INTRAOPERATIVE MACROSCOPIC LUNG APPEARANCE IN PREMATURE INFANTS WITH BODY WEIGHTS LESS THAN 1000 G UNDERGOING SURGICAL TREATMENT FOR PDA

JACEK WIETESKA, MACIEJ A. KAROLCZAK

2nd Department of Cardiac and General Pediatric Surgery, Medical University in Warsaw
Kierownik: prof. dr hab. M. A. Karolczak

The aim of the study was to assess the relationship between intraoperatively observed macroscopic pathologic findings in the left lung and the chosen clinical factors. The factors analyzed in the study were the following: neonatal gestational age and body weight, the age of the neonate at the time of surgery, the history of intrauterine infection and/or presence of active infection in the neonate, the history of ibuprofen treatment, and intraoperative diameter of the arterial duct.

Material and methods. The authors included a group of 126 preterm infants with body weight less than 1000 g undergoing surgical treatment for PDA in the 2nd Department of Cardiac and General Pediatric Surgery between January 2000 and May 2006 and analyzed the macroscopic intraoperative left lung appearance.

The average body weight of the neonates who participated in the study was 765.2 g, with the average gestational age 25.68 Hbd. According to the results of intraoperative macroscopic lung assessment, the neonates were classified into one of the following three groups:

0 – normal lungs or partially stiff lungs with emphysema focuses,
1 – limited macroscopic findings, focuses of limited atelectasis, lung congestion,
2 – severe pathologic findings in the pulmonary tissue, pulmonary hematomas, bleeding pulmonary surface, disseminated atelectasis, liver-like pulmonary tissue.

In the study, the statistical analysis of the relationship between pathological pulmonary findings (groups 0, 1, 2) and investigated factors was performed by the comparison of mean values (or median) of the investigated factor in the analyzed groups. The Kruskal-Wallis and the Mann-Whitney tests were used dependent of the analyzed factor. Additionally, for chosen factors (the infection presence and PDA diameter), their relationship with the lung macroscopic appearance was assessed with the use of the Spearman test.

Results. The pathological findings in the lungs were observed in the majority of the neonates (54%). The statistical analysis did not show any relationship between the pulmonary disorders and the majority of investigated factors.

Conclusions. 1. The authors found that a duct diameter of ≥ 4 mm correlates with the development of more severe disorders in the pulmonary tissue. 2. The authors emphasized the good results of surgical treatment of PDA and the lack of death in the perioperative period in that group of patients.

Key words: PDA, ELBW, thoracotomy, lungs

Patent ductus arteriosus (PDA) is observed in the majority of premature infants with extremely low body weight. The prevalence of PDA is higher with lower gestational age and lower body weight (1, 2). The relationship was demonstrated between the presence of PDA and not only the newborn gestational age but also the coexistence of respiratory distress and the general health condition of the newborn (3, 4). Significant left-to-right shunt through the arterial duct causes lung congestion, which can result in alveolar transudation. It can cause impaired alveolar ventilation, the development of atelectasis/emphysema focuses, and lung...
compliance impairment. Increased pulmonary blood flow results in the elevation of pulmonary resistance, which may lead to pulmonary congestion and the formation of hemorrhagic disorders in the pulmonary tissue.

The aim of the study was to assess the macroscopic lung pathologic findings in newborn infants with body weights less than 1000 g undergoing surgical treatment for PDA and to evaluate the relationship between the severity of these findings and the gestational age, body weight, the age of the newborn at the moment of surgical treatment of PDA, the presence of infection, previous medical treatment, and the diameter of arterial duct.

MATERIAL AND METHODS

Analytic group

126 neonates (67 girls and 59 boys) (proportion 1:1.5) with body weights less than 1000 g undergoing surgical treatment for PDA in our department from January 2000 to March 2006 were analyzed in the study. The gestational ages at the moment of delivery were 22-30 Hbd (average 26.67±1.73). The body weights in the study group were between 500 g and 1000 g (average 765.2 ± 147 g). The surgical treatment of all newborns was performed between the 3rd to 38th days after delivery. The majority of children (96 = 76%) were mechanically ventilated in the intraoperative period.

Qualification to the surgical treatment

The preliminary qualification was performed by pediatricians in individual neonatal centers on the basis of clinical symptoms and echocardiographic findings. The final qualification was done directly before surgery with the use of the following criteria:

1. The presence of a patent ductus arteriosus with the diameter not lower than 1.5 mm.
2. Left-to-right flow through the PDA visible in Doppler echocardiography.
3. Increased to 2 m/s blood flow velocity in the MPA.
4. The presence of diastolic backward flow in the descending aorta.

Surgical intervention

Access to the pleural cavity was achieved with the use of a limited (2-3 cm of length) left postero-lateral thoracotomy through the 3rd or 4th intercostal space. All surgeries were performed by the same operating team. The exact intraoperative assessment of accessible lung, including its pneumatization, consistency, and color, was performed in all cases. Each change in the blood supply, the presence of hematoma, focuses of atelectasis, as well as changes in lung consistency were noticed in the operating protocol. After the arterial duct had been surgically prepared, the measurement of its diameter was performed. Then the duct was closed with 2-0 silk suture. In one case it was closed with surgical vascular clamp because of duct wall damage and bleeding. The arterial blood pressure measurements were performed before and just after surgical ligation. All results were noted in the operating protocol.

RESULTS

According to the intraoperative macroscopic lung assessment all neonates were divided onto three following groups:

Group 0 – normal or partially stiff lungs with emphysema focuses (46%).

Group 1 – limited findings, focuses of limited atelectasis, lung congestion (26%).

Group 2 – severe pathologic findings in the pulmonary tissue, pulmonary hematomas, bleeding pulmonary surface, disseminated atelectasis, liver-like pulmonary tissue (28%).

In all groups the statistical analysis of noted pathological findings in the lungs was performed in correlation with the following factors: gestational age, newborn body weight, and age of the newborn at the time of surgery. The analysis also included the assessment of the relationship between the current lung appearance and the previous treatment with ibuprofen and the duct diameter.

1. Correlation between gestational age and intraoperative lung appearance

To assess the influence of gestational age on lung condition, the mean value of gestational age in the three groups formed on the basis of lung appearance (0, 1, 2) was calculated. No statistically significant differences in gestational age in these three groups (variation analysis, p=0.128005) were found.

2. Relationship between newborn body weight and intraoperative lung appearance

The mean values of body weight in the investigated groups were calculated. They were si-
milar in all groups. No statistically significant differences between mean values of body weight in these three groups (variation analysis, p=0.692031) were found.

3. Relationship between newborn age at the moment of surgery and intraoperative lung appearance

The mean newborn age at the moment of surgery and the median differences were assessed for all groups. The median value in the group with normal lungs was greater than in the other two groups, but the difference was not statistically significant (Kruskal-Wallis test; p=0.8605).

4. Relationship between previous ibuprofen treatment and intraoperative lung appearance

The history of previous ibuprofen treatment was positive in 33 neonates, negative in 86, and unknown in 7. The statistical analysis with the Mann-Whitney method showed no significant statistical differences between lung appearance and previous treatment with ibuprofen (p=0.7018).

5. Relationship between infection and intraoperative lung appearance

46 (39%) of the patients had no history of infection (group A), 36 (30.5%) had a history of previous intrauterine infection (group B), and 36 (30.5%) had an active infection ongoing during surgery (group C). In addition, a history of previous intraterine infection was found in 19 children in the group with active infection. There was no statistically significant relationship between lung appearance and affirmed infection (R=-0.04317; p=0.6425). Similar results were noticed in the analysis of lung appearance in the particular groups formed on the basis of the type of infection (Kruskal-Wallis test; p=0.4046).

After grouping all children with infections into one group, the statistical analysis (Mann-Whitney test) did not show any differences between the patients with and without infections (p=0.9011).

6. Correlation between intraoperative lung appearance and arterial duct diameter

To assess the relationship between intraoperative lung appearance and arterial duct diameter, the mean standard deviation (mean SD) was calculated in the groups with different lung appearances (0, 1, 2). The results are shown in tab. 1.

The analysis with the use of the Kruskal-Wallis test showed no significant statistical differences between the values of mean SD (p=0.2785). The relationship between the lung appearance in the 0-2 scale and the duct diameter assessed by the Spearman test was low (R=0.14; p=0.1103).

The results of the analysis of the two groups formed in accordance with the PDA diameter – group I – PDA diameter less than 4 mm, group II – PDA diameter equal or more than 4 mm.

The results for the three-degree scale of lung appearance are presented in tab. 1.

It is clearly seen that two times more children with stage 2 lung appearance had a duct diameter ≥ 4 mm. The number of children with a lung appearance assessed as stage 1 is similar in the two groups. Almost two times fewer children with normal lungs (stage 0) are in the group with duct diameter ≥ 4 mm.

The statistical analysis with chi² test showed a statistically significant difference between the lung macroscopic appearance and the duct diameter (p=0.0274)

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DISCUSSION

Patent ductus arteriosus is a frequent finding in the cardiovascular system in the newborn children. Premature infants with extremely low body weight are a special group in which the prevalence of patent ductus arteriosus is assessed to be up to 60% (5). The presence of a patent ductus arteriosus causes cardiovascular disturbances. Increased pulmonary blood flow and increased blood return from pulmonary vessels to the left atrium induces increased left ventricle workload and extension of the left atrium allowing for the blood shunt through the foramen ovale. The significant diastolic blood shunt from the aorta to the pulmonary artery disturbs intestinal perfusion (NEC), decreases blood supply to the kidneys, and diminishes blood flow in the central nervous system (intraventricular hemorrhage) (7).

In the accessible literature, the authors mainly assess the results of PDA treatment in relationship to the chosen method of treatment (1, 11). In many studies, the treatment results (efficacy, complications, period of mechanical ventilation, lung compliance) are analyzed in the aspect of neonatal age at the time of treatment (7, 12). In a large group of studies, a comparative analysis of medical treatment with indomethacin or ibuprofen was performed (13). Neonates with body weights less than 1000 g are particularly at risk for the development of complications with pharmacologic therapy and significantly more often are resistant to that treatment method (18, 19). In this group of patients, surgical treatment is recognized as the treatment of choice (14, 15, 17, 18). Cassady, (16) showed good results with surgical treatment and decreasing of the rate of NEC in a group of premature infants with body weights less than 1000 g who were undergoing surgery in the first day of life.

In our study, 86 neonates underwent surgical treatment without previous pharmacological treatment. In 33 neonates the surgical treatment was performed after unsuccessful treatment with ibuprofen. In all cases, surgical closure of the arterial duct was entirely successful and confirmed by echocardiography as the lack of blood flow through the duct.

Increased blood flow into the pulmonary circulation in connection with congenital lung immaturity, surfactant deficiency, and congenital infection in the premature infants can lead to significant impairment of lung function, intensification of the symptoms of respiratory distress syndrome of the newborn, and lengthening of the required time of mechanical ventilation.

The question about the relationship between the chronic lung disorders and the presence of patent ductus arteriosus still needs an answer. One must remember that the risk factors for broncho-pulmonary dysplasia and patent ductus arteriosus can be the same; therefore, it can be difficult to determine the impact of PDA on the development of bronchopulmonary dysplasia (7). There is ambiguous literature with regard to the relationship between the presence of PDA and the functional pulmonary impairment. Krauss did not show any differences in lung compliance in the neonates with patent ductus arteriosus in the 72nd – 96th hour of life. He also did not show any improvement in lung compliance in children after indomethacin treatment (20). An improvement in lung compliance was noticed by Yeh and Stefano (8, 21), and that improvement after surgical ligation was also shown by Gerhardt et Bancalari (22). Naulty (23) demonstrated the improvement in lung compliance in 9 of 11 surgically treated neonates.

In our study, we found macroscopic lung disorders in different stages of severity in 54% of patients during surgery. In the available literature we have not found any study on that topic and any analysis of their correlation with different factors. Three stages of pulmonary tissue appearance, far from completely precise, permitted us to perform the analysis of the relationship between the intensity of the lung disorder and the investigated factors. Despite the fact that intraoperative assessment is a subjective method, its use in a large group of patients by the same surgical team allows it to be legitimate. In our study, we did not find a significant relationship between macroscopic lung appearance and the following factors: gestational age, body weight, or neonate age at the time of surgery. We also did not demonstrate the influence of ibuprofen treatment on the severity of noticed lung disorders. In the conducted analysis, we did not confirm the correlation between the severity of lung findings and previous intrauterine infection or active neonatal infection. The only significant factor is the diameter of the arterial duct. Although we did not find any statistically significant differences with the use of the Kruskal-Wallis test in three groups formed according to macro-
scopic lung appearance, we found differences between the two groups with and without lung disorders. The analysis with the use of the Spearman test showed a low correlation between lung appearance (stages 0-2) and arterial duct diameter (R=0.15239; p=0.08846). In two groups formed accordingly to arterial duct diameter (group I – arterial diameter lower than 4 mm, group II – arterial diameter equal or greater than 4 mm), we found in group II two times more children with more severe lung macroscopic findings. However, the number of children with normal lungs in the group with arterial diameter equal or greater than 4 mm is almost two times lower.

Thus we can postulate that the diameter of the arterial duct is an important factor correlating with the development of the observed disorders in the lungs. This conclusion is in agreement with the results of the study performed by Kluckov, who demonstrated that in echocardiography the presence of PDA with a diameter greater than 1.5 mm in first 30 hours of life is the most essential factor of predicting a persisting patent arterial duct (10). We think that besides the factors analyzed in our study which influence the development of lung disorders, there are many other ones, including lung maturity, genetics, immunological maturity, treatment with surfactant, and type and time of mechanical ventilation. Subsequent long-term assessment of the treatment results and the analysis of the relationship between intraoperatively observed macroscopic lung findings and the other parameters of lung function, including the time of mechanical ventilation, oxygen requirements, and stay in the intensive care unit are necessary. The long-term analysis of that group of patients will allow the relationship between intraoperatively found macroscopic lung disorders and the development of late pulmonary complications, including broncho-pulmonary dysplasia, to be defined. The results of surgical treatment of patent ductus arteriosus in premature infants with body weights lower than 1000 g are very successful.

**CONCLUSIONS**

1. The macroscopic pathological findings in lung appearance were found in 54% of surgically treated newborns.
2. It is not possible to demonstrate a correlation between these changes and the majority of factors assessed in our study.
3. An arterial duct with a diameter greater than 4 mm correlates with the development of more severe disorders in the lungs.
4. The study group requires subsequent long-term analysis of the treatment results.
5. The results of surgical treatment of PDA in the group of premature infants under 1000 g are successful with no perioperative mortality.

**REFERENCES**