7 Patent Ductus Arteriosus

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Patent ductus arteriosus (PDA) is a postnatal communication between the main PA and the descending thoracic aorta due to the persistence of the fetal ductus arteriosus. In term infants, the ductus arteriosus normally closes at around 72 hours of age; however, in preterm infants, ductal closure is often delayed. In infants between 24 to 28 weeks' gestational age, 80-90% of PDAs remain open at 4 days of age.

Pathophysiology and Clinical Presentation

A PDA results in shunting of blood between the PA and aorta. The degree and direction of shunting depends of the size of the PDA (diameter and length), the pressure difference between the aorta and PA, and the difference between SVR and PVR. Normally after birth, closure is aided due to increased PaO_2 from lung expansion as well as other vasoconstrictive mediators like PGF2-alpha, acetylcholine, and bradykinin. In contrast to term infants, premature infants may have delayed PDA closure. Prenatally, the PDA is normally large and unrestrictive, and the PVR is elevated resulting in shunting of blood from the PA to the aorta. After birth, PVR falls due to factors including lung expansion and pulmonary vasodilation due to increased PaO_2. As PVR falls, the shunt through the PDA changes direction from right-to-left to left-to-right.

Premature infants have incomplete muscularization of the pulmonary arterioles, leading to a very rapid drop in PVR after birth. As such, in premature infants, a large PDA with a large left-to-right shunt can present with pulmonary vascular congestion as early as the first week of life. In addition, diastolic BP may be low due to "runoff" through the PDA, potentially leading to impaired myocardial and coronary perfusion and a "steal phenomenon" from peripheral organs like the kidney and intestine. The presence of retrograde flow in the abdominal aorta is associated with an increased risk for necrotizing enterocolitis (NEC) and feeding difficulties in this population. Unlike premature infants, term newborns experience a delay in the drop in PVR in the presence of a large PDA, such that a substantial left-to-right shunt is only expected to develop in the first 6-12 weeks of life.

Clinical signs and symptoms are dependent on the magnitude of the left-to-right shunt. A PDA with large left-to-right shunt may result in respiratory symptoms due to pulmonary edema, failure to thrive, with moderate-to-severe enlargement of the left-heart chambers (LA and LV) due to increased pulmonary venous return. Physical findings can range from a loud continuous murmur at the left infraclavicular area to a very soft murmur (a *very* large PDA will result in equal aortic and PA pressures with low-velocity flow across the PDA, which may result in a very soft murmur). The precordium is active and a gallop may be audible. The widened pulse pressure results in bounding pulses, with peripheral pulses being especially easy to palpate (e.g., palmar or digital pulses). A PDA with moderate left-to-right shunt may have less prominent pulmonary symptoms, and usually without failure to thrive; all the typical physical findings would be less prominent, but a continuous murmur and moderate left-heart enlargement are the rule. A PDA with small-to-moderate left-to-right shunt may be

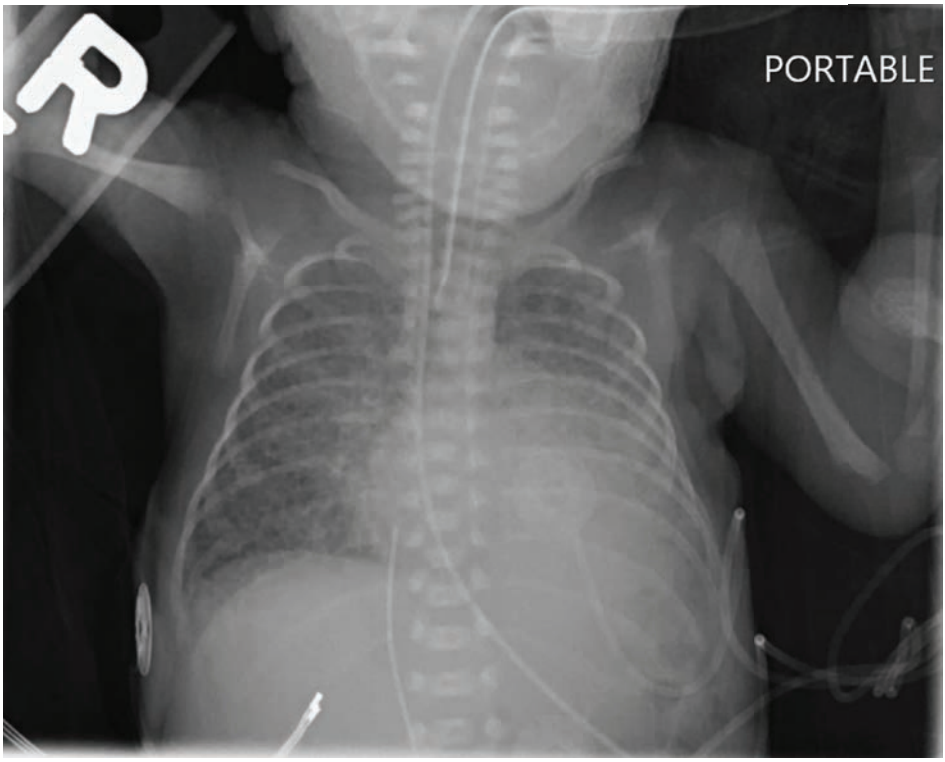

Figure 7-1. CXR of a patient with a large PDA demonstrating pulmonary edema.

asymptomatic, exhibit a continuous machinery murmur with normal precordial activity and normal pulses, and the left heart chambers may be mildly enlarged or normal. Finally, a tiny PDA with insignificant left-to-right shunt may present with either a soft continuous murmur, a soft long systolic-only murmur, or no murmur at all; the latter scenario of a tiny PDA without a murmur is referred to as a "silent PDA". In all cases of a tiny PDA with insignificant left-to-right shunt, patients are asymptomatic and the left heart structures must be of normal size; in fact, left heart enlargement in the setting of a tiny PDA should prompt the search for other causes of left heart enlargement.

PDA in the setting of other cardiac anomalies (e.g., coarctation, ductal-dependent lesions for systemic or pulmonary perfusion) will be considered elsewhere in this text.

Diagnosis

- **CXR (Figure 7-1).** May be normal with a small PDA. However, if moderate-to-large PDA, CXR will show cardiomegaly, increased pulmonary vascular markings, LA enlargement, and in severe cases, frank pulmonary edema.
- **ECG.** Most often normal. It may show LVH and combined ventricular hypertrophy in moderate-to-large PDA.
- **Echocardiogram (Figure 7-2).** The mainstay of diagnosis. In addition to assessing

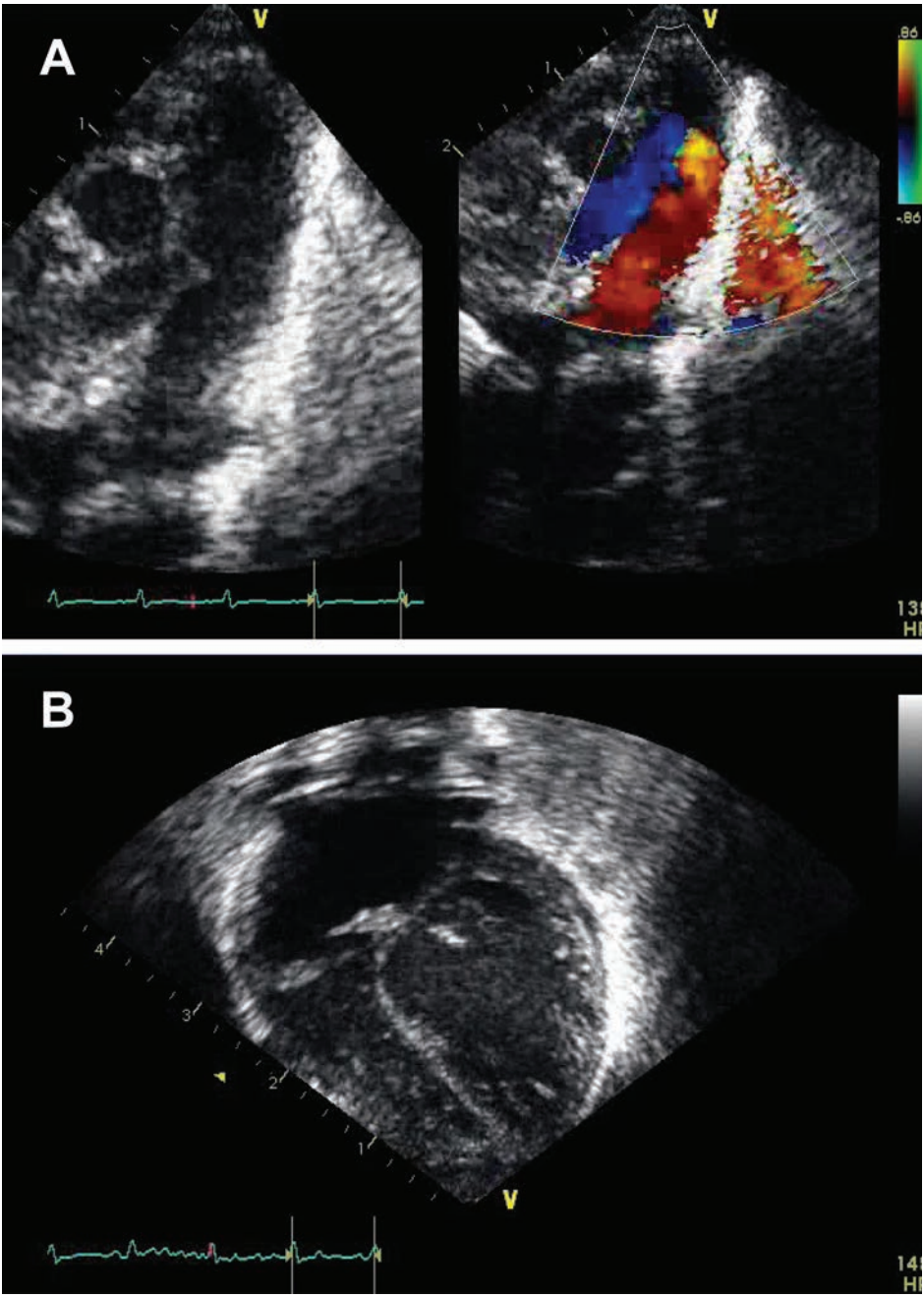

Figure 7-2. Echocardiographic images of a patient with a large PDA. Panel A shows a short-axis view demonstrating a large PDA with left-to-right shunting. Panel B shows left heart enlargement.

the presence and size of the PDA, it is important to ascertain shunt direction, morphology of the duct, arch sidedness, any concerns for aortic coarctation (which could be unmasked after PDA ligation), and origin of the coronary arteries (pulmonary origin of a coronary artery can lead to myocardial ischemia upon PDA ligation if unrecognized). Left heart enlargement is present if there is significant left-to-right shunting.

Medical Management

Medical, transcatheter, or surgical treatment is usually reserved for symptomatic PDAs in premature neonates; in this population treatment reduces the short-term need for mechanical ventilation but no long-term benefits have been established.

In term infants and older children, PDA closure is recommended in symptomatic patients or in asymptomatic patients with left heart enlargement. PDA closure is not required in those with tiny PDAs without left heart enlargement.

Conservative Management in the Premature Infant

- Modest fluid restriction to 120-130 mL/kg/day
- Lasix 0.5-1 mg/kg IV or 1-2 mg/kg PO every 8 to 12 hours
- Avoidance of further decrease in PVR
- Shunt limiting strategies: increased PEEP or permissive hypercapnia
- Use of vasoactive medications

Treatment with Ibuprofen or Indomethacin in the Premature Infant

If conservative management fails, treatment with cyclooxygenase inhibitors is the treatment of choice for pharmacologic closure of a symptomatic PDA. If the PDA closes or is significantly reduced in size >48 hours after the first course, no further doses are required. However, if the PDA fails to close, administration of a second course of treatment may be attempted. Efforts should be made to obtain an interval echocardiogram prior to initiating a second course of treatment.

Ibuprofen treatment:

- First dose: 10 mg/kg
- Second dose: 5 mg/kg (24 hours after first dose)
- Third dose: 5 mg/kg (24 hours after first dose)

If ibuprofen is not available, indomethacin may be used to treat a symptomatic PDA. Recommended dosage depends on the age of the infant at the time of treatment (Table 7-1). All dosages should be based on birth weight if the infant remains below birth weight early in life, or on current weight.

Contraindications to ibuprofen/indomethacin treatment include oliguria (urine output <0.6 mL/kg/hr), renal dysfunction (serum creatinine >1.6 mg/dL), NEC, coagulopathy, thrombocytopenia (platelet count <60,000 /uL), active bleeding, infection, or clinical conditions requiring ductal-dependent blood flow.

If the PDA remains symptomatic after the second course or if unable to provide a second course due to the contraindications noted above, surgical or transcatheter treatment may be considered.

Table 7-1. Dosing for indomethacin treatment of a PDA.

Age at first dose	First dose	Second dose	Third dose
< 48 Hours	0.2 mg/kg	0.1 mg/kg	0.1 mg/kg
2-7 Days	0.2 mg/kg	0.2 mg/kg	0.2 mg/kg
7 Days or older	0.2 mg/kg	0.25 mg/kg	0.25 mg/kg

Indications for Intervention in the Premature Infant

Surgical PDA ligation or transcatheter device closure may be required for those infants that fail medical management, have clinical instability, fail to wean off mechanical ventilation, or fail to have optimal growth in the setting of a PDA.

Anesthetic Considerations

For infants and children undergoing percutaneous ductal occlusion in the cardiac cath lab, general anesthesia is commonly achieved by a balanced technique utilizing low-dose narcotic, benzodiazepine, and anesthetic gas. This technique requires the establishment of an artificial airway, usually with an endotracheal tube. It is common practice for infants and children undergoing ductal occlusion in the cardiac cath lab to be extubated at the end of the procedure; the anesthetic is geared toward that end.

For those infants and children requiring surgical closure, age and weight determine where such closure takes place. Infants <1.5 kg are typically operated at the bedside in the NICU. For these patients, a standardized checklist is completed by the NICU prior to surgical closure (Table 7-2). Patients are commonly intubated prior to anesthesia team arrival and already have IV access in place. Prior to positioning, the patient is anesthetized and paralyzed to prevent extubation. Anesthesia is administered totally by IV means, as no anesthetic gases are available at the bedside. Prior to giving any narcotic, glycopyrrolate 10-20 mcg/kg IV is administered to prevent bradycardia. Fentanyl is most commonly used and the total dose for a case is often 10-20 mcg/kg. Muscle relaxation is achieved with rocuronium or vecuronium. Fresh or low-potassium blood should always be available at the bedside during surgery. Caution should be taken in these patients, as rapid administration of blood can cause hyperkalemia, hypocalcemia, and myocardial dysfunction due to citrate toxicity.

For patients undergoing surgical closure in the operating room, it is common to insert an arterial line for monitoring BP and evaluating blood gases, and a balanced anesthetic technique (combined IV and inhalational anesthesia) is used. It is uncommon to extubate patients immediately after surgery due to the higher doses of narcotics needed for a thoracotomy.

The ventilatory strategy should be to maintain normocarbia to slight hypercarbia, and minimize supplemental oxygen unless it is required for normal oxygen saturation. This strategy will help maintain PVR, reducing left-to-right shunting and diastolic runoff, which can lead to myocardial ischemia. Efforts to reduce diastolic runoff should include a conservative ventilation strategy, minimize anesthetic concentration, and maintain

SVR. The administration of phenylephrine 0.5-1 mcg/kg IV commonly restores SVR, raises the diastolic BP, and corrects coronary insufficiency if it occurs.

Catheter-Based Intervention

Transcatheter device closure of a PDA is an accepted method of closure in term infants and older children. Recently, availability of novel devices that can be delivered though smaller catheters has rendered percutaneous PDA device closure possible even in extremely low-birthweight infants weighing <1 kg. Device closure in infants <2.5 kg should be performed entirely through a venous (femoral or jugular) approach, with avoidance of placement of a femoral arterial catheter to avoid arterial injury. Upon reaching the ductus from a transvenous approach through the right heart, angiography is performed within the PDA to measure its length and diameter. A variety of devices with different shapes and sizes are available to treat a PDA, and most are delivered with catheters or sheaths <5 Fr in small children. Imaging the aorta during device placement to prevent aortic protrusion can be performed with angiography or echocardiography. It is also possible to perform PDA device closure in small infants entirely using echocardiography at the bedside in the NICU. For larger children >5 kg, arterial injury is much less likely, hence devices can be delivered to the PDA using a transvenous or transarterial (usually femoral) approach. PDA device closure in older children is an outpatient procedure.

Complications

Complications of device closure of PDA in small children less than 2 to 3 kg include device protrusion into the aorta or into the main PA near the left PA ostium. Aortic protrusion is more serious, as it can result in device-induced coarctation. Careful echo imaging of the region of the aortic isthmus should exclude patients with preexisting hypoplasia of the aortic isthmus or a true mild coarctation prior to the procedure, and intraprocedural echo can be used to aid with device placement to avoid this complication. In older children, significant aortic or PA device protrusion is less likely. Device embolization in larger children is typically managed by transcatheter device retrieval followed by placement of a more appropriately sized device. However, in very small children (less than 1.5 to 2 kg) device retrieval can be difficult and consideration should be given to surgical retrieval followed by surgical PDA ligation at the same time.

Surgical Intervention

Surgical ligation or division remains a common method used for PDA closure in premature infants. The standard approach involves a left posterolateral serratus-sparing thoracotomy via the fourth intercostal space using a short incision. The superior and inferior aspects of the ductus are dissected with care not to injure the PDA, which is very friable, especially in premature infants. All structures including the vagus nerve, left recurrent laryngeal nerve, and aortic arch should be readily identified. For small babies, a medium or medium-large titanium clip is used to occlude the PDA. The clip should be tested outside of the body prior to use since it is not possible to reposition or remove the clip once deployed. It is important to ascertain that the clip is all the way

Surgical PDA closures at TCH (1996-2016)
Median number of procedures per year: 11 (2-31)
Median age at surgery: 35 days (1 day - 13 years)
Median weight at surgery: 2.5 kg (0.5-28 kg)

around the ductus but not including the recurrent laryngeal nerve (that crosses behind the PDA) or the left mainstem bronchus (that also lies behind). A chest tube is placed at the discretion of the surgeon, based upon the friability of the lungs and potential for air leak.

In older patients, the PDA may be circumferentially dissected and either controlled with a silk ligature or divided between polypropelene ligatures. A chest tube is routinely placed in these patients.

It is possible to develop an aortic coarctation after PDA ligation. Patients that have a relatively small isthmus or concerns for developing an aortic coarctation should be carefully evaluated for the need to perform an aortic coarctation repair at the time of surgery. As such, these patients should undergo surgery in the OR rather than the NICU.

Complications

Some of the most critical technical complications that ought to be prevented are:

- Left vocal cord dysfunction from injury of the recurrent laryngeal nerve

Table 7-2. NICU checklist for patients undergoing PDA ligation in the NICU.

NICU Checklist for Bedside PDA Ligations
Day before surgery
- Preoperative orders placed in EPIC by CV Anesthesia NP - Hematocrit (Hct) checked with goal Hct >30 %. If Hct <30%, transfuse and recheck. NICU team to order blood transfusion and to recheck Hct level. - Type and screen sent, blood ordered for: 2 quarter units <7 day old blood to be delivered in bag on day of surgery - NPO orders written - CV surgeon consultation and consents signed (CHS team to arrange)
12 hours before/day of surgery
- Neobar removed by NICU respiratory therapy - Dedicated IV placed by NICU team or dedicated IV Port available by the morning of surgery - 2 suction setups available and working (one for surgeon, one for Anesthesia) - Blood warmer at bedside - Baby placed on K-pad (warming pad) - 2 pulse oximeters – one on right hand, second on either leg - 2 BP sources – one BP cuff on right arm, second cuff on either leg (leg cuff not needed if patient has UAC or lower extremity arterial line) - Internal temperature cable to bedside - Blood ordered from blood bank and brought to bedside in cooler 15 minutes prior to posted start time - Family at bedside 30 minutes prior to posted start time (for Anesthesia consent) - Area cleared of non-essential equipment, visitors and non-essential personnel. Toys/extra blankets off bed and "Surgery in Progress: DO NOT enter" sign posted
For any questions, please page the CHS Clinician on call.

- Chylothorax from disruption of lymphatic vessels and lymph nodes
- Aortic coarctation
- Ligation of incorrect structures

Postoperative Management of the Premature Infant

Nearly 50% of preterm infants may develop postligation cardiac syndrome (PLCS) after surgical PDA ligation. This syndrome is characterized by systemic hypotension and oxygenation failure often requiring vasoactive medications and prolonged mechanical ventilation. Low cardiac output is due to an acute increase in SVR and decreased preload. Symptoms usually begin 8 to 12 hours following intervention and tend to resolve 24 hours afterward.

Milrinone has been used to lower the afterload, with some benefit in infants with PLCS. Some other infants may require the use of other inotropes such as dopamine to improve their BP.