REVIEW ARTICLE
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Thoracoscopy in the treatment of persistent arterial ductus arteriosus in neonates

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INTRODUCTION

Patent ductus arteriosus (PDA) is a congenital deformity. The ductus arteriosus is essential for neonatal circulation, and normally after 2–3 days of life in terms of newborns, it closes. When occlusion does not occur, there is an increase in pulmonary flow associated with systemic hypoperfusion. The major risk factor for PDA is preterm birth and delayed canal closure, which is inversely proportional to gestational age (GA). An estimated 80% of infants with a GA between 25 and 28 weeks will present with PDA[1].

In 1977, indomethacin, a prostaglandin synthesis inhibitor agent, became the clinical therapy for ductus arteriosus closure in premature infants. However, in situations in which PDA is refractory to clinical management or when the side effects of clinical treatment outweigh the benefits, its surgical ligation is indicated[1].

Although open thoracic surgery is common for PDA ligation or clipping, thoracoscopic PDA closure is an alternative surgical procedure that requires a smaller incision, facilitates postoperative recovery, reduces pain, results in shorter hospital stay, and improves respiratory function. There is also a decrease in the incidence of chest wall deformity in the long term, including scoliosis and breast deformity, leading to better aesthetic results[2,3].

Minimally invasive surgery is increasingly performed in pediatrics, but the physiological characteristics of neonates are associated with a higher risk of intraoperative complications[4].

Collectively, the studies that make up the current literature on the subject are from centers with extensive experience in minimally invasive surgery, as such, there is still a need for more series of reports comparing thoracoscopy with standard thoracotomy in terms of efficacy, morbidity, and conversion rates, especially in neonates and premature babies[3,5]. Therefore, the objective of this study is to compare thoracoscopy with thoracotomy in the treatment of PDA in neonates.

METHODS

This study aimed to conduct a narrative review of the literature *via* an electronic search of the following databases: MEDLINE, SciELO, LILACS, and ScienceDirect. The articles were selected according to the search for the following DeCS descriptors: "Cardiac Surgical Procedures," "Congenital, Hereditary, and Neonatal Diseases and Abnormalities," "Ductus Arteriosus Patent," "Thoracoscopy," and "Minimally Invasive Surgical Procedures."

For the inclusion of articles, we selected mainly those published from 2015 to November 2020, without criteria for the language of origin. Personal communications, conference proceedings, case reports, and duplicates were excluded.

For better organization and applicability of this study, the Population, Intervention, Comparison, and Outcome (PICO) method was used. *(P) Study population:* full-term or premature neonate patients who submitted to thoracoscopy for the treatment of PDA; *(I) intervention:* thoracoscopy; *(C) comparison:* results of thoracoscopy with those of thoracotomy to treat PDA; *(O) outcome:* thoracoscopy is the procedure of choice for the treatment of PDA due to a decreased incidence of chest wall deformity, shorter hospital stay, and faster postoperative recovery.

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RESULTS

In the first stage, we actively searched for articles using descriptors and specific keywords. Thus, 109 articles were recognized, of which 32 were chosen according to their relevance based on the titles and abstracts. Subsequently, two duplicates were excluded. Table 1 summarizes the information from the most relevant articles: authors, year of publication, title, duration of the study, type of study, study description, patient group, study results, and limitations.

DISCUSSION

The arterial duct (AD) is an essential vascular conduit for fetal circulation because it enables communication between the systemic and the pulmonary circulation. The AD anatomically connects the left pulmonary artery to the descending aorta, allowing the passage of more oxygenated blood into the fetal systemic circulation[6].

After 24–48 h from birth, the AD undergoes physiological obliteration to ensure the functioning of the pulmonary circulation. However, the persistence of this communication may occur in the neonatal circulation[5,7]. If PDA is not treated, it can result in heart failure, endocarditis, ventricular hypertrophy, and systemic hypoperfusion[1,8].

Pathophysiology of PDA

When the AD fails to close, blood flow is maintained through it. However, the flow is reversed due to pulmonary and systemic pressure changes that occur after birth, as demonstrated in Figure 1[1].

The expansion of the lung abruptly decreases the pulmonary pressure and the loss of the placental circulation, which is of low pressure, and results in increased systemic pressure. Thus, the flow within the AD is reversed, with blood exiting the aorta and proceeding to the pulmonary artery[1]. This reversal causes an increase in the pulmonary circulation and associated systemic hypoperfusion, as the already oxygenated blood returns to the lung[1].

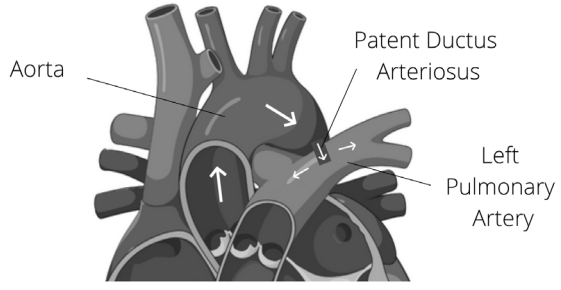

Figure 1. Blood flow with patent ductus arteriosus.

The PDA is related to three factors, namely, prostaglandins (PGs), O_2, and nitric oxide (NO). PGs are essential to maintain the patent ductus. In patients with PDA, the AD endothelium has a higher level of PG receptors[1]. In addition, the AD endothelium is less sensitive to O_2, which would cause its constriction[9,10].

Treatment

The goal is to close the PDA or minimize complications until its spontaneous closure[1]. For diagnostic confirmation, echocardiography is the gold standard, as it can assess the diameter of the AD and the flow through the shunt[11,12]. The clinical findings of the disease, the patient's weight, and the morphology of the duct are important factors for the choice of treatment[8].

The initial treatment is usually clinical. Surgery is utilized when the pharmacological approach is contraindicated, as in the case of complications, including necrotizing enterocolitis, intraventricular hemorrhage, and renal failure[8,13].

Percutaneous access is another option for AD closure[1,5,8,14,15]. However, comparative meta-analyses have shown that reoperations are more common in patients treated with percutaneous closure than with surgical ligation[5,16-18].

Thoracotomy

The goal is to directly ligate the AD. The incision is made laterally to the left and the duct is clipped. It is used in patients refractory to pharmacological treatment or contraindicated for clinical treatment[7].

This safe and reliable approach has similar mortality and complication rates to thoracoscopy[3]. However, there are observational data indicating that open surgery is associated with worsening neurodevelopment of the neonate[18]. In addition, the procedure presents some immediate complications, such as rib fractures, which could be avoided with thoracoscopy[3,14,15].

Thoracoscopy

Thoracoscopy is a minimally invasive method widely used as a treatment for aortic abnormalities, diaphragmatic hernia, and esophageal atresia. This is possible due to the optimization of surgical technologies and newly available equipment[1,8].

Multiple studies in the literature support the efficacy and safety of thoracoscopy as a form of treatment for PDA[19]. Complication rates range from 0.75–5% and the surgical success rate from 98.2–99.1%. Comparative studies between thoracotomy and thoracoscopy showed that there are no differences in safety or efficacy between the procedures[5]. However, there was a decrease in postoperative pain, in the incidence of chest wall deformities, such as scoliosis, and in surgical time and hospital stay after thoracoscopy[3,8].

Table 1. Information from most relevant articles included in the review.

Authors	Title	Duration of the study	Type of study	Description of the study	Patients	Results	Limitations
Muller, et al.[3]	Thoracoscopy Versus Open Surgery for Persistent Ductus Arteriosus and Vascular Ring (VA) Anomaly in Neonates and Infants.	1997–2016	RetrospectiveWW	Age, weight, echocardiography, preoperative symptoms, conversion rate, and short-term postoperative data were analyzed.	n=24 PDA: 13 VA: 11 Patients operated on due to PDA or vascular ring. Thoracoscopy was indicated for patients with clinical failure and/or PDA with hemodynamic symptoms. Thoracoscopy was indicated for patients with clinical failure and/or PDA with hemodynamic symptoms. The mean age was 34 days and the mean weight was 1800 g for patients with PDA.	The group that underwent thoracoscopy and the group that underwent thoracotomy did not have different short-term results (length of hospital stay, surgical time, and postoperative complications). Thoracoscopy causes less pain, especially in neonates and preterm infants. Minimally invasive surgery also causes a decrease in the risk of postoperative chest wall deformities.	Analyses of short-term results. All patients submitted to thoracoscopy due to persistent ductus arteriosus (PDA) were premature, except for one [gestational age (GA) = 37 weeks]. The mean GA was 29.5 weeks, and the mean weight was 1.255 g. The smallest neonate weighed 795 g, and his surgery was converted to thoracotomy due to lack of space. Three cases needed to be converted to thoracotomy due to anesthetic reasons. Conducted in only one institution.
Wei, et al.[5]	Comparison of Outcomes Following Thoracoscopic versus Thoracotomy Closure for Persistent Patent Ductus Arteriosus.	2000–2017	Retrospective	The following were analyzed: surgical time, length of hospital stay, postoperative complications, and reoperations. Exclusion criteria: weight <3.3 kg and/or presence of cardiac comorbidities requiring interventions and/or comorbidities that would require prolonged hospitalization or admission to the neonatal intensive care unit (ICU).	N = 173 Thoracoscopy: 127 Thoracotomy: 46 Patients who submitted to elective surgeries for treatment of PDA.	The length of hospital stay was shorter for patients who submitted to thoracoscopy (1.05 days) than for thoracotomy patients (2.27 days). During the study, conversion to thoracotomy was performed in seven patients; six due to lack of visualization and one due to ductal hemorrhage. Seven patients in the thoracoscopy group had a residual flow on PDA. One was diagnosed during thoracoscopy by transesophageal echocardiography and was converted to thoracotomy. Two others were diagnosed postoperatively and required reoperation. There was no difference in the rates of reoperation or complications, except for drain placement, in which there were rates of 50% in thoracotomy and 11% in thoracoscopy. One patient who submitted to thoracotomy suffered permanent vocal cord injury.	The prolonged thoracoscopy time may be due to the learning curve of the professionals at the institution. The study followed up on 58% of the patients for an average of 1 year. Conducted in only one institution.

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Table 1. Continuation

Authors	Title	Duration of the study	Type of study	Description of the study	Patients	Results	Limitations
Stankowski, et al[7]	Minimally Invasive Thoracoscopic Closure versus Thoracotomy in Children with Patent Ductus Arteriosus.	2003–2015	Retrospective	The patients were divided into two groups according to the surgical technique (thoracoscopy and thoracotomy). The following technical indices were analyzed: length of hospital stay, rate of patients with chest drains, and postoperative complications. Exclusion criteria: pre-existing cardiac abnormalities requiring simultaneous surgical intervention. During the follow-up period of the study, 22 patients were excluded; 4 due to perioperative death, 3 due to lack of data, and 15 due to conversion to thoracotomy.	N = 173 Patients were classified as low birth weight (LBW) and not low birth weight (NBPN). A greater number of patients with LBW who submitted to video-assisted thoracoscopic surgery (VATS) had heart failure and bronchopulmonary dysplasia at birth. Mean birth weight, weight at surgery, and age were lower in patients with BPN. In patients with NBPN, there was a greater mean diameter of the arterial duct.	Patients undergoing VATS spent less time with the chest drain and less time in the pediatric cardiothoracic ICU. Perioperative mortality was similar in both groups. Fewer complications in VATS, with a lower rate of blood transfusion. There were no statistically significant differences in mortalities.	Conducted in only one institution.
Stankowski, et al.[8]	Descriptive Review of Patent Ductus Arteriosus Ligation by Video-Assisted Thoracoscopy in Pediatric Population: 7-year Experience.	2012–2018	Retrospective	Cohort study was divided into two groups, namely, early phase (2012–2014) and late phase (2015–2018). Due to the learning curve of the institution, early and late outcomes were analyzed.	N = 127 2012–2014: N = 73 2015–2018: N = 54 Patients submitted to thoracoscopy after failure or contraindication of conservative clinical treatment. Mean age 1.7 years. 38.6% of patients were premature. Six patients (4.7%) had chromosomal abnormalities.	The average surgery time was 56.1 min, and that of the last 15 thoracoscopies was 38 min. The average conversion rate to thoracotomy was 16.5%. During the early phase, there was a 20% conversion to thoracotomy. During the late phase, there was a 5% conversion to thoracotomy. The mean number of days of hospitalization was 2.2 days. Only two patients who were discharged from the hospital experienced adverse effects during the follow-up period of the study. The patients who underwent thoracoscopy without conversion did not obtain chest deformities. The 5-year survival rate of the study was 93.6%.	The learning curve of the hospital staff, who started performing thoracoscopies in 2012, influenced the results of the initial phase (2012–2014). Conducted in only one institution.

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Table 1. Continuation

Authors	Title	Duration of the study	Type of study	Description of the study	Patients	Results	Limitations
Stankowski, et al.[24]	Conversion to Thoracotomy of Video-Assisted Thoracoscopic Closure of Patent Ductus Arteriosus.	2012–2017	Retrospective	The following were analyzed: preoperative period, in-hospital period, postoperative period, and rates, and reasons for surgery conversion.	N = 112 Thoracoscopy: 93 Thoracoscopy with conversion: 19 Patients who submitted to PDA closure by VATS technique. The patients were divided into two groups, namely, those who did not need conversion and those who required it.	The causes reported for conversion were as follows: incomplete closure of the duct (31.6%), ductal bleeding after clipping (26.3%), inadequate visualization (26.3%), cardiopulmonary instability after insufflation (10.5%), and injury of the pulmonary vein during preparation (5.3%). There was one death in each group in the immediate postoperative period. In the group requiring conversion, most of the patients required transfer to the neonatal ICU. Late postoperative period: All ducts presented successful closure. Two patients presented low-grade scoliosis.	Due to the learning curve, there was a reduction in the number of conversions in the last 2 years of the survey. The number of patients in the group of surgeries converted to thoracotomy was low for data comparisons.
Stankowski, et al.[25]	Surgical Closure of Patent Ductus Arteriosus in Extremely Low Birth Weight Infants Weighing Less than 750 grams.	2006–2016	Retrospective	The study was divided into two groups as follows: Early phase (2006–2012): all the patients underwent surgery by posterolateral thoracotomy (PT); Late phase (2012–2016): all the patients underwent VATS, requiring two conversions to PT. Inclusion criteria: birth weight <750 g, PDA with diameter ≥2 mm, left atrium to aorta ratio ≥ 1.5, presence of left to right shunt, and impaired cardiac performance. Exclusion criteria: PDA associated with any other cardiac abnormalities that needed to be surgically corrected in a classical manner.	N = 31 Thoracotomy: 16 Thoracoscopy: 15 (two conversions) Patients with primary pharmacological treatment failure.	All the patients survived the operation and were transferred to the ICU. Two children who underwent VATS required conversion; one due to hemodynamic instability and another due to difficulty in visualizing the channel. Nine children needed the insertion of a drain; seven after thoracotomy, and two after VATS. The mean mechanical ventilator time in the survivors was 19 days. Routine postoperative echocardiography confirmed complete duct closure in all the patients. During the follow-up period, two patients died at home 139 days and 310 days, respectively, after surgery. Late residual shunt occurred in two children during the study follow-up period. However, none of the shunts were hemodynamically significant, and so they did not require further treatment.	Conducted in only one institution.

Yet, the greatest limitation of thoracoscopy is the lack of training of professionals. Some studies showed that surgeons must perform at least 50 procedures to feel comfortable, and even more procedures are needed to reduce the surgical time of the thoracoscopic option. Therefore, the learning curve of surgeons should be taken into consideration. The more clinical cases a surgeon has performed, the more it is expected that the surgical time and the length of hospital stay will decrease[5,20,21].

Some studies have reported that demonstrated shorter hospital stay, while others found no such difference. However, the studies that did not find such a difference were carried out with fewer patients and mainly investigated premature infants. Therefore, there is currently a consensus that thoracoscopy reduces the length of stay in the neonatal intensive care unit (ICU). This may be due to the reduced need for placing drains in patients[5,7,22,23].

The technological development of minimally invasive surgical instruments for better adaptation to the bodies of neonates should improve compliance rates with the thoracoscopic method and decrease therapeutic costs[5,24,25].

Finally, thoracoscopy is more cost-effective than thoracotomy because there is less need for drains and re-intervention and lower complication rates, such as vocal cord injury and pneumothorax[5,24].

CONCLUSIONS

Based on the analyzed studies, it is possible to confirm that thoracoscopy and conventional surgery are equally safe and effective, regardless of the child's age. Thoracoscopy is associated with a shorter hospital and ICU stay, is less traumatic and painful, and has a shorter operative time, excellent cost–benefit ratio, good aesthetic results, and low rate of acute complications. Before the end of thoracoscopy, monitoring *via* transesophageal echocardiography is essential to verify residual flow regardless of the surgeon's experience. Conversion to conventional surgery is rare and does not result in increased complications. It is essential to have a specialized and trained team for the success of this procedure. Finally, more clinical studies comparing these techniques are needed to encourage the medical community to choose thoracoscopy as a surgical treatment for PDA.

AUTHORS' CONTRIBUTIONS

GCMV: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Visualization, Writing-original draft, Writing – review and editing. **MMJ:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing-original draft, Writing – review and editing. **JGMCB:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing-original draft, Writing – review and editing. **LABAP:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing-original draft, Writing – review and editing. **ALBG:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing-original draft, Writing – review and editing. **ACDA:** Conceptualization, Supervision, Validation, Visualization, Writing – review & editing. **AVT:** Conceptualization, Supervision, Validation, Visualization, Writing – review & editing.

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