Original Article

Descriptive review of patent ductus arteriosus ligation by video-assisted thoracoscopy in pediatric population: 7-year experience

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Background: Less invasive procedures such as video-assisted thoracoscopic surgery (VATS) are desirable for patent ductal artery (PDA) ligation when pharmacologic or conservative approaches fail. Studies done on VATS-PDA ligation showed better outcomes when compared to open thoracotomies, however, complication rates remain conflicting. Learning curve can be a postulated reason which may also precludes the acceptability. We therefore sought to report our single centered 7-year experience of PDA closure with VATS.

Methods: Single centered retrospective study of 127 patients who underwent PDA ligature with VATS from February 2012 to October 2018. The cohort was divided into two groups, i.e., 2012–2014 (early phase) and 2015–2018 (late phase) and were further compared. Early and late outcomes, including mortality and morbidity, were analyzed.

Results: The included patients had a mean age of 1.7 years. Among them, preterm infants accounted for 38.6%, there was no operative mortality. Six deaths (4.7%) occurred during in-hospital stay, predominantly in the neonatal intensive care unit (NICU) due to massive cerebral bleeding and cardiopulmonary failure. Overall conversion rate to thoracotomy was 16.5%. It decreased from 20% in early phase to less than 5% in late phase. Fifty patients (39.4%) required transfer to the NICU. The mean in-hospital stay for the remainders was only 2.2±1.6 days. All but two patients discharged home survived follow-up period without any adverse events and nobody among non-converted cases expressed concerns regarding chest deformity. A 5-year probability of survival estimated according to the Kaplan-Meier curve was 93.6%.

Conclusions: VATS is a safe as well as efficient method for closure of PDA that ensures satisfactory late cosmetic results. Postoperative mortality and extended hospital stay may be attributed to prematurity. Although learning curve exists it does not affect the safety and late outcomes.

Keywords: Patent ductus arteriosus (PDA); surgical treatment; video-assisted thoracoscopic surgery (VATS); safety; complications

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Introduction

Patent ductus arteriosus (PDA) is relatively common and reported to constitute 10% of all congenital heart disease (1). It is frequently seen in females and more prevalent in preterm babies possibly due to developmental immaturity (2). Persistent PDA if remain untreated, may results in ventricular hypertrophy, heart failure, reversal of shunt, infective endocarditis, aneurysmal dilation, failure to thrive and even early death (3). The initial treatment is usually pharmacologic, the surgical option is considered when conservative treatments are contraindicated (necrotizing enterocolitis, renal injury, intraventricular hemorrhage) or treatment failure is observed (4,5).

Previous work indicates that open thoracotomy is safe and reliable procedure (6). Recent observational data also suggests that open procedures are associated with poor neurodevelopmental outcomes (7). Less invasive, percutaneous catheter-based closure using coil embolization or such devices seems to be a favorable option in the older children and infants >4 kg only, and is associated with higher residual shunt (8-10). Notably, arterial injury seems to be consistently reported in preterm cohort who underwent percutaneous procedures (11). Nevertheless, the type of clinical settings, morphology of ductus, and patient's weight are important determinants of choosing the type procedure.

Over the past two decades, other less invasive procedures such as video-assisted thoracoscopy (VATS) have gained immense popularity. VATS-PDA ligation offers several advantages including preservation of muscular architecture of spine (12). Studies done on VATS-PDA ligation showed reduced surgical times, length of stay, better cosmetics when compared to open thoracotomies however complication rates remain conflicting among the centers (13-17). Learning curve may be a postulated reason (18). Nonetheless, limited data also precludes the acceptability of VATS procedure for PDA ligation among the centers. Very few studies evaluated the immediate clinical outcomes, complications and explored the long-term survival in patients undergoing PDA closure by VATS. We therefore sought to report our single centered 7-year experience of PDA closure with VATS.

Methods

With Institutional Review Board of Poznan University of Medical Sciences approval and waived consent we conducted this retrospective study between February 2012 and October 2018. Study data were collected and managed per protocol hosted at our institution. Patients' demographics, age, race, gender, body mass index (BMI), surgical history, length of hospital stay, the presence of complications, and long-term outcomes were collected.

Patient selection

We included single centered patients who underwent VATS-PDA closure in whom conservative treatment for PDA either failed or was contraindicated were enrolled in the study. None of them was an appropriate candidate for percutaneous closure. VATS was introduced in our center in 2012, we believed that there was a learning curve initially, hence we divided our included patients in two groups, i.e., 2012–2014 and 2015–2018.

Transthoracic echocardiography was performed in all patients before the surgery to confirm the presence of hemodynamically significant PDA. The exclusion criteria for VATS procedure were: diameter of PDA >9 mm, previous thoracotomy, previous history of left thoracic surgery, preexisting cardiac anomalies requiring simultaneous surgical intervention, endocarditis, calcified or aneurysmal PDA. Such criteria were observed in 6 patients (4.7%) who underwent surgical ligation of PDA through a posterolateral thoracotomy.

Technique of VATS closure

All procedures were performed by the same surgical team that consisted of two cardiac surgeons. All infants were operated in an infant incubator. The patients were anesthetized applying single-lumen, endotracheal intubation with isolated right lung ventilation. Endotracheal tube was adjusted immediately after the procedure to the supracarinal position. Midazolam, fentanyl, atracurium or pancuronium were used for induction and sevoflurane for anesthesia maintenance. Standard monitoring during the surgery included electrocardiogram, non-invasive blood pressure, capnography, pulse oximetry, central venous pressure.

The surgery was performed in right lateral decubitus positioning, the initial 5-mm incision was made along the 4^{th} or 5^{th} intercostal space (ICS) in anterior axillary line. The first port was used for the video-camera (Karl Storz Endoskope GmbH, Germany) and carbon dioxide insufflation. The thorax cavity was insufflated with CO_2 under pressure of 5–7 mmHg, to compress the left lung and

improve the visualization of the surgical field. The second and third 3-mm incisions in the 3rd and 6th ICSs in the posterior axillary line were made to place the instruments and clip applicator. The anatomical structures such as PDA, left pulmonary artery, descending aorta, recurrent laryngeal and vagus nerve were identified. Thereafter, carefully opening of the mediastinal pleura overlying the PDA was done, and the duct was gently and slowly dissected free from the surrounding tissues. After obtaining optimal visualization and magnification, an appropriate size of titanium clips (5, 8 or 10 mm) were chosen and were placed across to occlude the arterial duct. One or two titanium clips were enough to completely close the PDA. After adequate hemostasis was achieved, the CO_2 was aspirated from the thorax and the lung was re-expanded. The chest tubes were not routinely placed unless bleeding was expected or there was suspected lung injury. The chest tube, if necessary, was inserted through the first incision whereas the other holes for trocars were closed with single absorbable sutures.

Conversion to posterolateral thoracotomy, if necessary, was done through the anterior axillary line at 4th or 5th ICS. The mediastinal pleura was opened, PDA visualized and then dissected free from the surrounding tissues. The PDA was closed using titanium vascular clips. The chest tube was placed in all patients after conversion. Finally, the chest was closed in layers.

Early postoperative period and follow-up protocol

The postoperative echocardiography was routinely performed in the operating room to confirm the absence of ductal flow. Post-surgery, all patients were transferred to the pediatric cardiothoracic intensive care unit (P-CICU). Preterm infants requiring further treatment were treated in the neonatal ICU whereas the care was continued in pediatric cardiothoracic unit for other children. Chest X-ray was performed immediately after all surgeries to exclude hemothorax or pneumothorax and to confirm the proper position of the clip.

Outcomes were measured included not only mortality and morbidity but also the procedure time, need for intraoperative conversion, chest tubes insertion, length of hospital stay, blood transfusion, residual shunt and parents/patient's satisfaction with their surgical scars. Learning curve was ascertained and aforementioned variables were compared between two equal-in-length periods: early phase—from 2012 to 2014 (n=73); and late phase—from 2015–2018 (n=54). Clinical characteristics were comparable between both groups. The patients were followed up after discharge either by family physicians in majority and few by phone interview.

Statistical analysis

Continuous data variables were checked for normality with Shapiro-Wilk test. Normally distributed data was expressed as the means ± standard deviations and further compared with unpaired student *t*-test. Otherwise, they are presented as median with the range (min to max) and differences were calculated by means of the Mann-Whitney U test. Survival rate was stratified with the use of Kaplan-Meier method. Statistical significance was assumed at $P<0.05$. Statistical analysis was computed with SPSS Statistics 24 (IBM, USA) software.

Ethics approval

This study was approved by the Bioethics Committee at Poznan University of Medical Sciences (No. KB 40/18).

Results

One hundred twenty-seven patients with hemodynamically significant PDA underwent clipping via VATS. Median age at the time of surgery was 1.7 years, ranged from 10 days to 15.8 years. Forty-six patients weighed <2.5 kg at the time of the procedure constitute almost 36% of total population, not a trivial fraction (*Figure 1*). Other preoperative demographics selected clinical data and overall complication rates are summarized in *Table 1*.

Operative data

Intraoperative mortality was none. The overall mean surgery time was 56.1±33.1 minutes and was found to be comparable in both periods [57.5±34.6 *vs.* 54.4±31.2 minutes (ns)], however the mean surgery time of the last 15 procedures was 38 minutes. Although, intraoperative conversion rate from VATS to thoracotomy was more frequent by at least 50% in the early phase 13/73 (17.8%) *vs.* 6/54 (11.1%) statistical analysis revealed no significant difference (ns). Of note, only one conversion was noted during the last 25 procedures (4.0%). The most prevalent reason for conversion was noted to be incomplete PDA closure (n=7) followed by post-clipping ductal bleeding (n=5), inadequate visualization (n=5) cardiopulmonary instability

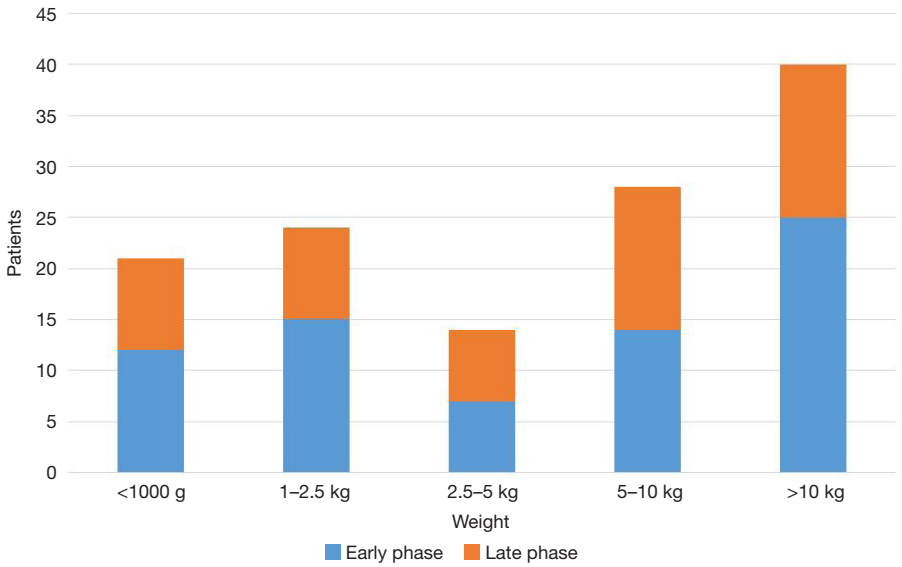

Figure 1 Distribution of patient weight at the surgery.

post-insufflation (n=2) and injury to pulmonary vein during preparation (n=1). Conversion was associated with significantly longer mean surgery time (100.1±47.1 *vs.* 47.3±20.5 minutes) and higher rate of blood transfusion (52.4% *vs.* 24.5%). Chest tube was placed in 27 patients (21.3%) and removed after 30.1±18.3 hours with median drainage of 27.4 mL.

In-hospital outcomes

Overall in-hospital mortality was 4.7% (n=6). Two preterm infants, weighting 700 and 2,000 g, died at the 40th and 48th hours after the surgery. The first infant underwent a complete PDA closure using VATS and died due to massive cerebral bleeding and the second one needed emergency conversion to thoracotomy and died due to cardiopulmonary failure. Four patients died during the treatment on the neonatal ICU at 3rd, 4th, 18th days after the procedure due to acute cardiopulmonary failure and at 20th day postoperatively due to cerebral bleeding.

Higher overall postoperative total complications rate was observed in the early phase (P=0.03, *Table 2*). Thoracotomy was performed in the early postoperative period in two children. One preterm infant weighing 890 g required open surgery 8 days post procedure due to lung injury and pneumothorax and another 7-year-old child 5-day post-procedure for surgical repair of chylothorax.

Seventy-five patients (59.1%) [median age: 2.8 years, median weight: 13.7 kg] were discharged home after mean in-hospital stay of 2.2±1.6 days. Fifty patients (39.4%) [median age: 32.6 days, median weight: 1.55 kg] were transferred to the neonatal ICU for continuity of care. Twenty-nine of them needed respiratory support with median time of mechanical ventilation 17.7 days. The mean length of stay at neonatology unit was 49.9±33.0 days.

Follow-up period

All patients completed the follow-up period for a median of (min to max) 4.0±1.9 years (1 month to 6.7 years). All but two patients discharged home survived follow-up period without any adverse events. Two children (preterm infants) who were discharged after 13- and 26-day treatment on neonatology unit died at home 139 and 310 days post-procedure, due to sudden infant death syndrome and cerebral disorders. A 5-year probability of survival after VATS closure of PDA stratified with the use of Kaplan-Meier method was 93.6% (*Figure 2*).

Residual ductal patency was detected in 2 children (1.6%) post procedure during the follow-up period. The pre-procedure diameter of the duct was 5 and 6 mm. In both cases, the residual shunts were noted to be hemodynamically insignificant not requiring any further treatment.

Among 106 patients (83.5%) who underwent successful VATS, 97.2% patients and parents were satisfied with the surgical scar. None of our patients had high-degree scoliosis

Table 1 Patient demographics, preoperative clinical data and postoperative complication rates

Preoperative demographics and selected clinical data	Value (n=127)
Female	79 (62.2)
Age at the surgery (years)	1.7 (10 days to 15.8 years)
Weight at the surgery (kg)	8.7 (0.7–64.0)
Preterm infants	49 (38.6)
Gestational age (weeks)	27.2±3.0
Birth weight (g)	1,043.5±522.3
PDA diameter (mm)	3.9±1.3
Chromosomal anomalies	6 (4.7)
Trisomy 21	5 (3.9)
Trisomy 13	1 (0.8)
Trisomy 18	0 (0)
Symptoms of heart failure	36 (28.3)
Symptoms of respiratory failure	51 (40.2)
Renal failure	6 (4.7)
Pulmonary hypertension	5 (3.9)
Fetal infection	24 (18.9)
Anemia of prematurity	33 (26.0)
Bronchopulmonary dysplasia	13 (10.2)
Intraventricular hemorrhage	28 (22.0)
Grad I/II	19 (15.0)
Grad III/IV	9 (7.1)
Postoperative complications	
Procedural mortality	0 (0)
Hospital mortality	2 (1.6)
Intraoperative conversion to thoracotomy	19 (15)
Late hospital conversion to thoracotomy	2 (1.6)
No. of patient with catecholamines	37 (29.1)
Blood products transfusions	37 (29.1)
Chylothorax	4 (3.1)
Chylothorax treated using chest tube	2 (1.6)
Pneumothorax	10 (7.9)
Pneumothorax treated using chest tube	5 (3.9)
Hemorrhages	1 (0.8)
Atelectasis	6 (4.7)
Recurrent laryngeal dysfunction	0 (0)
Transient recurrent laryngeal dysfunction	0 (0)
Permanent recurrent laryngeal dysfunction	0 (0)
Wound infection	0 (0)

Continuous variables are presented as mean ± standard deviation (if normally distributed) or median with the range, whereas categorical values are presented as the numbers (%). PDA, persistent ductus arteriosus.

or other musculoskeletal deformation requiring further treatment.

Preterm infants less than 1,000 g

Patients weighing at the time of surgery less than 1,000 g make up to 16.5% of all operated children. These infants were born before the 29th gestational week (22–29 weeks) with mean birth weight 702.9±128.2 g and presented significantly more symptoms of heart failure, respiratory failure, renal failure and intraventricular hemorrhage (47.6% *vs.* 18.8%; 100% *vs.* 28.3%; 9.5% *vs.* 3.8%; 52.4% *vs.* 16.0%) than patients weighing over 1,000 g. Patients weight did not affect the surgery related complications or duration of the procedure, however, the total complication rate was significantly higher in the smaller children <1,000 g (66.7% *vs.* 27.4%). The conversion rate was regardless of weight and remains at 14.3% in children weighing less than 1,000 g. One patient died at P-CICU (4.8%) and other 3 at neonatology unit. Overall mortality in this group of patients was 28.6% (n=6). A 5-year probability of survival estimated according to the Kaplan-Meier curve was 66.7% and it was significantly lower than calculated probability among children weighting over 1,000 g at the time of surgery (*Figure 3*).

Discussion

Overall during our study, the mortality rate was 6.3%. All who died were preterm infants. None death was related directly to the procedure and we demonstrated no intraoperative mortality. Postoperative morality of PDA ligation through posterolateral thoracotomy in the literature is described as minimal in older children and can reach up to 21% mortality among preterm infants (13,19-21). Several investigations that compared VATS with conventional thoracotomy revealed that both techniques were equal to one another in terms of their efficiency and safety (13,14,22).

In the present cohort of wide range of pediatric age and body weight, VATS-PDA ligation was carried out successfully and safely. The noted post-operative deaths (6.3%) seems relatively high, however mostly ostensible to premature consequences than surgical complications *per se* (23). Further analysis of these deaths revealed that those patients already had some degree of heart failure, respiratory failure, bronchopulmonary dysplasia, infection, anemia of prematurity or renal failure preoperatively. Additionally, our cohort represented 38.6% of premature

Table 2 Incidence of complications after VATS within two periods

Postoperative complications	Surgery between 2012–2014 (n=73)	Surgery between 2015–2018 (n=54)	P value
Procedural mortality	0 (0)	0 (0)	ns
In-hospital mortality	2 (2.7)	0 (0)	ns
Patients with complications	31 (42.5)	12 (22.2)	0.03
Overall conversion to thoracotomy	13 (17.8)	8 (14.8)	ns
Intraoperative conversion	13 (17.8)	6 (11.1)	ns
Late conversion	0 (0)	2 (3.7)	ns
Chylothorax	3 (4.1)	1 (1.9)	ns
Chylothorax treated with chest tube	1 (1.4)	1 (1.9)	ns
Pneumothorax	7 (9.6)	3 (5.6)	ns
Pneumothorax treated with chest tube	2 (2.7)	3 (5.6)	ns
Atelectasis	6 (8.2)	0 (0)	ns
Transient recurrent laryngeal dysfunction	0 (0)	0 (0)	ns
Permanent recurrent laryngeal dysfunction	0 (0)	0 (0)	ns
Residual shunt	2 (2.7)	0 (0)	ns
Residual shunt required reintervention	0 (0)	0 (0)	ns

Data are expressed as the numbers (%). VATS, video-assisted thoracoscopy; ns, not significant.

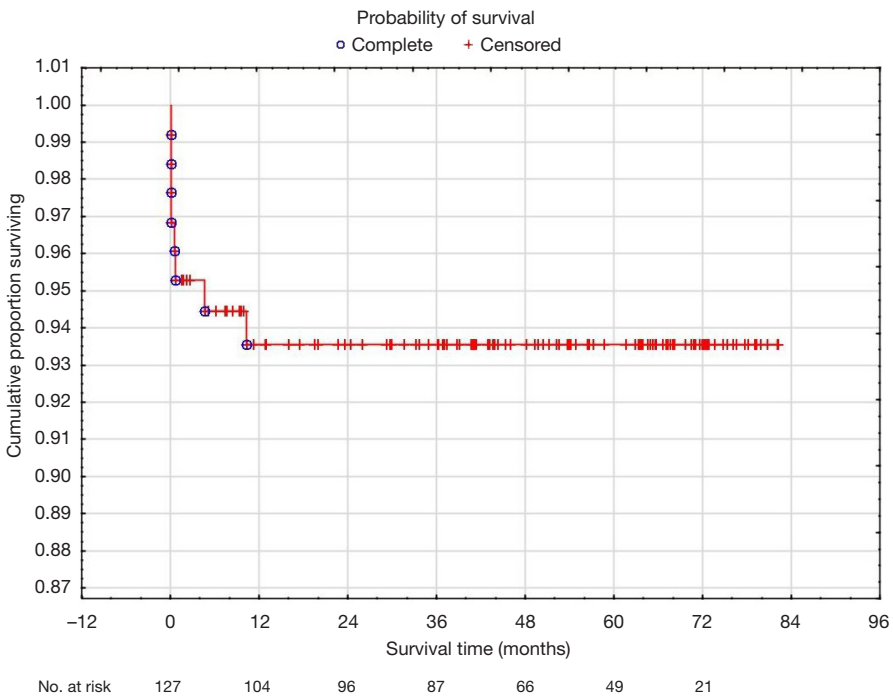

Figure 2 Kaplan-Meier survival curve of patients after video-assisted thoracoscopic PDA clipping. PDA, persistent ductus arteriosus.

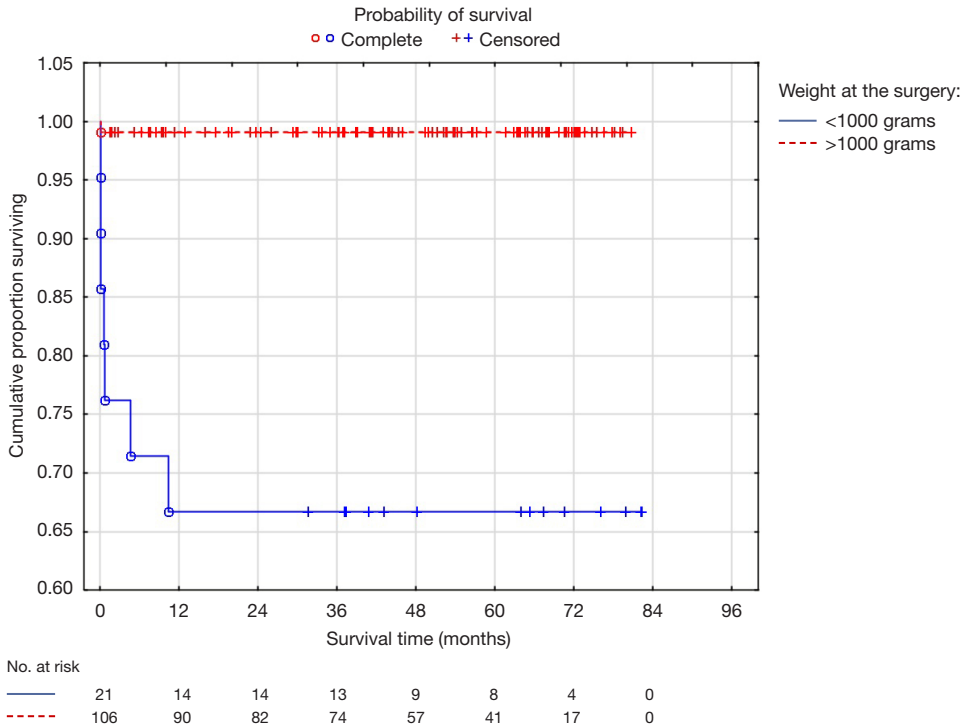

Figure 3 Kaplan-Meier survival curve of patients weighing less and more than 1,000 g.

infants—not a trivial fraction. We also observed extended mechanical ventilation and length of hospital stay possibly due to aforementioned reasons. The incidence of PDA is more common in females, our study also depicted more incidence in females (62%). The most difficult group of patients are preterm infants less than 1,000 g. This group presented both the highest overall complication rate and mortality with survival rate after 5 years only 66.7%. More attention must undoubtedly be focused on transport to operating room. All our patients were operated in the operating room, which is located next to the P-CICU. All Infants were operated in an infant incubator to reduce the potential risks of transportation such as hypothermia, dislocation of the tracheal tube or vascular line. Some investigations describe even surgery on bedside, to reduce the risk of transport of the smallest babies (24).

The rate of conversion from VATS to posterolateral thoracotomy in our study was 16.5%, however, 90% of these conversions were performed intra procedure whereas deemed necessary in 10% during the initial post-procedure days. Our conversion rate was relatively high from the previously observed rates of 0.3–12% in the literature (22). It is noteworthy that the intraprocedural conversion rate during the initial 2 years of early phase was 20.4%, which decreased significantly to less than 5% in the last 2 years of late phase. The reduction of conversion rate in the late phase of our study suggests the effect of learning curve—a known phenomenon in VATS procedures (25). This effect was also translated to reduction of the total postoperative complications (42.5% *vs.* 22.2%, P=0.03) in the late phase. All procedures were always performed by two same surgeons what enabled the standardization and the improvement of the technical skills that resulted in significant reduction of surgery time to 38 minutes in last 15 cases. We strongly believe that gaining surgical experience allowed us to avoid many technical and medical pitfalls. Lower prevalence of pulmonary complications in the late phase could be related to the meticulous PDA preparation and less compression of the lung. Nonetheless, this learning curve was observed without any effect on mortality.

Despite routine post procedural echocardiography, two of our patients had hemodynamically insignificant residual shunts during the initial post-operative days. The residual shunt after surgical closure are mostly rare and hemodynamically insignificant. However, none of them required any further treatment. Previous two large

numbered studies including 700 and 2,000 patients after thoracoscopic clipping of PDA reported late residual shunt rate of 0.6% and 0.2% (15,16). Nevertheless, investigators reported nil redo-procedure rate for residual shunts (26,27).

The incidence of post thoracotomy scoliosis is predominantly found in premature infants. We did not find any post-thoracotomy scoliosis or non-healing surgical scars in our group during follow ups, even in patients who underwent intra- or post-operative conversion to thoracotomy. Open thoracotomy involves significant muscle division, rupture of intercostal ligaments and rib spreading which may lead to imbalance of forces in muscular architecture and further attributes to scoliosis (28,29). Lawal *et al.* (12) also observed reduction of chest asymmetry, scoliosis and relatively better cosmetics results with VATS when compared to open procedures. Similar observations were also made by Chen *et al.* (13).

Our study is unique in its attempt to assess both short- and long-term complications of VATS in a large numbered cohort which includes almost 40% of preterm population. We also recognized the implication of learning curve in VATS-PDA ligation which may be responsible for increased complication in the early phase and may precludes its widespread usage. Our study is limited in being a retrospective analysis and therefore suffers some degree of confounding and bias. This investigation was a single-center and the results were analysed objectively without any control group hence the results may not be generalizable. Regardless, our results alienate with previous work. High early phase complications attributed to learning curve may falsely increase the total complication rate of the study but in general, reflects the trend of any new technique when introduced.

Conclusions

Overall, our results imply that VATS is a safe as well as efficient method for PDA ligation that ensures satisfactory late cosmetic results. Postoperative mortality and extended hospital stay may be attributed to prematurity. Although learning curve exists it does not affect the safety and late outcomes.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the Bioethics Committee at Poznan University of Medical Sciences (No. KB 40/18).

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