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# Thoracotomy Versus Sternotomy for Patent Ductus Arteriosus Closure in Preterm Neonates



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**Background.** To date, a posterolateral thoracotomy approach is considered the gold standard for surgical closure of patent ductus arteriosus (PDA), also in preterm neonates. However, a posterolateral thoracotomy approach can induce post-thoracotomy lung injury of the immature and vulnerable lungs of preterm neonates. Therefore, this study aims to compare a posterolateral thoracotomy and median sternotomy for surgical closure of PDA in preterm neonates.

**Methods.** Between September 2010 and November 2014, both surgical approaches were used to treat a symptomatic PDA in very and extremely preterm neonates. The hospital records of all these neonates were retrospectively reviewed to assess all-cause mortality and postoperative morbidity in both groups.

**Results.** Despite comparable preoperative patient profiles, the postoperative pulmonary complication rate was significantly lower in the median sternotomy group (52.9% vs 94.7%;  $P = .006$ ). Moreover, significantly lower

mean airway pressures (MAPs) were seen in the median sternotomy group directly after surgery ( $\Delta$ MAP median [interquartile range], 0.00 [2.13] vs 0.80 [1.67] cmH<sub>2</sub>O;  $P = .025$ ). Postoperative blood transfusion (median [interquartile range], 20 [14] vs 17 [16] mL;  $P = .661$ ) rates did not differ between both approaches. In addition, Kaplan-Meier survival analysis demonstrated no statistically significant differences between both groups.

**Conclusions.** In our experience, a median sternotomy approach for surgical PDA closure is at least noninferior to a posterolateral thoracotomy approach. Given the lower postoperative pulmonary complication rate and lower postoperative MAPs directly after surgery, the median sternotomy approach may be considered superior for preterm neonates with immature and vulnerable lungs.

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Patent ductus arteriosus (PDA) is one of the most common congenital cardiac defects and occurs predominantly in preterm neonates. The incidence of PDA in term neonates has been estimated to be 57 per 100,000 live births,<sup>1</sup> whereas every third preterm neonate with a very low birth weight, that is, less than 1500 grams, experiences a PDA.<sup>2</sup> Although spontaneous permanent PDA closure occurs in most very low birth weight neonates within the first year of life,<sup>3</sup> more than two-thirds of neonates delivered before 28 weeks of gestational age (GA) receive either pharmacologic or surgical closure of the PDA<sup>4,5</sup> with the intention to reduce respiratory insufficiency, heart failure, germinal matrix

intraventricular hemorrhage (GMIVH), bronchopulmonary dysplasia, necrotizing enterocolitis, and death.<sup>6,7</sup>

Although the first successful surgical PDA closure was performed by an anterolateral thoracotomy by Gross and Hubbard on August 26, 1938, most surgeons now prefer a left posterolateral thoracotomy approach for surgical closure of PDA in preterm neonates.<sup>8</sup> To circumvent post-thoracotomy lung injury of the immature and vulnerable lungs of preterm neonates, we adopted a median sternotomy approach for surgical closure of PDA in this specific patient population. In our concept, a median sternotomy approach might be preferred, because it allows equal ventilation of both lungs and circumvents extensive manipulation of these immature and vulnerable lungs.

Lehenbauer and colleagues<sup>9</sup> reported favorable morbidity and mortality results of a left thoracotomy approach in 166 extremely low birth weight infants. However, no comparisons of posterolateral thoracotomy

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and median sternotomy for surgical closure of PDA in preterm neonates are available in the literature to date. Therefore, this report aims to compare the clinical outcomes between these two surgical approaches for surgical PDA closure in very (28 to <32 weeks) and extremely (<28 weeks) preterm neonates.

## Patients and Methods

### *Study Sample and Data Collection*

Between September 2010 and November 2014, all subsequent very (28 to <32 weeks) and extremely (<28 weeks) preterm neonates undergoing isolated surgical PDA closure at the University Medical Centre Groningen were included in this study. Neonates were examined for the appearance of clinical symptoms indicative of a PDA (need for ventilator support, systolic murmur, widened pulse pressure, and hyperdynamic precordium). Those neonates with a clinical suspicion of a PDA underwent a transthoracic echocardiogram. When a hemodynamically significant PDA with left-to-right shunting was found on echocardiography, the respective neonate was considered to have a symptomatic PDA, and pharmacologic treatment with cyclooxygenase inhibitors (ibuprofen or indomethacin) was considered. The decision to use a second course of cyclooxygenase inhibitors was predominantly based on the response to the initial course of cyclooxygenase inhibitors. In case of contraindications for or failure of the above-mentioned pharmacologic treatment, surgical PDA closure was proposed.

During the study period, two different surgical approaches were used to treat patients with a symptomatic PDA. During the first period (September 2010 through July 2012), the traditional posterolateral thoracotomy approach was used. From July 2012 to November 2014, a median sternotomy approach for surgical PDA closure was adopted from the previously mentioned rationale. During this second period the surgical approach used was at the surgeon's discretion. There were no changes in our protocols for pharmacologic treatment (including pain management), enteral feeding, or ventilator management between both periods. In October 2010 (about the start point of this study), the Netherlands introduced a new national guideline on perinatal practice in which the lower limit for offering active intensive care was lowered from 25<sup>+0</sup> to 24<sup>+0</sup> weeks of GA.<sup>10</sup>

The hospital records of all neonates younger than 32 weeks GA undergoing surgical PDA closure by either a posterolateral thoracotomy or median sternotomy were retrospectively reviewed, and a comprehensive database, including demographic, preoperative, intraoperative, and postoperative data, was compiled. Mortality data were collected and checked by consulting the comprehensive Dutch Civil Registry. The medical ethics committee of the hospital waived the need for informed consent because data were retrospectively collected as part of routine medical care.

### *Study Objectives*

The objective of this study was to assess and compare the all-cause mortality and postoperative morbidity in both treatment groups. Because of our hypothesis that a median sternotomy may be less damaging in these critically ill preterm neonates, we were particularly interested in postoperative pulmonary morbidity and ventilatory requirements. Therefore, postoperative pulmonary complications (PPCs) (within 2 weeks after surgery) were considered as a primary composite outcome. We defined PPCs as either the presence of postoperative pleural effusion, pneumothorax, atelectasis, or pneumonia. Iatrogenic atelectasis because of overtly malpositioned endotracheal tube (mainly in right main stem bronchus) was excluded from analysis. The first author (A.J.F.P.V.) categorized the mentioned pulmonary complications according to the European Perioperative Clinical Outcome definitions. To verify the correct diagnosis of PPCs, a second observer (S.C.A.) reviewed this outcome variable independently. Moreover, the postoperative ventilatory requirements were analyzed. For this purpose, ventilator settings, including peak inspiratory pressure (PIP) and positive end expiratory pressure (PEEP), before and within 72 hours after surgery, were reviewed. Ventilatory pressures were analyzed directly before the operation and after the operation at 0, 12, 24, 48, and 72 hours. These data were retrieved from routine bedside registry records. Mean airway pressures (MAPs) were calculated using PIP, PEEP, inspiratory time, and total respiratory cycle time based on the following formula:  $MAP = (PIP - PEEP) \times (\text{inspiratory time} / \text{total respiratory cycle time}) + PEEP$ . In neonates who required high-frequency oscillatory ventilation, MAPs could be directly retrieved from the medical records. The ventilatory pressures were analyzed as change from baseline (denoted as  $\Delta PIP$ ,  $\Delta PEEP$ , and  $\Delta MAP$ , respectively).

### *Surgical PDA Closure Techniques*

All patients undergoing a posterolateral thoracotomy were placed in a right lateral decubitus position under general anesthesia. The left chest was entered through a standard left posterolateral muscle-splitting thoracotomy in the third or fourth intercostal space. The left lung was gently retracted for proper exposure, and the mediastinal pleura was incised over the proximal descending aorta. Then, the mediastinal pleura was retracted to expose and identify the left subclavian artery, the pulmonary trunk, and the PDA itself. The PDA was circumferentially dissected free and closed with at least one titanium hemoclip. Hemostasis was ascertained and the incised mediastinal pleura was closed with a running nonabsorbable polypropylene suture. Finally, the chest was drained with a small pleural catheter at the surgeon's discretion (n = 16; 84.2%) and closed in layers after local anesthetic infiltration.

All neonates undergoing a median sternotomy were placed in supine position under general anesthesia. A full median sternotomy was used for entering the chest, and both pleurae were kept intact as much as possible. Next,

the cranial portion of the pericardium was opened and gently suspended with traction sutures. The ascending aorta, the main pulmonary artery, both pulmonary arteries, and the PDA itself were identified. The PDA was dissected free and closed with at least one titanium hemoclip. Hemostasis was ascertained before closure, and a single chest tube was placed through a stab-wound incision to drain the anterior mediastinum. The sternum was closed in standard fashion with the use of synthetic absorbable sutures, and the presternal fascia, subcutaneous layers, and skin were routinely closed in layers.

All operations were performed in our level III neonatal intensive care unit (NICU), in the incubator, using operating room personnel. Apart from above-mentioned difference in locoregional pain relief, postoperative pain management was uniform between groups. Postoperative pain management was guided by the COMFORTneo scale.

### Statistical Analysis

Quantitative results were presented as median and interquartile range, whereas categorical data were expressed as numbers and percentages (%). Nonparametric tests were used to analyze our data. The Mann-Whitney *U* test was used when appropriate for continuous data, and the Pearson  $\chi^2$  or Fisher's exact test was used to evaluate categorical data. Survival was estimated with the Kaplan-Meier method. All statistical analyses were performed with IBM SPSS Statistics 22 software (IBM Inc, Armonk, NY). *P* values less than .05 were considered statistically significant.

## Results

### Demographic and Baseline Characteristics

From September 2010 to November 2014, 47 neonates with a hemodynamically significant PDA were eligible for isolated surgical PDA closure. Eleven neonates were excluded from this retrospective observational study because their gestational age at birth was  $\geq 32$  weeks. Therefore, 36 consecutive very (28 to  $< 32$  weeks) and extremely ( $< 28$  weeks) preterm neonates underwent surgical PDA closure via either a posterolateral thoracotomy ( $n = 19$ ) or median sternotomy ( $n = 17$ ). Patient demographic characteristics for both treatment groups are shown in Table 1. The preoperative patient profile in terms of demography and comorbidity was similar in both treatment arms, except the diagnosis of GMIVH was higher in the median sternotomy group. Preoperative ventilator settings did not differ significantly between the two treatment groups.

### Outcome Measurements

As shown in Table 2, the composite end point of pulmonary complications was significantly higher in the posterolateral thoracotomy group, mainly because of a higher incidence of pneumothoraces and atelectases in the posterolateral thoracotomy group. Moreover, the right lung was predominantly affected by atelectasis in

Table 1. Overview of Demographic Characteristics and Preoperative Clinical Condition

| Variable                               | Posterolateral Thoracotomy (n = 19) | Median Sternotomy (n = 17) |
|--|-------------------------------------|----------------------------|
| Male                                   | 11 (57.9%)                          | 13 (76.5%)                 |
| Gestational age, weeks + days          | 26 <sup>+4</sup> (19)               | 26 <sup>+0</sup> (12)      |
| Extremely preterm neonates             | 14 (73.7%)                          | 15 (88.2%)                 |
| Birth weight, g                        | 875 (35)                            | 900 (60)                   |
| Apgar score                            |                                     |                            |
| 1 min                                  | 4 (2)                               | 4 (3)                      |
| 5 min                                  | 7 (2)                               | 6 (2)                      |
| 10 min                                 | 8 (1)                               | 8 (3)                      |
| Age at operation, d                    | 28 (14)                             | 22 (11)                    |
| Weight at operation, g                 | 1173 (165)                          | 1138 (420)                 |
| Preoperative comorbidity               |                                     |                            |
| IRDS                                   | 19 (100.0%)                         | 16 (94.1%)                 |
| NEC                                    | 1 (5.3%)                            | 1 (5.9%)                   |
| Infection or sepsis                    | 8 (42.1%)                           | 9 (52.9%)                  |
| PVE                                    | 15 (78.9%)                          | 10 (58.8%)                 |
| GMIVH                                  | 2 (10.5%)                           | 9 (52.9%)                  |
| Posthemorrhagic ventricular dilatation | 1 (5.3%)                            | 3 (17.6%)                  |
| ROP                                    | 0 (0.0%)                            | 1 (5.9%)                   |
| Pulmonary hypertension                 | 2 (10.5%)                           | 1 (5.9%)                   |
| Associated cardiac anomaly             | 1 (5.3%)                            | 1 (5.9%)                   |
| Preoperative ventilator settings       |                                     |                            |
| PIP, cm H <sub>2</sub> O               | 24 (6)                              | 22 (6)                     |
| PEEP, cm H <sub>2</sub> O              | 6 (1)                               | 6 (1)                      |
| MAP, cm H <sub>2</sub> O               | 12.40 (3.47)                        | 12.00 (2.20)               |

Data are presented as median (interquartile range) or n (%).

GMIVH, germinal matrix intraventricular haemorrhage; IRDS, infant respiratory distress syndrome; MAP, mean airway pressure; NEC, necrotizing enterocolitis; PEEP, positive end expiratory pressure; PIP, peak inspiratory pressure; PVE, periventricular echodensity; ROP, retinopathy of prematurity.

the posterolateral thoracotomy group ( $n = 11$ ; 78.6%). Figure 1 shows an exemplary postoperative roentgenogram with pronounced right-sided atelectasis with midline shift in a preterm neonate who underwent surgical PDA closure by a posterolateral thoracotomy. Well-known complications, including thoracic duct injuries and left vocal fold paralysis (LVFP) with hoarseness and stridor, occurred only in neonates undergoing a posterolateral thoracotomy but were rare, thus not reaching statistical significance. The risk of wound-related complications such as infection (treated with antibiotics), wound dehiscence and cicatricial herniation (one cicatricial hernia at the drain insertion site in the median sternotomy group), was not significantly different between both surgical approaches. Postoperative echocardiographic follow-up showed a residual shunt over the ductus arteriosus in one neonate in the posterolateral thoracotomy group, whereas pericardial effusion was absent in both treatment groups. In addition, no neonates required any additional operative procedures. Moreover,

Table 2. Overview of Postoperative Outcome Measurements

| Variable                                 | Posterolateral Thoracotomy (n = 19) | Median Sternotomy (n = 17) | P Value           |
|--|-------------------------------------|----------------------------|-------------------|
| Mortality                                |                                     |                            |                   |
| 30-day mortality                         | 2 (10.5%)                           | 1 (5.9%)                   | 1.000             |
| Overall mortality                        | 4 (21.1%)                           | 5 (29.4%)                  | .706              |
| NICU length of stay, d                   | 37 (33)                             | 50 (57)                    | .471              |
| Volume of blood transfusion, mL          |                                     |                            |                   |
| Perioperative                            | 0 (0)                               | 0 (0)                      | .778              |
| Postoperative                            | 17 (16)                             | 20 (14)                    | .661              |
| Days receiving intravenous opiates       | 2 (1)                               | 5 (7)                      | .012 <sup>a</sup> |
| Thoracic duct injury                     | 1 (5.3%)                            | 0 (0.0%)                   | 1.000             |
| Left vocal fold paralysis                | 1 (5.3%)                            | 0 (0.0%)                   | 1.000             |
| Arrhythmia                               | 1 (5.3%)                            | 1 (5.9%)                   | 1.000             |
| Wound infection                          | 0 (0.0%)                            | 1 (5.9%)                   | .472              |
| Cicatricial hernia                       | 0 (0.0%)                            | 1 (5.9%)                   | .472              |
| Unsuccessful closure                     | 1 (5.3%)                            | 0 (0.0%)                   | 1.000             |
| Postoperative pulmonary complication     | 18 (94.7%)                          | 9 (52.9%)                  | .006 <sup>a</sup> |
| Pleural effusion                         | 3 (15.8%)                           | 0 (0.0%)                   | .231              |
| Pneumothorax                             | 6 (31.6%)                           | 0 (0.0%)                   | .020 <sup>a</sup> |
| Atelectasis                              | 14 (73.7%)                          | 7 (41.2%)                  | .048 <sup>a</sup> |
| Right                                    | 11                                  | 1                          |                   |
| Left                                     | 1                                   | 0                          |                   |
| Bilateral                                | 2                                   | 6                          |                   |
| Pneumonia                                | 1 (5.3%)                            | 2 (11.8%)                  | .593              |
| Duration to successful extubation, d     | 9 (7)                               | 10 (9)                     | .415              |
| Total duration of ventilatory support, d | 25.5 (23.0)                         | 32.0 (43.0)                | .832              |
| Postoperative HFOV                       | 0 (0.0%)                            | 2 (11.8%)                  | .216              |

<sup>a</sup>Statistically significant,  $P < .05$ .

The composite outcome pulmonary complications were defined as postoperative pleural effusion, pneumothorax, atelectasis, and pneumonia. An extubation was considered successful when a neonate did not require reintubation within 7 days of planned extubation. Data are presented as median (interquartile range) or n (%).

HFOV, high-frequency oscillatory ventilation; NICU, neonatal intensive care unit.



Figure 1. Postoperative roentgenogram with pronounced right-sided atelectasis with midline shift in a preterm neonate undergoing surgical patent ductus arteriosus closure by a posterolateral thoracotomy.

perioperative (immediately before and during surgery) and postoperative (up to 1 week) blood transfusion volumes were similar in both groups. However, the duration of intravenous opiate use (as a surrogate outcome measure for pain/discomfort given the strict adherence to our postoperative pain protocol, where opioids are dosed and withdrawn on the basis of COMFORTneo scores) was significantly longer in the median sternotomy approach.

In terms of postoperative mechanical ventilatory requirements, no significant differences in duration to successful extubation or total duration of ventilatory support were observed between both groups (Table 2). Nevertheless, a trend toward lower ventilatory pressures within the first 24 hours postoperatively was noted in neonates undergoing a median sternotomy approach (Figure 2). Only immediately after surgery (0 hours) were the  $\Delta$ MAP values significantly lower. On the other time-points (ie, 12, 24, 48, and 72 hours postoperatively), the difference did not reach statistical significance. The NICU length of stay did not differ significantly between both surgical approaches.

Both the 30-day and overall mortality were similar in the treatment groups (Table 2). In addition, survival

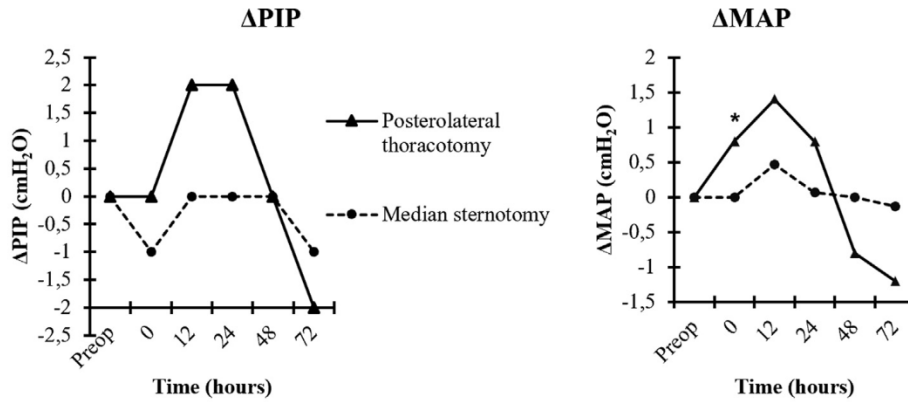


Figure 2. Postoperative ventilatory pressures. Ventilatory pressures were analyzed as change from baseline (denoted as  $\Delta$ PIP [peak inspiratory pressure],  $\Delta$ PEEP [positive end expiratory pressure], and  $\Delta$ MAP [mean airway pressure], respectively). Data are presented as median and interquartile range. An asterisk indicates a P value less than .05. (Preop, preoperative.)

|                                 | 0 hours     | 12 hours    | 24 hours    | 48 hours     | 72 hours     |
|---------------------------------|-------------|-------------|-------------|--------------|--------------|
| <b><math>\Delta</math> PIP</b>  |             |             |             |              |              |
| Posterolateral thoracotomy      | 0 (2)       | 2 (3)       | 2 (3)       | 0 (2)        | -2 (4)       |
| Median sternotomy               | -1 (4)      | 0 (5)       | 0 (5)       | 0 (3)        | -1 (3)       |
| P-value                         | .121        | .146        | .081        | .756         | .526         |
| <b><math>\Delta</math> PEEP</b> |             |             |             |              |              |
| Posterolateral thoracotomy      | 0 (1)       | 0 (1)       | 0 (1)       | 0 (2)        | 0 (2)        |
| Median sternotomy               | 0 (0)       | 0 (0)       | 1 (0)       | 0 (0)        | 0 (0)        |
| P-value                         | .285        | .594        | .433        | .731         | .941         |
| <b><math>\Delta</math> MAP</b>  |             |             |             |              |              |
| Posterolateral thoracotomy      | 0.80 (1.67) | 1.40 (2.20) | 0.80 (1.00) | -0.80 (2.33) | -1.20 (2.50) |
| Median sternotomy               | 0.00 (2.13) | 0.47 (2.00) | 0.07 (1.75) | 0.00 (2.48)  | -0.13 (2.45) |
| P-value                         | .025        | .057        | .087        | .639         | .402         |

analysis with the use of a Kaplan-Meier survival curve indicated no statistically significant differences between both treatment arms (Figure 3). No operative deaths occurred in either group. The leading cause of death was

bronchopulmonary dysplasia with pulmonary hypertension and respiratory insufficiency (n = 6), followed by necrotizing enterocolitis (n = 2) and pneumonia with sepsis (n = 1).

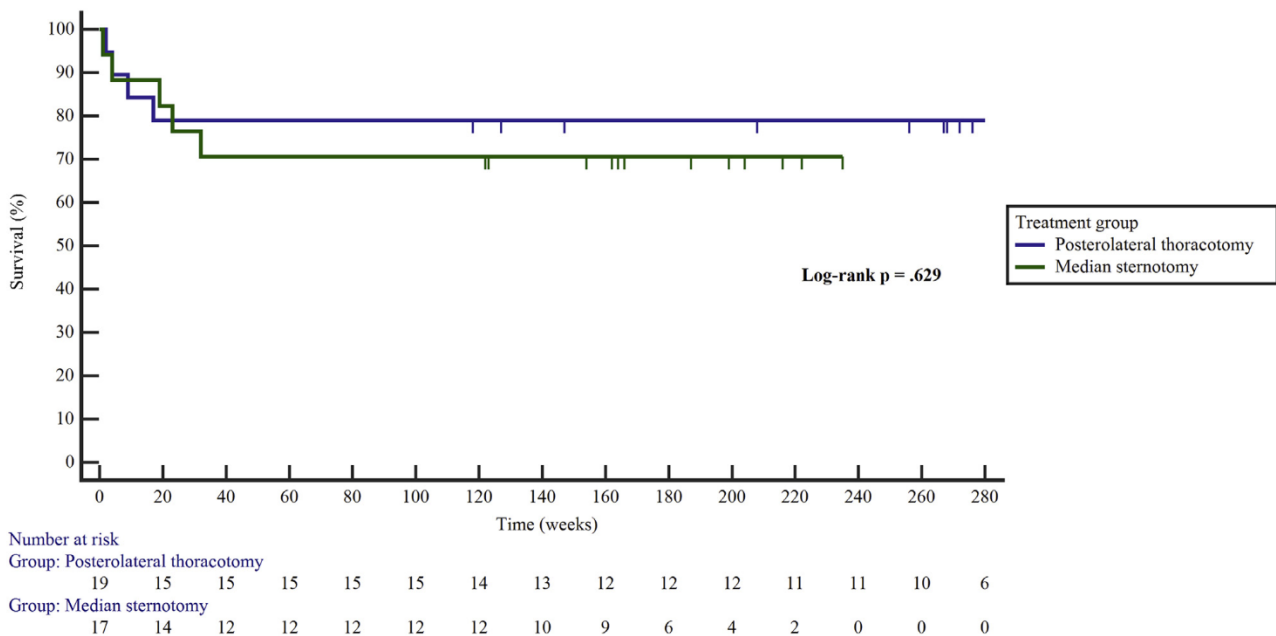


Figure 3. Kaplan-Meier survival analysis.

## Comment

The clinical importance, appropriate indication, and timing of closure of a PDA in preterm neonates remains a matter of ongoing debate. Nevertheless, medical and surgical closure remains an indispensable part of care with surgical closure occurring in approximately 25% of extremely low birth weight infants.<sup>11-13</sup> Evidence about the preferable approach for surgical PDA closure in preterm neonates is absent, and a posterolateral thoracotomy approach is considered to be the gold standard. However, post-thoracotomy lung injury, considerable pain, and potential long-term spinal and chest wall deformities are well recognized and apparently accepted drawbacks of a posterolateral thoracotomy.<sup>14</sup> To circumvent these adverse effects, we adopted a median sternotomy approach instead for surgical closure of PDA in this specific patient population. This report aims to compare for the first time the clinical outcomes between these two surgical approaches for surgical PDA closure in very and extremely preterm neonates.

In this study, we found a significantly lower postoperative pulmonary complication rate in preterm neonates who underwent surgical PDA closure by a median sternotomy approach compared with a posterolateral thoracotomy approach, which is in accordance to our hypothesis. Moreover, preterm neonates undergoing surgical procedure by a median sternotomy required lower ventilatory pressure within the initial postoperative period with significantly lower  $\Delta$ MAP values directly after surgery. The duration of intravenous opiate usage (as a possible surrogate outcome measure for pain/discomfort) was significantly longer in the median sternotomy approach. Well-known complications of surgical PDA closure, including thoracic duct injuries, LVFP, and wound-related complications, were uncommon and did not differ significantly between both surgical approaches. In addition, perioperative and postoperative blood transfusion volumes did not differ between both approaches. Finally, both the 30-day and overall mortality were similar in both groups.

In accordance with our findings, previous research from our hospital has shown that surgical PDA closure using a posterolateral thoracotomy approach results in significantly more asymmetrical bronchopulmonary injury in preterm neonates. This asymmetrical distribution of bronchopulmonary damage, in which the right lung was more seriously affected, is probably due to faster damage to the excessively and fully ventilated right lung in a right lateral decubitus position compared with the relatively protected left lung despite intraoperative handling of this left lung.<sup>15</sup> This rationale may also explain the significantly higher incidence of atelectasis in the posterolateral thoracotomy group, in which the right lung was predominantly affected by atelectasis ( $n = 11$ ; 78.6%). The explanation for the high incidence of pneumothoraces in the posterolateral thoracotomy in particular seems to be twofold. First, a well-known cause for pneumothoraces in preterm neonates is mechanical ventilation with high ventilatory pressures of the fragile

and immature lungs in order to achieve appropriate oxygenation and ventilation.<sup>16,17</sup> The significantly higher  $\Delta$ MAP values directly after surgery in the thoracotomy group may therefore, at least partially, be accounted for the significantly higher degree of pneumothoraces in this treatment group. Moreover, this phenomenon can explain the pneumothoraces seen on both sides in the posterolateral thoracotomy group. Secondly, in some ( $n = 3$ ; 15.8%) preterm neonates in the thoracotomy group, the chest was not routinely drained postoperatively, probably resulting in one pneumothorax in this subgroup.

In the adult population, post-thoracotomy lung injury has been studied more thoroughly, and an increasing body of evidence endorses above-mentioned concepts. Moreover, generation of reactive oxygen species as a result of ventilating with a high fraction of inspired oxygen and pulmonary capillary stress due to increased blood flow can contribute to injury of the excessively and fully ventilated right lung.<sup>18</sup> Therefore, in our opinion, a median sternotomy approach seems to be preferred in these critically ill preterm neonates to prevent (additional) lung injury, because it allows equal ventilation of both lungs and circumvents intraoperative manipulation of the left lung.

Although median sternotomy is generally regarded as a less painful approach, we found a counterintuitive longer duration of intravenous opiate usage in the median sternotomy group. A possible explanation for the counterintuitive, longer duration of intravenous opiate usage in the median sternotomy approach, may be found in the application of an intraoperative intercostal nerve block with long-acting levobupivacaine in the thoracotomy group. Apart from this difference in locoregional pain relief, postoperative pain management was uniform between groups. Postoperative pain management in our level III NICUs is strictly guided by the COMFORTneo scale. This is a well-known and commonly used behavior scale for pain and distress on NICUs in the Netherlands.<sup>19</sup> Our national and local pain protocol dictates the dose and duration for the use of opioids as guided by the COMFORTneo scale, with specific attention to a timely withdrawal given the risk for abstinence syndrome. Since the scores themselves were not always conscientiously recorded in the medical records and the postoperative pain protocol is generally well adhered to, we believe that the duration of opioids is reflecting pain most appropriately.

In contrast to previously reported research with reported incidences of LVFP ranging from 8.8% up to 40%, the incidence of LVFP was relatively low in this study ( $n = 1$ ; 2.8%).<sup>20-22</sup> This low incidence might be attributed to limited awareness of this potential complication of surgical PDA closure in general. However, we regard unawareness unlikely because neonates with persistent postextubation stridor after treatment with dexamethasone underwent flexible fiberoptic laryngoscopy to rule out LVFP. Awareness for LVFP after surgical PDA closure is essential, because LVFP carries significant long-term morbidity with feeding difficulties and the development of reactive airway disease due to chronic microaspiration.<sup>20</sup>

Owing to its retrospective nature and nonrandomized design, our study could be hampered by information and selection bias. Nevertheless, all data were collected in a comprehensive database with the use of established definitions. In addition, a historical difference existed between both treatment groups. In this light, the national Dutch policy change that lowered the limit offering active intensive care from 25<sup>+0</sup> to 24<sup>+0</sup> weeks of GA did not seem to affect our results.<sup>10</sup> Finally, the study sample size was relatively small. Because of its small sample size, potentially clinically relevant differences might not have reached statistical significance. Although a larger number of patients would be convenient to guarantee more indisputable evidence, we are convinced that our study shows interesting short- and mid-term results that acknowledge the lack of large, prospective, and randomized controlled comparisons.

Because surgical PDA closure aims at preventing long-term morbidity (among which bronchopulmonary dysplasia and GMIVH) and mortality, further research with larger sample size, multicenter, randomized controlled trials with long-term clinical follow-up will be necessary to determine whether a median sternotomy approach is associated with favorable long-term results as well. It might be hypothesized that favorable short-term results about pulmonary morbidity and ventilator requirements, as shown in this study, may lead to better (pulmonary) outcomes in the long run. Long-term data will also be needed to identify specific patient populations that would benefit most from a median sternotomy approach for surgical PDA closure. Ideally, a unified treatment algorithm should be developed for the (surgical) management of a PDA in preterm neonates.

In conclusion, we conducted a retrospective observational study to compare the clinical outcomes of surgical PDA closure through either posterolateral thoracotomy or median sternotomy in very and extremely preterm neonates. Our findings show that a median sternotomy approach is at least noninferior to a posterolateral thoracotomy approach for surgical PDA closure. Given the lower postoperative pulmonary complication rate and lower postoperative mean airway pressures needed directly after surgery, the median sternotomy approach may be considered superior for preterm neonates with immature and vulnerable lungs. In fact, these favorable short-term results about pulmonary morbidity and ventilator requirements might lead to better (pulmonary) outcomes in the long run. Therefore, these promising early outcomes warrant further research with long-term randomized controlled trials to determine the definite place of a median sternotomy approach in surgical PDA closure in preterm neonates.

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