Coronary artery perfusion and myocardial performance after patent ductus arteriosus ligation

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Objectives: To study coronary artery (CA) perfusion and myocardial performance after patent ductus arteriosus (PDA) ligation. The postoperative course in premature infants undergoing surgical ligation of PDA is often complicated by cardiorespiratory instability secondary to impaired left ventricular performance.

Methods: Serial echocardiography was performed before and after (1, 8, and 24 hours) PDA ligation to assess systolic (left ventricular output [LVO]) and diastolic (isovolumic relaxation time, E and A wave peak velocity) myocardial performance, and CA diastolic flow (CA velocity time integral and flow). The ratio of CA flow to LVO was calculated as a surrogate of coronary flow.

Results: A total of 20 infants (gestational age at birth, 26.3 ± 0.7 weeks) requiring PDA ligation at a median of 28.5 days (range, 9–40) after birth and weight of 780 g (range, 570–2840) were studied. A postoperative increase in the CA flow/LVO ratio was demonstrated. An early decrease in E and A wave peak velocity ($P < .05$) and increase in isovolumic relaxation time ($P < .05$) were demonstrated at 1 hour, before any clinical deterioration. A low baseline CA velocity time integral was associated with a low E/A ratio ($r = 0.63$, $P = .01$) at 1 hour and lower systolic blood pressure at 8 hours ($r = 0.5$, $P = .05$). The postoperative need for inotropes (n = 8) was associated with a low baseline CA velocity time integral at 1 hour (r = 0.52, $P < .05$), low LVO at 1 and 8 hours ($P < .05$), and increased oxygen requirement at 24 hours ($P < .05$).

Conclusions: PDA ligation is followed by altered CA perfusion. Perioperative evaluation of the CA perfusion can help identify neonates at risk of impaired myocardial performance, systolic hypotension, and the need for inotropes. (J Thorac Cardiovasc Surg 2012;143:1271-8)

Hemodynamically significant patent ductus arteriosus (hsPDA) is seen in about 40% of extremely low-birthweight infants.[1] One of the hallmarks of hsPDA is low diastolic blood pressure. Because coronary artery (CA) perfusion is dependent on the aortic diastolic pressure, premature infants with hsPDA might be susceptible to compromised CA flow and chronic myocardial ischemia.[2] This hypothesis is supported by previous data demonstrating ST-segment depression on the electrocardiogram[3] and elevations in plasma troponin[4] that normalized after therapeutic intervention in premature infants with a hsPDA. We have previously reported impaired left ventricular (LV) systolic performance after PDA ligation.[5] In that report, we speculated that the nature of the deterioration reflects an inability of the immature myocardium to tolerate an increase in LV afterload. Chronic myocardial hypoperfusion secondary to low CA diastolic flow might increase the likelihood of impaired myocardial performance when subjected to the stressor of PDA ligation and altered loading conditions. The effect of hsPDA on coronary blood flow and its relationship to postoperative myocardial performance remains unknown.

METHODS

Study Design

A prospective observational study of premature infants undergoing PDA ligation at an outborn quaternary neonatal intensive care unit (NICU).

Study Objective

The primary objective was to characterize the trends in CA blood flow after PDA ligation. The secondary objective was to investigate the relationship between the CA blood flow and indexes of myocardial performance after PDA ligation. We hypothesized a priori that the CA diastolic flow relative to LV output would increase after PDA ligation and that low flow was associated with impaired LV performance.

Study Population

Premature infants born at less than 32 weeks of gestation who underwent PDA ligation at the Hospital for Sick Children (Toronto, ON, Canada) from July 2006 to March 2007 were eligible for enrollment. Newborns with congenital heart disease, except for a patent foramen ovale, were excluded from the present study. The study received ethics approval, a priori, from the institutional research ethics board, and the parents provided parental consent.

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CHD

Abbreviations and Acronyms

CA = coronary artery
hsPDA = hemodynamically significant patent ductus arteriosus
LV = left ventricular
LVO = left ventricular output
NICU = neonatal intensive care unit
PDA = patent ductus arteriosus
PWD = pulse wave Doppler
SMA = superior mesenteric artery
VTI = velocity time integral
VTI_{dias} = CA diastolic VTI

hsPDA Diagnosis

hsPDA was clinically suspected by certain characteristic features (eg, murmur, wide pulse pressure, bounding pulses, and/or hyperdynamic precordium) or early-onset systemic hypotension. Comprehensive 2-dimensional (2D) echocardiography was performed on all patients to quantify ductal characteristics before deciding on surgical ligation. The hsPDA was defined by a transductal diameter >1.5 mm with unrestrictive (<1 m/s) left to right transductal flow on pulse wave Doppler (PWD) and clinical features of pulmonary overcirculation and/or systemic hypoperfusion.[6]

Medical Treatment

The usual medical practice at referring institutions consisted of fluid restriction and nonsteroidal anti-inflammatory treatment. Two courses (6 doses of 0.2 mg/kg at 12-hour intervals) of indomethacin were administered, unless adverse effects or contraindications prevented it.

Referral Process

The study population included neonates referred from 2 neighboring inborn tertiary units and neonates from the study site, which is an outborn center. Neonates with hsPDA who either failed to respond to medical management or in which indomethacin was contraindicated were considered suitable for duct ligation. The decision to perform PDA ligation was made by a dedicated neonatologist-led PDA ligation team. All neonates undergoing PDA ligation underwent comprehensive echocardiography by a member of the team to define the size of the PDA and the magnitude of the transductal shunt according to the degree of pulmonary overcirculation and/or systemic hypoperfusion. Only neonates with a ductus of sufficient size and high-order magnitude of flow, as adjudicated by echocardiographic markers and the director of the PDA ligation team, were referred for PDA ligation. PDA ligation was not performed in the first 7 days of life in any neonate, because of concern regarding reperfusion intraventricular hemorrhage. All neonates were admitted at least 6 hours before the procedure.

Preoperative Stabilization

All patients had a hemoglobin level greater than 100 g/L, platelet count greater than 100,000 mm^3, and international normalized ratio of 1 to 1.6 before surgical intervention. Neonates on high-frequency mode were switched to conventional ventilation at least 6 hours before surgery and enteral feeds withheld for similar duration. All neonates were transported from the referring hospital to the NICU at the surgical site by a dedicated neonatal transport team.

Surgical Procedure

The procedure was performed in the operating room by a cardiovascular surgeon, and all neonates were anesthetized with fentanyl and pancuronium. Newborns were placed in right lateral position and a left mid-axillary incision was made. The left lung was retracted, and the ductus arteriosus was mobilized. The ductus was then either ligated with sutures or metal clips according to the surgeon's preference, and an intercostal drain was placed prophylactically. Fluid boluses (normal saline) were administered in the case of hypotension or excessive fluid losses.

Postoperative Care

All neonates were transferred back to the NICU, and a morphine or fentanyl infusion was started. This was subsequently tapered for 6 to 24 hours depending on an objective assessment of pain using the Premature Infant Pain Profile score.[7] A chest radiograph was performed on all infants within 1 hour after surgery to assess lung inflation and exclude air leaks. The usual practice was to monitor blood gases every 8 hour, depending on the postoperative course. During the study period, hypotension was defined using either of the following methods: (1) mean arterial pressure less than for the corrected gestational age or (2) systolic blood pressure less than the third percentile for corrected gestational age. The fluid boluses of normal saline (10 mL/kg) and/or cardiotropes were administered to achieve normal blood pressure. If cardiotropic treatment was required, an infusion of dobutamine and/or dopamine at 5 to 10 μg/kg/min was started and titrated to a maximum of 20 μg/kg/min, followed by the addition of epinephrine, if necessary. The selection of dobutamine or dopamine was at the discretion of the attending neonatologist who remained unaware of the results of the echocardiogram. Adjunctive steroid therapy with hydrocortisone was considered after failure of at least 2 cardiotropic agents. The usual postoperative recovery period in the NICU was at least 24 hours.

Data Collection

Baseline neonatal characteristics, details of the antenatal course, and delivery and resuscitation and preligation morbidities were recorded. Clinical and 2D echocardiographic characteristics of the hsPDA, dosage and duration of indomethacin treatment, and rationale for surgical intervention were reviewed. Physiologic indexes of cardiorespiratory stability (eg, heart rate, arterial pressure, oxygen saturation, and temperature) were extracted from the electronic patient chart preoperatively and at 1, 4, 8, 12, and 24 hours after the procedure. The mean arterial pressure was measured directly using a transducer connected to an indwelling catheter. The mean airway pressure and oxygenation index were monitored at these points, as surrogates of the degree of respiratory support and the efficacy of oxygenation. The oxygenation index was calculated according to the oxygenation index = [(mean airway pressure/PaO_2) × FiO_2 × 100%], where PaO_2 is the partial pressure of oxygen and FiO_2 is the fractional inspired oxygen. Ventilation index was calculated as the [respiratory rate × (PIP − PEEP) × $PaCO_2$]/1000, where PIP is the positive inspired pressure, PEEP is the positive end-expiratory pressure, and $PaCO_2$ is the partial pressure of arterial carbon dioxide. The need for fluid boluses or blood transfusion, and the amount of cardiotropic support was also recorded during the same period.

2D Echocardiography

2D echocardiography was performed preoperatively (within 2 hours) and at 1, 8, and 24 hours after surgical intervention. 2D echocardiography was performed by a single operator (A.S.) using the Vivid 7 advantage cardiovascular ultrasound system (GE Medical Systems, Milwaukee, Wisconsin) with a 7.5- to 10-MHz, high-frequency phased array transducer probe. All images were saved to an optical disk for off-line analysis. Standard M-mode, 2D, PWD, continuous wave Doppler, and color Doppler evaluations were performed.

CA Indexes

The left anterior descending (LAD) CA was interrogated, because it is the main vessel supplying blood to the left ventricle and because previous