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Thoracoscopic ligation versus coil occlusion for patent ductus arteriosus: A matched cohort study of outcomes and cost

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Abstract
Background Coil occlusion (CO) and video-assisted thoracoscopic surgery (VATS) have both emerged as minimal access therapies for patent ductus arteriosus (PDA). These techniques have not previously been statistically compared.
Methods Twenty-four consecutive children undergoing VATS for PDA were each retrospectively matched by PDA diameter and child weight to two children undergoing CO (total 48) during the same time period. The two modalities were compared with respect to outcome and cost. Statistical analysis was performed using a Student's *t*-test and Mantel–Haenszel relative risk. Cost analysis from an institutional perspective was used to compare resource consumption.
Results Mean PDA diameter was 3.6 ± 1.2mm in both groups. Mean age and weight for VATS and CO children were 2.7 and 2.9 yrs and 13.2 and 13.1 kg, respectively. Mean surgical times were 94 ± 34 min for VATS and 50 ± 23 min for CO ($p < 0.0001$). Mean length of stay was 1.6 ± 0.2 days for VATS and 0.6 ± 0.2 days for CO (Mantel–Haenszel RR (95% CI) = 0.15 [0.07, 0.29], $p < 0.0001$). Mean fluoroscopy time with CO was 13 ± 7 min. No VATS or CO children required conversion to open surgical ligation. Two children in each arm (8% VATS, 4% CO) required indefinite antibiotic endarteritis prophylaxis for a persistent shunt. The cost per child was C$ 4282.80 (Canadian dollars) for VATS and C$ 3958.08 for CO.
Conclusions VATS is as efficacious for PDA closure as CO but requires longer surgical times and lengths of stay. Costs for each procedure are similar.

Keywords Patent ductus arteriosus · Coil occlusion · Coil embolization · Video-assisted thoracoscopic surgery · VATS · Pediatric

The incidence of patent ductus arteriosus (PDA) is 0.05% in term infants [1]. Large ducts can cause pulmonary overcirculation and left ventricular volume overload, which if left untreated eventually lead to congestive heart failure and pulmonary hypertension. Small to moderate size ducts are better tolerated but run an estimated bacterial endarteritis risk of 0.45% per year [1].

Surgical ligation for a PDA was first performed by thoracotomy in 1939 and for many decades remained the gold standard for management of this disorder [2]. In one series looking at a 46 year experience in 1108 full-term infants undergoing suture ligation and division through a thoracotomy, the persistent shunt rate was reported at about 3% [3]. Thoracotomy, however, is associated with

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considerable pain, a large scar and potential long-term chest wall and spinal deformity, as well as recurrent laryngeal nerve injury, infection, and effusion [4, 5].

Interventional radiological and thoracoscopic surgical techniques for the treatment of PDA have emerged as minimally invasive alternatives to the classic thoracotomy and ligation. The choice of each technique appears to be determined by local expertise and practice patterns. Coil occlusion (CO) is now a well established therapy for a PDA, while thoracosopic ligation is gaining popularity [6]. For premature children, the standard of care remains surgical repair through a thoracotomy, although thoracoscopic approaches have been utilized. The small size of these patients precludes arterial catheter access for embolization.

To date, there have been no studies comparing clinical efficacy and cost of thoracoscopic duct ligation and coil embolization, due to inadequate experience with thoracoscopy, short follow-up, and institutional biases for preferred therapies. Analysis of cost benefits have varied based on method of analysis, with some studies [7] showing equal costs associated with both techniques and other studies [8] showing the cost of coil occlusion to be about 54% of the cost of surgical closure. The aim of this study is to compare the clinical and cost outcome of PDA ligation at an institution with extensive experience in CO (Hospital for Sick Children, Toronto, Canada) to an institution routinely performing VATS (McMaster Children's Hospital, Hamilton, Canada).

Materials and methods

All children who underwent VATS for PDA at McMaster Children's Hospital were retrospectively identified. These children were each matched to two children that had undergone CO at the Hospital for Sick Children during the same time period. The primary match points were child weight, sex, and age, which were chosen to eliminate these factors as potential confounding variables. The indications for duct closure were volume overload and/or risk of endocarditis. Children with significant cardiac and non-cardiac comorbidities that could impact clinical outcome of duct closure as well as those with evidence of significant congestive heart failure were excluded. All premature children at both institutions had open surgical ligation rather than VATS or CO.

Outcomes measures included surgical time, fluoroscopy time, length of stay, need for chest tube drainage, complications, need for repeat occlusion procedures, and need for subsequent open duct ligation for a persistent PDA.

Statistical analysis was performed in consultation with a statistician using Mantel–Haenszel relative risk and Student's *t*-test, with significance set at the 0.05 level. The research protocol was approved by the institutional review boards at each institution.

Technique of thoracoscopic ligation

A general anesthetic was utilized with single-lung ventilation using either right mainstem intubation or a bronchial blocker, with the child in the right lateral decubitus position. Three or four ports were used, with 3.5 or 5 mm thoracoscopic instruments introduced to retract the lung anteriorly and expose the aorta and arterial duct. A posterior 10-mm port site was used to introduce the clip applier, and a single medium or large titanium clip applied to occlude the duct completely. After removing the instruments and expanding the lung, local anesthetic was infiltrated. A chest tube was used at the discretion of the surgeon, based on perceived risk of pneumothorax or bleeding. After recovery, children were given necessary analgesia and were generally discharged within 24 to 48 hours.

Technique of coil occlusion

After administering 150 IU/kg of heparin sulfate to the child while under general anaesthesia, the femoral artery was entered with a 5 Fr sheath, a descending aortogram performed and the duct diameter was measured at its insertion to the pulmonary artery. A 5 Fr coronary catheter was advanced across the duct from the aorta, and based upon the measured duct diameter, a detachable Giantruco coil of appropriate diameter (3, 5, or 8 mm) was inserted into the catheter and advanced with an 0.035 inch guide wire until the coil was positioned in the pulmonary end of the duct. The catheter was withdrawn until the coil was extruded and sat securely within the duct, straddling both the pulmonary and aortic ends. Contrast opacification was used to confirm closure and a second coil deployed if persistent pulmonary artery opacification was demonstrated. Children were typically discharged home the same day.

Cost analysis

Cost analysis was based on the average mean cost of resource usage between the two treatment arms. Data were collected on resources used during the time period from admission to hospital to primary discharge (unless post-operative complications required immediate readmission). Resources accounted for included operative/interventional radiology theatre costs, consisting of staff costs (salaries based on mid-range values for nursing, physicians and technical support staff), consumables (clips, coils,

catheters), drug usage (including anesthesia protocol as well as postoperative analgesia and antibiotic prophylaxis and thromboprophylaxis) intraoperative complication requirements, inpatient costs (including nights on the ward or in ICU) and postoperative costs, which included investigations (echocardiograms, chest radiographs), consumables (drains, catheters), and costs associated with management of postoperative complications. Overhead hotel cost of the hospital was assumed to be consistent between the two groups and incorporated into the number of nights each child stayed in-house.

Results

Twenty-four consecutive children underwent thoracoscopic ligation during the 6 year period from January, 1998 to February, 2004. Each child was matched to two children from a series of 319 CO procedures that were performed during the same time period (total of 48 matched CO patients). None of the patients were premature.

Table 1 depicts child demography for each treatment arm. Mean PDA diameter was 3.6 ± 1.2mm in both groups. Mean surgical times were 94 ± 34 min for VATS and 50 ± 23 min for CO ($p < 0.0001$). The mean surgical time for the first 12 thoracoscopic cases was 109 minutes and for the last 12 was 79 minutes. Mean fluoroscopy time with CO was 13 ± 7 min. The estimated total cost per child was C$ 4,282.80 (Canadian dollars) for VATS and C$ 3,958.08 for CO.

Chest tubes were placed in 9 of 24 (38%) VATS cases and removed within 36 hrs. In the VATS group, 17 children received intermittent dosing of narcotic analgesia, with a mean of 3.5 doses, two children were maintained on narcotic infusion until prior to discharge, two children received oral codeine as needed, and three children did not require narcotics. No children in the CO groups required narcotic analgesia. Mean length of stay was 1.6 ± 0.2 days for VATS and 0.6 ± 0.2 days for CO (Mantel–Haenszel RR (95% CI) = 0.15 [0.07, 0.29], $p < 0.0001$). No children in either group required subsequent open surgical ligation.

In the VATS group, 23 of 24 children had follow-up echocardiogram (one child was lost to follow-up), and the exam was not completed in one uncooperative child. Three children showed a residual shunt on echocardiography at 3 month follow-up however one was documented to close within 1 month. The remaining two children had residual shunts detected on echocardiogram not associated with a murmur, and so these children were not required to use antibiotic prophylaxis. No children have required any further procedures. Immediate assessment for shunt was not done post-VATS. There were no known cases of rib synostosis in any of the VATS children at last follow-up.

In the CO group, all children were continued on bacterial endocarditis prophylaxis for a period of six months post procedure to allow endothelization. Small leaks were detected in 21 of 48 (46%) of CO children immediately after the procedure. At 6 month follow-up, all leaks had resolved and antibiotics were discontinued. One child with congenital megakaryocytic thrombocytopenia had a postembolization angiogram showing complete closure but was found to have a small leak at follow-up echocardiography. This child remains on antibiotic prophylaxis.

Table 2 depicts the primary outcome measures for each treatment arm. There were no statistically significant differences in outcomes between treatment groups.

During the time period of this study, there were no premature babies undergoing coil embolism or thoracoscopic ligation. At the Hospital for Sick Children, all patients less than 2 kg and less than 28 days of age had surgical ligation through a thoracotomy ($n = 238$). At McMaster Children's Hospital, 150 premature children underwent open surgical ligation.

Table 1 Patient demographics

	Coil occlusion (CO)	Thoracoscopic Surgery (VATS)
Age (yrs)	2.9 ± 1.9	2.7 ± 2.4
Weight (kg)	12.9 ± 5.5	13.1 ± 7.2
Gender (M:F)	1:1	1:1

Discussion

Transcatheter duct closure was first introduced by Portsmann in 1967 using a polyvinyl alcohol foam plug [9]. This and other devices such as the Rashkind occluder have

Table 2 Outcome measures for each treatment arm

	Coil Occlusion (CO)	Thoracoscopic Surgery (VATS)
Operative time (min)*	50 ± 23	94 ± 34
Length of stay (days)*	0.6 ± 0.2	1.6 ± 0.2
Conversion rate to open surgical ligation	0/48 (0%)	0/48 (0%)
Need for subsequent procedure to close PDA	0/48 (0%)	0/24 (0%)
Need for ongoing antibiotic therapy due to residual shunt	2/48 (4%)	2/24 (8%)
Major complications	0/48 (0%)	0/24 (0%)
Cost (C$)	3958.08	4282.80

*$p < 0.0001$

C$ = Canadian dollars

fallen out of favor due to problems with a high residual shunt rate and high price. Current embolization techniques utilize the Cook detachable coil or the Gianturco (Dacron stranded double-helix stainless-steel spring) coil, which demonstrates a similar 6-month occlusion rate (78%) as the Rashkind occluder but at a much reduced cost (C$65 versus C$3,500) [10]. The major problem with the Gianturco coil is inadvertent embolization, occurring in approximately 3% of cases, with less common concerns being the potential for pulmonary artery stenosis, groin hematoma, and leg ischemia [11, 12]. The latter have improved with advancement of the learning curve.

The feasibility of a thoracoscopic approach for ligation of PDA was first reported by Laborde and colleagues [13] in 1993, followed soon thereafter by Rothenberg and colleagues [14]. Burke and colleagues [15] reported on 34 neonatal cases in which operative mortality was zero, four children required conversion to thoracotomy, and follow-up revealed no murmur in any child but residual flow in two children on echocardiography. Hines and colleagues [16] reviewed 59 children of which 21 were neonates (23 to 40 weeks gestation) and 21 were children (aged 1 to 24 months). Of the neonates, 18 were preterm, of which 17 were successfully ligated thoracoscopically (one conversion due to coagulopathy). Thoracoscopic ligation was also attempted in three term neonates, however two required conversion due to anatomic variance. Mean operative time for the neonates was 107 min, and there were no recurrent laryngeal or phrenic nerve injuries, postoperative effusions, chylo- or pneumothoraces related to the procedure, intraoperative bleeding, or deaths. Among the pediatric group, there was one conversion to thoracotomy for anatomic variance, two recurrent laryngeal nerve injuries, and no recurrence.

The two largest series of VATS PDA ligation have been reported by Nezafati et al. [17] and Villa et al. [18]. Nezafati et al. reported their experience with 300 children and showed no residual flow on immediate follow-up echocardiography, conversion to thoracotomy in three children, and transient recurrent laryngeal nerve palsy in two children. Villa et al., in a follow-up to Laborde's original report, presented a series of 703 cases. They excluded children with duct diameters >8 mm, previous thoracotomy, presence of calcifications, active infection, or aneurysm. Mean patient age was 3.0 ± 3.8 years and mean weight was 10.7 ± 8.0 kg. There were 22 low-birth-weight infants (≤2.5 kg). The duct was closed with two 9-mm titanium clips. Median operative time was 20 min. Echocardiography was performed immediately after operation. Residual duct patency was noted in 10 children, none of whom were low birth weight. Eight of these children underwent re-clipping and two were converted to thoracotomy. Subsequent follow-up showed an overall residual patency rate of 0.6% (4 of 703). There were five other conversions to thoracotomy, three for delayed residual shunt, and two for hemostasis. Chylothorax occurred in four children, of whom one required thoracoscopic treatment and the remaining resolved spontaneously. There were 18 children with transient recurrent laryngeal nerve palsy and three children in which the palsy persisted.

The experiences at the two institutions included in this study have been favorable for both modalities of treatment. CO can be performed safely as a same day procedure, resulting in a length of stay that is significantly less than VATS. Unlike VATS, narcotic analgesia is unnecessary with CO procedures and chest tubes are obviated. In this analysis, the length of procedure was significantly less for CO than for VATS. This likely reflects an ongoing learning curve for VATS, as larger series such as that of Villa show much shorter operative times.

Some potential risks are unique to CO. Foremost, there is a risk of coil embolization that may necessitate further interventional or surgical procedures. This risk relates to duct morphology that has been described elsewhere [19]. In general, ducts that are conical in shape with the narrowing on the pulmonary artery side are best suited to CO as the device becomes well seated. Ducts that are uniformly tubular or where the widest region is on the pulmonary arterial end have a higher risk of device embolization. Furthermore, as was suggested by the child in the CO group that had congenital thrombocytopenia, children with hypocoagulable states may also benefit from VATS over CO due to reduced ability to form clot. Finally, CO involves some radiation exposure with fluoroscopy.

Jacobs et al. [20] describe CO and VATS as complementary rather than competitive modalities, with equivalent efficacy with proper patient selection. In their retrospective review of 102 CO patients to 45 VATS patients, the investigators found that the therapeutic approach to PDA could be based primarily on the size and morphology of the duct. Specifically, they concluded that CO was most appropriate for ducts that were long and narrowest at the pulmonary artery side. VATS was most appropriate for ductal diameters greater than 3.0 mm so as to avoid use of multiple coils. VATS was not favored for calcified ducts or in patients with severe pleural scarring. In these cases, CO was favored (with multiple coils for large ducts), unless the duct was of the "window" type (Krichenko type B [19]; very short and wide), in which case thoracotomy was preferred.

The findings of our comparative study also suggest that VATS is a safe alternative to CO. Long-term duct closure rates were excellent in both groups. Although length of stay was longer than for CO, it was still relatively short, as was duration of chest tube in the children that required one. If there is no lung damage and hemostasis is secure, it is unlikely that children will require a chest tube, and it is the

experience of the authors that chest tube use decreased with increasing comfort with the operation. There were no conversions to open thoracotomy or recurrent laryngeal nerve injuries in this series, reflecting the very low rates of these complications in Villa's much larger series. We cannot comment on early postoperative residual shunts in the VATS group as echocardiography was not performed after surgery, however long-term follow-up showed an excellent closure rate. In the CO group, immediate small leaks occurred in 46% of children but were clinically inconsequential at long term, typically resolving with time.

We recommend that neonates and small children (<5 kg) have operative closure of their ducts as these early symptomatic children tend to have large ducts, and the potential for left pulmonary artery stenosis and aortic arch problems is greater than in the larger child. VATS is preferred for ducts that morphologically are not suited for CO, or in children with hypocoagulable conditions. CO with multiple coils is used for medium-sized ducts with good results. Ducts > 9mm (too large for clip application and CO) may require minithoracotomy closure unless the VATS surgeon is experienced in intracorporeal suturing. "Window" ducts should be repaired surgically through median sternotomy on bypass. Small and medium-sized ducts that are calcified and of appropriate morphology can be treated with CO, and otherwise with thoracotomy. In general, if CO is not available at a particular institution, VATS serves as a reasonable therapeutic alternative.

For premature children, most institutions perform PDA ligation through a thoracotomy incision, although VATS has been described for this population [21]. CO is not possible as arterial access is precluded by the small size of the patients. VATS is possible only in those children who are not on oscillatory ventilation. The benefit of VATS in premature children, however, is marginal. The magnification of the thoracoscope affords good visualization, and avoidance of a thoracotomy may reduce future incidence of scoliosis. Conversely, any additional benefits in terms of morbidity and outcome of this approach are difficult to demonstrate. Our institutions have not adopted VATS in the premature infants for this reason.

Both thoracoscopic surgery and coil occlusion are effective methods of treatment for patent ductus arteriosus, although coil occlusion is associated with shorter procedure time, shorter hospital stay, and less pain. In children that have unfavorable duct morphology or hypocoagulable conditions, or for institutions that do not have access to pediatric interventional cardiology, thoracoscopy provides an efficacious alternative that is similar in cost and outcome and is associated with minimal morbidity.

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