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Results of diaphragm agenesis repair

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Aim: assessment of short-term outcomes in children after diaphragmatic agenesis repair and selection of the optimal method for defect repair.
Materials and methods. This study involved 10 newborns with congenital diaphragmatic hernia (type D) who underwent surgery in one hospital between 2000 and 2023, followed by an assessment of complications, mortality, and the effectiveness of the thoracalization concept of the abdominal cavity.
Results. There were 6 (60%) male patients and 4 (40%) female patients. Right-sided diaphragmatic dome agenesis was diagnosed in 2 (20%) children and left-sided in 8 (80%). Early total mortality in this group was 60%. The surgical approach for treatment was thoracotomy in 80% (n=8) of cases, and in 2 (20%) cases transverse subcostal laparotomy was chosen. All diaphragmatic agenesis repairs were performed using patches (mostly made of polytetrafluoroethylene), with 8 of them applying the principle of thoracalization of the abdominal cavity. Indications for reoperations in our group included hernia recurrence – 2 cases (in one patient at 6 and 15 months) and intestinal obstruction caused by malrotation – 1 case.
Conclusions. Patients with diaphragmatic agenesis have higher mortality compared to the group with small and medium defects. The size of the diaphragmatic defect is an independent prognostic factor and may serve as a marker for the degree of pulmonary hypoplasia and pulmonary hypertension. The optimal method of surgical treatment is diaphragmatic repair using a synthetic polytetrafluoroethylene patch with thoracalization of the abdominal cavity.
The study was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethical Committee of these institutions. The informed consent of the children's parents was obtained for the research.
No conflict of interests was declared by the authors.
Keywords: congenital diaphragmatic hernia, diaphragm agenesis, recurrence, thoracalization, polytetrafluoroethylene.

Результати корекції агенезії діафрагми

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Мета: оцінка короткострокових результатів у дітей після хірургічної корекції агенезії діафрагми та вибір оптимального методу для корекції дефекту.
Матеріали та методи. У дослідженні взяло участь 10 новонароджених із вродженою діафрагмальною грижею (тип D), які пройшли хірургічне лікування в одній лікарні в період з 2000 по 2023 рік, з подальшою оцінкою ускладнень, летальності та ефективності концепції торакалізації черевної порожнини.
Результати. Хлопчиків-пацієнтів було 6 (60%), дівчат – 4 (40%). Агенезія правого купола діафрагми була діагностована у 2 (20%) пацієнтів, лівого – у 8 (80%). Рання загальна смертність у цій групі становила 60%. Хірургічна корекція здебільшого виконувалась через торакотомію у 80% (n=8) випадків, а у 2 (20%) випадках використовувалася поперечна підреберна лапаротомія. Всі операції з корекції агенезії діафрагми виконувалися із застосуванням латок (переважно з політетрафторетилену), причому у 8 випадках застосовувався принцип торакалізації черевної порожнини. Показаннями до повторних операцій у нашій групі були рецидив грижі – 2 випадки (в одного пацієнта на 6-му та 15-му місяцях) і кишкова непрохідність, спричинена мальротацією – 1 випадок.
Висновки. Пацієнти з агенезією діафрагми мають вищу смертність порівняно з групою із малими та середніми дефектами. Розмір дефекту діафрагми є незалежним прогностичним фактором і може слугувати маркером ступеня гіпоплазії легень та легеневої гіпертензії. Оптимальним методом хірургічного лікування є відновлення діафрагми із застосуванням синтетичної латки з політетрафторетиленом та торакалізації черевної порожнини.
Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження затверджено Локальним етичним комітетом цих закладів. Батьки дітей надали інформовану згоду на участь у дослідженні.
Автори заявляють про відсутність конфлікту інтересів.
Ключові слова: вроджена діафрагмальна грижа, агенезія діафрагми, рецидив, торакалізація, політетрафторетилен.

Introduction

Congenital diaphragmatic hernia (CDH), despite significant advances in prenatal diagnostics and intensive care, remains one of the leading causes of mortality and high morbidity in newborns [6,7]. Over the past 20 years, there has been a positive trend in the survival of children with corrected CDH; however, the mortality rate, depending on the hospital, remains quite high, ranging from 20% to 40% [20]. For comparison, in the 1980s, the mortality rate was approximately 50% [16,17].

Since the 1990s, there has been an increase in the use of advanced treatment methods such as fetoscopic endoluminal tracheal occlusion (FETO), extracorporeal membrane oxygenation (ECMO), high-frequency oscillatory ventilation and inhaled

nitric oxide for the management of CDH. The use of these techniques not only stabilized the condition of children with CDH during the preoperative period but also supported them postoperatively, thereby increasing the survival rate. However, not all authors agree with this assertion as some of the aforementioned methods have a traumatic effect and lack reliable evidence of benefit [21,23,28].

The survival rate of children with large defects, especially with agenesis (type D), is significantly lower, at 40–60%, compared to the group of patients with smaller defects. Additionally, in this group, there is a significantly higher percentage of recurrences and complications associated with CDH, which remains a challenge at present [5,9,25].

The aim of the study is an assessment of short-term outcomes in children after diaphragmatic agenesis repair and the selection of the optimal method for defect repair.

Materials and methods of the study

A retrospective analysis of surgical repair of CDH was conducted in 120 children from the high-risk group, who were treated at the National Children's Hospital «OHMATDYT» between 2000 and 2023. Preoperative preparation and subsequent treatment in the intensive care unit involved the use of a ventilation strategy (allowing hypercapnia, hyperoxia, hyperventilation), surfactant administration, intravenous vasodilators, neuromuscular blockade, and sedation.

According to the conducted analysis, 10 newborns diagnosed with diaphragmatic agenesis were included in the subsequent study. The type of the diaphragmatic defect was determined by the surgeon during the operation and was coded as «agenesis» or type D if the entire half of the diaphragm or a significant portion of it was absent (with a narrow short muscular rim mostly in the cartilaginous part of the ribs) and repair required fixation of the patch between the ribs from the front and back. Surgical repair of CDH was performed through a thoracic approach. The operation involved reducing the organs into the abdominal cavity and a repair of the diaphragmatic defect with the formation of a neo-dome without tension, which was achieved by closing it with a patch (tutoplast pericardium + polypropylene mesh, medical polytetrafluoroethylene (PTFE)) with thoracalization of the abdominal cavity.

Further patient assessment included assessment of physical development, and conducting X-rays to determine the presence of recurrence or other associated anomalies.

Results of the study

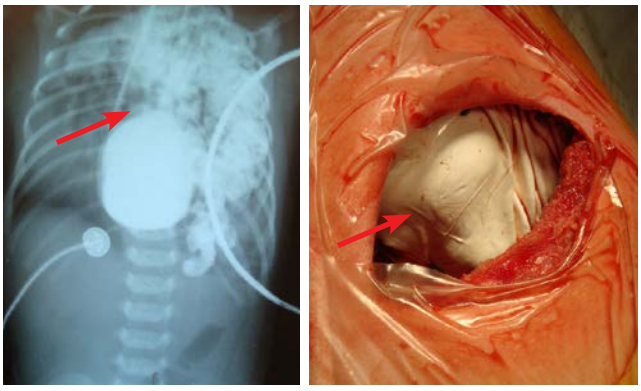
There were 120 children with CDH operated in our hospital within the period from 2000 to 2023. Among them, left-sided CDH predominated, accounting for 80.8% (n=97), while right-sided CDH accounted for 16.7% (n=20) and 2.5% (n=3) were bilateral. In cases of left-sided CDH, 23 patients died in the postoperative period (mortality rate of 23.7%) while in cases of right-sided CDH, 12 patients died (mortality rate of 60%). The overall early postoperative mortality in this group (excluding type D) was 27.2%.

Agenesis of the diaphragmatic dome (type D) was diagnosed in 10 (8,1%) patients. There were 6 (60%) male patients and 4 (40%) female patients. Right-sided agenesis was diagnosed in 2 (20%) children, while left-sided agenesis was found in 8 (80%) children. The average birth weight of the infants was 3063.3±393 g (ranging from 1780 g to 4800 g). There were no children with very low or extremely low birth weights.

Surgical management was primarily conducted through thoracotomy in the majority of cases, accounting for 80% (n=8), while in 2 (20%) cases a transverse subcostal laparotomy was chosen. All repairs of diaphragmatic agenesis were performed using the following patches: Gor-Tex (n=1), Tutoplast pericardium (n=1), Tutoplast pericardium + polypropylene mesh in a 'sandwich' configuration (n=1), and PTFE (n=7).

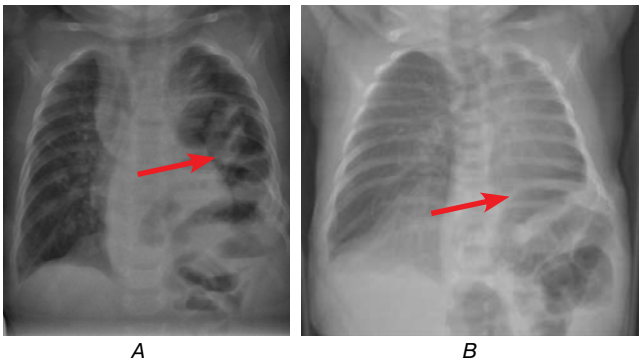
Despite the advancement in surgical techniques, a certain percentage of patients still require reoperations, especially in the group with diaphragmatic agenesis. Indications for reoperations in our cohort were found in 2 patients and included hernia recurrence 2 episodes in one patient at the age of 6 and 15 months) and intestinal obstruction caused by malrotation in another patient.

The repair of the diaphragmatic agenesis in 8 patients was performed using the thoracalization concept of the abdominal cavity. This involved thoracotomy access, closing the diaphragmatic defect with a synthetic patch and segmental cephalad translocation of the neo-dome, thereby increasing the volume of the abdominal cavity and decreasing the volume of the semi-empty pleural cavity. This results in the prevention of barotrauma injury of hypoplastic ipsilateral lung, prevention of abdominal



A B

Fig. 1. Chest and abdominal X-ray with gastrography of *patient G.:* A – 1 day old with agenesis of the left diaphragmatic dome. Contrasted loops of the intestine and stomach are located in the left hemithorax, the left diaphragmatic dome is not visualized and there is mediastinal shift to the right; B – a neo-dome formed using a PTFE patch (intraoperative photo)



A B

Fig. 2. X-ray of *patient G.*, 6 months old: A – recurrence of left-sided diaphragmatic hernia with bowel loops in the left hemithorax; B – X-ray taken on the 5th day after the surgery showing hypoplastic left lung with a neo-dome formed using thoracalization of the abdominal cavity principle

compartment syndrome, and no need for ventral hernia formation, reducing not only the degree of intraoperative trauma but also the risk of additional surgical interventions.

Early postoperative mortality in cases of agenesis of the right diaphragm dome was 50% (n=1), while in cases of left-sided agenesis 5 (62.5%) patients died. The overall mortality rate in this group is 60%.

We describe the short-term results of clinical observations after diaphragm agenesis repair in 2 newborn patients.

Clinical case 1

Boy G., was born from I pregnancy by cesarean section at 38 weeks of gestation with a birth weight of 2520 grams. Apgar score was 7/7 scores. Prenatally, the diagnosis was not established. The postnatal condition was severe due to respiratory distress, resulting in intubation and mechanical ventilation. According to clinical and radiological data, the diagnosis of left-sided CDH was established. The child was transferred to our hospital for surgical treatment 12 hours after birth.

According to X-ray data, the left hemithorax contains the stomach, colon, intestinal loops, and the left lobe of the liver (Fig. 1A). Preoperative stabilization was carried out using a ventilator, preductal O_2 saturation was 95–99% at a FiO_2 of 65%.

On the second day of life, the infant underwent surgery for left-sided CDH. The surgical approach involved anterolateral thoracotomy at the level of the eighth intercostal space. The left lung was hypoplastic, consisting of two lobes measuring 2.5×3.5 cm. The left hemithorax contained both small and large intestines, the left lobe of the liver, stomach, and spleen. After stepwise reduction of the organs into the abdominal cavity, agenesis of the left diaphragmatic dome with a narrow muscular rim on the anterior surface was identified. The defect was repaired using a synthetic patch of PTFE measuring 8×7 cm forming a neo-dome and thoracalization of the abdominal cavity was performed (Fig. 1B).

In the postoperative period, the child's condition remained severe due to respiratory distress, although the patient's hemodynamics did not require support. The child was on conventional mechanical ventilation, and by the second postoperative day, the oxygen concentration was successfully reduced from 100% to 42% with pre- and post-ductal saturations ranging from 91% to 95%.

Subsequently, the child's condition gradually improved. Enteral nutrition was initiated on the 5th postoperative day with a gradual transition to age-appropriate volume. The child was extubated on the 22nd postoperative day and transferred to the newborn department for further care. The child was discharged from the hospital on the 39th postoperative day with slight asymmetry of the left half of the chest during breathing.

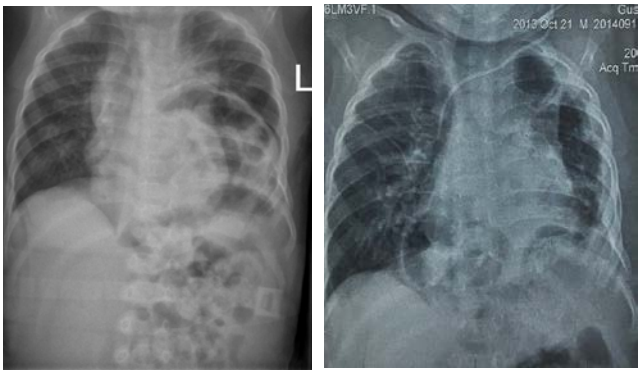
At the follow-up examination six months later, based on the radiological findings, the child was diagnosed with a recurrence of diaphragmatic hernia (Fig. 2A). During the surgery, there was a defect measuring 3×2 cm in the costovertebral area with a transverse colon and bowel loops present in the left hemithorax. The defect was repaired using an aortic valve (Dacron) with suturing to the prevertebral fascia and the PTFE patch in the posterolateral sector (Fig. 2B).

The patient was extubated on the second postoperative day and discharged from the hospital after 10 days.

The child subsequently developed according to age and at the follow-up examination one year and three months after the initial surgery based on radiological findings, a recurrent diaphragmatic hernia was detected. However, the child remained active, with no signs of respiratory distress (Fig. 3A).

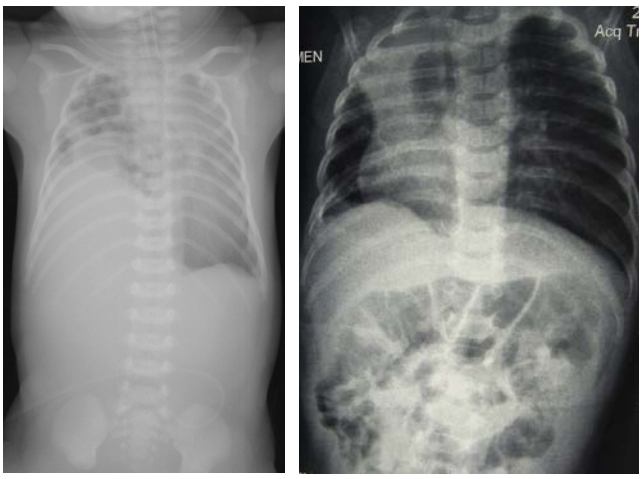
Intraoperatively, a defect (detachment of the patch) was found in the region of the mediastinal organs (esophagus, aorta) and the costovertebral angle. Considering the complexity of the anatomical zone and the absence of a muscular rim on the posterior aspect, it was decided to close the defect using a pedicled autopericardial flap (Fig. 3B). The child was extubated on the first postoperative day and discharged from the hospital on 14th postoperative day.

Throughout the 5-year follow-up period, the physical and intellectual development of the child corresponded to age-appropriate parameters, and no pathology of the respiratory system organs was detected.



A *B*

Fig. 3. X-ray of *patient G.*, 1 year and 3 months old: A – recurrent left-sided diaphragmatic hernia; B – follow-up X-ray taken on the 5th day after the surgery showing hypoplastic left lung with a neo-dome formed using thoracalization of the abdominal cavity principle



A *B*

Fig. 4. X-ray of the chest and abdomen of *patient C.*, 1 day old with right-sided CDH: A – the right diaphragmatic dome is not visualized and the mediastinum is shifted to the left; B – X-ray taken on the 4th day after the surgery showing the right lung is significantly hypoplastic and the mediastinum is now shifted to the center, a new dome on the right is segmentally higher

Clinical case 2

Boy C., was born from the II pregnancy by cesarean section at 37 weeks of gestation with a birth weight of 3260 grams. Apgar score was 5/7 scores. The diagnosis of the right-sided CDH was established prenatally at 36 weeks. He was intubated in the delivery room and after stabilization transferred to our center.

The diagnosis of right-sided CDH was confirmed by chest radiography (Fig. 4A). On the second day of life, surgical treatment of the CDH was performed. The approach involved a right-sided thoracotomy at the seventh intercostal space. The right hemithorax contained the right lobe of the liver, small intestine, and right segment of the colon. Upon revision, the right diaphragmatic dome was absent. Only a narrow muscular rim up to 4 cm in length was present along the anterior-medial surface. After the reduction of the organs into the abdominal cavity, repair of the diaphragmatic agenesis was performed using a PTFE patch measuring 8×8 cm to form a tension-free neodiaphragm (Fig. 4B).

The postoperative management was severe, accompanied by respiratory failure against the background of pulmonary hypertension, requiring high-frequency mechanical ventilation, as well as the use of dopamine and dobutamine to compensate for hemodynamics.

On the 15th postoperative day, the child underwent a re-preoperation due to intestinal obstruction. Adhesiolysis was performed to correct the malrotation. Subsequently, the postoperative period proceeded without complications. The child was extubated on the 30th postoperative day and discharged on the 45th day. The further development of the child was within normal physiological parameters.

Follow-up investigation within five postoperative years demonstrated an increase in the volume of the hypoplastic right lung with gradual normalization of the position of the mediastinum.

Follow-up observation of both children over a period of 7 years demonstrates normal physical and intellectual development.

Discussion

CDH remains a significant cause of neonatal mortality despite numerous advancements in intensive care. However, the application of modern therapeutic approaches has led to some improvement in these outcomes [3,10]. These approaches include ECMO, exogenous surfactant, inhaled nitric oxide (iNO), and high-frequency ventilation. Nonetheless, according to some authors, certain methods may lack proven benefits and could even be detrimental, potentially worsening survival rates or proving ineffective [6,13,22].

One of the key factors determining the survival of patients with congenital diaphragmatic hernia (CDH) is the degree of lung hypoplasia and pulmonary hypertension. However, the methods for preoperative assessment of lung hypoplasia often lack consistent effectiveness. Many hospitals use criteria such as preductal arterial PaO_2 or $PaCO_2$ levels, as a significant number of neonates who fail to achieve certain thresholds do not survive [4,12]. Other approaches include assessments based on prenatal diagnostics, birth weight, Apgar scores, and associated anomalies. Although these parameters are not specific predictors for CDH, they significantly influence morbidity and long-term survival outcomes [8,25]. In our hospital, we focus on achieving the operative treatment standards recommended by the CDH EURO Consortium, emphasizing preoperative stabilization of respiratory and cardiovascular systems, which has contributed to improved treatment outcomes for patients with CDH [24].

Assessing the potential size of the diaphragmatic defect is equally critical, as our study, along with others, confirms a correlation between defect size and survival rates. Patients with diaphragmatic agenesis exhibit higher mortality compared to those with small or moderate defects [2,5].

We classified the size of the diaphragmatic defect as «agenesis» or type D (according to the CDH Study Group classification) if the entire hemidiaphragm or a significant portion of it (over 90%) was absent, leaving only a narrow, short muscular rim, primarily in the costal cartilage region. This condition necessitated securing the patch to the ribs both anteriorly and posteriorly [11].

Mortality associated with CDH in cases of diaphragmatic agenesis (type D) is significantly higher compared to smaller defects. According to the data from the international CDH Study Group, the survival to discharge of patients with diaphragmatic agenesis was 54%, compared to 89% for those without agenesis ($P<0.001$). In our hospital, the mortality rate among patients with diaphragmatic agenesis was 60%, aligning with the reported international figures [18,19].

The diaphragmatic agenesis repair typically requires the use of a large patch to create a tension-free neodiaphragm and effectively reposition the abdominal contents into the abdominal cavity, considering the viscero-peritoneal disproportion. A critical aspect is the secure fixation of the patch to the ribs along its perimeter to ensure stability. Despite advancements in surgical techniques, a certain percentage of patients, particularly those with diaphragmatic agenesis, require reoperations. According to the literature, the recurrence rate in this group ranges from 30% to 80% [6,15,26,27]. In our study, three reoperations (30%) were performed in the subgroup of patients with diaphragmatic agenesis: one patient with left-sided CDH experienced two hernia recurrences (at 6 and 15 months after the initial surgery), and another patient with right-sided CDH developed intestinal obstruction due to malrotation.

We developed the thoracalization concept of the abdominal cavity for the surgical repair of large CDH defects, which offers significant pathophysiological advantages and is performed via a thoracotomy approach. This approach allows to increase abdominal cavity volume by utilizing the semi-empty pleural space, creating favorable conditions for the proper repositioning of organs herniated into the thoracic cavity. The formation of a dome-shaped neodiaphragm reduces the empty volume of the hemithorax, stabilizes the mediastinum, and lowers the risk of barotrauma to the hypoplastic lung. Additionally, the increased abdominal cavity volume helps prevent abdominal compartment syndrome, which is a critical factor in postoperative recovery [14,15].

Patients with hemidiaphragm agenesis exhibit high mortality rates and frequent surgical complications, including CDH recurrence, gastroesophageal reflux, ventral hernia formation, and intestinal obstruction. Long-term risks include repeated recurrences, pectus excavatum, and scoliosis, attributed

to the inability of synthetic patches to adapt to the child's growth, thereby exerting additional tension on the chest wall at fixation points [1,26,27]. These patients require prolonged follow-up and thorough evaluation of postoperative outcomes.

Conclusions

1. Patients with diaphragmatic agenesis have higher mortality compared to those with small to moderate defects. The size of the diaphragmatic defect is an independent prognostic factor and may serve as a marker for the degree of pulmonary hypoplasia, pulmonary hypertension and viscero-abdominal disproportion.

2. The optimal surgical management of CDH with large defect or diaphragm agenesis involves diaphragm repair using an oversized synthetic patch to form a neo-dome of diaphragm based on the concept of thoracolization of the abdominal cavity.

3. Further efforts should focus on accurate determining of the defect size prior to surgery, ideally prenatally, to precisely assess the relationship between the diaphragmatic defect and actual lung hypoplasia.

No conflict of interests was declared by the authors.

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