Induction of Ventricular Collapse by an Axial Flow Blood Pump

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An important consideration for clinical application of rotary blood pump based ventricular assist is the avoidance of ventricular collapse due to excessive operating speed. Because healthy animals do not typically demonstrate this phenomenon, it is difficult to evaluate control algorithms for avoiding suction in vivo. An acute hemodynamic study was thus conducted to determine the conditions under which suction could be induced. A 70 kg calf was implanted with an axial flow assist device (Nimbus/UOP IVAS; Nimbus Inc., Rancho Cordova, CA) cannulated from the left ventricular apex to ascending aorta. On initiation of pump operation, several vasodilator interventions were performed to alter preload, afterload, and contractility of the left ventricle. Initially, dobutamine increased contractility and heart rate ([HR] = 139; baseline = 70), but ventricular collapse was not achievable, even at the maximal pump speed of 15,000 rpm. Norepinephrine decreased HR ([HR] = 60), increased contractility, and increased systemic vascular resistance ([SVR] = 24; baseline = 15), resulting in ventricular collapse at a pump speed of 14,000 rpm. Isoproterenol (β agonist) increased HR ([HR] = 103) and decreased SVR ([SVR] = 12), but ventricular collapse was not achieved. Inferior vena cava occlusion reduced preload, and ventricular collapse was achieved at speeds as low as 11,000 rpm. Esmolol (β, antagonist) decreased HR ([HR] = 55) and contractility, and ventricular collapse was achieved at 11,500 rpm. Episodes of ventricular collapse were characterized initially by the pump output exceeding the venous return and the aortic valve remaining closed throughout the cardiac cycle. If continued, the mitral valve would remain open throughout the cardiac cycle. Using these unique states of the mitral and aortic valves, the onset of ventricular collapse could reliably be identified. It is hoped that the ability to detect the onset of ventricular collapse, rather than the event itself, will assist in the development and the evaluation of control algorithms for rotary ventricular assist devices. 


Ventricular assist devices (VADs) using atrial or ventricular cannulation establish a parallel pathway for blood flow from the pulmonary to the systemic vasculature,1,2 thus axial flow VADs add new hemodynamic states to the animal model. Decreased pulse pressure, and more notably, the possibility of the aortic valve remaining closed (and even of the mitral valve remaining open) at all points during the cardiac cycle may follow. Axial flow pumps, unlike passively filling pulsatile VADs, have the capacity to develop negative inflow pressure that actively suction blood into the ventricle.3 Therefore, the ventricular pressure may be less than the aortic pressure at all points during the cardiac cycle, precluding opening of the aortic valve. Further reductions in ventricular systolic pressure cause the mitral valve to remain open throughout ventricular systole.

To study these altered hemodynamic states, we conducted pharmacologic and hemodynamic interventions on an anesthetized calf.4 The pharmacologic interventions consisted of norepinephrine (α and β agonist), isoproterenol (β agonist), dobutamine (β agonist), and esmolol (β, antagonist). The hemodynamic intervention consisted of occlusion of the inferior vena cava (IVC) to reduce the preload to the left ventricle (LV). These were used to simulate various physiologic states, such as increased and decreased systemic vascular resistance ([SVR] mainly α, and β, effects), and increased and decreased HR and contractility.

Aortic valve status becomes one of the critical parameters while using an axial flow VAD. The aortic valve may be closed indefinitely because of the pressure difference across the pump, elevating the aortic pressure over the LV systolic pressure (i.e., at all points during the cardiac cycle). This establishes an area of hemostasis at the surface of the aortic valve that may facilitate the formation of thrombus5; if the aortic valve periodically opens, the thrombus may be ejected into the systemic circulation. The possibility that a fibrotic scar at the valve commissures might permanently disable the opening of the aortic valve is an additional morbidity risk, and represents a unique form of device induced cardiac pathology.

The point at which the aortic valve ceases to open is remarkable in that it precedes ventricular suction and collapse with an appreciable safety margin (i.e., ~1–2,000 rpm). With the pump operating at a point slightly below the speed required to close the aortic valve, the pump's output will nearly equal the venous return to the right atrium. As such, it can be viewed as the point of optimally unloading the ventricle.

The onset of ventricular collapse will be preceded by the mitral valve remaining open during systole. Therefore, it may be used as an indicator of imminent ventricular collapse.

Methods

In Vivo Data Acquisition

Use of in vivo studies in animals was necessary in this project because it is the only feasible way to obtain realistic hemody-
namic and physiologic data that accounts for all the intrinsic regulatory systems acting in the circulation. The experimental protocol was approved by the University of Pittsburgh Institutional Animal Care and Use Committee and performed according to National Institutes of Health (NIH) guidelines. These types of data are essential for characterizing the dynamics of the interaction between the native cardiovascular system and our assist device. Before explanation of the pump (Nimbus/Up? IVAS; Nimbus Inc., Rancho Cordova, CA) at the conclusion of a 30 day implantation study, one acute (3–6 hr) experiment was performed. Pharmacologic and hemodynamic alterations were instituted to induce ventricular collapse after anesthesia and left thoracotomy.

Cannulation at the apex of the LV allowed blood to enter the assist device, and the outflow of the device was anastomosed to the aorta. The pump was placed outside the chest cavity in a pocket under the skin as previously described.

Hemodynamic and device related data were acquired before and during all interventions. The hemodynamic signals included pump flow, pulmonary arterial flow, aortic pressure, pulmonary artery pressure, and LV pressure. In addition, motor current and pump speed were recorded directly from the device console. Pulmonary and pump flow measurements were obtained using ultrasonic perivascular flow transducers (A-Series Transonic; Ithaca, NY). All signals were sampled at 150 Hz and recorded using a Pentium personal computer implementing an analog-to-digital (A/D) acquisition board (Dataq, Akron, OH) and application software. During each intervention, the pump speed was increased in 1,000 rpm increments from the minimal (8,000 rpm) to the maximal (15,000 rpm) speed.

Five interventional conditions were completed, simulating various hemodynamic states. Four interventions were pharmacologic; one was hemodynamic. The pharmacologic interventions were administered as intravenous (IV) infusions, with dosage steadily increased to achieve the desired effect for each drug. The IVC occlusion was performed by manually occluding the vessel. For each of the interventions, ventricular collapse was determined using the criteria of a LV pressure <25 mmHg during ventricular systole. SVR was estimated by dividing the mean aortic pressure by the mean pulmonary artery flow tuntis in mmHg/L).

The interventions that resulted in ventricular collapse are described in Table 1. During the IVC occlusion, ventricular collapse occurred in which ventricular pressure increased the heart in a manner that increased heart rate (HR = 60 bpm) and contractility (Fig. 1). Ventricular collapse was achieved after a preload of 11,000 rpm. Ejection fraction (EF) = 55 and contractility was achieved at 11,500 rpm.

The interventions that did not induce ventricular collapse (HR = 139) and contractility, even at the highest pump speed (Fig. 1). Isoproterenol increased HR, and decreased SVR (Fig. 2), but did not achieve the results of Table 1.

Norepinephrine is a β1-receptor agonist, which increases systemic resistance and also lowers HR through β1 activity, responding to aortic pressure, which can simulate the conditions. Norepinephrine infusion at a rate of 0.2 µg/kg/min and arterial pressure approaching a systolic pressure of 120 mmHg. Thus, we observed an increase in heart rate at 12,000 rpm. Increases in cardiac output and ventricular collapse achievable (Fig. 2).

Isoproterenol is a non-selective β-receptor agonist and thus increasing cardiac output and systemic resistance with this intervention.
Figure 1. (Top) Increasing pump speed from 8,000 rpm to 14,000 rpm during dobutamine (β agonist) infusion. (Middle) Aortic pressure. (Bottom) Left ventricular (LV) pressure. Ventricular collapse was not achieved at any pump speed because ventricular systolic pressure was always more than 25 mmHg. The aortic valve continues to open during systole at all pump speeds because LV pressure exceeds the aortic pressure during systole of each cardiac cycle.

Figure 2. (Top) Increasing pump speed from 8,000 rpm to 14,000 rpm during norepinephrine (α and β agonist) infusion. (Bottom) Aortic pressure and left ventricular (LV) pressure. Ventricular collapse was achieved at 14,000 rpm where ventricular systolic pressure was always less than 25 mmHg. The aortic valve ceases to open during systole at pump speeds greater than 13,000 rpm because LV pressure is less than the aortic pressure during systole of each cardiac cycle.
collapse was unobtainable at all speeds because of the high cardiac throughput (e.g., more than 10 L/min; see Figure 3).

Dobutamine, a β₁ agonist, was administered by constant IV infusion at a rate of 5.3 µg/kg/min. It increased cardiac rate and contractility, simulating an exercising cardiovascular system. As with the isoproterenol infusion, ventricular collapse was unobtainable at all speeds because of the high cardiac throughput (e.g., more than 10 L/min; normal = 7 L/min).

Esmolol, a β₂ antagonist, reduces HR and contractility (SVR was increased through a reflex mechanism), thereby simulating cardiac insufficiency. Esmolol was administered by constant IV infusion at a rate of 16.7 µg/kg/min. The aortic valve remained closed at speeds greater than 9,000 rpm, but ventricular collapse was achieved at 11,500 rpm (Figure 4). It was also evident that once LV pressure approached zero, it was not reduced further with increasing speed; rather, inflow pressure continued to decrease, reaching −300 mmHg at times. The esmolol case, which represents a heart disease model, produced classic axial flow unloading and suction response: pulse pressure approached zero on full unloading. Beyond this point, the unstable oscillations of ventricular collapse were induced.

Inferior vena cava occlusion reduced the preload, as would an orthostatic challenge (e.g., standing from a supine position). The aortic valve was closed throughout systole at pump speeds more than 9,000 rpm. Ventricular collapse was obtained at speeds as low as 11,000 rpm (Figure 5). A sudden decrease in preload due to a change in posture simulates a transient type of hemodynamic challenge that the controller will routinely experience.

**Discussion and Conclusion**

Infusion of esmolol served as our acutely induced cardiac insufficiency model. Under these conditions, ventricular suction was demonstrated at much lower speeds than with interventions that simulated physical activity, such as isoproterenol infusion (dilation of vasculature supplying the muscle tissue as well as increased HR and contractility). The heart disease models also demonstrated prolonged intervals of aortic valve closure, as well as the development of high pressure differences across the pump (>300 mmHg peak pressure differences) during ventricular collapse.

A control algorithm's first priority should be to avoid operating points that are detrimental to the patient (i.e., "first, do no harm"). Not only should ventricular collapse be avoided, but the region of aortic valve closure 1,000–2,000 rpm before ventricular collapse might also be harmful to the patient. However, with a very weak native ventricle, the aortic valve may remain closed at unacceptable low systolic pressures. In this case, the speed may need to be reduced periodically to allow the aortic valve to open, thereby preventing permanent fibrotic stenosis of the aortic valve.

The finding that aortic valve closure and ventricular collapse are not achievable in elevated cardiac output states, and yet are easily induced in a weak ventricle, poses additional challenges in designing a robust controller to treat the most severely ill patients. Conversely, if recovery of ventricular function occurs, the controller will become less essential in maintaining the patient's quality of life.
Figure 4. (Top) Increasing pump speed from 9,000 rpm to 12,500 rpm during esmolol (β-agonist) infusion. (Bottom) Aortic pressure and left ventricular (LV) pressure. Ventricular collapse was achieved at 12,000 rpm where ventricular systolic pressure was always less than 25 mmHg. The aortic valve ceases to open during systole at pump speeds of more than 9,000 rpm because the LV pressure is less than the aortic pressure during systole of each cardiac cycle.

Figure 5. (Top) Increasing pump speed from 9,000 rpm to 12,500 rpm during the inferior vena cava occlusion. (Bottom) Aortic pressure and left ventricular (LV) pressure. Ventricular collapse was achieved at 11,000 rpm where ventricular systolic pressure was always less than 25 mmHg. The aortic valve ceases to open during systole at pump speeds more than 9,000 rpm because the LV pressure is less than the aortic pressure during systole of each cardiac cycle.
References