

Original Article

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The outcome of PDA ligation by mini-thoracotomy in premature neonates: A single hospital experience

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KEYWORDS

Patent ductus arteriosus,
Single lung ventilation,
Selective ventilation,
Prematurity,
Neonate,
Mini-thoracotomy

ABSTRACT

Background: Various thoracotomy practices have been employed for occlusion of patent ductus arteriosus (PDA) which are not amenable to medical management. We report our preliminary experience of using a mini-thoracotomy approach in small premature infants and determining survival outcomes in relation to factors such as gender, birth weight, age, and type of ventilation used intraoperatively.

Methods: Between January 2004 and December 2012, 52 consecutive premature infants with an echocardiographic diagnosis of isolated PDA, which are not amenable to medical treatment, were included. Those with chromosomal abnormalities, major cardiac congenital anomalies aside from septal defects, and infants who did not receive mechanical ventilation in the first week of life were excluded. The median gestational age was 28 weeks and the median gestational weight at surgery was 705g. The median PDA size was 3.8mm, ranging from 1.6 to 5mm. Twenty-nine patients were given non-selective ventilation and twenty-three were anesthetized using selective right-lung ventilation using a 2-F balloon catheter for arterial embolectomy. A left lateral mini-thoracotomy was performed in all infants and PDA closure achieved by double ligation using zero silk sutures.

Results: The median operative time and mean length of hospital stay were 45 minutes and 90 days, respectively. No major hemorrhage requiring blood transfusion occurred during the surgery. The survival rate until hospital discharge was 88.5%. There were no mortalities associated with the surgery itself. Six (11.5%) neonates died postoperatively because of prematurity (p-value=1.000). Pneumonia and atelectasis were among the few complications encountered post ligation. An interesting association was recognized between ventilation and surgical complications; that is neonates who underwent selective right ventilation did not experience any of the complications mentioned above in comparison to those who were put under non-selective ventilation (p-value <0.001).

Conclusion: Closure of PDA by double ligation via a left mini-thoracotomy in small premature infants proved to be safe and effective in providing pediatric surgeons adequate exposure within confined and delicate anatomic spaces. No mortalities or major complications were encountered.

INTRODUCTION

Patent ductus arteriosus (PDA) is a common complication observed in premature infants. Its incidence is inversely proportional to gestational age and birth weight. PDA is seen in 30% of infants born with a birth weight <1,500g, in 40% of those weighing 751-1,000g, and in more than 50% of those weighing 501-750g.

The management of PDA in premature infants is a controversial issue. The lack of robust evidence of the benefit or harm of available treatment options necessitates the need to balance it against the likelihood of spontaneous duct constriction, which occurs in approximately a third of extremely premature neonates. Despite this, nearly 70% of preterm infants (less than 28 weeks of gestation) will receive either medical or

surgical treatment. The rationale behind this is to decrease the likelihood of developing morbidities associated with prematurity and persistent PDA. These include intraventricular hemorrhage (IVH), bronchopulmonary dysplasia, necrotizing enterocolitis (NEC), renal dysfunction, prolonged use of assisted ventilation, and increased mortality.[1]

Current medical treatments for PDA are prostaglandin H₂ synthetase inhibitors, indomethacin, and ibuprofen. More recently, the effects of paracetamol are also being studied. Surgical management involves ligation of the PDA by either video-assisted thoracoscopic ligation (VATS) or thoracotomy.

This prospective study focuses on the closure of PDA by mini-thoracotomy in our institution. The aim is to present the survival outcomes of this approach in relation to variables such as gender, birth weight, and type of ventilation used intraoperatively.

METHODS

A total of 52 premature neonates, presenting with PDA were referred to our surgical unit between the year 2004 and 2012 after medical management failed to facilitate closure of the shunt. Surgical referral to our unit was decided by the attending neonatologist, following a failed response to the medical management (indomethacin/paracetamol).

All infants referred were included in the study, except those with chromosomal abnormalities, major cardiac congenital anomalies aside from septal defects, and infants who did not receive mechanical ventilation in the first week of life. Data collected included: patient demographics, gender, gestational age, weight, type of ventilation during the procedure, procedure time, length of hospital stay, chest tube insertion, the incidence of complications during hospitalization, and all-cause mortality.

Operative technique: All the 52 neonates underwent PDA ligation via a muscle-sparing left mini-thoracotomy. Patients underwent either selective right lung ventilation or normal two lung ventilation as per the anesthetist's assessment. After anesthetic induction, patients were placed laterally on their right side and a left mini-thoracotomy was performed in the fourth intercostal space. A small incision of 3cm was made at the level of the nipple. Intercostal muscles were cut by diathermy and the PDA was approached through the extra-pleural space. PDA closure was achieved by double ligation of the PDA using zero silk suture. Finally, layers were closed using 2-0 Vicryl suture for intercostal muscle incision and 5-0 nylon sutures for subcuticular skin closure.

Statistical analysis: For the descriptive analysis of categorical variables and continuous variables, data

were presented as frequencies (%) and medians (interquartile range), respectively. All categorical variables were analyzed using the Chi-Square test and Fisher's exact test and continuous variables were analyzed using the Mann-Whitney U test. Multivariate logistic regression analysis was used to calculate the odds ratio (OR) for factors associated with mortality. We used the statistical software SPSS 26 (SPSS Inc., Chicago, IL) for statistical analysis. P-values of 0.05 or less were considered statistically significant.

Ethical approval: This study was granted approval from the institution's responsible ethical committee (Ministry of Health Research Committee)

RESULTS

Of these 52 neonates, 31(59.6%) were males and 21 (40.4%) females (M:F 1.5:1). Our study included 33 (63.5%) very preterm (28-32 weeks) and 19 (36.5%) extremely preterm neonates (<28 weeks), in accordance with the WHO criteria. Forty-eight (92.3%) out of the 52 infants were extremely low birth weight (<1000g) and 4 (7.7%) belonged to the very low birth weight category (<1500g). Gestational age ranged between 24 to 31 weeks, with a mean and median of 28 weeks. The mean weight of premature neonates was approximately 740g and the median weight was 705g (range: 450g - 1000g). [Table 1] [Table 2].

The size of the PDA ranged from 1.6 to 5 mm in diameter; the mean and median size was 3.6mm and 3.8mm, respectively. Operative time ranged from 35 minutes to a maximum of 60 minutes, with a mean and median time of 46 and 45 minutes, respectively. Patients were admitted to the hospital for an average of 90 days including mortalities (range: 60 – 120 days) [Table 2]. The survival rate until hospital discharge was 88.5%.

During the procedure, 23 patients (44.2%) were given selective right lung ventilation and 29 patients (55.8%) normal ventilation as per the anesthetist's assessment. Intercostal chest drains (ICD) were routinely inserted in all the neonates. Twenty-three (79.3%) out of the 29 patients (normal two lung ventilation cohort) developed pneumonia and 4 (13.8%) developed atelectasis (p-value <0.001). Interestingly, most of the neonates that underwent normal ventilation (double lung ventilation) developed pneumonia; conversely, the neonates with selective lung ventilation had no complications as shown in Table 3. Other surgical complications such as pneumothorax, chylothorax, and vocal cord paralysis were not encountered. No deaths occurred during or immediately after the surgery. The patients were followed up until discharge or death, with follow-up echocardiography and clinical assessment suggesting no residual shunts.

Table 1: Patient characteristics			
		n	%
Gender	Female	21	40.4%
	Male	31	59.6%
Age ¹	Extremely premature	19	36.5%
	Very premature	33	63.5%
Weight ²	Very low	4	7.7%
	Extremely low	48	92.3%
Complication post-surgery	None	25	48.1%
	Atelectasis	4	7.7%
	Pneumonia	23	44.2%
Complication of prematurity	IVH	8	15.4%
	Lung hemorrhage	11	21.2%
	Sepsis	12	23.1%
	NEC	21	40.4%
Survival	Died	6	11.5%
	Survived	46	88.5%
Post-op day at which ICD ³ was removed	Day one	30	57.7%
	Day two	11	21.2%
	Day three	11	21.2%
Prematurity classification based on gestational age in weeks - late preterm (34 - <37), moderate preterm (32 - <34), very preterm (28 - <32) and extremely preterm (<28). [3]			
² Based on birth weight: low (< 2500g), very low (< 1500g) and extremely low (< 1000g) birth weight. [4]			
³ ICD: Intercostal Chest Drain			

Table 2: Descriptive statistics			
	Mean	SD	Median
Weight (grams)	739.4	169	705
Gestational age (weeks)	28.1	1.7	28
Hospital stay (days)	90.2	23.1	97.5
Size of PDA (mm)	3.6	0.9	3.8

Table 3: Relationship between ventilation and surgical complications							
Ventilation	Complication post-surgery						P-value
	None		Atelectasis		Pneumonia		
	n	%	n	%	n	%	
One lung	23	100%	0	0.0%	0	0.0%	<0.001
Two lungs	2	6.9%	4	13.8%	23	79.3%	

The overall mortality rate was 11.5% (6/52). No deaths were attributed to the surgery performed. Four male infants died on days 50, 58, 60, and 70, respectively and 2 female infants died on days 48 and 55,

respectively (p-value 1.000) owing to prematurity-related complications. Male infants were 1.4 times more likely to die as compared to females, but this association was not statistically significant [OR 1.407,

95% CI (0.234,8.480), p-value 1.000]. All the deaths (12.5%) occurred in neonates with extremely low birth weight (p-value 1.000). According to the WHO classification of prematurity [3], four extremely premature and two very premature neonates died (p-value 0.175).

Noticeably, there was a higher incidence of mortality in the extremely premature neonates with low birth weight and in the male gender. However, the relationship between gender, gestational weight, gestational age [OR 0.242, 95% CI (0.40,1.472), p-value 0.175], size of PDA [OR 0.540, 95% CI (0.213,1.372), p-value 0.309] and mortality was not statistically significant as seen in Table 4 and Table 5.

Table 4: Relationship between patient characteristics and survival

		Died		Survived		P-value
		n	%	n	%	
Gender	Female	2	9.5%	19	90.5%	1.000
	Male	4	12.9%	27	87.1%	
Weight	Very low	0	0.0%	4	100.0%	1.000
	Extremely low	6	12.5%	42	87.5%	
Age	Extremely premature	4	21.1%	15	78.9%	0.175
	Very premature	2	6.1%	31	93.9%	

Table 5: Relationship between size of PDA and survival

		Size of PDA		P-value
		Mean	SD	
Survival	Died	3.2	1.3	0.309
	Survived	3.7	0.8	

Table 6: Relationship between age and weight to complications of prematurity

		Complication of prematurity								P-value
		IVH		Lung hemorrhage		Sepsis		NEC		
		n	%	n	%	n	%	n	%	
Weight	Very low	1	25.0%	0	0.0%	3	75.0%	0	0.0%	0.046
	Extremely low	7	14.6%	11	22.9%	9	18.8%	21	43.8%	
Age	Extremely premature	3	15.8%	2	10.5%	2	10.5%	12	63.2%	0.058
	Very premature	5	15.2%	9	27.3%	10	30.3%	9	27.3%	

Necrotizing enterocolitis (NEC) was observed to be the most common complication seen in premature neonates included in our study. Four infants died because of NEC and 2 infants died due to sepsis. Most of the complications encountered, especially NEC, occurred in extremely premature infants with low birth weight. A statistically significant association can

be seen between gestational age [p-value 0.058], weight [p-value 0.046] and prematurity complications [Table 6]. Association between PDA size and complications, both surgical and those related to prematurity, were found to be not statistically significant [p-value 0.732 and 0.399] [Table 7].

Table 7: Kruskal Wallis test for the relation between the size of PDA and complications

		Size of PDA		P-value
		Mean	SD	
Complications post-surgery	None	3.7	0.8	0.732
	Atelectasis	3.9	0.4	
	Pneumonia	3.5	1.0	
Complications of prematurity	IVH	4.1	0.4	0.399
	Lung hemorrhage	3.7	0.8	
	Sepsis	3.6	0.5	
	NEC	3.4	1.1	

DISCUSSION

With regards to survival outcome, there was no statistically significant association found between any of the patient characteristics studied and patients’ survival. (Gender p-1.000, weight p-1.000, age p-0.175). Similarly, there was no statistically significant relationship exists between the size of PDA and survival outcome (P-0.309).

In our study, four complications of prematurity were seen. These being: intraventricular hemorrhage, lung hemorrhage, sepsis, and NEC. Extremely low birth weight, as compared to gestational age, was found to be a statistically significant risk factor for developing the above-mentioned complications, with NEC affecting 43.8%, lung hemorrhage affecting 22.9%, sepsis affecting 18.8%, and IVH affecting 14.6%. (p-0.046).

With regards to the surgical procedure, a statistically significant association was found between the type of ventilation used during the surgery and the incidence of surgical complications. Patients who underwent selective one-lung ventilation experienced neither atelectasis nor pneumonia. Whereas 79.3% of patients who had two lung ventilation encountered postoperative pneumonia, and 13.8% encountered atelectasis (p-value <0.001).

This association sheds a light on the importance of assessing the role of anesthesia on the surgical outcome of PDA closure. The literature review regarding the type of ventilation used during the surgery is deficient. However, Janvier et al. [2] studied the role of adequate analgesia as part of the anesthesia regimen for surgical closure of a PDA in premature infants. The study found that a wide variability of anesthetic techniques was used for PDA ligation and that such variations were the only factors associated with postoperative instability. It concluded that a minimum of 10.5 mcg/kg of fentanyl equivalent as a component of the anesthetic regimen promotes postoperative res-

piratory stability. The effects of adequate analgesia were crucial in the perioperative period, in controlling the physiological stress response as well as providing extended pain relief to promote respiratory stability.[2]

Given that, further studies should be carried out to evaluate the role of anesthesia, with a particular focus on ventilation and anesthetic agents used. Furthermore, a standard protocol, independent of the anesthetist’s preference and expertise, should be implemented to ensure the best outcome. A meta-analysis is also needed to combine the contradicting results of studies comparing ligation by mini-thoracotomy with its surgical alternative video-assisted thoracoscopic surgery (VATS).

Vanamo et al. published a study comparing VATS and open ligation in neonates (excluding preterm babies) and older children. No perioperative mortality occurred in either group or faster recovery period was observed with VATS; however, a higher tendency of post-operative complications particularly recurrent laryngeal nerve palsy was noticed in the VATS group. The recurrence rate of residual shunt one year after the initial operation was 1.7% for open ligation and 2% for VATS.[5]

Open ligation has success rates of 77% to 100% but with higher possibilities of postoperative complications such as severe scoliosis, recurrent laryngeal nerve palsy, and respiratory compromise to name a few. In comparison, the success rates of thoracoscopy are 88% to 98% with minimal chest wall trauma and deformities and lower risk of complications. [6]. Vocal cord palsy (VCP) is known to be one of the most frequent complications encountered after cardiothoracic procedures (Open surgery or VATS). Results from two meta-analyses evaluating the incidence of VCP after surgical closure of PDA revealed an increased occur-

rence of VCP in preterm infants (9% and 11.7%) particularly in neonates with low birth weight, low gestational age, and low weight at the time of surgery.[7-9] However, none of the above-mentioned complications were encountered in our study.

VATS and conventional thoracotomy have both been proven to be safe and effective in infants including extremely premature neonates with low birth weight.[10-13] Post-operative survival between the two groups remains similar but some studies have favored VATS over open surgery as it is minimally invasive; results in lesser complications, shorter postoperative stay, rapid recovery, aesthetic cosmetic scar, and better patient and parental satisfaction.[14]

In order to resolve the controversy regarding the optimal management of PDA, a comprehensive study is needed that takes into account all of the following variables: the size of the PDA shunt, the duration of exposure to symptomatic PDA, use of indomethacin including its dose and timing, and surgical ligation. In addition to the effects of the general care given to the premature infant which includes administering antenatal surfactant, corticosteroids, and mechanical ventilation.

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It is important to keep in mind that our study was restricted to a single center and included a limited number of participants. Additionally, neurodevelopmental events, which might be attributed to the surgery, anesthesia, or perioperative hemodynamic compromise, were not studied.

CONCLUSION

Closure of PDA by mini-thoracotomy in our institution was found to be safe with no procedure-related mortality or major complications. It is a useful option in neonates with failed medical management of PDA especially in preemies where performing VATS is challenging.

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