End-diastolic flow reversal limits the efficacy of pediatric intra-aortic balloon pump counterpulsation

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Background: Counterpulsation with an intra-aortic balloon pump (IABP) has not achieved the same success or clinical use in pediatric patients as in adults. In a pediatric animal model, IABP efficacy was investigated to determine whether IABP timing with a high-fidelity blood pressure signal may improve counterpulsation therapy versus a low-fidelity signal.

Methods: In Yorkshire piglets (n = 19; weight, 13.0 ± 0.5 kg) with coronary ligation-induced acute ischemic left ventricular failure, pediatric IABPs (5 or 7 mL) were placed in the descending thoracic aorta. Inflation and deflation were timed with traditional criteria from low-fidelity (fluid-filled) and high-fidelity (micromanometer) blood pressure signals during 1:1 support. Aortic, carotid, and coronary hemodynamics were measured with pressure and flow transducers. Myocardial oxygen consumption was calculated from coronary sinus and arterial blood samples. Left ventricular myocardial blood flow and end-organ blood flow were measured with microspheres.

Results: Despite significant suprasystolic diastolic augmentation and afterload reduction at heart rates of 105 ± 3 beats per minute, left ventricular myocardial blood flow, myocardial oxygen consumption, the myocardial oxygen supply/demand relationship, cardiac output, and end-organ blood flow did not change. Statistically significant end-diastolic coronary, carotid, and aortic flow reversal occurred with IABP deflation. Inflation and deflation timed with a high-fidelity versus low-fidelity signal did not attenuate systemic flow reversal or improve the myocardial oxygen supply/demand relationship.

Conclusions: Systemic end-diastolic flow reversal limited counterpulsation efficacy in a pediatric model of acute left ventricular failure. Adjustment of IABP inflation and deflation timing with traditional criteria and a high-fidelity blood pressure waveform did not improve IABP efficacy or attenuate flow reversal. End-diastolic flow reversal may limit the efficacy of IABP counterpulsation therapy in pediatric patients with traditional timing criteria. Investigation of alternative deflation timing strategies is warranted. (J Thorac Cardiovasc Surg 2014;147:1660-7)

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Counterpulsation with an intra-aortic balloon pump (IABP) is the most common mechanical circulatory support strategy for a variety of cardiac pathologies in adults.[1] Yet, IABP therapy in pediatric patients has not demonstrated the same degree of efficacy and has not gained widespread clinical use.[2] Differences between adult and pediatric anatomy and physiology may limit the efficacy of IABP therapy in neonates, infants, and children.

In this study, we examined IABP counterpulsation in a pediatric model of acute ischemic left ventricular failure. We tested the hypothesis that the efficacy of pediatric IABP therapy is improved with a high-fidelity (micromanometer) rather than a traditional low-fidelity (fluid-filled) arterial blood pressure signal used to adjust IABP inflation and deflation timing.

METHODS

All animals received humane care and were handled in accordance with the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996). Experimental procedures followed animal study protocols approved by the University of Louisville (Louisville, Ky) Institutional Animal Care and Use Committee.

Experimental Design

Piglets (n = 19; weight, 13.0 ± 0.5 kg) were instrumented surgically to determine aortic, carotid, and coronary artery hemodynamics. Myocardial oxygen consumption (MVO_2) was calculated from coronary sinus and arterial blood gas data. Left ventricular myocardial blood flow and regional

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Abbreviations and Acronyms

AoF = aortic flow
AoP = aortic pressure
bpm = beats per minute
IABP = intra-aortic balloon pump
LAD = left anterior descending
LADF = LAD flow
LAP = left atrial pressure
LVP = left ventricular pressure
MVO_2 = myocardial oxygen consumption

end-organ blood flow were determined with neutron-activated 15-μm microspheres. Sequential coronary ligation was performed to induce acute ischemic left ventricular failure. A pediatric IABP was placed in the descending thoracic aorta.

In each animal, hemodynamic waveforms (15-second data epochs), blood gases, and end-organ blood flows were measured at steady state during the following experimental test conditions: (1) normal baseline (IABP off), (2) coronary ligation-induced left ventricular failure (IABP off), (3) IABP support with timing adjusted to the arterial blood pressure waveform acquired with a low-fidelity (<20-Hz response) fluid-filled catheter in the radial artery, and (4) IABP support with timing adjusted to the arterial pressure waveform acquired with a high-fidelity (<5-kHz response) micromanometer pressure transducer in the aortic root. Measurements were recorded during 1:1 counterpulsation support in which each aortic valve closure initiated rapid balloon inflation and each end diastole initiated rapid balloon deflation.

Of note, an aortic root pressure waveform transduced by a high-fidelity catheter results in a more precise waveform morphology with a more pronounced dicrotic notch, less signal gain, and less phase distortion.[3] Consequently, a high-fidelity signal was presumed to enable more accurate inflation and deflation timing of the IABP.

Surgical Preparation

Animals were fasted, preanesthetized with intramuscular ketamine (30 mg/kg) and acepromazine (0.2 mg/kg), and anesthetized with isoflurane (1.5%-3%) and room air. A left lateral thoracotomy was performed, and the left and right carotid artery and jugular vein were exposed through neck incisions. A single-tip high-fidelity micromanometer catheter (2.5 Fr, SPR-524; Millar Instruments, Houston, Tex) was placed in the left atrium. A dual-tip high-fidelity micromanometer catheter (5 Fr, SPC-721; Millar Instruments) was advanced retrograde from the ascending aorta into the left ventricle. Transit-time ultrasonic flow probes (T205; Transonics, Ithaca, NY) were placed around the aortic root, left carotid artery, and left anterior descending (LAD) coronary artery to measure volumetric blood flows. Sampling catheters were introduced into the coronary sinus via the hemiazygous vein, pulmonary artery, and right carotid artery to sample blood and measure blood gases. An infusion catheter was introduced into the left atrium for serial injections of microspheres during each experimental test condition to determine end-organ blood flows throughout the body.[4] A blood-sampling catheter was introduced into the right femoral artery for simultaneous withdrawal of a microsphere reference blood-flow sample during each test condition. A fluid-filled pressure-monitoring catheter (24-gauge Angiocath; Becton Dickinson, Sandy, Utah) was inserted into the right radial artery.

The animal was anticoagulated with a bolus injection of heparin (300 U/kg) and subsequent small boluses of heparin to maintain an activated clotting time of greater than 300 seconds. An IABP catheter (5 or 7 mL; Datascope, Fairfield, NJ) was inserted via a left femoral artery cut down and advanced until the tip was distal to the left subclavian artery, as confirmed by digital palpation. Balloon timing was manually adjusted with the arterial pressure waveform (fluid-filled radial artery catheter or aortic root Millar catheter) displayed on the IABP console (System 97; Datascope). Balloon inflation and deflation were timed to maximize aortic diastolic pressure augmentation and minimize aortic end-diastolic pressure (afterload).

Induction of Ischemic Left Ventricular Failure

Intravenous lidocaine (20-mg bolus, 20-mg/h infusion) and esmolol (5-mg/kg bolus, 50-μg/kg per minute infusion) were administered to prevent arrhythmia. Sequential coronary ligation of branches of the LAD induced acute ischemic left ventricular failure. Target cardiac dysfunction was achieved when 3 of 4 criteria were met: approximate reduction of (1) left ventricular cardiac output by 25%, (2) mean aortic pressure by 10 mm Hg, (3) mixed venous O_2 saturation by 10%, and (4) an elevation of left atrial pressure (LAP) and/or left ventricular end-diastolic pressure by 5 mm Hg. Animals with life-threatening hypotension were supported with boluses of intravenous normal saline and continuous infusion of phenylephrine and/or epinephrine to effect.

Blood Gas Analysis

During each experimental test condition, blood samples were simultaneously withdrawn from the coronary sinus, pulmonary artery, and right carotid artery. Samples were processed with a blood gas analyzer ($IRMA_{SL}$ Blood Analysis System; Diametrics Medical, Roseville, Minn) to measure hemoglobin content ([Hb] g/dL) and hemoglobin oxygen saturation (% O_2 Sat). Oxygen content ($[O_2]$) was calculated for each blood sample:

$$[O_2] = \frac{\%O_2\text{Sat} \times [\text{Hb}] \times O_2\text{capacity of Hb } (1.34 \text{ ml } O_2/\text{g})}{100} = [\text{mL } O_2/100 \text{ mL}]$$

Total myocardial oxygen consumption (MVO_2) was calculated as follows:

$$MVO_2 = \left([O_2]_a\right) - \left([O_2]_{cs}\right) \times MBF = [\text{mL/min/g}]$$

$[O_2]_a$ = arterial oxygen content, $[O_2]_{cs}$ = coronary sinus oxygen content, MBF = total myocardial blood flow in mL/min/100 g as determined by the microsphere method.

End-Organ Blood Flow Measurements

During each experimental test condition, a different color (isotope label) of 15-μm neutron-activated microspheres (1×10^6 microspheres in 0.4-mL suspension; Biopal, Worcester, Mass) was injected into the left atrium, followed by a 4-mL saline flush. The microsphere technique enabled the measurement of regional end-organ blood flow in vascular beds of interest, as previously described.[4,5] During microsphere injection, a reference blood-flow sample was drawn from the femoral artery at a rate of 4 mL/min for 60 seconds with a calibrated syringe pump (Harvard Apparatus, Holliston, Mass). The withdrawal sample acted as a reference to determine organ-specific flows in mL/min per gram of tissue.[4]

Necropsy and Microsphere Analysis

After completion of the experimental protocol, animals were euthanized with an increase in anesthetic depth and an intravenous bolus injection of supersaturated KCl. After euthanasia, the heart was harvested and weighed. The ventricles were dissected from the atria. The left ventricle was dissected from the right ventricle. The brain, lungs, kidneys, pancreas, liver, spleen, and adrenals were harvested and weighed.

Tissue and reference blood samples were sent to BioPAL, Inc (Worcester, Mass) for radioactive assay and automated calculation of blood flow in mL/min per gram for each sample during each experimental test condition. Tissue and blood samples were bombarded with neutrons to transiently activate each

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