of chronic IHF was monitored by weekly echocardiographic measurement of LV ejection fraction (EF). Animals were maintained in IHF for an average of 47 ± 8 days before acute LVAD implant.

Surgical preparation and instrumentation

Chronic IHF animals ($n = 10$) were implanted with the HeartWare HVAD (HeartWare, Miami Lakes, FL) CF LVAD to study acute hemodynamic responses to pump speed modulation strategies. Fluid-filled arterial and venous catheters were inserted into the right carotid artery and jugular vein, respectively, for fluid or drug administration and blood collection. The LVAD was implanted at the LV apex and anastomosed to the proximal descending thoracic aorta without the use of cardiopulmonary bypass.

The LVADs were controlled with an intermediary controller unit (CDAS DAQ Interface, HeartWare) and a custom LabVIEW (National Instruments Corp, Austin, TX) operator program. This proprietary control system allowed for basic LVAD control (pump off/on, constant rpm operation) and LVAD speed modulation through user-defined rpm increases and decreases for specified durations. The animals were instrumented with high-fidelity pressure catheters (Millar Instruments, Houston, TX) to measure left atrial and aortic pressure and a pressure-volume admittance catheter to measure LV pressure and volume (ADV500; Transonic Systems, Ithaca, NY). Flow probes (Transonic Systems) were placed for measurement of pulmonary artery, left main coronary artery, aortic, and LVAD flows. LVAD motor current, voltage, and speed (rpm) were simultaneously recorded by the LVAD controller. LV volumes and wall motion were measured with three-dimensional transesophageal echocardiography (iE33 and X7–2t transducer; Philips Healthcare, Andover, MA).

Experimental protocol

Baseline hemodynamic measurements were recorded before and immediately after LVAD implant with the device off and outflow graft clamped. After establishing IHF baseline, the LVAD was operated in constant speed and speed modulation modes. The constant speed conditions were set at pump speeds of 2,900 rpm and 3,200 rpm. The speed modulation conditions were created by positive and negative step changes in pump speed (rpm) with equal magnitude and duration (Figure 1). Modulation profiles were tested using 2 pump speed conditions: low relative pulse speed (RPS; ±25%) of 3,200 ± 800 rpm and high RPS (±38%) of 2,900 ± 1,100 rpm. Speed modulation profiles achieved equal maximum motor speed (4,000 rpm).

Asynchronous (19, 38, 60 cycles/min) and synchronous (counterpulse and copulse) modulations were applied at each pump speed condition, totaling 10 speed modulation profiles (Figure 2). Synchronous LVAD cycle rates were matched to the animal's heart rate with a 0.02-second offset to allow the LVAD flow modulation to transition between counterpulse and copulse during the synchronous data set (180 seconds). Baseline hemodynamic values were recorded for each speed test condition to verify return to IHF steady-state.

Myocardial oxygen consumption

Paired blood samples from the carotid artery and coronary sinus were collected to determine the LV myocardial oxygen consumption ($LVVO_2$) for each test condition and processed using a GEM Premier 4000 blood gas analyzer (Instrumentation

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