Mechanical cavopulmonary assist maintains pulmonary and cerebral blood flow in a piglet model of a bidirectional cavopulmonary shunt with high pulmonary vascular resistance

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Objectives: We tested mechanical cavopulmonary blood flow assist by incorporating a novel miniature centrifugal pump into a 1½-ventricle type cavopulmonary connection in neonatal pigs.

Methods: Nine 3-week-old piglets (mean body weight, 10.2 kg) were used: mechanical cavopulmonary assist (n = 6) and controls (n = 3). A bidirectional cavopulmonary connection between the superior vena cava and the main pulmonary artery was created. The superior vena cava and pulmonary artery were also connected by cannulas with an interposed centrifugal pump. The cavoarterial mechanical cavopulmonary assist was performed at pump speeds of 1500, 2000, 2500, and 3000 rpm. Retrograde superior vena caval flow was limited by a band on the superior vena cava. A bidirectional cavopulmonary connection was created in the control animals, which then had a pure 1½-ventricle repair physiology without mechanical support. Hemodynamics, blood gas, and cerebral blood flow measured by ultrasound were analyzed. Catheter-based dilatation of the surgically created superior vena cava obstruction was tested.

Results: Incremental increases in pump speed augmented bidirectional cavopulmonary shunt blood flow ($P = .03$) and diminished superior vena caval pressure ($P = .03$), thereby improving cerebral perfusion pressure. Pump flow of 3000 rpm was equivalent to baseline superior vena caval flow (before caval flow, 392 ± 48 mL/min vs MCPA, 371 ± 120 mL/min; mean ± SD; P = not significant). The mechanical cavopulmonary assist group had higher Doppler velocities of the middle cerebral artery and higher transcerebral oxygen difference ($P < .05$) than controls. Balloon dilatation of the superior vena cava band was successful.

Conclusions: Mechanical cavopulmonary assist maintained bidirectional cavopulmonary shunt flow, thereby sustaining primary bilateral cavopulmonary shunt physiology in a neonatal pig model of high pulmonary vascular resistance. The mechanical cavopulmonary assist maintained cerebral blood flow and metabolism with an adequate transcerebral pressure gradient.

CHD

Overall outcomes of patients with hypoplastic left heart syndrome have improved over the past 2 decades with advances in surgical and perioperative therapeutic strategies.[1,2] However, all forms of current stage 1 surgical palliation have an inherently unstable ''in-parallel'' circulation. We have hypothesized that this is a cause of early and interim morbidity and mortality.[3-5] ''In-series'' physiology is established at the time of the stage II bidirectional cavopulmonary shunt (BCPS). Morbidity and mortality are diminished with stage II physiology. One might therefore also hypothesize that surgical outcomes might be improved by primary application of an in-series palliation with a BCPS in the neonatal or early infantile period. The first attempt of a primary BCPS in a 5-week-old infant with hypoplastic left heart syndrome, by Dr William I. Norwood in 1977, resulted in early death with progressive desaturation.[6] Subsequent series of early BCPS application in early infancy also showed high mortality mainly related to severe hypoxemia and pulmonary artery (PA) thrombosis.[7,8]

Immaturity of the peripheral pulmonary vasculature and high pulmonary vascular resistance (PVR) preclude successful application of a primary BCPS in neonates and small infants. Peripheral pulmonary vasculature develops in the months after birth so that PVR becomes low enough to create a cavopulmonary connection usually at 5 to 6 months of age. We hypothesized that establishment of a primary BCPS circulation in neonates might be feasible if the lungs are assisted by a mechanical pump, thereby overcoming the problems related to pulmonary vascular immaturity. This proof-of-concept study was designed to test a ''mechanical cavopulmonary assist'' (MCPA) system as a means to improve forward BCPS flow in the presence of high PVR, much as is seen in the human neonate. We examined

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Abbreviations and Acronyms

BCPS = bidirectional cavopulmonary shunt
CPB = cardiopulmonary bypass
CPP = cerebral perfusion pressure
JB = jugular bulb
MCA = middle cerebral artery
MCPA = mechanical cavopulmonary assist
NS = not significant
PA = pulmonary artery
PVR = pulmonary vascular resistance
RA = right atrium
SVC = superior vena cava

assisted pulmonary blood flow rates and cerebral blood flow. As a second component, we sought to demonstrate the possibility of a catheter-based completion to unassisted BCPS circulation.

MATERIALS AND METHODS

All experimental protocols were approved by the Animal Care Committee at the Hospital for Sick Children. Nine 3-week-old pigs (mean body weight, 10.2 kg) were divided into two groups: the MCPA group (n = 6) and the control group (n = 3). The animals were premedicated with ketamine (20 mg/kg), atropine (0.02 mg/kg), and acepromazine (2 mg/kg) before endotrachial intubation. Mechanical ventilation (Air-Shields Inc, Hatboro, Pa) was maintained with a tidal volume of 10 to 15 mL/kg and 50% oxygen and 2% isoflurane. Minor ventilator adjustments were made to maintain normal blood gas values (partial pressure of carbon dioxide, 35–45 mm Hg; pH, 7.35–7.44). Temperature was maintained at 37°C with a thermal heating pad placed under the animals. The left femoral artery and vein, the right internal jugular vein, and the jugular bulb (JB) were cannulated for pressure monitoring and blood sampling. The heart was exposed through a median sternotomy and the pericardium suspended. The superior vena cava (SVC) and main PA were completely mobilized. The bilateral azygos veins were ligated and divided to mobilize the SVC. Direct left atrial and distal PA pressures were monitored via 3F catheters. SVC and aortic blood flow was measured by an ultrasonic flow probe (Transonic Systems, Ithaca, NY) before surgery.

After systemic heparinization (400 U/kg), a temporary shunt was created between the SVC and right atrium (RA) with 12F right-angled venous cannulas. The SVC was transected at its junction to the RA, and the RA was oversewn. The main PA was partially clamped, and a transverse incision was made on the anterior wall of the main PA approximately 1 cm above the pulmonary ring. The SVC was anastomosed to the main PA in an end-to-side fashion with 5-0 or 6-0 polypropylene sutures (Ethicon, Inc, Somerville, NJ) (Figure 1, *A*). The SVC was anastomosed to the main PA, as opposed to the right PA, because in pigs the right PA is posterior, making the anastomosis in that location technically impractical. The final anatomy was that of a 1½-ventricle repair. The temporary SVC-to-RA shunt was eliminated after completion of the anastomosis. A 10F arterial cannula was inserted into the main PA distal to the BCPS anastomosis. The 5 mL–prime miniature centrifugal pump[9] was then connected via the cannulas placed in the SVC and the distal main PA (Figure 1, *B*), and MCPA was initiated and carried out to a maximum of 2 hours. Retrograde SVC flow caused by the pump and right ventricular pulsatility was limited by a band placed on the SVC between the cannula and anastomotic site. A tourniquet was initially used and later was replaced by a metal wire band once hemodynamic stability was achieved (Figure 1, *C*). Pump initiation without the SVC band led to hemodynamic instability related to circular blood flow. The band tightness was adjusted to the level that yielded systemic hemodynamic stability, indicating that circular blood flow was now not clinically significant. A BCPS was created in the control animals under a temporary shunt as described above. After the anastomosis, the cannulas placed in the SVC and RA were removed, making a pure 1½-ventricle repair physiology without mechanical support.

The hematocrit value was maintained at a baseline level with supplemental blood from a donor pig if necessary. In the MCPA group, blood gas and hemodynamics were analyzed every 10 minutes at pump speeds of 1500, 2000, 2500, and 3000 rpm. The blood gas was analyzed 10 minutes after BCPS creation in the control group. Centrifugal pump flow was continuously monitored by an ultrasonic flow probe (Transonic Systems, Ithaca, NY). Finally, an 8F Mullins dilatation catheter (NuMED, Inc, Hopkinton, NY) was inserted via the right internal jugular vein to the SVC across the band, and the surgically created obstruction was dilated when the pump flow was terminated and the SVC cannula was removed.

Evaluation of Cerebral Blood Flow and Metabolism

Cerebral perfusion pressure (CPP) was calculated using the difference between mean arterial and JB pressures. Transcerebral oxygen and lactate differences were calculated from arterial and JB partial oxygen pressures and lactate levels. Peak systolic, diastolic, and mean velocities and velocity time integral of the right middle cerebral artery (MCA) were measured by transcranial Doppler ultrasound (Vivid 7; GE Vingmed, Horten, Norway) using a 5- to 8-MHz probe to estimate cerebral blood flow volume[10] at baseline and 10 minutes after maximal MCPA of 3000 rpm in the MCPA group. Doppler ultrasound was performed at baseline and 10 minutes after BCPS creation in the control group.

Statistical Methods

Data are presented as means ± standard deviations. Comparisons between preoperative and postoperative values were performed by the paired *t* test. Comparisons of the values between the MCPA and control groups were performed by Wilcoxon rank–sum test. Changes in hemodynamic and metabolic parameters were determined by 1-way analysis of variance, followed by a post hoc test using the Bonferroni multiple comparisons test.

RESULTS

The Effect of Pump Speed on Hemodynamics and Metabolism

Incremental increases in the centrifugal pump speed augmented BCPS blood flow ($P = .03$) and diminished SVC pressure ($P = .03$), thereby improving CPP ($P = .03$) (Table 1). The final pump flow of 3000 rpm was equivalent to the SVC flow before the procedure (pre-SVC flow, 392 ± 48 mL/min, vs MCPA, 371 ± 120 mL/min; mean ± SD; P = not significant [NS]). All MCPA animals were hemodynamically stable, well ventilated, and oxygenated until being humanely killed 2 hours after pump initiation.

Effects of Mechanical Lung Assist on 1½-Ventricle Repair Physiology

Hemodynamics, metabolism, and cerebral blood flow patterns were compared between the MCPA group and the control animals. No statistical differences in baseline parameters were noted between the groups (Table 2). Comparisons in hemodynamics and metabolism between the MCPA group with a pump speed of 3000 rpm and the control group are