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# Perioperative anesthetic management of premature neonates weighing less than 1500 grams undergoing transcatheter PDA (TC-PDA) closure: An institutional anesthetic experience☆

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ABSTRACT

*Objectives:* The aim of our study is to describe the various anesthetic techniques and intraoperative management used during transcatheter closure of hemodynamically significant PDAs in VLBW premature infants weighing less than 1.5 kg and their potential impact on postoperative outcomes using a retrospective chart review.
*Design:* A retrospective electronic medical chart review was performed in infants who underwent Transcatheter Patent Ductus Arteriosus (TC-PDA) closure at an academic institution between January 1, 2008 and October 4th 2019. Only premature patients with isolated PDA weighing less than 1500 g at the time of the procedure were included in the study.
*Setting:* Single Institutional Hospital.
*Participants:* Premature patients with isolated PDA weighing less than 1500 g at the time of the procedure.
*Interventions:* None.
*Measurements and main results:* Interprocedurally, there was no evidence of device embolization or clinically significant vascular obstruction on follow-up echocardiography, and inotropic or vasoactive infusions were not required. All patients survived and were discharged from the hospital after a mean of 86.4 ± 48.49 days (median 74, range 40–180) following initial admission to the NICU. At 7 post-operative days, freedom from ventilatory support reached 70% in all patients. Incidences of device embolization or clinically significant vascular obstruction were not noted on follow-up echocardiography.
*Conclusions:* Though our preliminary findings show promising outcomes following TC-PDA closure relative to traditional surgical approaches, further investigations with higher patient volume are needed to validate these promising observations.

## 1. Introduction

Patent Ductus Arteriosus (PDA) account for 5–10% of congenital heart disease, occurring in 33% of infants with very low birth weight (VLBW) and up to 65% of infants with extremely low birth weight (ELBW) [1–3]. Recently, advancements in percutaneous PDA occlusion devices and transcatheter therapy, once limited to children and adults, have made successful closure feasible in premature neonates that would have traditionally limited patient treatment to medical treatment therapy or surgical ligation. Though first

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described in 1967, transcutaneous PDA (TC-PDA) closure in very preterm infants has historically been excluded from the use of occlusion devices due to catheter and introducer size constraints despite having the same sized PDAs as their older counterparts [4–6]. While limited devices exist to accommodate this novel patient population, successful PDA closure has been reported in several patients <1 kg [4,7–9]. Despite the perioperative and anesthetic challenges inherent to caring for the premature neonate, the potential post-procedural benefits of a less invasive percutaneous approach may offer more favorable outcomes when compared to surgical ligation [10]. We have found that implementing a multidisciplinary program may offer the additional benefits of providing optimal care to these delicate patients by incorporating safeguards to mitigate anticipated difficulties encountered during the perioperative period. Our institutional Preemie Duct Occlusion Program (PDOP) integrates a multidisciplinary team approach to streamline the care of premature babies with PDA requiring interventional closure. This article describes our perioperative anesthetic experience and outcomes after implementing an integrated interdisciplinary TC-PDA closure program for preterm infants weighing less than 1.5 kg at a single institution.

## 2. Methods

A retrospective electronic medical chart review was performed in infants who underwent TC-PDA closure at a single academic institution between January 1, 2008, and October 4thst, 2019. Only premature patients with isolated PDA weighing less than 1500 g during the procedure were included in the study. Patient characteristics and data were determined based on previously performed diagnostics, provider notes, laboratory values, and procedurally related anesthetic and interventional documentation throughout hospital admission. Patients weighing greater than 1.5 kg at the time of intervention were excluded from the study. Approval for this study was obtained from the Institutional Review Board. Patient demographics including gestational age, weight, and preoperative laboratory investigations were collected for comparison. Intraoperative anesthetic data included intraoperative vasoactive support required throughout the case as well as medications used for anesthetic induction and maintenance. Ventilation strategy, numerical ventilation parameters (range), and incidence of significant cardiac events requiring intervention were collected. Post-operative data included procedurally-related bleeding complications, central nervous system (CNS) events (both hemorrhagic and ischemic), number of post-operative days to extubation, overall mortality, days to hospital discharge, and survival to hospital discharge were recorded. Normally distributed, continuous variables were expressed as a mean±standard deviation. Categorical variables were expressed as a number and percentage of the total.

## 3. Results

Electronic medical records were reviewed for thirty-five premature TC-PDA closures performed during a 15-month time period. Of these 35 patients, 10 infants weighed less than 1500 g at the time of device placement, had a mean gestational age of 25.65 ± 2.13 weeks, and were all American Society of Anesthesiologists' (ASA) Physical Status Classification of 4. Of these patients, two extremely low birth weight patients (<1 kg) were included in the study and weighed between 835 and 910 g. The remaining eight patients included very low birth weight infants (less than 1500 g). The range of weight for all patients was between 835 g and 1400 g (Table 1). Gender was evenly distributed between all patients. The mean weight of all patients was 1142 ± 178.73 g with an average patient age was 36.1 ± 6.15 days old. All but one patient underwent successful TC-PDA closure. The single unsuccessful case was converted to surgical ligation at the time of initial intervention due to vascular obstruction of the non-deployed device. MVP devices (MVP 3Q or MVP 5Q) were used in all patients that underwent successful TC-PDA closure. Femoral venous access was obtained in all cases and no vascular complications were observed perioperatively (Table 2).

Intraoperatively, half of all patients received the volatile inhalational agent Sevoflurane for anesthetic maintenance. All but one patient received intravenous fentanyl for anesthetic induction, while one patient received ketamine. Neuromuscular blockage was accomplished using cisatricurium in all patients (Table 3). The mean $FiO_2$ requirement for all patients was 49.71 ± 11.46%. Maximal

**Table 1**
Patient DemographicsMean±Sd; Median; (Range)N(%).

| TABLE 1 PATIENT DEMOGRAPHICS | Mean +/- SD; Median; (Range) | N(%) |
|---|---|---|
| **Age** | | |
| Gestational Age at Birth (weeks) | 25.65+/-2.13; 26; (23-28.43) | 10(100) |
| Gestational Age at Time of Procedure (weeks) | 30.81+/-2.65; 32.31; (27-34.29) | 10(100) |
| **Weight** | | |
| Weight at birth (grams) | 730+/-109.34; 690; (620-930) | 10(100) |
| Weight at the time of procedure (grams) | 1142+/-178.73;1197.5;(835-1400) | 10(100) |
| **Gender** | | |
| Male | | 5(50) |
| **Additional Cardiac Diagnosis** | | |
| Yes | | 9(90) |
| No | | 1(10) |
| **Cardiac Diagnosis** | | |
| Valvulopathy | | 2(20) |
| PFO/ASD | | 9(90) |
| VSD | | 1(10) |

**Table 2**
Procedural Characteristics Mean±Sd; Median; (Range)N(%).

| TABLE 2 PROCEDURAL CHARACTERISTICS | Mean +/- SD; Median; (Range) | N(%) |
|---|---|---|
| **Device** | | |
| MVP-3Q | | 6(60) |
| MVP-5Q | | 3(30) |
| **Intraoperative Laboratory Studies** | | |
| Initial Hemoglobin (g/dL) | 10.84+/- 1.59; 11.15; (8.4-13.8) | |
| **Vascular Access** | | |
| Right Femoral Vein | | 8(80) |
| Left Femoral Vein | | 2(20) |
| 4Fr Femoral Venous Sheath | | 10(100) |
| Total Femoral Venous Sheath Time (Minutes) | 48.1+/- 19.46; 46.5; (27-84) | 10(100) |
| **Procedural Complications** | | |
| Conversion to surgical ligation intraprocedure | | 1(10) |
| Device Embolization | | 0(0) |
| Vascular Injury | | 0(0) |
| Vascular Obstruction Post Device Deployment | | 0(0) |
| Residual Shunt Present Post Device Deployment | | 0(0) |

peak inspiratory pressures and positive end expiratory pressure of 27.5 ± 5.45 cmH2O and 6.25 ± 1.39 cm/H2O, respectively (Table 4). The lowest temperature noted intraoperatively averaged 36.3 ± 0.45° Celsius with two patients experiencing intraoperative hypothermia, defined as temperature less than 36° Celsius, that resolved prior to post-operative admission to the NICU. Unexpected intraoperative code events, accidental extubation requiring reintubation, intraoperative requirement for inotropic or vasoactive infusions, hemodynamically significant arrhythmias, vascular trauma, or device embolization were not noted in any patient (Table 4). All patients were ventilated in the catheterization suit using standard Drager Apollo ventilators during interventional procedures. Overall, the mean OR time was 131.1 min while the mean procedural time was 70.3 min. Total OR time reflects total anesthesia time during patient encounters. Total Procedural time reflects the time from initial sheath insertion to the time of removal of sheaths following device deployment.

Post-operatively, one patient developed a pulmonary hypertensive crisis on post-operative day one. Two patients developed postoperative infections (E.Coli pneumonia and urinary tract infection; CONS Bacteremia). One patient developed chylous effusions after unsuccessful device placement requiring subsequent surgical ligation. No mortality events were noted in any patients within the study and all patients were discharged from the hospital after a mean of 86.4 ± 48.49 days (median 74, range 40–180) following initial admission to NICU. At 7 post-operative days (POD), freedom from ventilatory support reached 70% in all patients. Technical Success was achieved in 9 (90%) patients, all of which were closed with the MVP device. No patient experienced device migration after deployment (Table 5).

## 4. Discussion

Though PDA percutaneous closure was first described in 1967, very preterm infants (<32 weeks old at birth) have remained excluded from advances in occlusion devices due to catheter and introducer size constraints despite having the same sized PDAs as their older counterparts [4–6]. Though there are limited devices manufactured to accommodate this novel patient population, successful PDA closure has been reported in numerous publications [4,7–9]. Newer devices including the Amplatzer Ductal Occluder II (ADO-II AS, St. Jude Medical, Minneapolis, MN) have recently shown promise to address size concerns. Aside from size limitations, placement of occlusion devices within preterm neonates remains limited by the ability to establish vascular access, risk of device embolization, vessel obstruction by device components, exposure to continuous fluoroscopy, and contrast administration. However, reports of successful PDA closure with the amplatzer vascular plug II (AVPII) demonstrate a favorable 88% success rate of percutaneous PDA closure in 52 very preterm infants (range 1.2–3.9 kg), noting post-procedural improvements in respiratory status including less exposure to mechanical ventilation [4]. Despite these advancements in transcatheter PDA closure, there exist a paucity of literature describing the safe anesthetic management of this vulnerable patient population.

PDAs present a number of significant clinical issues related to mortality and significant morbidities including pulmonary hemorrhage, respiratory distress syndrome (RDS), prolonged mechanical support, BPD, Retinopathy of prematurity (ROP), renal dysfunction, intraventricular hemorrhage (IVH), hypotension, heart failure, periventricular leukomalacia (PVL), necrotizing enterocolitis (NEC) as well as cerebral palsy at later stages in life [2,3]. Administration of antenatal magnesium sulfate, postnatal infections, inappropriate fluid therapy during the first week of life, phototherapy, presence of severe respiratory distress, elevated serum osmolality, intrauterine growth retardation, thrombocytopenia, and genetic predisposition may increase the risk of PDA in neonates [11–16].Clinical features consistent with hemodynamically significant PDAs including the classic cardiac murmur in the setting of a hyperdynamic precordium, respiratory deterioration necessitating intervention, widening of pulse pressures, hypotension, and metabolic acidosis all complicate the anesthetic management of these patients [17].

The challenges inherent to preterm neonates obviates the need for providers to determine what constitutes hemodynamically compromised patients based on PDA classification in order to guide successful perioperative anesthetic care. Anesthetically the comorbidities associated with prematurity including prolonged ventilatory support, bronchopulmonary dysplasia, pulmonary

**Table 3**
Individual Patient Characteristics And Anesthetic Characteristics.

| TABLE 3 INDIVIDUAL PATIENT CHARACTERISTICS AND ANESTHETIC CHARACTERISTICS | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient | Gestational Age at Birth (Answer: Weeks) | Day of Life (Answer: Days) | Post-Conceptual Age at the time of procedure (Answer: Weeks) | Gender | Weight at Birth (grams) | Weight at Catheterization (Grams) | Height (cm) | BMI | Intraoperative Volatile Utilized | Primary Anesthetic Used for Induction, Fentanyl | Total Induction Dose of Fentanyl (mcg/kg) | Total Intraoperative Dose of Fentanyl (mcg/kg) | Primary Anesthetic Used for Induction, Midazolam | Total Induction Dose of Midazolam (mg/kg) | Total Intraoperative Dose of Midazolam | Primary Anesthetic Used for Induction, Ketamine | Total Induction Dose of Ketamine (mg/kg) | Total Intraoperative Dose of Ketamine (mg/kg) | Primary Paralytic Used for Induction, Cisatracurium (mg/kg) | Total Induction Dose of Cisatracurium (mg/kg) | Total Intraoperative Dose of Cisatracurium (mg/kg) | Nitric Oxide Administered Intraoperatively | Transfusion Required Intraoperatively | Total RBCS Transfused Intraoperatively (cc/kg) | Inotropes Required Intraoperatively | Intraoperative Cardiac Arrest | Uncuffed Endotracheal Tube Size | Total OR Time (Minutes) |
| 1 | 24 | 35 | 29 | Female | 710 | 1200 | 32 | 11.72 | Yes | Yes | 1.67 | 4.17 | No | | | No | | | Yes | 0.25 | 0.75 | No | No | | No | No | 3 | 145 |
| 2 | 26 | 44 | 32.28 | Female | 930 | 1400 | 38.7 | 9.88 | Yes | Yes | 3.38 | 7.55 | Yes | 0.14 | 0.14 | No | | | Yes | 0.45 | 0.81 | No | No | | No | No | 3 | 135 |
| 3 | 27.71 | 35 | 32.71 | Male | 690 | 1260 | 37 | 9.2 | Yes | Yes | 7.94 | 15.87 | No | | | No | | | Yes | 0.4 | 0.6 | No | No | | No | No | 3 | 110 |
| 4 | 28.43 | 40 | 34.14 | Female | 920 | 1320 | 40.5 | 8.05 | Yes | Yes | 7.58 | 10.3 | No | | | No | | | Yes | 0.38 | 1.52 | No | Yes | 22.73 | No | No | 3 | 264 |
| 5 | 27.9 | 29 | 32.04 | Male | 690 | 1200 | 38 | 8.31 | No | Yes | 2.08 | 10.42 | No | | | No | | | Yes | 0.33 | 0.67 | No | No | | No | No | 3 | 120 |
| 6 | 26 | 44 | 32.29 | Male | 650 | 1195 | 34 | 10.34 | Yes | Yes | 1.67 | 9.46 | No | | 0.17 | No | | | Yes | 0.33 | 0.67 | No | No | | No | No | 3 | 137 |
| 7 | 23 | 27 | 26.86 | Male | 670 | 910 | 33 | 8.36 | No | No | | | No | | | Yes | 1.1 | 2.2 | Yes | 1.1 | 1.01 | No | No | | No | No | 2.5 | 56 |
| 8 | 23 | 30 | 27.29 | Male | 760 | 1030 | 35.8 | 8.04 | No | Yes | 1.94 | 4.85 | No | | | No | | | Yes | 0.97 | 2 | No | No | | No | No | 2.5 | 120 |
| 9 | 27 | 37 | 32.29 | Female | 660 | 1070 | 35.4 | 8.54 | No | Yes | 3.74 | 23.36 | No | | | No | | | Yes | 0.37 | 1.21 | No | No | | No | No | 3 | 138 |
| 10 | 23.43 | 30 | 27.72 | Female | 620 | 835 | 33 | 7.67 | No | Yes | 1.2 | 2.4 | No | | | No | | | Yes | 0.19 | 0.19 | No | No | | No | No | 2.5 | 86 |

**Table 4**
Intraoperative Characteristics.

| TABLE 4 INTRAOPERATIVE CHARACTERISTICS | Mean +/- SD; Median; (Range) | N(%) |
|---|---|---|
| **Time** | | |
| Total OR Time (minutes) | 131.1+/-54.08; 127.5; (56-208) | 10(100) |
| Total Procedural Time (minutes) | 70.3+/- 48.80; 64.5; (29-203) | 10(100) |
| **Ventilator** | | |
| Maximum Peak Inspiratory Pressure (cmH2o) | 27.5+/- 5.45; 25; (22-37) | 8(80) |
| Maximum Positive End Expiratory Pressure (cmH2O) | 6.25+/- 1.39; 6; (4-8) | 8(80) |
| Maximum Respiratory Rate (Breaths Per Minute) | 42.5+/-8.15; 40.5; (34-60) | 10(100) |
| Mean FiO2 (%) | 49.71+/- 11.46; 44.93; (37-69.22) | 10(100) |
| **Vitals** | | |
| Minimum Intraoperative Temp. (Degrees Celcius) | 36.3+/- 0.45; 36.45; (35.3-36.7) | 10(100) |
| Maximum Intraoperative Temp. (Degrees Celcius) | 37.38+/-0.41; 37.3; (36.8-38.1) | 10(100) |
| **Drugs** | | |
| Total Intraoperative Fentanyl (mcg/kg) | 12.04+/- 9.44; 9.46; (2.4-30.3) | 9(90) |
| Total Intraoperative Cisatricurium (mg/kg) | 0.94+/- 0.52; 0.78; (0.19-2) | 10(100) |

**Table 5**
Post-Operative Characteristics.

| TABLE 5 POST-OPERATIVE CHARACTERISTICS | Mean +/- SD; Median; (Range) | N(%) |
|---|---|---|
| **Extubation** | | |
| Number of Days to Extubation (Days) | 10.1+/-12.31; 6.5; (1-43) | 10(100) |
| **Post-Procedural Complications** | | |
| Persistent Left Pulmonary Artery Obstruction | | 0(0) |
| Persistent Aortic Obstruction | | 1(10) |
| Post-Operative Infection | | 1(1) |
| Post-Operative Pulmonary HTN | | 1(10) |
| Ionotropic Support 24 Hours Post-Procedure | | 1(10) |
| Blood Transfusion 48 Hours Post-Procedure | | 0(0) |
| Chylothorax Post-Procedure | | 1(10) |
| Interventricular Hemorrhage Post-Procedure | | 1(10) |

hypertension, and necrotizing enterocolitis are likely to be complicated in the presence of a PDA [18]. With the risk of adverse events (AEs) being inversely related to patient weight at the time of catheterization [19], an expected increase in adverse events is not unexpected in premature neonates weighing less than 4 kg relative to heavier patients receiving percutaneous PDA closure. Despite reports of technical success as high as 88%, limitations to successful percutaneous PDA closure include aortic isthmus narrowing or left pulmonary artery obstruction despite excellent device positioning with complete device closure [20].

As previous data has shown that mechanical ventilation increases the risk of chronic lung disease in very preterm infants [21], improvements within respiratory status following percutaneous closure offer potential benefits over the potential morbidities incurred with invasive surgical intervention. Unmeasured effects including improvements in nutrition and positive linear growth following successful percutaneous closure may also contribute to overall post-procedural clinical improvement [20].

The safe application of TC-PDA closure devices in smaller patients including preterm infants [9,22–24] has resulted in a growing trend in the number of these patients referred for closure by neonatologists [25]. Nearly 50% of premature infants are estimated to have a PDA at birth, resulting in significant comorbidities such as congestive heart failure, renal failure, and necrotizing enterocolitis in the setting of persistent diastolic hypotension [26]. The presence of respiratory distress syndrome (RDS) necessitating prolonged mechanical ventilation may result in the development of bronchopulmonary dysplasia (BPD) from chronic hypoxemia that can further exacerbate comorbidities inherent to this fragile population [2,3]. The management of sequalae resulting from pulmonary over-circulation can be challenging, making closure of the PDA of particular benefit for the preterm infant [26,27]. Additionally, the risks inherent to undergoing open thoracic ligation including pneumothorax, phrenic nerve palsy, bleeding, vocal cord paralysis, chylothorax, and scoliosis [28,29] may also be avoided with successful device placement. Transcatheter closure may also offer faster post-operative recovery with decreased mortality compared with surgical ligation [9]. Though new data continues to emerge regarding PDA closure in very small neonates, a paucity of data exist describing a safe means of caring for this niche of patients undergoing TC-PDA closure.

## 5. Our institutional experience

The Preemie Duct Occlusion Program (PDOP) was created within our institution to develop a multidisciplinary team approach to streamline the care of these premature babies with patent ductus arteriosus (PDA). The goal of this program is to improve patient clinical outcomes and enhance education and academic endeavors specific to this vulnerable patient population.

Through the implementation of our institutional transcatheter PDA protocol and increasing experience, we have consistently and safely accomplished the task of reducing the risks inherent to transporting these extremely fragile patients out of their secure environment in the NICU into the catheterization suite for device closure. We have found that a smooth perioperative experience relies in

the incorporation of several key perioperative considerations when preparing to perform TC-PDA closures.

## 6. Considerations

### 6.1. Thermoregulation

Due to a high surface area to body weight ratio, and low body fat percentage, VLBW and ELBW neonates are at significant risk of hypothermia and its consequences (i.e., impaired wound healing, coagulopathy). To prevent heat loss during transport, our NICU neonates are transported in their Giraffe Isolette (GE Healthcare, Chicago, Illinois). Isolettes offer the ability to provide active warming and temperature monitoring. In addition, the lid can be closed completely, providing protection from a cold environment. However, the cumbrous nature of the isolette does add a degree of difficulty to transport.

### 6.2. Ventilation

Neonates for PDA closure at our institution have properly sized cuffless endotracheal tubes (ETT) placed in situ preprocedural by the NICU team. Our protocol incorporates the task of securing the airway in the NICU prior to transport to avoid inefficiencies and environmental exposures inherent to intubating in the lab while minimizing ventilatory leaks. Intubation occurs at least 24 h prior to the procedure, and requires a discussion among the anesthesiologist, interventional cardiologist, and NICU physician.

Due to their extremely small size (frequently $<$1500 g), this patient population is at risk of either accidental extubation or right sided bronchial intubation with even minute movements of the ETT. Simply flexing or extending the head, as may occur when moving from the isolette to the table, can have a significant effect on the ETT position.

Pulmonary overcirculation from a PDA, in addition to an immature pulmonary system, can make ventilation of the extremely premature neonate challenging. Ventilation strategies must also take into account the effect fractional inspired oxygen concentration (FiO2), carbon dioxide, and acidosis/alkalosis have on the shunt magnitude across the PDA, and thus the degree of pulmo-nary overcirculation. Our ventilation mode of choice for transport is the BIO-MED Crossvent: CV2i+ (BIO-MED Devices, Guilford, CT). The Crossvent is easy to set up, has few moving parts, and provides simple to manageable control over FiO2, inspiratory pressure, and positive end expiratory pressure. The anesthesia provider ventilating the patient has independent control over the respiratory rate.

#### 6.2.1. Pre-procedural management

Following referral for patient evaluation and approval for procedural candidacy, patients are transported to our facility for pre-operative optimization and procedural intervention. Establishing consistent pre-operative optimization practices in the NICU has allowed for smoother transitions in patient care immediately prior to intervention. These practices minimize patient exposure to ambient temperatures that may result in hypothermia and optimize overall time management upon entering the catheterization suite. On admission, patients are prophylactically intubated by the NICU team within one day of intervention and adequate peripheral intravenous (ideally in the upper extremities) is established. Patients routinely receive uncuffed standard endotracheal tubes during intubation to ensure appropriate sizing and an acceptable amount of leak is present. Care is taken to avoid the right leg or groin for procedural access. Additionally, orogastric tubes are inserted and serve as a radiological marker for the aorta at the time of catheterization. Metabolic blood panels are obtained the morning of intervention to optimize and correct any abnormal findings before proceeding to the catheterization suite. Ionized calcium is corrected to above 1.0 mmol/L while magnesium is corrected above 2.0mEq/L. Patients are transfused to achieve optimal hematocrit of 30% and platelets 75,000 and 100,000 cells/mm$^3$ depending on patient postmenstrual age week (PMA). Coagulation studies are obtained in patients with known hepatic pathology, cholestasis, or are on anti-coagulation therapy. Review of preoperative glucose trends provide additional insight regarding incidences in hypo and/or hyperglycemia that may occur intraoperatively. The evaluation of markers of malnutrition including hypoalbuminemia should be noted and considered when anesthetic plans involve the administration of highly protein bound agents that may warrant dose reduction in the setting of protein depletion. Hypoalbuminemia in the setting of a low phosphorus may indicate compromised muscular strength that could potentially result in respiratory fatigue and subsequent reintubation after percutaneous closure.

Immature thermoregulatory control and liver function within the preterm infant present additional challenges of hypothermia and hypoglycemia. The presence of underdeveloped thin skin leads to increased evaporative water loss and hypovolemia [30] making it imperative that a sufficient and continuous glucose-containing solution is provided similar in concentration to the predetermined preoperative glucose maintenance fluids used in the NICU. Premature infants are prone to rapid decreases in temperature when exposed to ambient temperatures during all aspects of perioperative care and active measures to minimize opportunities for heat loss should be taken. To accommodate these needs, transportation to the hybrid catheterization suite involves a dedicated team consisting of the circulating nursing staff, respiratory therapist, and cardiac anesthesiology team using heated cribs with underbody warmers to minimize ambient heat losses. Additionally, the hybrid suite should be adequately warmed prior to entering with warm blankets, radiant warmers, and clear plastic draping available to facilitate patient transfer to the procedural bed. Ventilation is supported throughout transport using portable neonatal ventilators that provide controlled ventilation until arrival to the procedural suite.

#### 6.2.2. Perioperative anesthetic management

Upon arrival to the catheterization lab, the patient is transferred to the procedural bed and reconnected to anesthesia ventilator. Lung compliance and endotracheal tube should be manually assessed to ensure satisfactory leak and tube positioning prior to draping of the patient. Standard monitoring involves placement of ECG pads on the back of the patient to allow transthoracic echocardiography

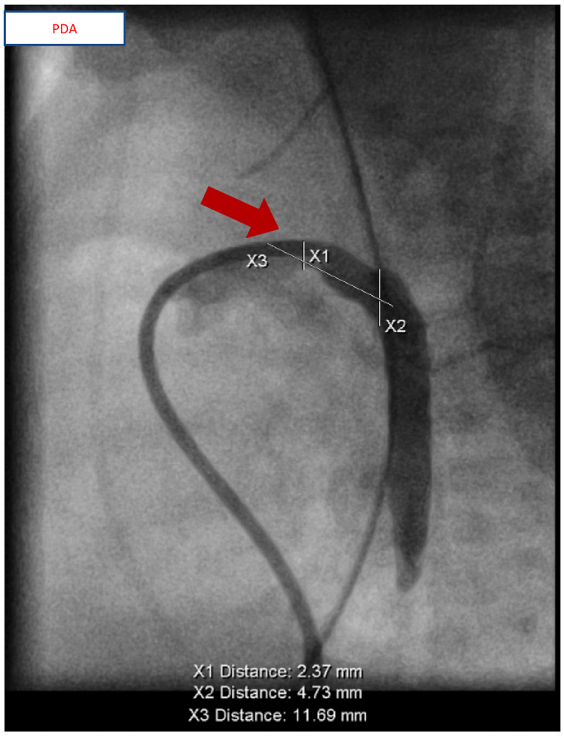
(TTE) throughout the case. Dual measurements of both pre and post ductal oximetry and noninvasive blood pressure monitoring are ideal, but not required. An arterial line is typically not necessary and may be risky for vessel damage and thrombosis. It is essential to monitor glucose, ionized calcium, hemoglobin, and lactate at regular intervals during the case. Given that many premature infants have a history of interventricular hemorrhage it has been our practice to avoid the use of routine intravenous dosing of heparin. Intraoperative venous catheter and vascular patency are maintained with periodic flushing of dilute heparinized saline into the venous sheath placed by the interventionalist. Adequate preload and cardiac contractility should be maintained while avoiding large fluctuations in systemic vascular resistance (SVR) or pulmonary vascular resistance (PVR) that may result in unbalanced blood flow. Factors that induce small changes in increase PVR such as hypoxia, hypercarbia, and acidosis can incite sudden clinical deterioration [31]. Clinically hypovolemic patients may manifest after prolonged fasting periods, despite the presence of maintenance fluids requiring correction to establish adequate hydration and volume status prior to induction to augment systemic blood flow by lowering blood viscosity. Successful induction of general anesthesia in premature neonates should be tailored to the current degree of respiratory support, baseline pre-ductal and post-ductal oxygen saturations that may be used clinically to assess shunt fraction. Our institution has favored combinations of intravenous Fentanyl (1-2mcg/kg) with non-depolarizing neuromuscular blockade using cisatricurium or rocuronium several minutes prior to local anesthetic placement by the cardiologist. Given the short procedural time and local anesthetic administered at the site of catheter placement, our practice has favored the avoidance of the volatile anesthetic agents that may further exacerbate hemodynamic lability intraoperatively.

#### 6.2.3. *Ventilation strategy*

In premature patients who are mechanically ventilated, permissive hypercapnia is allowed as it has been shown to decrease pulmonary morbidity in patients receiving mechanical ventilation. Hypoventilation is generally avoided with $pCO_2$ levels maintained between 40 and 59 mmHg as $pCO_2$ levels less than 39 mmHg and greater than 60 mmHg have been shown to increase risk of intraventricular hemorrhage in preterm infants [32]. Volume targeted ventilation has been shown to demonstrate an advantage over other modes of ventilation in reducing the incidence of bronchopulmonary dysplasia, duration of ventilation, any IVH, IVH grade 3 or 4, PVL, pneumothorax, failure of primary mode of ventilation, hypocarbia, mean airway pressure and days of supplemental oxygen administration [33]. However, the ability of the anesthesiologist to deliver appropriate volume-targeted ventilation depends upon the availability of appropriate ventilators. Overall, our patients required an average $FiO_2$ of roughly 60% to maintain oxygen saturations greater than 90% with mean PIPs below 30cm$H_2O$ and PEEPs below 8cm$H_2O$

#### 6.2.4. *Intra-procedural management*

Following patient positioning and assurance of adequate ventilation and tube positioning a baseline transthoracic echocardiogram




*Angiographic intraprocedural catheterization demonstrating PDA prior to device deployment.*

**Image 1.** Angiographic intraprocedural catheterization demonstrating PDA prior to device deployment.

is performed to evaluate the size, shape, and doppler flow through the PDA. During this time, vigilance is required as mild pressure on the chest and abdomen by the echocardiographer can significantly compromise ventilation. Typically, the procedure is performed through a single femoral venous sheath to eliminate the need for arterial access that may risk vascular injury due to the small size of the femoral artery relative to a standard arterial introducer sheath. Significant hemodynamic changes may be noted with introduction of the venous delivery catheter as it traverses the tricuspid valve and right ventricular outflow track following sampling of a baseline venous blood gas. Once inside the pulmonary artery, the catheter is advanced through the PDA and into the aorta to obtain additional catheterization data and arterial blood gas measurements to ensure that metabolic acidosis is not present. Positioning of the device prior to deployment may result in intraoperative hemodynamic lability or arrhythmias in the setting of vascular obstruction within the aorta or pulmonary artery. Closed loop communication including all personnel involved during this time allows for prompt recognition and treatment of any hemodynamic derangements that may occur immediately prior to device deployment. Supplemental oxygen is provided during this time as needed to maintain optimal age-appropriate saturations. Transthoracic echocardiography is performed at this time, functioning as a surrogate to aortic angiography by avoiding additional exposure to IV contrast agents to demonstrate wide patency of the proximal descending aorta and branch pulmonary arteries (Image 1). Following device deployment and confirmation of successful positioning, the venous sheath is removed, and the patient is undraped (Image 2). Active warming measures during this time should be immediately reinstituted prior to patient transport to the NICU. In the event of unsuccessful device placement, a pediatric cardiac surgeon is routinely available for immediate surgical conversion within the hybrid suite.

## 7. Limitations

Even at a single institution with guideline-driven approach to PDA management, the decision to refer for percutaneous closure was at the discretion of the attending physician, with marked variability in the timing of referral for percutaneous closure. Thus, it becomes necessary to identify pre-operative and intraoperative characteristics that may aid in the establishment of a more uniform means of identifying and referring patients that would benefit from percutaneous PDA closure. Additionally, Since the present study was conducted at a major academic center, the risk of referral bias is recognized.

## 8. Conclusion

Preliminary findings show promising outcomes in decreased mortality and survival to hospital discharge following TC-PDA closure. Our institutional experience has favored ventilation strategies that maintain peak airway pressures less than 30cmH20 with an FiO2 appropriate to maintain intraoperative oxygen saturations greater than 92%. Our overall intraoperative experience demonstrated a lack of significant intraoperative cardiac events requiring intervention or need for inotropic support to maintain adequate perfusion pressures through the duration of TC-PDA closure with both anesthetic techniques. Overall, muscle relaxants (cisatricurium) were routinely used to ease ventilation, help prevent accidental extubation due to a moving patient, and provide optimum operating conditions. Benzodiazepines (midazolam) and opioids (fentanyl) were employed to safely achieve sedation and analgesia without the need for intraoperative vasoactive agents. Despite these promising findings, further investigations with higher patient volume are needed to validate these promising observations.

## Ethics statement

Informed consent was obtained from all individual participant(s) involved in this study for the publication of their images. Participants provided their agreement for the use, analysis, and publication of their personal and/or medical images, understanding fully the purpose of their use in the study, and the context in which they would be displayed. The consent process was designed and implemented in accordance with the ethical standards of the Declaration of Helsinki and its later amendment.

## Author contribution statement

Mikel Gorbea: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

## Data availability statement

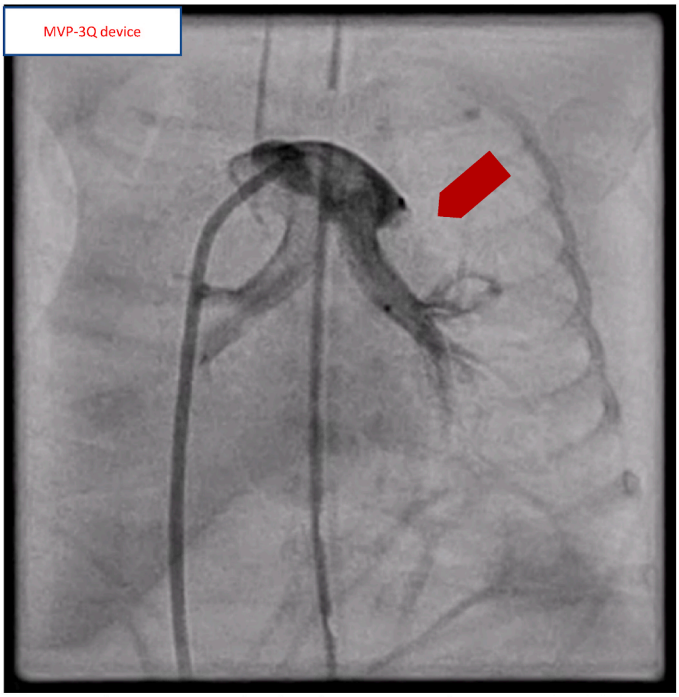
Data included in article/supp. material/referenced in article.

## Additional information

No additional information is available for this paper.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.




*Angiographic intraprocedural catheterization demonstrating MVP-3Q device within PDA immediately following device deployment*

**Image 2.** Angiographic intraprocedural catheterization demonstrating MVP-3Q device within PDA immediately following device deployment.

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