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"Immortalis est ingenii memoria" Seneca



Natalia Gheorghiu - Pioneer of Pediatric Surgery in Moldova

## SURGICAL TREATMENT OF THE ACHALASIA IN CHILDREN. SINGLE CENTER EXPERIENCE

## Razumovsky A.Yu., Mitupov Z.B., Alkhasov A. B., Bataev S.M., StepanenkoN.S., Zadvernuk A.S., Chubko D.I, Petrov A.P, Ignatiev R.O.

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## ABSTRACT

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**Purpose:** Achalasia of the esophagus is a rare disorder in children; its symptom can mimic common childhood illnesses. In this study, the tactics of managing children with the corresponding pathology and evaluating the effectiveness of ongoing surgical treatment at the Filatov Children Hospital are considered.

**Materials:** From 1991 to 2016, in the Filatov Children Hospitalwas treated 39 patients with achalasia. Since 2011, all patients (27 cases) have undergone laparoscopic Hellercardiomyotomy with Dorfundoplication. The average age was 9.9 (4-15) years. The most frequent symptoms were vomiting (81%) and dysphagia (70%). Weight loss was observed in 48.1% of patients and chronic cough in 25%.

**Results:** All children underwent laparoscopic Hellercardiomyotomy with Dorfundoplication. Intraoperative complication - damage to the mucosa of the esophagus occurred during cardiomyotomy in 2 cases (7.4%), which were cured during the laparoscopic procedure. There were no open procedures. Six (22.2%) required repeated intervention: pneumatic dilations (n = 2), balloon dilatation (n = 2) and re-surgery (n = 2).

**Conclusion:** In our study, laparoscopic Hellercardiomyotomy in the case of achalasia of the esophagus is effective in 77.8% of children. We recommend this operation with Dorfundoplication, and believe that it is the operation of choice in the treatment of achalasia in children.

Key words: Achalasia; cardiomyotomy; fundoplication; complication

## INTRODUCTION

Idiopathic achalasia is a rare primary disorder of esophageal motility with a morbidity rate of 1 per 100,000 people. Achalasia is characterized by a lack of peristalsis of the esophagus of the body and a violation of relaxation of the lower esophageal sphincter (LES) due to the progressive destruction and degeneration of neurons in the muscle plexus. Unfortunately, the cause of neuronal degeneration is still unknown [3]. The aperistals and the dislaxation of LES subsequently lead to the retention of food and saliva in the esophagus, leading to typical symptoms of achalasia, namely, dysphagia, chest pain, regurgitation of undigested food, and weight loss.

Traditionally, the most commonly used treatment options are endoscopic pneumodilation and Heller's laparoscopic myotomy. Although pneumodi-lation is characterized by relapses and the need for re-treatment, Heller's myotomy is considered to be a more effective therapy for a long time. However, a small proportion of patients suffer from persistent or recurring symptoms after surgery. This study is aimed at assessing the effectiveness of Geller's cardiomyo-tomy with Douro fundoplication as a treatment for patients with achalasia.

## **MATERIALS AND METHODS**

In the period from 1991 to 2016, 39 patients with achalasia were treated in the N. Filatov Children's Hospital. Since 2011, all patients (27 cases) have undergone laparoscopic cardiomyotomy according to Geller with fundoplication according to the Dor. The average age was 9.9 (4-15) years. The average body mass index (BMI) is 16.9 kg/m2; with a minimum value of 11.4 kg/m2, with a maximum value of 30.4 kg/m2. Table 1 presents the clinical manifestations of the disease in our patients:

As can be seen from the table, the leading manifestations of the disease were vomiting and dysphagia in eating, which were present in almost all children with esophagus achalasia. In the over-whelming majority of observations (74%), children and parents noted the need to take a sip of water while eating. The lag in physical development and weight loss, which is the result of violations of nutritional status, was present in all children, but the degree of its severity was not the same. In 7 cases, there were respiratory manifestations of the disease in the form of a cough arising at night as a result of chronic regurgitation.

All patients underwent a comprehensive examination, including a general clinical examination, radiography of the abdominal cavity organs, fluoroscopy of the esophagus with contrast material, esophagus fibroscopy, and ultrasound examination of the abdominal cavity organs and, in some cases, computed tomography.

Clinical symptoms	Number of patients	%
Vomitting	22	81,5
Disphagia	19	70
Need to take a sip of water while eating	20	74
Pain on swallowing	8	30
Grade 3 hypotrophy	2	7
Grade 2 hypotrophy	7	26
Grade 1 hypotrophy	4	15
Night Cough	7	25

Table 1. Clinical manifestations of the disease

A characteristic radiographic evidence of achalasia of the esophagus is the absence of a gastric gas bubble in the survey radiography of the abdominal cavity (fig. 1). The leading diagnostic method is fluoroscopy of the esophagus with contrast material, which we carry out with barium sulfate, in an upright position. Depending on the age, the volume of the low-density barium suspension is between 50 and 200 ml. The study reveals a more or less pronounced expansion of the esophagus, a delay in the barium suspension above the cardia, in some cases a prolonged, and characteristic narrowing of the cardia in the form of a gradually tapering outline – «beak bird» (fig. 2).

The first portion of the contrast medium enters the stomach in a thin stream, and then the contrast medium enters the stomach after a delay. A significant expansion of the esophagus, as a rule, is not detected in children [2].

Esophagofibroscopy reveals the expansion of the esophagus, esophagitis. With a slight increase in the esophagus, its pronounced transverse folding, an abundance of mucus, and the remains of food eaten the day before are found. Cardia has the shape of an outlet or funnel. With a significant expansion of the esophagus and its deformation, it is sometimes difficult to find a cardia, but it is freely passable for an esophagoscope.



Fig. 1. The survey radiography of the abdominal cavity.



Fig. 2. X-ray examination of the esophagus with barium sulfate.

Ultrasound diagnostics (fig. 3) and computed tomography (fig. 4) are performed in order to exclude volumetric formations of the thoracic and abdominal cavities, which can lead to violation of the esophageal patency.

All children underwent laparoscopic cardio-myotomy for Geller with gastropexy.

Technique of operation: the patient is lying on his back under general anesthesia, and the surgeon stands between the patient's legs. Pneumoperitoneum is maintained at a pressure of 10-14 mm Hg. Five trocars are introduced into the abdominal cavity (fig. 5). In this case, depending on the age and weight of the patient, we use trocar with a diameter of 3, 3.5 and 5 mm.



Fig. 3. Ultrasonic picture of achalasia of the esophagus



Fig. 4. Computer tomography of achalasia of the esophagus.

The first trocar introduced method of open laparoscopy through the umbilicus. Through this trocar into the abdominal cavity insufflated CO2 (pressure 10-14 mm Hg). In the same trocar, we introduce a telescope with an angular optics of 30° (4-5 mm). After superimposition of carboxypeperito-neum and revision of the abdominal cavity, we introduce four additional trocar for endoinstrument, with a diameter of 3 or 3.5 mm. After examining the abdominal cavity, we lower the stomach and abdominal section of the esophagus into the abdominal cavity. We perform a partial mobilization of the lower part of the stomach to the left of the esophagus. Further, we dissect the peritoneum above the esophagus by means of mono- or bipolar coagulation and we mobilize the abdominal esophagus.

After mobilization of the stomach and abdominal esophagus, it is necessary to note the myotomy line by a hook of monopolar coagulation. After this, we conduct an out-of-plane cardiomyo-tomy with simultaneous traction in the transverse direction by two instruments. The myotomy line should be formed approximately 4 cm above and 2 cm below the esophageal-gastric junction. The mucous membrane of the esophagus is excreted on the 1/2 circumference of the esophagus. Then we pass to gastropexy. The lower part of the stomach is attached alternately to both edges of the cutting line with separate nodal seams (Ethibond 3/0).

Recently, in order to eliminate the inconsistency of the joints and eliminate tension in the gastropexia region, we perform mobilization of the stomach bottom with the intersection of the short arteries of the stomach.





Fig. 5. A - Laparoscopy cardiomiotomy (location of trocars): 1 - trocar is installed through the navel (telescope), 2 - trocar in the right hypochondrium, 3 - trocar under the xiphoid process, 4 - trocar in the left hypochondrium, 5 - trocar in the left iliac region. B - Laparoscopic cardiomyotomy, gastropexy (endophotography.)

#### RESULTS

All patients are discharged home in a satisfactory condition. Cases of conversion was not. The average operation time is 75 minutes. The average stay in the hospital was 6 days. The average postoperative day for which they started to drink - 1, take food - 2. The intraoperative complication - damage to the mucous membrane of the esophagus occurred during myotomy in 2 cases (7.4%). Defect of the mucosa is sewn by separate sutures (Ethibond 3/0). Sealing of the seams of the esophagus mucosa after suturing is verified by injecting air through the gastric tube.

Six children (22.2%) required repeated intervention: pneumodilatation (n = 2), balloon dilatation (n = 2) and repeated surgery (n = 2).

Cases of relapse, apparently, are associated with insufficient mobilization of the muscular layer in cardiomyotomy, the presence of a cicatricial process in the field of cardia, and deformation of the stomach after surgery.

## DISCUSSION

Based on a comparative analysis of the longterm results, 431 cardiodilations and 468 esophago-cardiomyotomies at the Mayo clinic showed excellent and good results in 65% and 85% of patients, respectively. Unsatisfactory results after conservative treatment were observed 3 times more often, 19% and 6%, respectively [17]. Some authors believe that cardiodilation justifies itself in 50% of cases [6].

The main drawback of cardiomyotomy is the occurrence of gastroesophageal reflux. In the long term after the operation of Geller, the incidence of gastroesophageal reflux is 52%, reflux esophagitis 17%, hernia of the esophageal aperture 9%. [11]. In patients with high acidity of gastric juice, this leads to reflux esophagitis and the formation of esophageal stenosis. All this served as an excuse for supplementing Geller's operation with antireflux operations such as Nissen's fundoplication [4], Toupet [21], Belsey [12], Dor [13]. Some authors, in the case of achalasia, prefer Dor fundoplication in laparoscopic Geller's cardiomyotomy [16, 18, 20]. While other authors prefer fundoplication by Toupet. So, A. Kilic and co-authors in 93% of cases performed fundoplication, of which 75% by Toupet, 16% by Dor and 1% by Belsey. C. Smith gives a series of observations of 209 patients who performed gastric dysfunction in Toupet in 86.6% of cases, and in 12% of cases according to the Dor and, correspondingly, 1.4% of operations without fundoplication [10, 19].

In order to reduce the number of repeated interventions due to the recurrence of achalasia of the esophagus after laparoscopic cardiomyotomy, Jafri M. and co-authors suggest performing intraoperative manometry to determine the adequacy of myotomy [9]. For the first time, data on the use of intraoperative manometry belong to Hill L., who published the results of transthoracic cardiomyotomy. In 94% of cases, a good result was obtained [7, 8]. In the largest series of observations (139 patients) of laparoscopic cardiomyotomy using intraoperative manometry, the case of relapse of pressure in the NPS was observed in 1 patient and symptoms of

dysphagia in 7% of cases [5]. Interesting data lead C. Smith and co-authors, who analyzed the results of treatment of 209 patients with esophagus achalasia. In the first group (154 patients), various conservative methods of treatment were used before cardiomyotomy: balloon cardiomyelitis, injections of botulinum toxin, and subsequently both methods. In this group, the level of mucosal perforations during cardiomyotomy was 9.7%, whereas in patients who did not use conservative methods of treatment (the second group), this indicator was 3.6%. Late postoperative complications in the form of severe dysphagia and complications from the lungs in the first group occurred twice as often. Also, the authors cite data on insufficient myotomy, which is manifested by severe symptoms of the disease after surgery. In the first group, additional procedures were required in 19.5% of cases, including repeated myotomy and esophagology, and in the second group in 10.1% of cases. Given these data, the authors recommend that conservative treatment methods should not be performed for those patients who are scheduled for cardiomyotomy [19].

Endoscopic treatments for achalasia - the apparent absence of POEM in the pediatric population. It has the combined advantages of endoscopic procedure with long-term effectiveness of surgical myotomy. Until 2015, a study conducted by Caldaro et al. Was conducted only in adults with proven safety and efficacy [1]. The findings showed that he had a shorter surgery time, lower complication rates, faster feeding time, a longer myotomy, and a faster discharge [8]. A single-centered experience of 26 patients with an age interval of 6 - 17 years demonstrated successful treatment for 2 years C 20% development of reflux [2]. Given recent acquaintance with children, there may be a need to move to standard treatment, when even more experienced endoscopists will be available and trained to provide comparable or improved results for achalasia [19].

## CONCLUSION

As the literature data and own observations show, surgical treatment of esophagal ahalasia with a good functional result is possible with the use of minimally invasive methods. In our opinion, and in the opinion of a number of authors, laparoscopic cardiomyotomy with fundoplication can be considered an operation of choice for achalasia of the esophagus, since they possess all the advantages of minimally invasive interventions and have the same results as in open operations. Laparoscopic cardiomyotomy according to Geller during achalasia is effective in 77.8% of children. We are considering a laparoscopic cardiomyotomy according to Geller with Dor fundoplication - the operation of choice in the treatment of achalasia in children.

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## ASPECTS OF INTRA-OPERATIVE INACTIVATION AND METHODS OF SURGICAL RESOLUTION OF RESIDUAL CAVITIES IN PULMONARY HYDATID CYST IN CHILDREN

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## ABSTRACT

The study includes a complex analysis of clinical, imaging, morpho-pathological and laboratory observations, as well as the results of the medical and surgical treatment of 150 patients, aged 3-17 years, with pulmonary hydatidosis, of which 135 with primary hydatidosis and 15 with recurrent hydatidosis. Thus, the results of this study allow us to conclude that intraoperative use of 2% silver nitrate solution allows effective antiparasitic inactivation of hydatid larval cyst elements and adequate disinfection of residual cavities, which contributes to a significant reduction in the incidence of recurrent cases and postoperative septic complications. The residual cavity capitonnage with intraoperative filling using "LitAr" preparation represents an optimal way of resolving residual cavities in major hydatid cyst with the presence of bronchial fistulas and in hydatid cyst complicated with rupture, ensuring fast postoperative re-expansion of the restant parenchyma, it being superior to pneumonostomy.

Key words: hydatid cyst, lung, children, treatment

## INTRODUCTION

Hydatid disease is a cyclozoonotic parasitic disease caused by the larval form of Echinococcus granulosus, quite rarely encountered in Western countries and considered endemic, with major public health problems in several regions of the globe [1, 4, 53], including the Republic of Moldova [30, 48]. Although parasitic cystic lesions are most commonly found in the liver (54.2-70%) and lungs (20-33.3%), the hydatid metacestode may involve any tissue and organ including: muscles (5%), bones %), kidneys (2%), heart (1%), pancreas (1%), central nervous system (1%), spleen (1%) etc. [20, 27]. Some authors consider that in children, compared to adults, the lungs are most affected; the incidence of lung forms being about 68%, giant or multiple hydatid cysts are not a rarity [7, 17, 33].

At present, chemotherapeutic preparations for the conservative treatment of hydatidosis are available, such as benzimidazole derivatives (albendazole, mebenazole) or their combination with pyrazinoisoquinoline derivatives, but no conclusive evidence of their curative efficacy exists [6, 37]. Moreover, a harmful action of these preparations on vital organs [26] has been recorded. In this context, surgical intervention is the treatment of choice of the hydatid cyst of various localization. It requires to unconditionally comply with some important principles that significantly influence the evolution and the disease treatment [23], among which: cyst evacuation with complete removal of parasitic larval cyst elements, deworming and avoiding the intra-operative contamination and the residual cavity resolution [8, 43, 46]. Despite the multitude of technical precautions and the diversity of protoscolicide substances, the intraoperative contami-nation with hydatid larval cyst content is quite common, causing 10% of postoperative recurrences [43]. The optimal way of the residual cavity resolution in both the lung and liver hydatid cyst, the attitude towards pericystic parenchyma, especially in complicated and recurrent forms of the disease, are contradictory. Although various surgical, conservative and radical techniques are proposed [16, 45, 52], the rate of postoperative morbidity in hydatid disease is still high, ranging between 12.5% and 25%, with one or more associated complications [35, 52].

The objective of the study was to carry out a comparative evaluation of the *in vitro* and *in vivo* protoscolicidal effect of some chemical compounds, such as 0.5%, 1% and 2% silver nitrate, as an attempt to intra-operatively inactivate the hydatid larval cyst, and to elucidate some surgical technique peculiarities in the postechinococcectomic residual cavities resolution.

## **MATERIAL AND METHODS**

The study includes a complex analysis of clinical, imaging, morpho-pathological and laboratory observations, as well as the results of the medical and surgical treatment of 150 patients, aged 3-17 years, with pulmonary hydatidosis, of which 135 with primary hydatidosis and 15 with recurrent hydatidosis.

The elements of hydatid cyst and daughter-vesicles served as material for the experimental study, obtained through the puncture of hydatid metacestode (without any parasiticide treatment), as well as parasitic larval cyst totally removed (laminar cuticle together with the proligerous membrane, obtained after pericystectomy). The native material, collected intra-operatively, was subjected to the histopatholo-gical study, recording on the video camera without any additional coloring methods. In addition to silver nitrate, we also used other scolicide agents: 10% and 20% hypertonic saline solution, 95% alcohol, 2% mebendazole suspension, 3% hydrogen peroxide, 10% iodopovidone.

The following morphopathological changes were taken into consideration when analyzing the effectiveness of the scolicide agent: the degree of the chemical agent penetration into the tissues of the germ elements; the disappearance of their active movements; the intensity of their coloring (from brown to black); the presence of objective signs of damage to the structure of the wall and organs of the germ elements; chaotic distribution of hooks. The duration of exposure of the parasiticide solutions used in hydatidosis was 1, 2, 5, 10, 15, 20 and 30 min, respectively (table 1). In order to document the results obtained, a microscope video camera was used.

The topographic study of pulmonary hydatido-sis showed that in 77 (51.3%) cases the right lung was affected, in 54 (36%) cases - the left lung was affected, and in 19 (12.7%) both. Concomitant lung and liver involvement was found in 26 children (17.3%), of which: right lung + liver involvement - 11, left lung + liver involvement - 8, bilateral lung hydatid cyst + liver - 5 cases. In 2 children, some polyorganic forms were found with concomitant damage to the lungs, liver, spleen, brain, and kidneys. In 64% of cases, large and giant cystic formations (the volume of the parasitic larval cyst exceeded 500 ml) were diagnosed, affecting mainly the right lung - 31 cases, the left lung - 18 cases; the lungs and the liver being simultaneously involved in 15 children. Of the total number of patients, in 19 (12.7%) some clinical-evolutionary forms were found which were complicated with: infected lung hydatid cyst - 4 cases; hydatid cyst rupture in bronchus - 11; simultaneous rupture of hydatid cyst in bronchus and pleural cavity - 4. The distribution of patients by age showed the predominance of children aged 7-14 years both in the group of boys (51, 69%) and girls (60.66%). The analysis of the distribution of patients by sex showed that 59.3% were male and 40.7% female.

Diagnostic imaging methods included chest X-ray, computed tomography with and without reconstruction, pulmonary perfusion scintigraphy, hepatic scintigraphy, ultrasound of the lungs and abdominal organs.

The anesthesiology of patients in the study group was performed with the Drager Fabius plus anesthesia workstation, the Infiniti Vista XL multifunction monitor, the Scio Four Oxi plus gas analyzer. Rapid induction was performed with Sevoflurane through the facial mask. Catheterization of two and more peripheral veins was performed, the central vein catheterization being abandoned. For premedication, the intravenous administration of Atropine sulphate solution with Diazepam solution was used. Opiates (Fentanyl), myoplegia with Atracurium or Pipecuronium bromide were used for basic anesthesia.

After 100% oxygen preventive hyperventila-tion, tracheal intubation was carried out, assisted breathing being performed with the apparatus in pressure-controlled ventilation mode, peak inspiratory pressure - 20 mm col. (max. 30-40 mm col. of water), positive end expiratory pressure - 5-10 mm col. of water. Subsequently, Isoflurane (minimum alveolar concentration <1) was infused, which had a lower influence on pulmonary hypoxic vasoconstriction. In the unipulmonary intubation, a bronchial tube with lumen with or without a cuff was used, depending on the child's age and airway dimensions.

In the unipulmonary intubation, assisted mechanical and manual ventilations proved to be useful, depending on the surgery stage, with the temporary arrest of short-term breathing in the inspiration or expiration phase. Under the control of the monitoring indices (FiO2, SaO<sup>2</sup>, ETCO<sup>2</sup>) the optimal ventilation regime was established by changing the respiratory volume and respiratory rate.

#### RESULTS

The results of the experimental study show that the sensitivity of the germ elements to the scolicide solutions used (table 1) depends, to a large extent, on the clinical-evolutionary stages of the parasitic disease and the degree of maturation of the germ elements: the "younger" they are, the more sensitive to the scolicide agents they are, therefore the metascolex (a degenerative form of protoscolex) was significantly more sensitive compared to orthoscolex.

The germ elements in the daughter vesicles of the maternal membrane are well protected and, therefore, resistant to the action of scolicide solutions as compared to free protoscolex.

According to the final results of the *"in vitro"* study, 10% and 20% hypertonic saline solutions, 2% mebendazole, 3% oxygen peroxide have shown to be less effective in inactivating hydatid germ elements even at an exposure of 15-20 minutes. Higher inactivation possibilities included 96% alcohol and 10% povidone iodine. Some higher comparative results were recorded when using silver nitrate. Thus, signs of the germ elements inactivation were observed within the first 5-7 minutes after using this preparation in 1% concentration, while 2% concentration was effective even within the first 2 minutes after administration.

The results of the action of 1-2% silver nitrate on the structural elements of the parasitic larval cyst and the fibrous capsule in the lung hydatid cyst in children presented a major interest. Chitin and fibrous capsule fragments, treated with this substance, were subjected to the morphopathological study (63 cases). After treating the fibrous capsule with 1% and 2% silver nitrate, some variable structural degenerative changes were observed, strictly depending on the solution concentration and the exposure period. Under the action of 1% silver nitrate for 1.5-2 minutes, there was a moderate decomplexation of the syncytium structure of the proligerous membrane with marked syncytium imbibition and pronounced argentophilia, as well as the syncytium cell adhesion to the ratatinated pseudoglobulins.

Table	1. E	fficacy	of p	oarasi	ticidal	solutions	depend-
ing on	the	durati	on o	of the	expos	ure	

No.	Preparation used	No. of test	Duration of exposure	Scolicide effect
1.	NaCl 10 %	30	15-20 min	Absent
2.	NaCl 20 %	30	15-20 min	+
3.	Ethanol 96 %	30	15-20 min	++
4.	Mebendazole Susp. 2 %	30	15-20 min	Absent
5.	H2O2 3 %	30	15-20 min	+
6.	Povidone iodine 10 %	30	10-15 min	+
7.	Povidone iodine 10 %	30	25-30 min	++
8.	Silver nitrate 0,25 %	30	15-20 min	+
9.	Silver nitrate 0,5 %	30	15-20 min	+
10.	Silver nitrate 1 %	30	5-7 min	++
11.	Silver nitrate 2 %	30	1-1,5 min	++
12	Silver nitrate 2 %	30	2-2,5 min	+++

At an exposure for 4-5 min. of the preparation, there was recorded the complete decomplexation of the proligerous membrane, with the necrotic degeneration of the proligerous syncytium and the reticular net, its ejection, with denaturation and coagulation processes, the lamellar tunica having a marbled appearance.

At 2 % silver nitrate exposure for 2 minutes there was determined a more active degeneration in the proligerous membrane, manifested by total or subtotal necrosis, with mild argentophilia, rendering it a granular appearance. The action of 1% and 2% silver nitrate for 2-3 minutes causes major denaturation and coagulation with total disintegration of the parasitic elements (fig. 1). At the fibrous capsule level, the preparation soaks in its superficial layers, forming a strict demarcation area between the layer of eosinophilic necrosis and granulation. Within these limits there is a dystrophy of the connective fibers, in some places their disjunction being observed, followed by aseptic necrosis. After 3-5 minutes, the swelling of cytoplasmic fibroblasts is observed, sometimes seconded by a micro-vacuolation, the nuclei being ratatinated. The fibroblasts on the area adjacent to silver nitrate action became more succulent. A more advanced and deeper aseptic necrosis was determined at an exposure for 5-7 minutes, in some cases reaching the fibrovascular layer. In some sectors the penetration of the preparation into the adjacent lung parenchyma was observed. As a rule, the pericystic bronchial net remains intact, except the bronchi that open up into the residual cavity.



Fig. 1. Microscopic aspect of protoscolex treated with 2% silver nitrate

The results obtained show that 2% silver nitrate has marked necrotic action and it can be used in pulmonary hydatidosis as an elective substance in the intraoperative inactivation of the hydatid larval cyst. The scolicide and bactericidal action of 2% silver nitrate, along with its necrolytic action, provides favorable conditions for both the obliteration of the postechinococcoectomy residual cavity and for the prophylaxis of relapses and postoperative complications. Administration of this preparation reduces the risk of parasite germ elements dissemination, as well as intra- and post-operative complications, relapses. The choice of appropriate anesthesiological assistance in surgical interventions in lung hydatid cyst in children has been made according to factors that influence the pulmonary ventilation/perfusion ratio and increase the risk of developing hypoxaemia, including: lateral position of the patient, pneumothorax, in some cases the need for one-lung intubation, etc. To prevent the development of atelectasis and obturation of the intubation tube with blood clots and biological fluids, assisted pulmonary ventilation was performed under permanent positive pressure conditions at expiration. Only patients with adequate self-respiration were extubated, as well as cough reflex being restored and satisfactory muscular tonus being present due to restored consciousness.

Surgical techniques were applied and managed according to the topography and dimensions of the hydatid cyst. They included:

- pulmonary echinococcectomy+Delbet capitonnage of the residual cavity - 33 cases;
- echinococcectomy + residual cavity capitonnage with suture application in overleveled bursae with absorbable wire "to-and-fro" - 56 cases;
- echinococcectomy + residual cavity capitonnage with suture application in overleveled bursae with absorbable wire "to-and-fro" with application of "LitAr" material - 44 cases;
- echinococcectomy + pneumonostomy 18 cases;
- economical marginal cyst-pericystectomy resections (12 cases);

The predominant use of echinococcectomy with the residual cavity resolution by application of sutures in overleveled bursae with absorbable wire "to-and-fro" was imposed by some negative moments that develop after the Delbet capitonnage of the residual cavity. All the dehiscences of the capitonnage sutures observed in the study group in children with uncomplicated lung hydatid cyst (3 patients) occurred when using this method, the persistence of residual spaces being found in 11 cases.

Difficulties in resolving residual cavities also occur in the case of overleveled "to and fro" cappitonage, especially in large cystic formations and deep intrapulmonary formations. In these cases, there is a real risk of developing pulmonary collapse caused by persistent air leakage from secondary bronchial fistulas (2 cases), residual cavity infection (1 case), long persistence of residual spaces in major cysts (4 cases) (fig. 2). In view of these inconveniences, the method was completed using "LitAr" plastic material, the process being particularly useful in these cases.







Fig. 2. Patient V, 13 years old. Preoperative chest X-ray (A) - giant pulmonary hydatid cyst of the right lung; the presence of residual spaces after capitonnage at discharge (B) and 30 days post-operatively (C)

Some serious problems in resolving residual cavities occur in complicated hydatid cyst, these patients being hospitalized late. Morphopathological investigations have confirmed that the capitonnage of the residual cavities in these cases may be a failure due to the presence of marked inflammatory-destructive phenomena of the fibrous capsule layers and pericystic pulmonary tissue. In major cysts and in forms complicated with rupture, resolved by suturing fistulas with external drainage of the residual cavity (cystostomy) and the pleural cavity, significant postoperative morbidity was determined due to long persistence of the residual cavity (30 - 112 days) (fig. 3, 4), aerostatic disorders (12 cases), and the development of serious complications manifested by the destructive pleuro-pulmonary process (3 cases), postoperative suppurative pleurisy (2 cases), compressive pneumothorax (6 cases) (fig. 5).





Fig. 3. Patient A., 10 years. Preoperative computed tomography. Hydatic cyst in the lower lobe of the left lung

To fill the residual cavity subjected to capitonnage, we used plastic material "LitAr" (42 cases) which is a collagen preparation with hydroxyapatite. The preparation was applied concurrently with the capitonnage of residual cavities, filling 2/3 of the volume of these spaces. The use of this plastic material allowed to obtain stable aerostasis and haemostasis in the postechinococcectomic residual cavity in most cases (fig. 7), except 2 patients with infected hydatid larval cyst complicated with rupture in which only the observed fistula was sutured and filled, the residual cavities being drained. According to the results obtained, this method is not sufficient for a stable aerostasis, so it was subsequently abandoned.



Fig. 4. Patient A., 10 years. A – chest X-ray performed on the 3rd postoperative day: the presence of the residual cavity with fluid drained out(A, B), which is maintained on the  $38^{th}$  day after surgery (C, D)



Fig. 5. Patient L., 10 years. Postoperative chest X-ray performed 6 days after surgery. Compressive pneumothorax on the right with the residual cavity visualization

Cystostomy (pneumostomy) proved to be an effective method in uncomplicated hydatid cysts without inflammatory changes of the pericystic parenchyma, localized predominantly in the peripheral lung areas and without the presence of major bronchial fistulas (fig. 6).

To perform an efficient filling, it was necessary, along with the capitonnage of the residual cavities, to fill at least 2/3 of the volume of the residual spaces. This procedure also represents an effective method of prophylaxis of postoperative complications. The period of time that ensures a satisfactory filling of the residual cavity is 20-25 days, during which acceleration of the local repairing phenomena takes place. The adverse reaction was recorded in one case by the development of pleurasy resolved without major therapeutic problems. This method was particularly useful in major or complicated lung hydatid cyst, usually accompanied by marked pleuropulmonary inflammatory phenomena and bronchial fistulas, thereby avoiding pulmonary resection operations.



Fig. 6. Patient P., 9 years old. A - preoperative chest X-ray: the presence of a large formation in the lower lobe of the left lung; B - chest X-ray 10 days postoperatively: the presence of a residual cavity; C - chest X-ray 60 days postoperatively

Cases of the lung hydatid cyst recurrence were recorded in 6 (4%) patients, of which 1 patient was reoperated 3 times and one female patient twice, the number of surgical reinterventions reaching 11 (7.33%). Cases of death in the study group were not recorded.

## DISCUSSIONS

Surgical intervention is the optimal treatment in lung hydatid cyst [18]. Surgical removal of the intact hydatid larval cyst remains the preferred option in the surgical treatment of this disea se with any location, intraoperative contamination being the main cause of multiple secondary hydatidosis. In this context, several substances with a protoscolicidal action have been proposed for the intra-operative inactivation of parasitic elements, including: formalin, thymol, ethanol 95%, hypertonic saline solution 20%, hypertonic glucose solution, povidone iodine, cetrimide, octenidine hydrochloride, chlorhexidine gluconate, hot water, etc. [13, 14, 22, 36]. The increased toxicity and the development of adverse reactions and serious complications induced by these preparations necessitated to search for new scolicide agents with less harmful action on the macro-organism and with increased efficiency in inactivating this parasitic agent [12,34,41]. For this purpose, there were tested several compounds obtained from plants and microorganisms [3, 32, 42], chenodeoxycholic acid, an effective bile stones dissolving agent [44], sodium arsenite [49], silver nanoparticles [40], and biogenic selenium [31]. The results of these experimental studies are at the discussion stage, opinions being often contradictory [29]. It is important that during the process of intra-operative inactivation, the active migration phenomenon of protoscolex is also taken into account [5].



Fig. 7. Patient C. 3 years. A - Preoperative X-ray: Major hydatid cyst in the upper lobe of the right lung. B - postoperative X-ray at discharge (12th day). C - chest X-ray 1 year after surgery. D - pulmonary scintigraphy (perfusion) performed 1 year after surgery. E - postoperative pulmonary scintigraphy of patient C. performed 2 years after surgery

Several techniques have been proposed to remove the hydatid larval cyst dependent on intra-operative conditions, including enucleation (Ugon procedure) plus capitonnage, cystotomy with bronchial fistulas closure plus capitonnage (Possadas procedure), cyst-pericystectomy (Perez-Fontana method), pneumostomy, lung resections, etc. [10, 24, 38].

In the literature there is also controversy regarding the attitude towards the residual cavities after the removal of the hydatid larval cyst [45]. Although parasitic cyst enucleation is only possible in 21.4% of adults and 16% of children [10], some authors believe that using this procedure along with bronchial fistulas closure should be a standard surgical technique, because the residual cavity capitonnage, does not have significant beneficial effects in postoperative evolution [19]. At the same time, several authors opt for cystotomy with the capitonnage of the residual cavity and the preservation of the pericystic parenchyma, the avoidance of the bronchial-pleural fistulas and the prevention of the abscess formation within the residual cavities are important advantages of this technique [2, 11, 28, 51].

There is a risk that capitonnage of the residual cavities will cause the disfigurement of lung parenchyma, which may influence the postoperative re-expansion of the lung [38], and in complicated forms of the disease it can lead to infection, the laceration of the pulmonary tissue and the insufficiency of the capitonnage sutures [45]. The non-capitonnage procedure with pneumonostomy is considered a safe and effective alternative technique by several authors, who concluded that the capitonnage procedure does not have any advantages in terms of hospitalization length, duration of air removal through the chest tube or prevention of some complications such as empyema, persistence of fistulas and air leaks, recurrence [15, 16, 24, 47]. This technical procedure of creating a direct communication between the residual cavity and pleural space, with the removal of bronchial fistulas and external drainage in pulmonary echinococcectomy was proposed by Yacoubian H.D. and Dajani T. (1963).

Pulmonary resections, justified under certain conditions [52], should be performed with caution even in the case of infected hydatid cysts, giant or multiple cysts involving the same lobe [21, 25], some technical procedures being preferred with the preservation of the pulmonary parenchyma [39], especially in children and endemic areas, where the risk of recurrence is a real concern [9].

Thus, the results of this study allow us to conclude that:

- Intraoperative use of 2% silver nitrate solution allows effective antiparasitic inactivation of hydatid larval cyst elements and adequate disinfection of residual cavities, which contributes to a significant reduction in the incidence of recurrent cases and postoperative septic complications.
- 2. The use of contemporaneous inhalers of Sevoflurane, Isoflurane in the general anesthesia regimens in lung surgery in children allows adequate management and safe control of the level of anesthesia and analgesia with minimal implications for hypoxic pulmonary vasoconstriction.
- 3. The residual cavity capitonnage with intraoperative filling using "LitAr" preparation represents an optimal way of resolving residual cavities in major hydatid cyst with the presence of bronchial fistulas and in hydatid cyst complicated with rupture, ensuring fast postoperative re-expansion of the restant parenchyma, it being superior to pneumonostomy.

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## ABSTRACT

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In Clinic of Vertebrology, Orthopedics and Traumotology of the "N.Georgiu" Scientifically - Practical Center of Children's Surgery 29 patients with spine deformations after traumatic injuries in the acute stage have been pre- and postoperatively examined with a follow-up of 1 to 5 years. Children were aged between 3 and 17 years. The main goals of surgical interventions were: elimination of the compression factor, deformation and disbalance, correction and spine stabilization. The comparative analysis of the quality of the life of patients (according to a questionnaire "EQ-5D"), before and after surgical intervention, has shown that the quality of the life of patients improved, in comparison with the preoperative period, from 12,7±0,3 points to 7,7±0,1. The distant results of surgical treatment were good– 85,1%, satisfactory – 11,2 % and unsatisfactory – 3,7%.

Conclusion: 1. In fresh cases of the complicated spinal - marrow trauma with mild and average degree of a neurologic symptomatology (D degree on Frenkel's scale) the preference was given to the closed, indirect decompression. At a serious neurologic symptomatology (A, B, C degree) carried out open decompression and revision of dural bag's contents; 2. Optimum method of correction the complicated spinal - marrow trauma were: forward spine release; dorsal correction and backbone fixation by a metal construction.

Key words: spine deformations; traumatic injuries; spine stabilization, children

## **INTRODUCTION**

Traumatic spine deformations at children represent the cause that influences the main peculiarities of the spinal column: its safety and stability; initially it is manifesting by pains, statics infringements, and internals' dysfunction, subsequently it leads to severe decrease of quality of life. The choice of surgical and therapeutic options in the management of traumatic spine deformations at children is still controversial. So (for example) patients with fractures like AI according to AO/ASIF classification don't need in surgical treatment. However, it is proved on a big clinical material [12] the fact that compression fractures like AI with depression of forward (ventral) part of the spine on 5 mm (>5), or average more than on 3 mm at children leads to formation of kyphosis deformation. One experts recommend in urgent cases forward decompression of a spinal cord at the level of damage [2, 8, 9], but others prefer decompressing-stabilizing operations with back or back-lateral access [5, 11]. The majority of available literary references belong to studying of spine injury at adults.

Work's goal: Rising of treatment's efficiency at traumatic deformations of thoracal and lumbar spine department at children by means of development differentiated surgical tactics.

## **MATERIAL AND METHODS**

29 patients with traumatic injuries thoracal and lumbar spine department have been pre- and

postoperatively examined with a follow-up of 1 to 5 years, in Clinic of Vertebrology, Orthopedics and Traumotology of the Scientifically - practical Center of Children's Surgery "N.Georgiu" (2008-2012). Children were aged between 3 and 17 years; they were predominantly boys – (56 %).

The evaluation included collecting of anamnesis data, clinical examination, labs and imaging (standard radiography/ with functional tests, magnetic resonance).

The type of fracture was estimated on Denis classification (1983) and AO/ASIF scale (Gertzbein S.D. 1994) extent of neurological disturbances on the scale of Frankel (1969) modified for children's age, pelvic functions JOA agrees. All patients were operating in terms from several hours to 5 weeks from the trauma moment.

Injuries of vertebras at one level became perceptible at 21 (72,4%) patients, two and more at 8 (27,6%). The combination of spine and spinal cord injuries took place at 9 (31%) patients, damages like All took place at 2 patients, BI types at 2, and CIII at 5. Depth of neurological disturbances on the scale of Frankel was: A-5 (55,6%), V-2 (22.2%), S-1 (11,1%), D -1 (11,1%). Disturbances functions of pelvic organs on the scale of JOA were: 1-5(55,6) patients, 2-2 (22.2%) and 3-2(22.2%). Therapy according to the NASCIS-II protocol carried out to patients with the complicated spinal trauma from the moment of hospitalization.

The indication to operative treatment was spine instability (on F.Denis) at which there are damages of two or more backbone's colons, according to AO/ ASIF classification (Gertzbein S.D., 1994) : AII-AIII (explosive fractures) – 14 (48,3%) and BI (distraction - flexion on type of "seat belts" ("seifti-belt")) – 4 (13,8%), CII-III (dislocation-fractures) – 5 (17,2%) patients. AI (compression fractures with height's depression of forward department of vertebral body more than on 5 mm (>5°), and height's depression of average department more than on 3 mm) were observed at 6 (20,7%) patients.

The main goals of surgical interventions were: elimination of the compression factor, deformation and disbalance, correction and spine stabilization. Surgery allowed obtaining the following results:

- Reposition (reduction) of the body of displaced vertebras;
- Reconstruction of forward and average spine columns;
- Restoration of physiological spine profiles (frontal and sagittal);
- 4. Restoration of normal anatomy of the vertebral channel;
- 5. Stabilization of the spine-impellent segment.

**Clinical case.** *Patient K.*, 3 years old. There is a combined trauma, the closed fracture and vertebra dislocation L1 (type C III), the bottom paraplegia (type A).

*Operation:* Wide laminectomy Th XII, L1, LII, vertebral channel's revision, indirect reposition; fixation by CD system.





Fig 1. Before operation. L1 dislocation-fracture, symptom of a double vertebra





Fig. 2. After operation. In 2 years after operation neurological disturbances of type A passed to type D.

## **RESULTS AND DISCUSSIONS**

Reposition and stabilization interventions which are combining with a partial resection of curve process of joints at seifti-belt damage were carried out for the best adaptation of back osteal structures at the reposition.

Decompressing and stabilization interventions in combination with back and lateral back autospondilodezis were carried out at patients with complicated traumas. The remote results were tracking in terms from 1 to 5 years. Local deformation (kyphosis, depression of body's height) was partially or completely eliminated. There is no negative dynamics after expeditious treatment in cases where neurological symptomatology wasn't noted. In 1 case transition of type A to type D is noted. In 8 cases of the complicated trauma there was regress of a neurological symptomatology, on 1-2 degrees on Frankel.

Questioning and medical examination in polyclinic were carried out at 28 patients. 20 patients returned to study. Constructions are removed at 2 patients in remote period (3 years) - 1 breakage of hinge, 1 screw.

Partial loss of the reached kyphosis correction (to 20%), in cases of "short" bracing of two vertebral motive segments at 2 patients was observed. Intraoperative complications: not recognizable wrong screws carrying out (2). Early complications: sacrum decubitus (1), infection of urinary ways (1), superficial inflammation of an operational wound (1). Late complications: 3 cases of metal construction breakages, in 1 with correction loss.

For objectivity of results we used a Denis's scale (1984) for the pain and operability syndrome's assessment: at 14 (53,8%) patients - P1 degree (there is no pain), 9 (34,6%) - P2 (the infrequent weak pains which aren't demanding treatment) and at 3 (11,5%) - P3 (the average intensity, sometimes demanding applications of drugs).

## **CONCLUSION:**

1. In fresh cases of the complicated spinal marrow trauma with mild and average degree of a neurologic symptomatology (degree of D on Frenkel) the preference was given to the closed, indirect decompression. At a serious neurologic symptomatology (A, B, C degree) carried out open decompression and revision of dural bag's contents.

2. The early surgical intervention leads to pain syndrome's cupping, restoration of a vertebral form, elimination of the spine deformation and stabilization of the damaged segment, using *only back access*.

3. Compression fractures like AI with depression of forward (ventral) part of the spine on 5 mm (>5°), or average more than on 3 mm at children needs to operate for the purpose of prevention of the kyphotic deformation's formation.

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## ABSTRACT

**Objectives.** Surgical management of patients with benign biliary strictures and biliary lesions is a current issue for discussion and raises many scientific research directions. The purpose of this study was to systematize our experience in the treatment of benign biliary strictures, analyzing both immediate and remote complex results.

**Material and methods.** Between 1989-2015 years, there were 203 hospitalized patients with benign biliary strictures in Surgery Department no. 2 of Public Institution, State Medical and Pharmaceutical University (PI SMPhU) "Nicolae Testemitanu". The study is conducted as part of postdoctoral research; thesis/ dissertation title is Clinical-functional efficiency of modern surgical treatment of benig biliary strictures according to immediate and remote clinical results and was approved by the Science Council of PI SMPhU "Nicolae Testemițanu" and Ethical Committee (EC) of Ministry of Health (MoH). Clinical evaluation included several consecutive steps: 1) setting the etiopathogenic diagnosis; 2) pre-operatory decompression of the biliary tree; 3) reconstructive surgical act. In the case of biliary strictures, after the initial assessment, bilio digestive derivations were performed according to the level of the obstacle, preferring the bilio-jejunal on isolated loop en Y a la Roux.

**Conclusions.** The iatrogenic stricture of bile duct has a complicated evolution, with many surgeries, requiring many hospitalizations. It should be endeavored to detect them in a timely manner and to prevent septic complications. In the first phase biliary tree decompression will be used, and after decreasing the inflammatory process biliary-digestive reconstruction will be performed. These patients require a complex remote monitoring and analysis of health status.

Key words: biliary strictures; etiopathogenic diagnosis; hepaticojejunostomy; reconstructive surgery act

## **INTRODUCTION**

Bile duct lesions that occur most often after a cholecystectomy, present a formidable challenge for surgical services that require a complex approach for optimal management. If the injury is not recognized in time or has been poorly managed, then serious complications can occur, such as cholangitis, biliary cirrhosis or portal hypertension. These complications involve considerable a cost for treatment, loss of employment and long-term disability [6, 18].

The incidence of biliary injuries during open cholecystectomy is reported to be about 0.1-0.2%. The incidence of biliary injuries during laparoscopic cholecystectomy is certainly greater than the one following open cholecystectomy and according to published data varies between 0.4-0.6% [6, 22]. It is also noteworthy that after laparoscopic cholecystectomy bile injuries are more severe and complex than those encountered during an open cholecystectomy [1, 4, 12].

In order to define the types of biliary lesions (BL) there have been proposed several classifications of BL, but none is universally accepted because each has its own limitations. Among them, a fundamental role is played by Bismuth's classification and Strasberg's classification, which are most commonly used by practitioners. Bismuth's classification addresses the group of patients presenting an established biliary

stricture and distributes patients based on the level of damage, which is a determining factor of the evolutionary result [5]. Dr. Sikora amended type III strictures in type IIIa / IIIb, according to Bismuth, depending on the level of confluence of hepatic ducts, being intact or destroyed [20]. Strasberg's classification applies to acute injury with bile leaks, lateral damage and sectioning [21]. A subgroup of transections (type E according to Strasberg) incorporates Bismuth classification. The major disadvantage of these classifications is that some important factors affecting the result are not presented, such as the vascular lesions, time until recognition of the damage, the presence of biliary fistula (internal/external), portal hypertension, liver function, and the presence or absence of previous reparatory operations.

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The Hannover classification is the most refined in terms of the combination of classification of Strasberg and Bismuth and is addressed directly to the assessment of biliary-vascular lesions [3]. Hopefully a comprehensive classification system, universally accepted at all levels of surgical services, will be proposed in the near future and will mandatorily include all the relevant parameters that influence long-term outcome [12].

A detailed clinical evaluation and a thorough preoperative preparation are important factors for a successful management of a patient with BL. The major preoperative aim is to document the degree of liver dysfunction, to establish the exact level and type of stricture, the presence or absence of biliary infection, and to investigate possible complications such as secondary biliary cirrhosis and portal hypertension or possible biliary fistula. Besides BL diagnosis, it is also equally important to detect the associated medical risk factors, especially liver disease coexistence, electrolyte dysfunction, coagulation, metabolic or in association with infection disorders.

In this context, our study focuses on what happens after the damage has already been produced and the surgical modality for solving the existing problems [16]. The moment of BL repairs is critical, especially when we realize that the first attempt to repair is the best in terms of long-term outcome. The outcome of main bile duct injury is an increase of diameter, wall thickening, an increase in proliferative connective cells and an increase in elastic fibers. One important relevant aspect is the presence of inflammatory infiltrate in the wall of bile duct wall. In an elective situation, a minimum period of 3 months after the injury and reconstruction is optimal for the resolution of edema and tissue inflammation from the biliary-hepatic region and for a proximal dilatation of the biliary tree [6, 11]. In patients with an total external biliary fistula, the interval from injury to reconstruction can be extended to six months, in order to provide the appropriate surgical management, which will ensure the return of externalized bile in the digestive tract, avoiding electrolyte disturbances and development of acholia [8]. Unjustified haste in trying to solve an injury at an early stage by reconstruction is associated with a high risk of bile leak postoperatively - 30%, forming a distant stricture - 25% and a high mortality - 30%.

The aim of the management of bile stricture is to restore the flow of bile in the gastrointestinal tract through a bypass that prevents reflux cholangitis, biliary sludge duct which is formed due to stasis and the formation of gallstones, re-stricture of the bile duct or chronic progressive liver injury. The surgical reconstruction is superior to other techniques, such as percutaneous or endoscopic (balloon dilation or stenting). Hepaticojejunostomy (HJA) is the gold standard in the treatment of biliary strictures. The key surgical principles associated with a successful reconstruction of biliary stricture are the exposure of healthy, well-vascularized stump bile that drains the entire liver, and preparation of a corresponding segment of intestine (usually a loop Roux-en-Y of jejunum> 80 cm) to make close edges and tension free anastomosis – mucosa to mucosa [13, 15]. Hepp-Couinaud technique for accessing the left hepatic duct under the base of the quadratus lobe enables repair of high lesions, performing a bypass with reliable results. A side-to-side HJA, performed through a longitudinal incision of the left hepatic duct, produces a large anastomosis, minimizes the dissection behind the biliary tract and reduces the risk of excessive devascularization of liver ducts [2, 23].

The data from a few tertiary centers presents the

postoperative mortality ranging from 5% to 8%. In the last decade, with perfected surgical techniques and management of biliary strictures addressed, there is a considerable decrease in operative mortality with many consistent series reporting *zero* perioperative deaths [14]. Risk factors adversely affecting the survival rate are: age, repeated reconstructive surgery, significant comorbid medical condition, sepsis, bile, and secondary biliary cirrhosis [9].

Several factors must be considered when discussing the long-term outcomes after reconstruction addressed to biliary strictures. Several tertiary care centers reported a satisfactory result in 80-90% of patients. Important factors, presented at scientific forums, underline that predictors of adverse outcome typically include proximal strictures (Bismuth type 3 and 4), multiple previous attempts of reconstruction, presence of parenchymal liver disease, portal hypertension, difficult biliary anastomosis, biliary sepsis, lack of experience of the surgeon [18, 19].

Psychosocial repercussions of BL are high; most patients are in the most productive years of their lives. When faced with a serious post-operative complication, requiring major surgical reconstruction carried out by several specialists, a program with integrity assessment and rehabilitation is needed, being a major cost to the health system. Despite the excellent results in long-term reconstructive surgery, Quality of life (QoL) is modest and not well documented. Current studies are often incomplete and do not allow these goals to be established on this difficult issue.

#### **MATERIALS AND METHODS**

In the present study, 203 patients with iatrogenic biliary lesions secondary to laparoscopic or open cholecystectomy, gastric resections, admitted at the Surgery Clinic no. 2 between the 1989-2015 years, were looked after (fig. 1).





The mean age of the 203 patients was 49.15  $\pm$  0.94 years, in the range: 21-78 years old, they were 37 (18.2%) men and 166 (81.8%) women. Depending on the symptoms presented and the clinical manifestations of patients with postoperative biliary strictures the following clinical picture is found at the time of admission for reconstructive intervention: presence of biliary colic in 103 (50.7  $\pm$  4.93%) cases;

jaundice in 157 (77.3  $\pm$  3.34%) cases; cutaneous pruritus in 104 (51.2  $\pm$  7.36%) cases; hepatomegaly -32 (15.8  $\pm$  6.45%) cases; fatigue in 140 (69.0  $\pm$  3.91%) cases; presence of external biliary fistula in 137 (67.5  $\pm$  4.01%) cases. Stated symptomatic was directly correlated with the presence of chronic biliary-hepatic suffering, motivated by supported biliary injury and followed by reparative operations or drainage of the biliary tree. The intensity of clinical signs was explained by the degree of drainage of the biliary tree, the amount of bile that got in the digestive tract, the presence of local septic complications, or angiocholitis, the transient or persistent mechanical jaundice, the degree of hepatic failure.

Direct etiologic cause of postoperative biliary strictures in 91 (44.8%) of the cases were the consequences of lesion of the MBD during a traditional cholecystectomy. Usually these are cases of acute cholecystitis or situations with major fibrosis with deformation of the report of the gallbladder and biliary-vascular complex. The major complexity of cases imposed them to be resolved by traditional access, often during night shifts with inadequate anesthesical relaxation, difficult access to subhepatic space, adding a possible inadequate incision by size. In 107 (52.7%) cases the lesion was secondary to laparoscopic cholecystectomy. These situations often are motivated by scleroatrophic cholecystitis, anatomical abnormalities, bleeding during surgery. Clinical experience was 16 (7.88%) cases of lesions, which constituted 0.05% of all clinical cases of cholecystectomy operated during this period. The remaining 187 (92.12%) cases were from other surgical services. Gastric resection for complicated callous ulcers with penetration caused iatrogenic injury just in 5 (2.5%) cases. An important point is that over time from the lesions to its finding in our study was 7.29  $\pm$  0.49 days, which increased the gravity of patients at the stage of drainage of biliary tree and obviously had a major impact on biliary stricture formation. An important criterion in increasing complexity of strictures furtherly developed was that 99 ( $48.8 \pm 5.02\%$ ) of patients had two or more drainage operations or plastic MBD at the time of lesion. Any repeated trauma obviously increases the local inflammatory process, grade of fibrous tissue and develops a difficult biliary stump due to the excessive fibroplastic process and changed local anatomy. In the remaining 104 (51.2  $\pm$  4.90%) of cases there is only one intervention, thanks to the presence of partial lesions with retention preservation of MBD path. Timely detection of these patients prevented septic complications and limitation of re-operation just in order to restore MBD on the Kehr or Robson drainage. The presence of small lesions often makes us technically easier to resolve the biliary drainage through minimally invasive endoscopic methods often associated with percutaneous echo-guidance. Endoscopic stenting was possible at 15 (7.39%) patients, which excluded the need for open intervention. As a result, it provides natural bile flow into the duodenum and satisfactory physiological preparation and qualitative precondition for reconstructive interventions.

We also conducted a comparative study of diagnostic imaging methods, which allowed us comparative evaluation of sensitivity and specificity, negative and positive predictive values for the diagnosis of patients with benign biliary strictures. Imaging examinations (ultrasound, CT, MRCP, ERCP, CPTH and cholangio-fistulography) showed conclusive pictures of the biliary tree, intra- and extrahepatic sectors, the degree of expansion, distal discontinuous extra hepatic bile duct and even invisible in some cases. They were used to discover the level of stricture and state of different sectors of biliary tree, the biliary wall thickness above the obstacle and the presence of endobiliary inclusions. Preoperative visualization of the biliary tree was obtained by cholangio-fistulography in 29 (14.29%) cases, by ERCP in 157 (77.34%) cases and by CPTH in 19 (9.36%) cases.

The performed imaging examination allowed to systematize the level of strictures. So in our study, 6 (3.0%) patients were reported as type I, 92 (45.3%) type II, 90 (44.3%) as a type III, 15 (7.4%)- type IV and type V - 0 (Table 2). Bile duct dilation above stricture was more than 1.5 cm at 77 (37.93%) patients, from 1.5 to 2.0 cm at 102 (50.25%) patients, and more 2.0 cm at 7 patients. This moment was of great importance to the formation of biliodigestive anastomosis. Biliodigestive derivations are essential to rebuilding the biliary tree and restoring properly the biliodigestive flow. Any reconstruction of biliary channel, in our experience, fulfilled the following requirements: a) excision of fibrous tissue from proximal biliary channel; b) formation of a wide anastomosis; c) presence of an intact mucous membrane without any inflammatory processes at 3600 of the anastomosis line; d) good vascularization on suture line; e) lack of tension on the anastomosis line. Currently achieving biliary-digestive derivations using Roux loop has become a recognized standard in biliary strictures surgery. But notable advances were recorded in terms of forming the hepaticojejunoanas-tomosis. Technological development of applying this anastomosis was directly related to evolution in processing the biliary stump and suture material. In current practice, anastomosis is performed with ordinary sutures, which are passed through all layers. We allow as PDS suture material, Vicril 4 / 0-5 / 0. We focus on a good hermeticism, applying sutures with 2-3 mm step. On posterior lip the nodes are applied facing the lumen, and on the anterior - the outside. Suture line is reinforced with sero-serous sutures up to 5 in number, only when needed. For strictures type I and II according to Bismuth, an end-to-side choledocojejunostomy using hepatic duct and Roux loop is already a recognized norm. It was carried out in 86 (42.4 ± 5.33%) cases of our study sample. We accept as PDS suture material, Vicril 3 / 0-4 / 0. In this situation, usually we have a

pretty "long" stump, which adjusts well to the intestinal mucosa. The surgeon had extra-tissue for maneuvers when preparing the common hepatic stump allowing to apply sutures only on healthy tissue.

In case of Bismuth type III strictures hepaticojejunostomy was faced with a small biliary stump, it requires continuing the incision longitudinally on the left channel, after the preparing it from the hepatic hilum. In our experience, we had special cases, with intrahepatic anatomical positioning situation without adequate exteriorization in hilum which did not assure us an anastomosis mouth of proper dimensions. We resorted to mobilizing right hepatic duct and extending the incision longitudinally. Just this way we could ensure a broad and functional anastomosis. We accepted tas PDS suture material, Vicril 5/0-6/0. Usually these high derivations require mandatory drainage of anastomosis mouth. The drainage was performed according to the Veolker procedure, separately for each biliary channel and for 2-3 months. Hepaticojejunostomy was carried out in 102 (50.2  $\pm$  4.95%) cases, there were long incisions on both channels liver in 47 of them (23.15%).

For strictures of type IV, when liver channels junction is completely destroyed, leaving two separate channels in the wound would bring up technical difficulties for reconstructive surgery. Intraoperatively liver channels will be released of parenchyma and fibrous tissue. The essential element that must guide surgery is resection till healthy tissue. They conducted separate anastomoses with each bile duct with Roux loop using 5/0 ordinary resorbable suture in single plan under surgical optical control in 15 (7.4  $\pm$ 6.99%) cases. We had situations when the right hepatic duct was very short and we had to section and anastomosis separately paramedian right and lateral right channels. Anastomoses were finished with separate drainage of both channels according to Veo-Iker procedure for a period of 6 months. The anastomosed loop required mandatorily serosa-muscle sutures with liver capsule with non-resorbable material, which excluded traction at the anastomosis level postoperatively.

## RESULTS

The postoperative evolution was favorable; the length of hospitalization was  $11.97 \pm 0.16$  days, with amplitude from 8.00 - to 20.00 days. Postoperative mortality was absent at the stage of reconstructive operations. Immediate postoperative complications after surgical reconstruction operations were recorded in 69 ( $34.0 \pm 5.70\%$ ) cases. Most feared postoperative complication was the postoperative abscess, found at 1 ( $11.74 \pm 1.4\%$ ) patient. The situation was resolved by echo-guided percutaneous drainage with no need to solve classically. Transitory bile leak during first 72 hours after surgery was most frequent, evaluated at 24 ( $34.8 \pm 9.93\%$ ) patients, did not require additional interventions, being clarified with

the rehabilitation of intestinal passage after surgery. Wound infection was recorded at 15 (21.7  $\pm$  11.01%) patients and was resolved by conservative aseptic dressings. Alarming postoperative complications were partial anastomosis dehiscence established in 12 (17.4 ± 11.43%) cases. These cases were resolved conservatively, due to intraoperative drainage with anastomosis drainage system both posteriorly and anteriorly together with transanastomotic drainage after Veolker. Postoperative bleeding complications were encountered in version of wound hematoma - 9 (13.0 ± 11.89%) cases, recreation resolved by the cutting of infection through widened dressings with anesthetically potentiation. Postoperative pulmonary complications were recorded in 7 (10.1 ± 12.30%) cases, mostly pneumonia or bronchopneumonia due to prolonged intubation. The serious consequences of biliary infection were scored in episodes of cholangitis at 1 (11.74  $\pm$  1.4%) patient. Clinic situation was solved through targeted antibacterial and infusion therapy. The statistical correlation of clinical status, biochemical indices, level of stricture with postoperative morbidity showed that they influenced the arousal of complications (p = 0.01).

Remote surveillance on average was 29.89 ± 0.48 months, with amplitude range from 2.00 to 68.00 months. Excellent or good results were obtained at 134 (66.01%) patients, while 69 (33.99%) remaining patients showed reasonable or weak results. To assess quality of life in remote postoperative stage with a periodicity of 3 and then every 6 months postoperatively was used the assessment system represented by J. Terblanche. We mention four fundamental groups for evaluation scale. All results were measured with a digital database. In this assessment, we noticed that the best evolution in terms of indicators of inquiry have been established for the group I, evaluated in 123 (60.6  $\pm$  4.41%) cases with a truthfulness of  $p_{1,2}$ <0.001; t = 5.38. These patients demonstrated a sustainable recovery and a lack of complaints from the hepatobiliary system, with a full reinstatement in social activity. Group II cumulated satisfactory results observed in 39 (19.2  $\pm$  6.31%) cases with a truthfulness of p<sub>23</sub>> 0.05; t = 1.10. All patients were in good state of health, only episodically had clinical transient signs of a chronic liver and biliopathy. The last did not have any serious impact. These states were corrected by diet, hepatoprotective therapy, which were received episodically in the hospital. Group III represented patients who presented complaints at the time of the tests exam and hepatobiliary function disorders. These patients were registered in 18 (8.9  $\pm$  6.91%) observations and truthfulness of  $p_{3,4}$  > 0.05; t = 0.25. All of them required episodically surgical hospitalization with hepatoprotective infusion treatment under multidisciplinary control, which included hepatobiliary surgeon, hepatologist, gastroenterolo-gist, endoscopist. Making treatments allowed health compensation and avoidance of hepatobiliary suf-

fering progression. An unfortunate impact was that the vast majority of them have changed their profile and social activity regime. Group IV accounted patients with recurrent biliary stricture and essential disturbance of hepatobiliary function on reflux angiocholitis background or of severe cholestatic hepatitis. These situations we noticed at 23 (11.3 ± 6.75%) patients with a truthfulness of  $p_{1.4}$  <0.001; t = 6.12. In all 23 cases were found strictures of hepaticojejunoanastomosis, we performed plastic surgery of hepaticojejunoanastomosis with plastic elements of Heineke-Mikulicz type. Intervention aimed to liquidate the stricture and anastomotic restoration within the present tissues on anastomosis line. All cases had an intraoperative fibroplastic process on hepatojejunostomy level while the bile duct was not directly involved, presenting normal tissue. This moment was decisive in omitting the need to restore the anastomosis and achieve only a plasty of anastomosis mouth using 5/0 PDS atraumatic suture only in single plane and separate drainage of both liver channels. Drains were maintained for up to six months, having a housing role in order to stabilize the formation of the anastomosis mouth. The achieved postoperative results were very good. It's worth noticing that the issue of HJA strictures or anastomosis restricture require further study and has a major scientific actuality. Thus are analyzed and studied effects of complications on patient including its implications and their resounding on quality of life, disease progression and prognosis as well the impact on remote survival.

## **ISCUSSIONS**

latrogenic strictures of main biliary ducts are characterized by a high degree of severity, with the tendency to a more proximal location, more frequently found in recent years. Most restorative and temporary drainage interventions on biliary ducts require a new biliary-digestive intervention [6, 7].

In surgery for benign biliary strictures, reconstruction of biliary system through HJA has become a standard procedure. The anastomosis is performed through modern suture in a single layer mucosa-to-mucosa using a jejunal arm Roux-en-Y. It was proved to be safe and feasible, even in high reconstructions simultaneously applying on several bile ducts [6, 8, 15].

When Performing HJA, different types of suture of bile stump are applied to the intestine. Particularly important is the distance of suture application, the depth and the type of the suture. In current practice, anastomosis is performed with ordinary sutures that are passed through all layers. PDS suture material, Vycril 4/0-5/0 are accepted. We focus on a good eremitism, using sutures with a 2-3 mm step. The posterior lip is performed with the nodes in the lumen, and the anterior one with the nodes outside. Suture line is strengthened with up to 5 anterior sero-serous sutures only when necessary [17].

Regardless of biliary stump level, the precise mucosa-to-mucosa suture in a single plan of discontinued sutures and the placement of transanastomotic drainage tubes ensured a sufficient anastomosis with bile flow or remote strictures. It is quite important during high anastomosis, on the hilum level to drain each bile duct separately. Long-term outcome for these cases was reported as being comparable to low hepatico-jejuno-anastomosis [10, 23].

Hepp-Couinaud technique relies on left extrahepatic hepatic duct. Fascia incision concentrated around the hepatic artery, portal vein and represents the "hilarium plaque", which allows easy exposure of the extrahepatic left hepatic duct. Left hepatic duct is an excellent choice for repairing proximal strictures, because it is located under 4th segment and makes an optimal access to the stoma. In addition, it has a rich blood supply that is not affected by iatrogenic lesions, unlike the fragile blood supply of the common hepatic duct.

Remote results of HJA on Roux- en-Y loop are reported as very good by the majority of publications in the field, with excellent results in 85% of cases.

At least 5 years after the reconstruction are considered an optimal period of postoperative evaluation of the results. A series of studies underlines that two thirds of complications occur within 2 years, 80% within 5 years, while 20% of failures may occur 5 years after the operation. According to Leslie H. Blumgart, 40% of re-strictures were identified after more than five years since the reconstructive surgery. Therefore, monitoring during the first five years or more is necessary in evaluating the results. In choosing the critical length of time, the professionals should consider comparing the results from different series of treatments.

Large international experience in studying the quality of life (QoL) presents promising opportunities of this method for all branches of clinical medicine and can be used with traditional indicators for monitoring the effectiveness of surgical treatment. There is currently no data on the level of disability and postoperative rehabilitation after reconstructive surgery. Therefore, we consider it important to study the future quality of life of patients with iatrogenic lesions and scar biliary strictures. The effectiveness of bilio-digestive anastomoses should be evaluated in the immediate postoperative period and in time. Research of QoL can help solving the problem of patients' rehabilitation and their return to normal life.

## CONCLUSIONS

The diagnosis and management of benign biliary strictures remain a challenge. Given the risks of septic biliary complications, the costs and the high associated morbidity due to repeated surgeries, an accurate diagnosis is crucial. A detailed medical his-

tory and a multidisciplinary approach to guide the treatment goals, is important in ensuring a satisfactory lasting outcome after surgery.

Factors such as the detailed knowledge of the patient's medical history or embracing a multidiscipli-nary approach in managing treatment objectives have important contribution to a satisfactory and lasting outcome.

The definitive goal of surgical management is to restore bile flow in the proximal gastrointestinal tract that prevents any reflux cholangitis, re-strictures of the biliary tree and chronic hepatobiliary pain.

The reconstructive surgical act addressed to iatrogenic biliary strictures is directly related to the localization. Choosing the appropriate reconstructive surgical method to address iatrogenic biliary strictures depends on their localization. For type I strictures, an end-to-side choledochojejunostomy with a Roux-en-Y excluded loop is optimal. For the type II, the solution consists of a choledochojejunostomy with a Roux-en-Y single loop, and case of a high upper extension of the stricture, we proceeded to hepaticojejunostomy with a Roux-en-Y excluded loop.

For type III stenosis, an end-to-side hepaticojejunostomy with a Roux-en-Y excluded loop and transanastomotic drainage of the right and left hepatic ducts is applied. For type IV, a double hepaticojejunostomy with a Roux-en-Y excluded loop and mandatory transanastomotic drainage of both ducts is preferred.

A unified method for remote assessment of patients with postoperative biliary stricture would make possible a good estimation of the occurring complications and quality of life (QoL). Curently, it is important to know and evaluate the impact of biliary strictures and reconstructive operations on the patient's health and rehabilitation based on biomedical, physiological and socio-economic indices. Study of QoL, among the multitude of factors related to health, would allow a deeper analysis of multifactorial components of human health according to WHO criteria, namely the medical-physiological, psychological and social problems of the patient.

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## ABSTRACT

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**Introduction.** Once medical progresses have improved, which determined health care and therapeutic result improvement, rising the quality of life has become a major desideratum, with important contribution in the elaboration of the therapeutical decision

**Materials and methods.** It has been realized a bidirectional clinical trial for a period of 11 years, which evaluated the surgical impact on the quality of life of 97 patients, diagnosed with hepatic cirrhosis. The research took place at Surgery nr2 department, hepatobiliopancreatic surgery department of the Republican Hospital in 2005-2016 period. The patients in the study, benefited of selective, scheduled surgical treatment. The quality of life was assessed using the SF-36 and SF-LDQOL questionnaires.

**Results.** Postoperatively, patients with liver cirrhosis and associated portal hypertension (89%) noted a significant improvement in the quality of life in both the control group ( $p \le 0,002$ ) and the preoperative stage ( $p \le 0,001$ ). Remarkable in all the operated patients, in the first year after the intervention, the quality of life improved in moderate/good quantification in 78.9% of patients.

**Conclusion.** Patients with liver cirrhosis have significant impairments in quality of life. The possibility of improving the quality of life is in direct relation to the stage of liver cirrhosis, type of the surgical intervention and rate of postoperative complications. Life quality assessment studies are useful, because it provides important information for optimizing therapeutic methods, reduction of morbidity and improving prognosis.

Key words: cirrhosis; liver; portal hypertension

## **INTRODUCTION**

The Liver cirrhosis is considered a disease-generating various complication developmental leading in most cases limiting or temporary losing of working capacity, with significant economic consequences both on society and the individual level [1, 2]. In the Republic of Moldova, compared to the other EU countries, is recording the highest mortality by chronic liver diseases: 116 deaths per 100,000 males and 99.4 deaths per 100,000 female populations respectively [1, 3, 10]. Multimodal treatment (hepatotropic, endoscopic, surgical) of cirrhosis has become a current medical practice [4, 5]. The goals of treatment of this serious disease are the reduction of mortality by stopping the progression of liver disease by stage complications and a consequent reduction in the inflammatory process metabolism and the improvement of quality of life that includes physical, mental and social welfare [6, 7, 11]. Has been demonstrated, clearly, the negative impact of hepatic cirrhosis on the quality of life. Social support, social stigma, personal vulnerability of the disease with the tendency towards complications, style of coping are the factors involved in adapting the individual to the disease, their seriousness being directly correlated with the deterioration of the quality of life [8, 9, 13].

In this context, from the unfortunate impact of liver cirrhosis on the quality of life, is required to be controlled through effective treatments, an interdisciplinary, integrated and coherent approach, and a proper conduct of post-treatment surveillance at a distance. Managing symptoms and maintaining a maximum possible degree of hepatic functionality is the main purpose of medical professionals focused on the ill person. According to Romanciuc I. (2013), contribution of Quality of Life (QoL) in developing therapeutic decision remains an important topic for patients and physicians [8, 12]. There is a necessity of studies of evaluating the quality of life through specific questionnaires dedicated to liver disease, capable throughout the various stages of therapy, to provide a comprehensive image of the perception of patients about their health status [14, 116]. The aim of this study is to evaluate quality of life for patients with liver cirrhosis who were surgically assisted and identify the elements of differentiation of the evolution of quality of life after the treatment with severity of liver disease and surgical gesture, selectively practiced within the complex scheme of portal hypertension cirogene therapy [15].

## MATERIAL AND METHODS

The study was qualified by exploration and quantitative approach of quality of life. The study material consisted of patients diagnosed with LC, surgically treated and followed during the study period 2005 -2016 within the Surgery Clinic No.2, State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Moldova.

The research protocol was approved by the Research Ethics Committee of the "Nicolae Testimitanu" University of Medicine and Pharmacy, Chisinau, Republic of Moldova (favorable opinion from the Minutes No. 59 of 18.06.2015, CEC President-Prof. M. Gavriliuc). All evaluated subjects received detailed information on the methodology of the study. The patients signed an informed consent to enroll in the study.

The diagnosis of LC was clinically, laboratory and morphological imaging held, data that allowed calculation of the disease scores: Child-Pugh and MELD.

In the mentioned period, 118 patients were operated. Among them were enrolled in basic research sample a total of 97 patients.

Inclusion criteria in the study:

- · history of surgical treatment for liver cirrhosis;
- age over 16 years;
- confirmed diagnosis of liver cirrhosis;
- ability to understand the questionnaire;
- informed consent for enrollment in the study. Exclusion criteria in the study:
- severe language deficiencies, which make it impossible to complete the questionnaire;
- hepatocarcinoma developed on the background of cirrhosis;
- concomitant haematological diseases;
- patients who for various reasons have dropped monitoring.

Conventionally, from point of view of statistical terms, all respondents were subdivided into three groups according to surgical method applied by the same medical team:

- subgroup A consisting of 57 patients (58.7%), which benefited from the azigo-portal devascularisation + traditional splenectomy (SPLT);
- subgroup B, consisting of 27 patients (27.8%), which had surgery through a minimally invasive method - DVA + laparoscopic splenectomy (Spll).
- subgroup C, consisting of 13 patients (13.4%) which received the liver transplant.

In the studied case, the choice of the type of

surgery was made according to the general state, portal obstruction and topography of spleno-portal venous spindle, evolutionary stage of liver cirrhosis, possible pathological lesions. Thus, adapted to each case, the surgical interventions were intended with radicality. The majority (83%) were practiced under the following technical conditions: splenomegaly stage III-IV (83.4%), severe hemorrhagic syndrome (78%), important perisplenism (49%), the presence of lymph nodes in the lienal hill (31%), the pancreas tail located intrahilar (41%), fascicular variation of splenic vascular pedicle (7%).

The surgical indications, selectively imposed on liver cirrhosis complications:

• liver cirrhosis, portal hypertension, severe splenomegaly;

• liver cirrhosis, portal hypertension, 3-degree varices with bleeding risk;

• liver cirrhosis, portal hypertension, severe splenomegaly, the presence of one or more episodes of esophageal bleeding;

• liver cirrhosis, portal hypertension, giant splenomegaly, with compression elements (splenic infarct, subcapsular haematoma);

• liver cirrhosis, portal hypertension, severe pancytopenia, induced by antiviral therapy;

• liver cirrhosis, portal hypertension, autoimmune splenomegaly.

To achieve the goal and achieve the objectives, patient quality of life was assessed in parallel with the clinical-biological and imagistic data of the preoperative cytorellular patient and at an interval of 1-3-5 years post-surgical, to be able to ascertain the implications of the surgical therapy on the quality of life. Assessing the impact on quality of life was achieved by generic SF-36 questionnaire used to determine the value of mental component summary (MCS) and physical component summary (PCS) and the specific SF-LDQOL (9 fields, 36 items). The last one was developed by Dr. Fasiha Kanwal (2008), with the written consent of that was translated in Romanian [11]. The SF-36 questionnaire contains 36 questions that assess: functional status - physical function (questions 3 a-j), limiting health (questions 4a- d), bodily pain (questions 7- 8), general health (questions 1, 11 - d), and the mental component summary (MCS) scales composed of: vitality (questions 9a, 9e, 9g, 9i), social function (questions 6, 10), emotional role (questions 5a-c), mental health (9b questions, 9c, 9d, 9f, 9h).

The research has been completed with the SF-LDQOL contains 36 questions that assess: symptoms related to the disease (questions 1 - f), the consequences of liver disease (questions 2a-c), concentration/memory (questions 3, 4a, 4b, 5), the problems caused by disease sleep (questions 11a-e), isolation (questions 12a-e), hope (questions 13a-c), stigma liver disease (questions 14a-d), the function/sexual issues (questions 7,9a-b, 10). For all scales studied, scores (score) was from 0 to 100.

The statistical analysis was performed with the statistical analysis software GraphPad Prism 4 (*GraphPad Software*, California, SUA). The results are presented as absolute and relative values (binary data), mean and confidence interval of 95% (continuous data type).

## RESULTS

The clinical characteristics of the patients included in the study, depending on the surgery performed are shown in table 1.

# Table 1. Clinical charact eristics of patients enrolled in the study, depending on the surgery performed.

Parameter	All subjects (n=97)	DVA+SPLT (n=57)	DVA+SPLL (n=27)	TH (n=17)
The etiology of cirrhosis • liver cirrhosis HBV • liver cirrhosis HCV • liver cirrhosis HBV + HCV	54 (55.7%) 28 (28.9 %) 16 (16.5 %)	33 (57.9%) 10 (17.5%) 14 (24.6%)	20 (74.1%) 7 (25.9%) -	1 (7.6%) 11 (84.6%) 1 (7.6%)
Clinical signs • ascites • jaundice • variceal haemor- rhage in anamnesis • severe splenomegaly	15 (15.5%) 11 (11.3%) 19 (19.6%) 71 (73,2%)	2 (3.5%) 2 (3.5%) 7 (12.3%) 49 (85.9%)	3 (11.1%) - 5 (18.5%) 11 (40.7%)	10 (76.9%) 9 (69.2%) 7 (53.8%) 11 (8.4%)
Impaired liver function <ul> <li>Child C score</li> <li>BEA A/B score</li> <li>Previous antiviral treatment</li> </ul>	15 (15.5%) 15 (72.2%) 17 (17.5%)	1 (1.7%) 3 (3.2%) 7 (22.3%)	1 (3.7%) 3 (11.1%) 5 (18.5%)	13 (100%) 11 (9%) 5 (39.4%)

In all patient groups, the symptoms of liver impairment were identified. The collected data confirms the existence of social issues: diminishing social activities, the limitation of work capacity, the impossibility of satisfying physical and psychological needs. The analysis of the general group revealed that 72% of the respondents did not have a job. Invalidity grade II-III had 82%; in 10% of the patients, the diagnosis was documented less than 3 years ago, 45% - 3-5 years ago and 18% - more than 5 years ago. Most patients accused asthenic syndrome (96%) and severe splenomegaly (73%).

In 83.4% of cases, patients were under hepatotropic syndrome, 14.4% of cases were followed by antiviral medication and 2.1% of hormone therapy.

By processing the data of the SF-36 questionnaire, it was shown that preoperatively, most patients in the study group had a severe impairment of quality of life, of varying degrees. Significant differences were noted between the overall health status of the investigated group vs. control group (practically healthy individuals) (table 2). Table 2. Comparison of the quality of life, according to SF-36, in patients with liver cirrhosis (initial, preoperative) vs. healthy people

Qualitu-of-life parameters	Cirrhotic patients (n=45)	Healthy subjects (n=20)	р
Physical function (PF)	61 [37-69]	93 [70-80]	<0.001
Physical Role (PR)	33 [27-78]	81 [75-81]	<0.001
Somatic Pain (BP)	54 [32-61]	74 [60-75]	<0.05
General Health (GH)	49 [21-58]	65 [54-66]	<0.05
Vitality (VT)	51 [26-46]	61 [53-68]	<0.001
Social function (SF)	62 [23-52]	78 [62-78]	<0.05
Emotional Role (RE)	43 [31-68]	75 [62-69]	<0.001
Mental Health (SM)	65 [33-59]	67 [52-62]	<0.05
Summarized physical health status (SSF)	38	52	<0.05
Summarized mental health status (SSP)	43	46	<0.001

Note: statistical analysis: Fisher test. The data are presented as [extreme] median.

It is noted that the most affected aspects, compared to the benchmark score, were the psychological and functional status, social and family life, and professional activity.

The influential of analysis of Child-Pugh score on life quality prior to surgery (table 4), revealed that overall health status is significantly lower in patients with Child C score, compared to those in Child A and B classes, who in most cases were hepatically decompensated and undergoing to liver transplantation.

The current study reveals an improvement in the quality of life of the operated patients, translated by improving the physical and psychological function compared to the preoperative level (table3).

From the dynamics of the obtained results, it is noticed that postoperatively, the patients with liver cirrhosis and associated portal hypertension noted an improvement of the quality of life, in relation to both the control batch ( $p \le 0.002$ ) and the preoperative ( $p \le 0.001$ ). It is worth noting that, in all patients of the operated group, in the first postoperative year, improvements in quality of life have occurred, with moderate/good increases in over 78.9% of patients. In our series, postoperative satisfaction was good, 85.3%, and the SF-LDQOL score improved significantly versus pretreatment.

The beneficial effect of surgery on quality of life is documented by the significant increase of emotional and global status level, and from functional scale only social status did not change essentially. SF-LDQOL scoring data of analysis at one post-operative year, recorded on the physical and emotional factors items in two categories of patients (SPLT versus SPLL), shows higher net differences for the SPLIT lot. This trend disappears at 3 and 5 years of monitoring, when there is no significant difference in both groups on the scale of vitality and social functioning, which is explained by the fact that the somatic state of the patients treated for liver cirrhosis worsens over time, through parenchymal and vascular decompensations.

Laparoscopic operations and postoperative benefits in terms of quality of life of this intervention exceed, in many aspects, the results of classical surgery in the first postoperative year.

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## Table 3. SF-LDQOL score: The evolution of postoperative quality of life at 1-3-5 years

		Preopera-		
Domains	Up to 1 year	Up to 3 years	Up to 5 years	tive
1. Symptoms related to liver disease	71.73 ± 6.87*	69.16 ± 9.37*	70.0 ± 12.07*	66.6± 8.04
2. Consequences of liver disease	67.15 ± 6.85*	65.14 ± 9.33*	66.4 ± 13.69*	63.2± 11.32
3. Concentration and Memory	66.1 ± 9.30*	60.12 ± 9.30*	65.3 ± 12.26*	77.7± 9.17
4. Problems caused by the disease	51.13 ± 6.91*	37.7 ± 9.41*	61.2 ± 11.29** t <sub>L1C, L0</sub> =2.34	51.3± 7.09
5. Sleep	54.5 ± 6.90*	53.0 ± 9.41*	57.0 ±11.58 t <sub>L1C, L0</sub> =1.99	54.9+ 9.08
6. Isolation	66.67 ± 6.52*	71.5 ± 8.89*	64.4 ± 11.58*	71.2± 14.03
7. Норе	63.3 ± 6.40*	58.3 ± 8.72*	54.7 ± 13.71*	63.2± 10.11
8. Stigma of liver disease	74.42 ± 6.01*	63.7 ± 8.19*	77.3 ± 11.03*	75.7± 13.17
9. Sexual function / issues	62.7 ± 6.64*	71.2 ± 9.05*	68.8 ± 9.98*	65.1± 13.07

Laparoscopic operations and postoperative benefits in terms of quality of life of this intervention exceed, in many aspects, the results of classical surgery in the first postoperative year. Following the evolution of liver disease severity, measured in the studied cases by Child-Pugh score, was noticed that the choice of surgery after well-defined indications, it is a way of effective treatment of cirogene portal hypertension. In most of these cases (67% of patients) we noticed that interfering in relation to liver disease complicated postoperative course had a major negative impact on quality of life. It is emphasized that the analysis of specific liver disease symptoms, self-reported in the analyzed sample, recorded a lower level of the phenomenon studied in decompensated cirrhotic patients, Child C class, who benefited from hepatic transplantation. This tells us the highest scale parameters: social, psychological and functional emotional. Therefore, the quality of life of the patients in the selected and operated casuistry, in cases where they underwent liver transplantation, was clearly superior to the other types of interventions. The analysis of the results reveals that this qualitative increase in living conditions is also due to complex therapeutic and interventional measures of organizational, social, family and community elements. The results of the study show that, if preoperatively, 79% of operated patients experienced a quality of life impairment due to reduced household activities they could make, at 12 months postoperatively, only 36% of patients still had this problem.

On the studied lot, they were recorded 17 cases (17.5%) who had various postoperative complications, predominated by venous thrombosis shaft – 5 cases (5.15%) of conservative treatment received antithrombotic; the emergence abscess of LEFT under diaphragm - 3 cases solved by eco-guided external drainage installed; parietal suppurations - 4 cases and ascites - 5 cases.

In terms of the SF-LDQOL score, it was found that in those who presented complications, psycho-emotional and physical status was significantly lower (p=0.030 and p=0.001, respectively). One postoperative year, 7 patients had post-operative outcomes which, however, did not associate with a significant decrease in quality of life. An important deterioration in quality of life was present at 3 patients with portal vein thrombosis and secondary ascites - a specific complication of post splenectomy. Discussion with patients on control, clinical, ultrasound and endoscopic examination, performed at 3 years postoperatively, and analysis of outcomes after hepatic cirrhosis surgery, have confirmed the relapse of esophageal varices (6 cases), ascites (7 cases), portal vein thrombosis (4 cases). The analysis of the answers to the questionnaires in these cases found that the overall satisfaction level of these patients were significantly affected (25.6%). Scoring achieved post-treatment for the overall health status/quality of life status recorded significant differences between pre- and post-therapeutic trials and revealed an improvement from 25.6% to 51.3%, on the account of physical factors (36%) and emotional (16%). We are summing up that screening and therapeutic support programs implemented after surgery and endoscopic curative antiviral treatment have increased the quality of life of patients in the study group, having surgery for liver cirrhosis.

#### DISCUSSIONS

Hepatic cirrhosis is a public health problem, is a major cause of morbidity and mortality induced by the development of evolutional complications. In past years, has been paid more attention to the quality of life of these patients [16, 17, 20]. The results obtained from this study were compared to the data from literature, showed that the quality of life of patients with liver cirrhosis had decreased significantly, physical and psycho-emotional functions declined. Therefore, the importance of quality of life controlled by effective treatments raised [19]. Treatment of hepatic cirrhosis is complex, multimodal, and includes a combination of endoscopic and surgical methods, as well as a multidisciplinary approach. Of all the specific questionnaires tested regarding the quality of life assessment of patients with chronic liver disease, the short-form SF-LDQOL questionnaire showed the best performance.

In the clinic, with the application of the SF-36 generic score, appreciated by the users for simplicity but also criticized for the lack of suggestive parameters, we translated, validated and implemented in

practice the SF-LDQOL questionnaire as a measure of the quality of life of patients with diseases chronic liver disease. The study shows that the use of the short-form SF-LDQOL questionnaire contributes to collecting static and dynamic life quality data at different stages, pre- and post-operative [18].

The results obtained post-operatively at a distance confirm the beneficial effect of surgical interventions on the quality of life for the selected cases of patients with liver cirrhosis. Improvements were seen at approximately 78-82% of patients operated, influenced, net to favorable, as follows: hepatic transplantation, azygo-portal devascularization and laparoscopic approach splenectomy, azygo-portal devascularization and splenectomy. Traditional approach, which confirms the beneficial effect of portal hypertension surgery through cirrhosis in selected cases. The data obtained once again justifies the importance of assessing the quality of life, and introducing it into the monitoring programs of the cirrhotic patient operated.

#### **CONCLUSIONS:**

- 1. Patients with liver cirrhosis have significant impairments in quality of life. The possibility of improving the quality of life is in direct relation to the stage of liver cirrhosis, type of the surgical intervention and rate of postoperative complications.
- Life quality assessment studies are useful, 2. because it provides important information for optimizing therapeutic methods, reduction of morbidity and improving prognosis.

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#### ABSTRACT

ᆔ

**Aim:** to delineate the symptomatic features and to emphasize the necessity of early diagnosis and complete surgical excision of rectal duplications.

**Method.** We undertook a retrospective and contemporary review of all patients. Clinical recordings, preoperative evaluations, intraoperative and histological findings, and current patients' condition were studied.

**Results.** Age of the six patients ranged from new-born to 13 years. There was a broad spectrum of clinical presentation: two children were seen after previous therapy elsewhere with a mistaken diagnosis of perianal fistula, respectively undefined abdominal pain; two presented with exstrophic duplication of the rectum; one neonate was seen with an anal cleft and one infant with rectal bleeding and retrorectal palpable tumour. Paraclinical investigations established preoperative diagnosis in one patient, aided it in two others, and detected associated anomalies in two further patients. All duplications were "in toto" removed using laparotomy (n = 1), transanal (n = 1), or perineal sagittal approach(n = 4). All duplications had contact with the rectum. Smooth muscle coat and intestinal epithelial layer were histological demonstrated in each case.

**Conclusions.** Rectal duplications are rare anomalies. Clinical manifestations may include abdominal pain, obstipation, rectal bleeding, urinary or bowel obstruction, rectal polyp, perianal fistula, perineal abscess, and pelvic, abdominal, retroperitoneal or perineal mass. Early diagnosis avoids prolonged symptomatic treatment and unnecessary operative procedures. Complete excision is curative.

Key words: rectal duplication; exstrophic duplication of the rectum

## **INTRODUCTION**

Congenital duplications of the alimentary tract are rare but potentially dangerous anomalies. There is no sex predominance. Any segment of the intestinal tract may be concerned, but small bowel is more involved. Among the 764 cases of Daudet [1], 490 (64%) were small bowel duplications (57% jejunum and ileum, 7% duodenum), and 38 (about 5%) were duplications of the rectum.

Duplications are cystic or tubular structures located usually adjacent to the mesenteric border, but other locations were also reported [2, 3, 4]. Rectal duplication may have diverse presentations, which include bowel or urinary obstruction, haemorrhage, infection, perforation, chronic obstipation, perianal fistula, perineal abscess, tumour of the labia major, exophytic tumour of the perineum, asymptomatic mass, pelvic floor hernia [5, 6, 7, 8, 9, 10, 11, 12, 13, 14]. Therefore the diagnostic is often delayed or incorrect. The early complete excision is the choice therapy of the alimentary tract duplications. That is particularly important in rectal duplications because of the risk of late malignant changes [15, 16, 17].

## **MATERIAL AND METHODS**

This review encompasses 6 patients with clinically different manifestations, 4 of them diagnosed and cured by first admission, while 2 have been treated elsewhere over a long time period for perineal abscess, respectively undefined abdominal pain. All patients were diagnosed and treated in our department from September 1992 to march 1996. This study used the patients charts, preoperative investigations, intraoperative findings and histological examinations. All patients underwent clinical follow-up 12 - 22 y (mean 17 y) postoperative.

**Case 1 (Surgery 09/1992)**. An 11-month-old boy was brought to our clinic after a 5 months history of perineal abscess. He was twice operated but symptoms did not disappeared. At admission he presented an inflamed retroanal fistula and had painful defecation. Putrid secretion flowed throughout fistula. Sonography findings were compatible with a retrorectal cystic tumour. After 7 days of antibiotic therapy and local betajodine bath the inflammation ceased. By a posterior sagittal approach the retrorectal cystic tumour was removed. Histological examination revealed colonic structures.

**Case 2 (Surgery 03/1993)**. An 11-days-old male was admitted with a mucosal-lined skin defect and an exophytic mass left perineal. The mass in contiguity with the rectum had a separate perineal opening (fig. 1). Clinical examination revealed hemi-hypertrophy with asymmetry of the pelvis, hip luxation, left thigh hypotrophy, and clubfoot on the left side. The following investigations were performed: plain x-ray and sonography of the pelvis and abdo-

men, echocardiography, micturating cystourethrogram, diuretic nephroscintigram, cystoscopy with retrograde ureteropyelography, magnetic resonance imaging (MRI), and urodynamic examination. These investigations showed the absence of musculus gluteus maximus and musculus piriformis, absence of sacrotuberous and sacrospinosus ligament, no foramen ischiadicum majus and minus. Instead of the last two there was a defect where through part of the colon and left kidney herniated subcutaneously in the gluteal region. Additionally, the patient had an aortic isthmus stenosis, PDA, bilateral vesicoureteral reflux, caudal regression syndrome, tethered cord, lumbosacral lipoma, At 3-months the perineal mass was excised and histologicaly identified as colonic structure. The left kidney was relocated in the pelvis using a vicryl-net. Two years later the left kidney herniated again. A plasty with prolene-net was achieved. Twenty two years postoperatively the patient has regular bowel movements, normal renal function, no urinary infections, and good function of extremities. He is on medical therapy for hypertension.

**Case 3 (Surgery 09/1993).** A 3-days-old female infant with a birth weight of 3210g was brought to our department with an anal cleft at "3 o'clock" (with patient in supination). Pelvic sonography showed no pathologic findings. A contrast enema was carried out: there was a diverticular structure communicating with the rectum. A transanal resection followed when the child was 3 weeks old. The postoperative course was uneventful. Histological examination diagnosed colonic structures.

Case 4 (Surgery 07/1994). A 6-year-old female presented with an exophytic mass (7x5cm) of the labia minora (fig. 2). The mass covered by epithelium, had a lumen with an opening onto the vulva which through a probe was easy introduced. No other anomalies of outer genitalia, meatus urethrae or anus were observed. Paraclinical investigations detected a left ureteral duplication with ureteric ectopia and upper pole dysplasia, and vesicoureteral reflux of the lower pole. By a paramedian anterior sagittal approach the exophitic mass was excised. Intraoperatively a contact between the mass and the rectal wall was found. The histological diagnosis was rectal duplication covered by colonic and ectopic gastric mucosa. The dysplastic upper pole of the left kidney was removed by a subcostal incision.

**Case 5 (Surgery 02/1996)**. A 13 ½ -yr-old boy was brought to our department after being treated over a long period for undefined abdominal pain. No pathological findings at physical examination were found. The sonography showed a precaval, subhepatic cyst with a diameter of 3 cm. Nuclear magnetic resonance scans (NMR) demonstrated the cyst located in the retroperitoneum. The cyst ended in the right side of the rectal wall and was filled with grey fluidly-mucous content (Fig. 3). The excision was carried out through a right supra-umbilical transverse laparotomy. A tailgut cyst lined by epithelium with gastric mucosa ectopy was demonstrated by histological examination.

**Case 6 (Surgery 03/1996).** A 3-month-old female infant was admitted for rectal bleeding. Rectal examination revealed walnut size tumour on the posterior wall of the rectum. Sonography showed a 3 x 2 cm cystic structure between sacrum and rectum. This tumour was removed by a posterior sagittal approach. The rectum and duplication shared a muscular layer. Six days after the operation a small dehiscence of the wound occurred. This closed spontaneously 10 days later. Histopathological exam identified a tailgut cyst with included ectopic gastric mucosa.







The explanations of this material are presented in the text (red.)

## RESULTS

The age at presentation of the 6 patients ranged from new-born to 13  $\frac{1}{2}$  years (mean 3 4/12 yr.). The female: male ratio was 4 : 2. There was a broad spectrum of clinical presentation:

- two patients presented with extrophied perineal mass: one of them had multiple associated anomalies (case 2), the other only renal associated anomalies (case 4).
- one neonate female was diagnosed with an anal cleft at "3 o'clock" (case 3).
- one patient was seen because of rectal bleeding (case 6).
- two patients came to us after previous therapy elsewhere: the first with perineal swelling was twice operated erroneously for perianal fistula (case 1), the second treated for chronic abdominal pain (case 5) with medications.

The preoperative diagnosis was extrophy of the rectum in 2 patients (cases 2 and 4), retrorectal cystic tumour in 2 (cases 1 and 6), diverticular rectal duplication in 1 (case 3), and retroperioneal cystic tumour in 1 (case 5).

In three cases the preoperative diagnosis (associated anomalies excepted) was by clinical means only (cases: 2, 3, and 4), twice by clinical examination and sonography (cases:1and 6), once by sonography and MRI (case 5).

The surgical approach was perineal sagittal in 4 patient (posterior median in 2, posterior paramedian in 1, anterior paramedian in 1), transanal in 1, and laparotomy in 1.

Complete excision of the tumour was accomplished in each patient. All patients had intraoperative and postoperative antibiotic therapy, and were drained for 2 - 5 days postoperatively. Recovery was uneventful in all patients, except for a small wound dehiscence (case 6). Histological anatomy is shown in table I. The follow-up (mean 17 years postoperative) shows good function, good cosmesis in all cases, without complaints due to rectal duplication.

Table 1. Histological anatomy of the excised structures

>Small muscle coat	all
>Intestinal mucosa* - including crypts of Lieberkühn	all
>Gastric mucosa heterotopy	n = 3

\*Taylgut cyst mucosa: cylindrical, transitional and squamous epithel, crypts of Lieberkühn

## DISCUSSION

The embryogenesis of these abnormalities is uncertain [9, 18]. The most satisfactory theories of alimentary tract duplications are the partial twining theory and that relating to the residua of the neurenteric canal. The dorsal anatomic location of most duplications is supportive of this last theory [9]. However more duplications have been found in other sites on the bowel circumference [2, 3, 4]. Perineal exophytic mass or tumour of the labia majora are other possible presentation forms of rectal duplications [19, 20, 21, 22, 23]. Two of our patients had a very special duplication form: the rectum extrophy (cases: 2 and 4). Another one has a retroperitoneal, prerenal cystic duplication with the caudal end in the lateral wall of the rectum (case 5).

Clinic examination and sonography in the case of 5 patients provided enough information to submit the patients for surgery. A patient needed supplementary MRI investigation to improve diagnosis (case 5). Because high rate of associated anomalies, all patients with rectal duplications will be thoroughly clinically and, in doubt, paraclinically examined.

Differential diagnosis of rectal duplications enclose all pelvic, and some abdominal and perineal tumours. Rectal duplications can be confused with rectal polyps, haemorrhoids, anal fistula (case1), and perirectal abscess [8, 10, 11, 24]. No patient in this series had duplication of the bladder, urethra or genitalia [25, 26, 27]. Only one patient had a unilateral ureteral duplication (case 4). There were no duplications in our patients communicating with urinary tract or intraspinal space [28, 29]. All lesions presented here fulfilled the criteria for alimentary tract duplications as defined by Ladd and Gross (30): a) contiguity with and strong adherence to same part of the alimentary tract; b) a smooth muscle coat; c) a mucosal lining consisting of one or more types of cells normally observed in the alimentary tract.

Presence of heterotopic gastric mucosa may be a source of rectal bleeding [7]. Malignant degeneration in rectal duplication in adults age is possible [15, 16, 17]. Carcinoid tumour in a rectal duplication in children have been also reported [31]. Therefore completely surgical excision is required.

### COMCLUSIONS

These observations showed that the child with rectal duplication is a good candidate for surgical procedures planed to cure completely the child's suffering. Early diagnosis avoids prolonged symptomatic treatment and unnecessary surgical procedures.

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## ABSTRACT

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This article includes the management of one clinical case. A 27 years old patient was urgently hospitalized with upper digestive hemorrhage diagnosis, caused by Dieulafoy disease. The primary diagnosis was confused and needs more pre- and intraoperative confirmations. Histological and morphological examinations confirmed the clinical diagnosis. The surgical treatment and intensive care contribute to removal of vital risk and better therapeutic outcome.

Key words: Dieulafoy disease; hemorrhage; histology, treatment

## INTRODUCTION

Angiodysplasias of the gastro-intestinal tract are vascular abnormalities situated in the wall structure of digestive tract organs, from the esophagus to anus. They are often acquired and, more rarely, congenital, clinically appreciated or latent, evolving on their own or in association with other pathologies. Fontch P. defines angiodisplazia as an idiopathic syndrome consisting of ectasia of intestinal submucosa, with or without ectasia of overlying mucosa capillaries [3, 4, 6, 7, 8].

Dieulafoy disease represents an arterial angiodysplasia characterized by anomaly of vascular development of the stomach submucosa, with the presence of large arterial erosions in the absence of vasculitis with the formation of acute ulcers, often complicated with digestive haemorrhage [2, 4, 7]. Similar cases were described at autopsy by Gallard (1884). The detailed clinical picture was described by Dieulafoy G. (1998), being distinguished as a separate nosologic form – simple ulcers [3, 4, 5].

Clinical features of the disease are:

- It is characterized by proximal stomach lesion, localization of ulcers on the posterior wall, small curvature (60-80%), at a distance of up to 6 cm from the esophagus junction [2, 7];
- It occurs between 16-96 years (average 50-60 years), the ratio of men: women being 2:1;
- It is presented as a source of superior digestive hemorrhage (0.3-5.8%), recurrent (18-100%), cataclysmic hemorrhages in 1/3 of patients [1, 3, 4];

 Clinical development is characterized by: sudden onset without abdominal pain; active hemorrhage (hematemesis, melena) [2, 8];

Predisposing factors are: chronic alcoholism, salicylates and steroids administration, stress. The absence of ulcerative anamnesis is important [2, 8].

The Dieulafoy ulcer may be located on the way of the digestive tract and may be associated with other pathologies such as: gastric and duodenal ulcers, Mallory-Weiss syndrome, Crohn's disease, gastric cancer [2, 4, 6].

Histomorphologically it is characterized by: the presence of large arteries in the ulcerous defect of the stomach mucosa, dysplasia of muscular substrate vessels and lymphocytic infiltration [2, 4, 6].

Diagnosis of Dieulafoy disease in the multidisciplinary study of causes of digestive hemorrhages is based on endoscopic techniques (48-98%), selective angiography results (30%) and histomorphological study (20%). All of these methods are used to identify Dieulafoy disease, assess the localization of vascular fistula, and evaluate treatment outcomes [2, 4, 7].

**Clinical case:** Patient S., aged 27 years old, is hospitalized urgently for a specific symptom of superior digestive hemorrhage: repeated vomiting with fresh blood and clots, vertigo, headache, general weakness, melena. From the past, it is known that in 2012 he suffered the first upper gastrointestinal hemorrhage, and he was treated conservatively under stationary conditions. He was healed and discharged with the diagnosis of Mallory-Weiss syndrome, receiving recommendations for ambulatory treatment. The general exam reveals that at the admission, the patient is in a general serious condition. The visible skin and mucosa are pale and clean. Cold sweats, hypotension – 90/60 mmHg, tachycardia, FCC-120 bpm /min.

The patient presented a hypovolemic shock. The nasogastric tube evokes gastric content –hematemesis, fresh clots. Rectal exam – rectal ampoule with changed blood content. Laboratory samples show post hemorrhagic anemia – Hb - 70 g / l; erythrocytes –  $2.4 \cdot 10^{12}$  g /l.

The admission diagnosis focused on Mallory-Weiss syndrome complicated with superior digestive hemorrhage gr. II-III; hypovolemic shock. The diagnosis has been endoscopically confirmed. Two flat defects of 1.8-1.3 cm and 1.5-0.3 cm, fibrin-coated, are determined in the esophageal junction. Emergency treatment in the intensive care unit includes correction of volume and hematic correction, antiulcer medication, hemostatic. The patient is in clinical and hemodynamic improvement. More than 18 hours after hospitalization, the hemorrhage is re-evaluated. Repeated endoscopic control is performed, the source of hemorrhage cannot be appreciated due to inconclusive endoscopic signs. The Blackmore probe for the Mallory-Weiss syndrome was applied, the upper digestive hemorrhage being stopped.

For a differential diagnosis of superior digestive hemorrhage with digestive angiodysplasia, repeated endoscopic control was performed over 48 hours after admission, attesting to the presence of 2 mucosal rupture of 2.0 cm and 1.4 cm in diameter, which covered the gastroesophageal junction with fibrin. In the posterior subcardial area on fornix – a 0.5 cm pitched defect with freshly fixed thrombus, laminar hemorrhage.

Endoscopic diagnosis: Dieulafoy's disease complicated with repeated, active digestive hemorrhage. Surgical treatment is indicated immediately.

Intraoperative endoscopic control confirmed: the stomach of normal size and shape, elastic walls. In the stomach lumen – coffee grounds hemorrhage, the glossy pale mucosa of the stomach. Preserved relief of the fornix, esophageal and cardiopulmonary varicose veins were absent. In the posterior subcardial area of fornix, a 0.5 cm pitched defect with a freshly fixed thrombus was assessed.

Gastric resection is practiced. In the proximal subcardial region of the stomach, on the large curvature - the posterior wall, at 3.0 cm from the esophagus junction, there is a mucosal ulceration of 3.0 mm, covered with a fresh thrombus, fixed without signs of active hemorrhage. Blood clotting in the jet was seen in the removal of the clot. The resection was performed in the direction of the large curvature (fig. 1). In the gastro-splenic ligament, large vessels were found which do not correspond to the anatomical realities. The particularities of the clinical case: diagnostic and therapeutic problems with major impact on pre- and postoperative clinical development. The uncertain diagnosis has contributed to errors in therapeutic conduct. The histomorphological diagnosis confirmed the clinical diagnosis of Dieulafoy Disease (fig. 2, 3, 4).







Fig. 1. a) Endoscopic view, b) Intraoperative, c) Postoperative



Fig. 2. A - piece of the gastric wall in the region adjacent to the Dieulafoy lesion: 1) mucosa without signs of inflammation, 2) sSubmucosa, 3) artery dilated with blood stasis. H-E. x100; B - A piece of the gastric wall in the region adjacent to the Dieulafoy lesion: 1) gastric mucosa without signs of inflammation, 2) artery with eroded walls, 3) hemorrhage and mucosal lesion adjacent to the eroded vessel, 4) Dilated arteries in submucosa. H-E. x40; C - hemorrhage outbreak with mucosal eruption. H-E. x200

## DISCUSSIONS

Gastrointestinal angiodysplasias are responsible for approximately 6% of gastrointestinal tract hemorrhages and 1.2-8% of hemorrhages located in the upper digestive tract. This is the fourth cause of digestive hemorrhage after ulcer disease, varicose hemorrhage and colon diverticulosis, all of which cause 85% of digestive hemorrhage [1, 6, 7, 8].

Concomitant with the more frequent use of contemporary imaging methods (endoscopic and angiographic), the incidence of angiodysplasia diagnosis has increased, patients being included in the category of idiopathic digestive hemorrhage.

According to the Camillieri classification (1996), clinical, histological arterial-venous malformations are divided into [6, 8]:

- Type I arteriovenous malformations with predominance of dysplastic veins with the small intestine / colon wall;
- Type II Osler-Webber-Rendu disease;
- Type III haemartomatous vascular lesions encountered in Peutz-Jeghers syndrome, blue rubber blue nevus and Klipper-Trenaunay syndrome;
- Type IV gastrointestinal angiodysplasia, localized predominantly on the right colon, associated with aortic stenosis, (Heyde syndrome);
- Type V Massive gastrointestinal bleeding caused by submucosa lesion with large vessel (Dieulafoy Disease).

## CONCLUSIONS

Dieulafoy's disease is a rare cause of digestive bleeding, being identified as a cause of obscure bleeding. Diagnosis of pathology is difficult and complex (endoscopy, selective angiography and histological examination). EFGDS intraoperatively confirms clinical diagnosis. Surgical interventions are prevalent, and it is necessary to minimize "blind" resections.

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## ПЕРВЫЙ ОПЫТ ЛАПАРОСКОПИЧЕСКОГО ЛЕЧЕНИЯ КОМПРЕССИОННОГО СТЕНОЗА ЧРЕВНОГО СТВОЛА У ДЕТЕЙ

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## ABSTRACT

## THE FIRST EXPERIENCE OF LAPAROSCOPIC TREATMENT OF COMPRESSIONAL STENOSIS OF THE TRUNCUS CEALIACUS IN CHILDREN

The paper describes a rare case of compression stenosis of the celiac trunk in a 17-year-old girl with periodic abdominal pain. The examination revealed a narrowing of the celiac trunk more than 50% of its lumen. It was found that the stenosing agent is the median arched ligament of the diaphragm. The girl underwent laparoscopic dissection of the arcuate ligament of the diaphragm, which led to the reduction of clinical manifestations of the disease.

In addition, there are 3 more such observations of the authors, 2 of which also had a positive postoperative result. One patient refused surgical intervention.

The authors emphasize the effectiveness of the laparoscopic approach to the treatment of patients with compression stenosis of the celiac trunk and give a literature review devoted to this topic.

Key words: compression stenosis of the celiac trunk; children; "angina abdominalis", surgical treatment

## введение

При обследовании пациентов с сильными болями в животе, не поддающимися лечению, врачу следует помнить о таком редком заболевании, как стеноз чревного ствола (СЧС), приводящем к ишемии органов брюшной полости.

Сужение чревного ствола может быть обусловлено как интравазальными причинами (атеросклероз), так и экстравазальными (сдавление чревного ствола срединной дугообразной связкой диафрагмы, внутренними ножками диафрагмы, гипертрофированными узлами чревного сплетения или увеличенными лимфатическими узлами).

Сравнительная частота изолированного сдавления чревного ствола извне и многообразие вызывающих его причин позволили выделить его в самостоятельный синдром, который называют также синдром Данбара, по фамилии врача, впервые описавшего результаты хирургического лечения пациентов с данным заболеванием.

Истинная распространённость заболевания неизвестна. Связано это с тем, что не все пациенты с компрессионным стенозом чревного ствола (далее в тексте КСЧС) (≈10-24%) [1], имеют какие-либо жалобы. Выраженные клинические проявления возникают лишь у небольшой части из них.

Клиническая картина, возникающая при данной патологии, не отличается специфичностью, и проявляется симптомами различных гастроэнтерологических заболеваний. Наиболее частой жалобой, побуждающей людей с данным заболеванием обратиться за помощью к врачу, является выраженная боль в животе, которая может локализоваться в любой его части, но наиболее часто - в эпигастральной области. Боль может носить постоянный или приступообразный характер, усиливаться под воздействием провоцирующих факторов (приём пищи, физическая нагрузка, психоэмоциональное напряжение). Чаще всего возникновение или усиление боли связано с приёмом пищи и зависит от её количества. Как правило, боль возникает через 15-20 минут после еды, и через 1-2 часа стихает. Страх перед возобновлением болей нередко заставляет больных ограничивать её количество, что приводит к постепенной потере веса. Вторым по значимости фактором, провоцирующим болевой приступ, является физическая нагрузка (поднятие тяжестей, физический труд, особенно в согнутом положении, длительная ходьба или бег). Болевой приступ может быть также спровоцирован психоэмоциональным стрессом [2].

Считается, что в генезе болевого синдрома при КСЧС наряду с ишемическим фактором, связанным с нарушением гемодинамики в чревном стволе и связанных с ним артериях брюшной полости, определяющую роль играют раздражающие факторы, обусловленные травмированием ганглиев чревного сплетения. Дело в том, что вследствие конституциональных особенностей у этих больных срединная диафрагмальная связка расположена низко и непосредственно контактирует с межганглионарными комиссурами и правым чревным ганглием (рис. 1, 2). Поэтому в процессе физических нагрузок и дыхательных движений происходит раздражение симпатических проводников с возникновением болевого синдрома и гипокинезии желудка [3]. Кроме того, больных с КСЧС могут беспокоить: ощущение тяжести и распирания в надчревной области; отрыжка; изжога; тошнота; рвота; ощущение горечи во рту; запоры и диарея. Встречаются и нейровегетативные расстройства: головные боли; сердцебиение; повышенное потоотделение; одышка; затруднение дыхания; ощущение пульсации в животе; плохая переносимость тепла и холода; слабость; быстрая утомляемость и снижение работоспособности [2]. Приводим клинический пример успешного лечения пациента с выраженными проявлениями СКЧС.

#### Нормальная анатомия



Рис. 1. Взаиморасположение чревного ствола и срединной дугообразной связки в норме. Иллюстрация J.A.- Cienfuegosandall., 2010.

КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ

Больная Н. 17 лет поступила в ДГКБ №13 им. Н.Ф. Филатова в сентябре 2016 года с жалобами на выраженные схваткообразные боли в эпигастральной области, беспокоящие её в течение последних нескольких лет. Девочка отмечала, что боли возникали после занятий спортом, приёма пищи и стрессовых ситуациях. За последний 1,5 года больная похудела на 3 кг. Впервые диагноз был заподозрен при выполнении УЗИ брюшной полости, по данным которого была выявлена зона сужения чревного ствола и увеличение скорости кровотока в этой области (> 300 см/сек) (рис. 3).



Рис. 3. УЗИ брюшной полости. Зона сужения чревного ствола с усилением кровотока до 322,4 см/сек.

В связи с чем была выполнена компьютерная томография органов брюшной полости и выявлено зона сужение чревного ствола до 1,5 мм с посстенотическим расширением до 8,8 мм (рис. 4).



Рис. 4. КТ брюшной полости. Зона сужения чревного ствола с постстенотическим расширением.

При ангиографическом исследовании выявлен локальный участок стеноза чревного ствола сразу у

Сдавление чревного ствола срединной дугообразной связкой



Рис. 2. Взаиморасположение чревного ствола и срединной дугообразной связки при КСЧС. J.A.- Cienfuegosandall., 2010.

места отхождения его от аорты (1,2 мм), протяжённостью 4,5 мм (рис. 5).



Рис. 5. Ангиографическое исследование при стенозе чревного ствола

Было решено выполнить ребёнку лапароскопическую ревизию чревного ствола.

Доступ выполнялся через печёночно-желудочную связку. Для обнаружения чревного ствола мобилизованы основные ветви чревного ствола: общая печёночная и левая желудочная артерии (рис. 6А). Выявлено, что сужение чревного ствола обусловлено сдавлением его срединной дугообразной связкой (рис. 6Б), которая была рассечена (рис. 6В, 6Г).

При контрольном обследовании через 4 месяца девочка жалоб не предъявляет, отмечает полное исчезновение болей в животе. Данные проведённых инструментальных методов обследования также подтвердили положительную динамику (рис. 7, 8, 9).



Рис. 6. А - лапароскопическое рассечение срединной дугообразной связки; Б - эндоскопическая картина после выделения основных ветвей чревного ствола; В - срединная дугообразная связка; Г - этап рассечения срединной дугообразной связки. Чревный ствол после рассечения срединной дугообразной связки: 1 чревный ствол; 2 - общая печёночная артерия; 3 - левая желудочная артерия; 4 - срединная дугообразная связка



Рис. 7. УЗИ брюшной полости. А - до операции. Vs до 322,4 см/сек. Б - после операции. Vs 132 см/сек. ЧС – чревный ствол; ОПА – общая печёночная артерия; СА – селезёночная артерия.



Рис. 8. КТ брюшной полости, 3D-реконструкция: А - до операции. Б - после операции



Рис. 9. Ангиографическое исследование: А - до операции;.Б - после операции

Всего в нашем отделении наблюдалось 4 пациента со стенозом чревного ствола, 3 из них были оперированы. У всех пациентов причиной стеноза чревного ствола явилось сдавление его срединной дугообразной связкой. Всем детям была выполнена лапароскопическая декомпрессия стеноза чревного ствола (таб. 1).

4-й пациент был оперирован по поводу воронкообразной деформации грудной клетки. Послеоперационный период осложнился кровотечением из эрозивно-язвенных поражений желудочно-кишечного тракта. При обследовании был выявлен стеноз чревного ствола. Однако, от радикального лечения стеноза чревного ствола родители ребёнка отказались.

	Пациент	Длитель- ность операции	Кой- ко-день	Допплерография Vs. до/Vs. после	Срок наблюде- ния
1	Д. 17 лет	75 мин	6	300/132 см/сек	4 мес.
2	Д. 15 лет	40 мин	3	192/170 см/сек	2,5 мес.
3	М. 14 лет	80 мин	3	265/180 см/сек	1 мес.

Таблица 1. Результаты лечения пациентов со стенозом чревного ствола

#### обсуждение

Открытие феномена компрессионного стеноза чревного ствола связано с историей изучения абдоминальной ишемической болезни. «angina abdominalis» (абдоминальная Термин ишемическая болезнь) был введён в 1903 г. G. Bacelli. Первоначально причину заболевания связывали исключительно с атеросклерозом сосудов брюшной полости. Однако, в 1963 г. Р.-Т. Harjola сообщил о больном с симптомами «брюшной ангины», причиной которой было экстравазальное сдавление чревного ствола рубцово-изменённой ганглионарной тканью чревного сплетения. В 1965 г. американский врач J. D. Dunbar описал результаты хирургического лечения 13 больных со сдавлением чревного ствола срединной дугообразной связкой диафрагмы [4]. В серии его наблюдений пациентам была выполнена декомпрессия чревного ствола открытым способом.

Стремление современной хирургии к минимальной инвазивности заставило искать новые подходы и в лечении КСЧС. Были предложены эндоваскулярные методики лечения данного заболевания. Однако, постоянное давление диафрагмальной связки на стентированный сосуд ведёт к постепенному разрушению стента, что в итоге приводит к рецидиву заболевания. Поэтому широкого применения эндоваскулярное лечение не получило [5]. В начале XXI века стали появляться единичные наблюдения о лапароскопическом лечении пациентов с КСЧС [6-8]. Однако необходимо отметить, что их суммарное количество невелико, а крупные статистические исследования отсутствуют.

Вопросы диагностики и тактики лечения при КСЧС до сих пор во многом остаются нерешёнными. Учитывая стёртую и неспецифическую клиническую картину при данном заболевании, диагноз зачастую ставится методом исключения после безуспешного лечения различных гастроэнтерологических заболеваний [9]. К настоящему моменту не выработано однозначных диагностических критериев, являющихся показанием к операции. В каждом случае вопрос решается индивидуально. Показания к оперативному лечению ставятся при наличии симптомов заболевания и доказанной с помощью инструментальных методов диагностики (УЗИ, КТ с контрастированием, ангиография). В представленном наблюдении каждый из перечисленных выше методов диагностики свидетельствовал в пользу предполагаемого диагноза. Однако мы сочли необходимым продублировать все методы диагностики для точной верификации диагноза.

Таким образом, приведенное наблюдение демонстрирует, что одной из причин абдоминального болевого синдрома может быть компрессионный стеноз чревного ствола. Это следует учитывать в повседневной практике хирурга и иметь данную нозологическую форму заболевания в обширном перечне заболеваний, для которых характерны подобные клинические проявления заболевания с целью проведения дифференциальной диагностики. Что касается избранного метода лечения, следует констатировать, что лечение с использованием миниинвазивных методов лечения демонстрирует высокую ее эффективность.

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## МОРФОЛОГИЧЕСКАЯ ДИАГНОСТИКА ЖЕЛУДОЧНО-КИШЕЧНЫХ ПЕРФОРАЦИЙ У НОВОРОЖДЕННЫХ И ЕЁ ПРАКТИЧЕСКОЕ ЗНАЧЕНИЕ

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## ABSTRACT

## MORPHOLOGICAL DIAGNOSE OF GASTRO-INTESTINAL PERFORATIONS IN NEWBORNS

Reasons, morphogenesis of gastro-intestinal perforations in newborns are introduced in this article. Clinical and morphological distinctions between perforated NEK and isolated gastrointestinal perforations are discussed. Morphogenesis of gastrointestinal perforations in newborns is a basis for prescribe correct medical tactic and choice of surgical method.

Key words: necrotizing enterocolitis, newborns, isolated gastrointestinal perforation, morphological study.

## ВСТУПЛЕНИЕ

В последние годы имеется тенденция к увеличению количества перфораций желудочнокишечного тракта (ЖКТ) у новорожденных, которые довольно часто являются одной из основных причин тяжелогосепсисаилетальностиуданногоконтингента детей. По данным литературы летальность при перфорациях ЖКТ у новорожденных составляет 30% - 60% от общего числа оперированных детей и может достигать 100% у недоношенных детей с тяжелой сопутствующей патологией [1]. Количество таких пациентов растет из года в год, что связано с увеличением числа выживших доношенных и недоношенных детей, в том числе и детей с критически низкой массой тела, благодаря достижениям в неонатологии, неонатальной хирурии и интенсивной терапии, приведшим к повышению качества оказания медицинской помощи новорожденным с неблагоприятными перинатальными факторами.

Параллельно с увеличением перфораций ЖКТ на фоне врожденных пороков развития, увеличивается и количество перфораций, обусловленных некротическим энтероколитом (НЭК), спонтанных (или изолированных) перфораций ЖКТ [2]. В современной детской хирургии спонтанные перфорации (СП) рассматриваются как самостоятельная нозологическая единица среди других перфораций ЖКТ [3]. По данням литературы перфорации, обусловленные НЭК, составляют приблизительно 53% от общего количества перфораций ЖКТ у новорожденных, СП – 27%, на 18% всех перфораций приходятся перфорации при врожденных пороках развития ЖКТ, а на 2% перфоративные аппендициты, дивертикулиты Меккеля и ятрогенные перфорации [4, 5, 6, 7].

Факторы риска, которые обусловливают развитие перфораций ЖКТ, до сегодняшнего дня остаються мало изученными [8]. Можно смело признать, что проблема перфораций ЖКТ у новорожденных является не только актуальной, но и достаточно новой в детской хирургии.

Цель работы – изучить клиникоморфологические особенности перфораций ЖКТ у новорожденных и на основании данных морфологических исследований предложить мероприятия по улучшению результатов лечения таких пациентов.

## МАТЕРИАЛ И МЕТОДЫ ИССЛЕДОВАНИЯ

Под нашим наблюдением последние 15 лет находилось 75 новорожденных с перфорациями ЖКТ. Среди них детей с перфоративными НЭК было 39 (52,0%), со СП – 20 (26,67%), с желудочно-кишечными перфорациями на фоне врожденной кишечной непроходимости – 13 (17,33%), у 1 новорожденного перфоративный апендицит, у 1 – перфоративный дивертикулит Меккеля, у 1 – ятрогенная перфорация прямой кишки.

Отмечается приблизительно двухкратное преобладание мальчиков над девочками (48 и 27 новорожденных соответственно). Недоношенных детей было 58 (77,33%). Из них недоношенных с НЭК – 33 ребенка, с СП – 17, с врожденной кишечной непроходимостью – 7 и 1 недоношенный с гангренозно–перфоративным апендицитом.

Всем детям проводилось клинико– лабораторное обследование, инструментальные методы исследования (рентгенография органов брюшной полости, рентгенологическое контрастное исследование ЖКТ, УЗИ органов брюшной полости и другие), а также морфологическое исследование операционного материала с целью верификации диагноза. Контроль за состоянием ребенка осуществлялся круглосуточно реаниматологом отделения реанимации и интенсивной терапии новорожденных и детским хирургом.

Для гистологического исследования операцонный материалл фиксировали в 10% расстворе нейтрального формалина и после стандартной проводки заливали в парафин. В дальнейшем парафиновые срезы толщиной 5–7 мкм окрашивали гематоксилином–еозином и пикрофуксином по Ван Гизону. Исследование и фотографирование гистологических препаратов проводилось на микроскопе «Axio Imager 2» from Carl Zeiss.

## РЕЗУЛЬТАТЫ И ОБСУЖДЕНИЕ

Акушерский, гинекологический и соматический анамнез у 65 матерей (86,67%) был отягощен (гестоз, хроническая маточна-плацентарная недостаточность, пиелонефрит, анемия, сахарный диабет).

Причинами перфораций ЖКТ у исследуемой группы пациентов были:

- НЭК 39 детей (52,0%);
- C∏ 20 (26,67%);
- врожденная кишечная непроходимость 13 (17,33%);
- гангренозно-перфоративный апендицит 1 (1,33%);

гангренозно-перфоративный дивертикулитит Меккеля – 1 (1,33%);

ятрогенная перфорация прямой кишки – 1 (1,33%).

Из 13 новорожденных с врожденной кишечной непроходимостью атрезия тонкой кишки наблюдалась у 6 детей, мекониальный илеус – у 3, болезнь Гиршпрунга – у 2, заворот тонкой кишки – у 4 новорожденных. По локализации перфорации распределились следующим образом:

- желудок 13;
- двенадцатиперстная кишка 6;
- тощая кишка 17;
- подвздошная кишки 27;
- ободочная кишки 9;
- аппендикс 1;
- дивертикул Меккеля 1;
- прямая кишка 1.

В 33 (44,0%) случаях поражения полого органа были локализованными, у 42 (56,0%) новорожденных поражения кишки были обширными, с вовлечением в патологический процесс больших площадей стенок полых органов.

Перфорации ЖКТ у новорожденных были интра– и постнатальные. Среди наших клинических наблюдений у 22 (29,33%) новорожденных были интранатальные перфорации, у 53 (70,67%) детей – постнатальные, которые всегда сопровождались разлитым гнойно-фибринозным и каловым перитонитами (рис. 1, 2).



Рис. 1. Разлитой каловый перитонит у новорожденного с множественными перфорациями ободочной кишки (интраоперационное фото).



Рис.2. Вид перфоративного НЭК (интраоперационное фото)

Мы выявили следующие клиникоморфологические различия между перфорациями ЖКТ на почве НЭК и СП, которые приводим в таблице 1. Факторами риска в возникновении и развитии перфораций, обусловленных НЭК, являются хроническая гипоксия плода и интенсивное энтеральное кормление, которое вызывает перераспределение системного и регионарного кровотока и ишемию подвздошной кишки. Наиболее вероятными факторами риска появления СП органов ЖКТ являются хроническая внутриутробна гипоксия, острая асфиксия в родах и патология органов дыхания, при которых необходимой была интубация трахеи. Респираторный дистресссиндром виступает в качестве ведущего фактора риска при СП ЖКТ. Среди СП ЖКТ у новородженных имеет место 3,5-кратне увеличение в группе высоких перфораций в сравнении с з низкими перфорациями (35,0% против 10,25%). Спонтанные перфорации локализовались у желудке (12), двенадцатиперстой кишке (4), тощей кишке (3) и толстой кишке (1), то есть высоке расположение перфораций имело место у 19 новородженных из 20 исследуемых.

Nº	Клинические признаки	НЭК	СП
1.	Середний гестационный возраст (нед.)	32,5	27,2
2.	Средний вес при рождении (г)	1645	880
3.	Интубация трахеи	61,54%	100%
4.	пупочный катетер	61,54%	100%
5.	перинатальная энцефалопатия	66,67%	55,0%
6.	Врожденная кардиопатия	64,10%	55,0%
7.	Локализация перфорации	Нижние отделы ЖКТ	Верхние отделы ЖКТ
8.	Кишечный пневматоз	66,67%	-
9.	Летальность	41,02%	5%

Таблиця №1. Клинические различия между СП и перфорациями при НЭК

Перфорации ЖКТ при НЭК локализовались в тощей кишке у 12 новорожденных, подвздошной кишке – у 22 детей, в толстой кишке – у 5 (таблица 2). Макроскопически кишечник и желудок при СП имели нормальний вид, кроме наличия изолированной перфорации с локальным патологическим процессом, без распростронения последнего на большие площади стенки полого органа. Кишечник при перфоративных НЭК имел распостраненные поражения с вовлечением в патологический процесс больших площадей стенок кишки и всех её слоёв – (рис. 2).

Nº	Отделл ЖКТ	НЭК	СП
1.	Желудок	-	12
2.	Двенадцатипертная кишка	_	4
3.	Тощяя кишка	12	3
4.	Подвздошная кишка	22	-
5.	Толстая кишка	5	1

Сравнительное изучение клинических биоптатов перфораций ЖКТ у новорожденных показало наличие ишемии в стенке полого органа при двух патологиях. Однако, при СП имела место врожденная мышечная гипоплазия стенка, которая является главным морфологичпеским отличием между СП и перфорациями на фоне НЭК. Все СП имели изолированный, или сегментарный, мышечный дефект стенки полого органа без вовлечения в патологический процесс обширный площадей стенки желудка или кишки (рис. 3 А, Б, В).



Рис. 3. А - сосудисто-мышечная дисплазия стенки тонкой кишки при СП: 1 - резкое истончение кругового слоя мишечной оболочки стенки кишки; 2 - аневризма сосуда в подслизистом слое. Б - язвенный дефект слизистой оболочки тонкой кишки с широким кровоизлиянием в перифокальные ткани при СП. В - сосудисто-мишечная дисплазия стенки тонкой кишки при СП. Мышечний слой отсутствует, на его месте сосудистая мальформация. Г - некроз стенки подвздошной кишки при перфоративном НЭК с вираженой лейкоцитарной инфильтрацией (1) и пневматозом (2). Окр. Г-Э. Х 10, об. 40.

Перфорации при НЭК имели выраженый воспалительный процесс перифокальных тканей с вовлечением в патологический процесс больших участков кишичной стенки, некрозом её слоёв и некрозом стенки слизистой оболочки (рис. 3 Г).

Все новорожденные с перфорациями ЖКТ были прооперированы. Хирургическая тактика отличалась в зависимости от общего состояния новорожденного, уровня перфорации, её морфологических особенностей и распространенности патологического процесса. Нами были выполнены следующие оперрации:

- лапароцентез (у детей с тяжелой сопутствующей патологией и экстремально низкой массой тела) – 11;
- формирование межкишечных анастомозов 23;
- иссечение краев и ушивание перфораций 20;
- 4. наложение кишечных стом 19;
- 5. аппендэктомия 1;
- 6. дивертикулэктомия 1.

Послеоперационная летальность при перфоративных НЭК составила 38,46% (умерло 15 новорожденных), при СП ЖКТ – 5% (умер

1 ребенок). Основной причиной смерти был тяжелый неонатальний сепсис з полиорганной недостаточностью.

## выводы:

Поскольку между перфорациями ЖКТ у новорожденных существуют клинические и морфологические отличия, морфологическая диагностика очень важна в выборе адекватной хирургической тактики в каждом отдельно взятом клиническом случае.

Морфологическая диагностика желудочно-ки-

шечных перфораций у новорожденных позволяет оценить прогноз заболевания. Так, при СП прогноз лечения детей является благоприятным.

Ведущим фактором риска при СП является дистресс–синдром, при перфорацях на фоне НЭК – хроническая гипоксия плода и интенсивное энтеральное питание.

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## EMBRIOLOGICAL AND ANATOMICAL BASES IN SURGERY OF CONGENITAL STRUCTURAL DEFECTS OF THE DIAPHRAGM

(Review of literature)

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## INTRODUCTION

Congenital diaphragmatic defects are one of the leading causes of morbidity and mortality in neonates. Often the defect dimensions, precise anatomical details or defect type directly influence the prognosis of these malformations [1]. For a surgeon, knowing the aspect of embryology and surgical anatomy of the diaphragm is critical in understanding the mechanisms of development of normal variations and congenital malformations that are rarely encountered in surgical practice [31].

## **EMBRYOLOGY**

The diaphragm is a critical organ in maintaining normal breathing, and is also a barrier between thoracic and abdominal cavities [9, 10, 28]. Being closely linked to the formation of body cavities, the structural elements of the diaphragm begin to develop in early gestation [9], in the 4<sup>th</sup> to 12<sup>th</sup> week of intrauterine development [27,37]. The diaphragm is derived from several embryonic sources, some of them being unidentified [35]. At present, the diaphragm is thought to be derived from four mesodermal structures [8], including: *transverse septum*, two lateral pleuroperitoneal envelopes, dorsal mesentery of the esophagus, and the body wall muscles [4, 11].

The anterior region of the diaphragm originates in the transverse septum, and later this tissue develops into the mature central tendon and the non-muscular mesenchyme [32]. The transverse septum is the first structure in development of the diaphragm and initially serves as a barrier between the thoracic and abdominal cavities [35], and as a coherent mesodermal structure is formed at the end of the third week of gestation. In the fourth week of gestation, the incomplete separation of pericardial and peritoneal cavities takes place, with the formation of two adjacent esophageal apertures (pericardioperitoneal canal). Originally located at the occipital level, superior to cervical somites (C3), this embryonic structure represents a frontal caudal dorsal inclination, initially connected to the body wall, and the ends at the cranial edges of the middle intestine. During the descending migration, the transverse septum passes past the cervical segments III, IV and V, a process accompanied by the migration of myogenic stem cells from these somites and the local differentiation of myoblasts into the tissue of the pleuropericardial folds, referred to as the posthepatic mesenchymal plaque. The transverse septum does not extend all the way to the dorsal wall, the pleural and peritoneal cavities remain open, being called pleuroperitoneal ducts (canals) (20, 41).

In the 5<sup>th</sup> week of gestation, neural structures in the cervical IV and V segments of the spinal cord develop. Nerve fibers penetrate into the transverse septum through the pleuropericardial folds, where they form the phrenic nerve. The detachment of these folds from the somatopleure to form the pericardium, determines the localization of the phrenic nerve between the pericardium and the mediastinal pleura [11, 41].

Pleuroperitoneal folds are two transient structures formed by the fusion of pleuropericardial folds [9], located on either side of the esophagus, attached to the dorsolateral wall of the body, with the free edge protruding at the caudal end of the pericardioperitoneal canals [35], with the transverse septum. In the  $6^{th} - 8^{th}$  week of gestation, growing medially and ventrally, these folds merge with the dorsal mesentery of the esophagus and a portion of the transverse septum, causing separation of the pleural and peritoneal cavities. Closure of the communications is also determined by the extensive increase of the liver tissue and muscle structures in these membranes, from which only a small dorsolateral portion of the diaphragm will develop [4, 27, 41].

The dorsal mesentery of the esophagus contributes to the attachment of the middle intestine to the trunk wall, eventually forming the median portion of the diaphragm. The crura of the diaphragm develop from muscle fibers growing in the esophageal mesentery [4].

The contribution of the muscle wall of the trunk to the formation of the lateral diaphragm portion is determined by the enlargement of pleural cavities during weeks 9-12 of gestation. As a result, the body wall is divided into two layers: external, from which the thoracic wall will later develop, and internal, embedded in the diaphragm [41].

Several hypotheses attempt to explain the origin of congenital diaphragmatic defects. According to some, congenital diaphragmatic hernias are a consequence of the vicious development of the lung or the developmental disturbances of the phrenic nerve [21]. Other scientists believe that the origin of the congenital diaphragmatic hernias is in the non-muscular portions of the fetal diaphragm and results from the failure of fusion of one or several of these embryonic structures [8, 11, 13, 45]. In cases where the membranes merge and the muscle fibers fail to migrate from the cervical myotomes, a hernia with sac appears [11]. The development of these defects is based on some disorders of the retinoid signaling embryogenic mechanisms and of some transcription factors [2, 16, 34, 43]. For example, Bochdalek hernia (the abnormal development of the pleuroperitoneal fold) results in the typical posterolateral defect [9], and the fusion defect of the transverse septum with the lateral wall of the trunk leads to the anterior diaphragmatic hernia (Morgagni hernia) [46].

## CLASSIFICATION

Classification of diaphragmatic hernias proposed by Harrington S.W. in the 1930s. proved to be quite widespread. The author distinguished two main types of diaphragmatic hernias: traumatic and non-traumatic [14, 44], including:

## I. Non-traumatic hernias:

- A. Congenital hernias (usually without sac):
- 1. through the pleuroperitoneal hiatus (Bochdalek foramen);
- 2. through a space left by the partial absence of the diaphragm (posterior part);
- 3. through the esophageal hiatus (as a result of muscle deficiency);
- through the esophageal hiatus in the case of a short congenital esophagus (the stomach remains partially or entirely above the diaphragm);
- 5. through the anterior subcostosternal spaces (foramen of Morgagni) with the presence of the hernial sac.
- B. Hernias acquired after birth:
- through the esophageal hiatus (it usually has a hernial sac);
- through the fusion region of the diaphragmatic primordium;
- 3. other locations.

## II. Traumatic hernias:

- A. Direct injuries in any part where an object can penetrate into the diaphragm;
  B. Indirect injuries - at any point, but usually at the embryological fusion points;
- C. Diaphragm rupture following inflammatory necrosis (subphrenic abscess, necrosis due to drainage tube pressure).

Jackson R.L., and Welcome H.C. (1941) [23] classified the diaphragmatic hernias into 3 groups:

- 1. Congenital (true and false);
- 2. Acquired (true and false);
- 3. Traumatic (true and false).
- In 1952, Gudbjerg C.E. [18] argued that the lack

of a clear classification of diaphragmatic abnormalities was determined by the uncertainty regarding their pathogenesis and proposed a new classification, reuniting diaphragmatic abnormalities into three groups:

- 1. Diaphragmatic hernias:
- a) congenital (true with sac and false without sac);
- b) traumatic
  - 2. Relaxation of the diaphragm:
- a) congenital (defective development of the musculature);
- b) paralytic (resection of the phrenic nerve, tumors).
  - 3. Absence of the diaphragm.

The classification of diaphragmatic hernias proposed by Petrovskii B.V. (1966), quite useful in practical activity, included the following forms: 1) congenital - diaphragmopleural, hiatal, parasternal, phrenopericardial hernias and 2) acquired, divided into traumatic and non-traumatic[5]. In 1988, Isakov Iu.F. proposed the classification of congenital diaphragmatic hernias, namely : 1) embryonic hernias (false); 2) fetal hernias (true hernias) and 3) relaxation of the diaphragm [5].

In 2007, Trojan V.V. [5] proposed an anatomical classification of the congenital diaphragmatic hernias:

- 1. Hernias of the posterior region of the diaphragm.
- 2. Hernias of the diaphragmatic vault.
- 3. Hernias of the anterior region of the diaphragm:
  - a) Retrosternal hernias (true);
  - b) Phrenicopericardial hernias.
- 4. Hiatal hernias:
  - a) Oesophageal hernias;
  - b) Para-oesophageal hernias.

Based on some intraoperative observations, some authors have tried to classify the congenital diaphragmatic defects, according to their dimensions, into: A) defects surrounded by muscles; B) small defects (less than 50%); C) major defects (over 50%) and D) absence of the hemidiaphragm [36].

It is believed that most congenital diaphragmatic defects develop in "classical" locations such as posterolateral (Bochdalek), parasternal (Morgagni-Larrey hernia) and central and anterior hernia (Cantrell transverse septum hernia) [1], several concomitant diaphragmatic defects being observed in some cases [6, 25].

The congenital diaphragmatic defects originating from the lumbocostal triangle are the most prevalent and were first described in 1848 by Vincent Alexander Bochdalek, who reported an incidence ranging from 5% to 25% of the total diaphragmatic hernias [1]. Although Bochdalek hernia manifests in neonatal period by severe progressive respiratory distress [54], cases of late-onset manifestations were reported in adults [19, 33]. More often (up to 90% of cases) the malformation is found on the left, rarely the bilateral form being detected [26].

In 1959, Bingham described an anatomical entity characterized by the absence of the hemidiaphragm (diaphragmatic agenesia), distinct from the posterolateral defects [49]. Cases of bilateral absence of the diaphragm are also described [48].

The congenital Morgagni hernia is relatively rare, constituting approximately 3-5% of all types of congenital diaphragmatic hernias. Approximately 90% of this type of hernias appear on the right, 2% on the left, and in 8% of the cases bilateral forms are found. The hernial sac is present in over 95% of cases [15]. Although congenital Morgagni hernia is specific to children, asymptomatic forms were primarily diagnosed in adults and even in elderly patients [30, 50].

The congenital intrapericardial diaphragmatic hernia is characterized by herniation of abdominal viscera in the pericardial cavity, being caused by developmental anomalies of the retrosternal transverse septum with persistence of the pericardioperitoneal canal. This entity is also referred to as peritoneopericardial diaphragmatic hernia, which may be associated with other congenital defects at the midline and pentalogy of Cantrell [24, 38]. The first case of peritoneopericardial diaphragmatic hernia was described in 1903 by De Cardinal and Bourderou [42].

The central tendon defects are casuistically diagnosed, characterized by congenital hernia of the abdominal content through the central tendon of the diaphragm. The embryogenic aspects of these defects remain unclear [9, 29].

Diaphragmatic eventrations, a nosological entity described in the literature as diaphragm atrophy, non-paralytic eventration, neurogenic aplasia of the diaphragm, etc., are congenital defects of rare development of the muscle portion of the diaphragm. From a histological point of view, it is characterized by fibro-elastic changes, which replace the muscular tissue layer and extend between the pleura and the peritoneum, keeping the diaphragm anatomical structure intact, thereby differentiating from the congenital diaphragmatic hernias and diaphragmatic paralysis. The incidence of this malformation is below 0.05% [53]. The left hemidiaphragm is more frequently affected. Congenital diaphragmatic eventrations are divided into: complete, partial and bilateral. Partial eventrations, based on the embryological segments that contribute to the formation of the normal diaphragm, can be classified into the following types: anterior, posterolateral and medial [17, 52]. Multiple eventrations of a single hemidiaphragm are also reported [51].

In 1774, Jean Louis Petit was the first to observe this entity during the necropsy, the term *eventration* was later proposed by Beclard (1829) [47]. In 1923, Morrison published the first case of diaphragmatic eventration subjected to surgical treatment [22, 53].

## ANATOMY

The diaphragm is a dome-shaped musculofibrous septum that separates the thoracic cavity from the abdominal cavity, maintaining the pressure gradient between the two cavities and participating in the regulation of esophageal contractions, being the most important respiratory muscle. The name of the organ comes from the words of Greek origin dia (between) and phragma (fence) [12, 31, 39, 40]. The main element of the diaphragm is the phrenic muscle, covered by a homonymous fascia (upper and lower), parietal pleura (upper), peritoneum (on the abdominal side) and traversed by vessels, nerves and esophagus. The diaphragm vault consists of two domes: right one, a slightly higher one, the top of which corresponds to the intercostal IV space on the right medioclavicular line and the left one, with the highest point on the V rib level along the left medioclavicular line [7].

The diaphragm consists of a central non-contracting tendon, considered central aponeurosis, two major muscular portions (costal and crural diaphragm) and a minor sternal muscle portion [4, 41].

The lumbar (crural) side of the diaphragm (pars lumbalis) is represented by the pillars of the diaphragm (right and left) - the strongest part of the diaphragm [7]. The right diaphragm pillar is located on the anterior surface of the lumbar vertebrae (L1- $_4$  on the right and L<sub>1.2</sub> on the left), on the intervertebral discs and the anterior longitudinal ligament. The right diaphragm pillar, larger than the left, is directed towards the middle of the central tendon, on both sides of the upper median plane, forming by branching, in more than 60% of individuals, the esophageal hiatus, in the rest of the cases, both pillars of the diaphragm participate in its formation. Split muscle fibers meet again to form the anterior edge of the aorta hiatus. Although the esophageal pillar is made up of muscular and tendinous tissue, only the tendinous side is strong enough to deal with sutures during surgery. The left diaphragm pillar is facing up, to the left of the esophageal hiatus. A portion of this pillar reaches the central tendon [4].

There are also described accessory pillars (intermediate), placed laterally by the main pillars, represented by muscular bundles originated on the vertebral body L2, which, with the lateral pillars, delimit a narrow space for the splanchnic nerves [7].

The lateral pillars (or the arches bundles) start from the medial arcuate ligament, (*lig. arcuatum mediale*), passing as a bridge over the psoas muscle, coming onto the body of the first lumbar vertebra and the intervertebral disc L1-L2, and laterally at the top of the transversal apophysis L1, sometimes L2, and the lateral arcuate ligament (*lig. arcuatum laterale*) that passes over the quadratus lumborum muscle, joining the tip of the transverse apophysis L1 and/or L2 with the lower edge of the free end of the 12<sup>th</sup> rib. Through the space delimited by the lateral and medial pillars, the sympathetic chain and the ascending lumbar veins pass, which continue with the azygos veins (on the right) and hemiazygos veins (on the left). The median arcuate ligament (*lig. arcuatum medianum*) contributes to preaortic solidarising of the two diaphragmatic pillars, consisting of aponeurotico-tendinous fibers [7].

The costal part of the diaphragm (*pars costalis*) originates from the inner surface and the upper edges of the six lower (caudal) ribs and radiates in the central tendon [11]. At the limit of the costal and lumbar portions, the muscle fibers are missing, giving rise to a triangular space with its base at the 12<sup>th</sup> rib (lumbocostal triangle, Bochdalek). This area, covered only by the diaphragm fasciae, parietal pleura (upper) and the retrorenal fascia of the parietal (lower) peritoneum, makes it possible to spread infections from the thoracic cavity (with subpleural adipose connective tissue) in the retroperitoneal space ( with pararenal adipose tissue, Gerota) in double directions [7, 11].

The sternal part (*pars sternalis*) of the diaphragm is the smallest and extends from the posterior surface of the right muscle and behind the xiphoid process to the central tendon of the diaphragm. Laterally to the sternal portion of the diaphragm, the coastal parts are. Between these portions, the diaphragm is covered only by connective tissue, the sternocostal triangle or foramina of Morgagni is on the right, and sternocostal triangle or Larrey's triangle is on the left [11].

The central tendon is an aponeurotic form, which has the shape of a clover (trefoil) leaf and consists of three leaflets (one anterior and two lateral) separated by slight crevices. Between the anterior and the lateral right leaflet, moved posteriorly, there is the inferior vena cava which is inextensible and ovoid, being crossed by the homonymous vein and bordered by tendinous fibers, some of them being circularly arranged, others radially oriented and ascending towards the vein adventitia, solidarising with the orifice border. Thus, the circulatory onset of the lower vena cava is not influenced by the diaphragm movements during breathing [4, 7]. The vascularization of the diaphragm occurs in the branches of the pericardophrenic, musculophrenic, upper and lower diaphragmatic arteries, which form a rich anastomotic network with the VI-IX intercostal arteries, the subcostal arteries and the branches of the internal thoracic artery. Two veins, accompany the homonymous arteries and flow into the azygos veins, internal thoracic veins and inferior vena cava, at this level being made cavocaval and portacaval anastomoses [7].

The diaphragm innervation is ensured by the phrenic nerves that originate in the cervical plexus (C3-C4), to which they reach around the inferior vena cava orifice (right) and lateral and anterior (left), respectively, dividing, consecutively, in an anterior and a posterior branch. Some of the posterior branches continue with the phrenico-abdominal ones that penetrate the diaphragm, being distributed in the subdiaphragmatic parietal and visceral peritoneum with the ligaments of the supramesocolic organs, especially the liver. At the diaphragm motor innervation, intercostal IX-XI nerves participate, oriented especially to the periphery of the coastal portion. Pain, which radiates to the right shoulder and the supraclavicular region in hepatobiliary disorders, and those radiating to the left shoulder, in pancreatic and spleen diseases (Eiselsberg sign), are transmitted via the phrenico-abdominal branches and the trunk of the phrenic nerve [7].

Therefore, the various congenital diaphragmatic defects require a thorough evaluation, with rigorous documentation of anatomical forms in order to elucidate the biology of the development of these malformations and the individual adaptation of the surgical reconstruction.

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## SURGICAL INTERVENTION SPECIFICS OF RESECTION OF EX-TREMITY SOFT TISSUE SARCOMAS IN CHILDREN

(Review of literature)

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The integrated approach in the treatment of soft tissue sarcomas in children and adolescents at various stages includes conservative methods and tactics of surgical removal of neoplasms.

The main tasks of the surgical stage of treatment are to remove the tumor in a single block without damaging it, to ensure maximum functionality of the affected organ and to prevent local recurrence. However, in connection with the need for radical tumor removal, significant tissue defects requiring reconstructive manipulation are often formed during surgery. Determining a sufficient resection width is an important aspect of ensuring adequate volume of surgical intervention.

According to the literature, over 300 histological types of soft tissue sarcoma have been described. These tumors are of mesodermal and less often neuroectodermal origin, and are localized in different parts of the body. The morphological classification developed by WHO experts comprises 15 types of tumor process in terms of histogenesis. According to statistics, among all bone and soft tissue tumors, malignant neoplasms in the foot and ankle region account for about 4% of cases [1]. Soft tissue sarcomas are rare tumors and in most cases are localized in the extremity region [1].

These neoplasms are represented by a heterogeneous group of malignant tumors that are created from primitive mesenchymal tissues and account for 7% of all childhood tumors [2].

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## Table 1. Histogenetic classification of soft tissuesarcomas

Tissue type	Tumor type	
	Malignant mesenchymoma	
Mesenchyme	Мухота	
	Desmoid (invasive form)	
Fibrous tissue	Fibrosarcoma	
Adipose tissue	Liposarcoma	
	Malignant hemangioendothelioma	
Vascular tissue	Malignant hemangiopericytoma	
	Malignant lymphangiosarcoma	
Muscle tissue	Rhabdomyosarcoma (from striated muscles)	
	Leiomyosarcoma (from smooth muscles)	
Synovial tissue	Synovial sarcoma	
	Malignant neurinoma (schwannoma) – from neuroectodermal membranes	
INERVE sheaths	Perineural fibrosarcoma – from connective tissue membranes	

# Diagram 1. Distribution of histological variants of soft tissue sarcomas by frequency of occurrence in children



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Rhabdomyosarcoma is a tumor of the striated muscles. It is the most common soft tissue sarcoma in children aged 0 to 14 years and comprises 50% of all tumors in this age group [3]. The remaining soft tissue sarcomas in children account for approximately 3% of the total number of soft tissue sarcomas [4], and include neoplasms of: connective tissue (e.g. desmoid fibromatosis), peripheral nervous system (e.g. malignant tumors of peripheral nerve sheaths), smooth muscle (e.g. leiomyosarcoma), vascular tissue (blood and lymphatic vessels, e.g. angiosarcoma) [5].

Non-rhabdoid soft tissue sarcomas are more common in adolescents and adults [5]. Most of the information on the treatment of young patients was based on the tactics of conducting adult patients. Such soft tissue sarcomas can develop in any part of the body, but more often occur in the extremities and upper body [6-8] and are rarely localized in the brain [9]. The clinical presentation can be asymptomatic or, for example, with the involvement of nerve structures in the process, accompanied by pain syndrome. Systemic symptoms in the form of fever, weight loss, increased night sweats are practically not found [10].

From the point of view of the histological picture, rhabdomyosarcoma and Ewing sarcoma can be easily distinguished from other sarcomas. However, other soft tissue sarcomas are more difficult to differentiate. To make an accurate diagnosis, a biopsy is necessary. The use of fine needle biopsy is not desirable in view of the low informative nature of the sample. An open biopsy is crucial for the complete histological characterization of the sample, for performing immunohistochemical, cytogenetic analysis, fluorescence [11, 12], cryoconservation in biobanks, etc. Longitudinal sections are used on the extremities for surgical access, which allows to a greater extent to preserve the skin and to reduce the irradiation zone. The use of trepanobiopsy may be accompanied by the formation of a hematoma, which complicates the subsequent resection of the tumor. To plan an informative biopsy of the affected area, ultrasound diagnosis, CT, or MRT studies are needed [13]. Excisional biopsy is suitable only for small superficial neoplasms (<3 cm in diameter) and is not standard [14, 15]. Execution of excisional biopsy is associated with a greater risk of non-radical surgery. Further, on the background of chemoradiotherapy, it is difficult to distinguish scar tissue from a possible residual tumor. Therefore, in the beginning it is advisable to perform a nonexcisional biopsy, to conduct further therapy followed by a radical operation. The criteria for successful treatment are the histological form, the size and location of the neoplasm, the degree of malignancy, the presence of local and distant metastases, the stage of the disease, the response to polychemotherapy and radiation therapy. Treatment of soft tissue sarcomas is poorly effective without a surgical stage. The ability to perform complete neoplasm resection is the most

important prognostic factor for survival [16-24].

The interrelation between the resection margin and the recurrence of the disease is an important issue in oncology surgery. Despite a large number of scientific developments in this direction, at present there are no clear criteria for estimating the sufficient resection width [25].

Children with an unplanned resection of nonrhabdomyosarcoma soft tissue sarcoma need a re-excision of the postoperative cicatrix. In such patients, tumor cells are often found in scar tissue, since initially it is fairly difficult to remove a tumor radically, and unplanned resection is associated with suspected benign neoplasm and is performed without taking into account the possible malignancy of the process [26, 27]. In the research by Qureshi Y.A. et al. the retrospective analysis showed that an unplanned initial excision of soft tissue sarcoma leads to an increased risk of local recurrence, metastasis and fatal case. For tumors of a high degree of malignancy, these parameters were the highest [28]. For some types of children's nonrhabdomyosarcoma soft tissue sarcomas, the prognosis is more favorable. For example, infantile fibrosarcoma, which is most often found in infants and children under the age of 5, has a good prognosis, is sensitive to polychemotherapy, and as a rule, is resectable [4].

Children with localized unresectable forms of nonrhabdomyosarcoma soft tissue sarcoma have an unfavorable outcome. Only about one third of patients who receive therapy regain their health [29-32].

In the analysis of American and European centers, it was established that those patients, whose planned removal of soft tissue sarcoma was performed fully, have better survival rates compared to patients who underwent non-radical resection. The best results were noted in cases where radiotherapy was also performed [31]. Therefore, each patient needs an individual approach. Therapy planning should be carried out before the start of treatment [7, 33-37].

The tasks of surgical treatment of extremity soft tissue sarcomas are to remove the tumor in a single block, to prevent local recurrence, and to provide maximum functionality [38].

Over the past decades, approaches to treating sarcomas have undergone significant changes, primary amputations are increasingly being replaced by organ preservation surgeries [39]. But in cases where central vessels and nerves are involved in the tumor process, or there is severe bleeding from the tumor tissue, which can not be stopped conservatively, amputation remains the only correct treatment option [40]. When resecting soft tissue sarcomas with damage to bone structures, modern methods of prosthetics help to achieve good functional results.

Peripheral nerves, as a rule, are not involved in the tumor process or are easily isolated with preservation of the nerve sheaths. In cases where the nerve is diseased, it is necessary to resect it altogether with the tumor in a single block. In adult patients, neural grafts often do not function, which is probably related to age, but can be successfully used in children. In complete resection of the sciatic nerve, the extremity functionality is preserved [41]. In the postoperative period, due to the risk of decubitus formation, knee orthoses should be used with caution, among other things because of the reduced sensitivity of the extremity [42].

If possible, it is necessary to avoid removing the periosteum, especially in the femur, since its excision with subsequent radiation therapy increases the risk of pathological fractures [43]. The periosteum should be resected in cases where it is likely to be involved in the tumor process. In this case, the area of bone resection is recommended to be fixated [44], however, there is no reliable data on the stabilization efficiency in this case [45, 46]. The frequency of occurrence of pathological fractures in such patients is extremely small and is associated with the dose of radiation therapy, most often they occur in the femur [47]. In some cases, bone fixation may be supplemented with a pedicled fibular graft [48].

In successful surgical treatment of patients an important point is a wide excision of the primary tumor (of the whole block without damage to the tumor, with sufficient margin of healthy tissue). Resection should be performed outside the pseudocapsule of the tumor, through normal unaffected tissue. Intraoperative damage to the tumor structure (i.e., intralesional surgery or resection) leads to an increase in the frequency of local recurrences [38].

The presence of tumor cells in the resection margin also affects the frequency of local recurrences [38, 49-55], increases the risk of distant metastases, and decreases survival rates [54, 56]. The resection margin is positive if the tumor cells are histologically determined in the edge of the tissue being resected. For intraoperative evaluation it is reasonable to use express histological diagnostics, which reduces the risk of non-radical surgery. Its technique is a removal of the tumor, followed by a small resection of surrounding tissues and their urgent histological evaluation.

In case of patients with non-radical resection, if possible, it is necessary to perform a resection with complete excision of the remaining tumor edges [57]. It is necessary to take into account the volumes of repeated surgery, the possibility of traumatizing the neurovascular structures, and also the fact that in patients with R1 resection, the frequency of local recurrences was 30% greater as compared to R0 resection, where the frequency of local recurrences was 5-10% [58, 59].

When a tumor is resected, healthy tissue should encircle the pathological area. The required thickness of the resected noninvolved tissue remains debatable. According to literature data, it is recommended to remove at least 1 cm margin from the tumor edge or the resection margin should include a fascial barrier [52, 60]. In practice, it is not always possible to remove a tumor with a margin of 1 cm, especially when large vessels are involved in the tumor process [60]. A combination of reconstructive surgery and adjuvant radiotherapy helps to achieve good results, which is associated with a good tumor sensitivity to radiation therapy [61, 63, 64]. Tumors of high degree of malignancy are the ones most prone to local recurrence [62, 63, 64], which reasonably worsens the prognosis of the disease.

In patients with locally advanced form of extremity soft tissue sarcoma, it is advisable to use isolated chemotherapeutic perfusion. Performing this procedure with the use of alpha-tumor necrosis factor allows to preserve the extremity in 81% of cases [65].

In the study by Kandel R. et al. it was shown that the size of the surgical margin from the tumor edge does not significantly affect the overall survival of patients [39]. From the point of view of the operating surgeon, it is safer to make a sufficient margin, but in some cases the possibility of maintaining the functionality of the operated region is possible only with a microscopic margin from the tumor border that is confirmed by express histological diagnostics. Despite a large number of scientific developments, at present there are no clear criteria for assessing the sufficient width of the resection.

However, major surgery with a wide surgical margin, which is accompanied by significant defects in soft and bone tissues, is often appropriate for patients with locally advanced form of extremity soft tissue sarcoma. The use of plastic reconstructive surgery techniques, for example, closure of defects with a local advanced flap, free fasciocutaneous flap, musculocutaneous flap, osteocutaneous flap or split-skin grafts can reduce functional disorders even with large resection volumes or in cases of tumor localization in close proximity to anatomically important structures, which is accompanied by a significant improvement in the quality of life of such patients.

For plastic surgery, the defects that arise after extensive resection of the neoplasms, notably in the back and side surfaces of the foot, are of particular complexity. This is due to the anatomical features of this area and the direct participation of the foot in the movement of the body and the wearing of shoes [66-69]. One of the common options for closing such defects is the use of a local advanced flap. It is possible to use a free split-skin graft, however, during walking in the postoperative period this tissue, as a rule, does not withstand a significant load. The cosmetic result and innervation in the area of the transplanted graft are also impaired, the intraoperative interval time increases. The technique of performing a local advanced flap requires speciall skills which not all children's surgeons possess [70].

For resections larger than 3 cm<sup>2</sup> and without involvement of bone structures in the tumor process, it is practical to use a free fasciocutaneous or musculocutaneous flap, as well as to close defects with local tissues. When bone tissue is involved in the tumor process, it is also possible to perform replacement of defects with free flaps, including osteocutaneous grafts. Defects of large sizes can be closed in several stages of reconstructive surgeries [71, 72].

The use of plastic surgery techniques to close large defects in the area of the distant neoplasm allows rapid healing of the surgical wounds and recovery of the patient in the postoperative period, provided that sufficient blood supply to the tissues is preserved, which increases the effectiveness of treatment due to the timely delivery of adjuvant radiation and/or chemotherapy.

The use of the fasciocutaneous sural flap has positively proved itself for the closure of defects in the heel and ankle area due to its plasticity and good blood supply [73-76]. The inflow of blood to this flap is due to the artery of calf, which, descending between the heads of gastrocnemius muscle, is a continuation of the popliteal artery. It is accompanied by veins and medial sural cutaneous nerve, which branches from the tibial nerve. Its formation should be started at least 5 cm proximal of the lateral malleolus, which is a favorable condition for preserving adequate anastomosis of the flap with the peroneal artery [77-79]. Mendieta et al. report on the successful recovery of sensitivity in the sural flap due to the connection of the transected nerve of the graft with the cutaneous branch of the superficial fibular nerve [80]. Tan et al. report on a series of such successful reconstructions of nerves with the preservation of the overall viability of the sural flap [81]. These works are of particular interest from the point of view of restoring the sensitivity of the flap, especially in cases of large resection volumes, and require further observation. A medial plantar flap is used to close small defects of the foot soft tissues with the preservation of innervation of the graft [82, 83].

Special attention should be paid to rotational axial pedicled flaps with the ability to rotate the graft from 90 to 180 degrees. Dong et al. reported on similar successful operations in 20 patients with extensive defects in the shin and foot area. All the flaps remained viable, the size of soft tissue defects ranged from  $2 \times 8$  cm to  $10 \times 20$  cm. In 12 patients the places of graft harvesting were closed with local tissues, in 8 cases a split cutaneous thigh flap was used [84]. In some cases free microvascular grafts may be used to close large volumes of resection, for example, a fasciocutaneous flap from the anterolateral surface of the thigh or from the parascapular area, as well as a flap from the latissimus dorsi with or without a cutaneous area. After taking the

flap from the anterolateral surface of the thigh, depending on the age and volume of the thigh, with a flap width of up to 10 cm, it is possible to close the defect with local tissues, whereas in case of larger grafts the defects should be closed with split-skin grafts. If it is necessary to use a free graft to close a foot defect, preference should be given to the flap from the front surface of the thigh, which is connected with a more favorable functional and cosmetic result due to the well-developed subcutaneous fat, as compared to the flap from the parascapular area. The blood supply of the parascapular fasciocutaneous flap occurs due to the branches of the arteria circumflexa scapulae emerging from the triangular space between major and minor teres muscles and the long head of the triceps muscle of arm. Depending on the age and body surface area of the child, the flap width can vary up to 12 cm wide and 25 cm long, which allows closing the defect of the donor wound with local tissues [85-87].

While using locally advanced flaps, there is a probability of spreading the tumor process to the graft harvesting area due to possible contamination of healthy tissues by tumor cells [88], however, according to the literature, such cases are isolated, and the positive effect of plastic reconstructive surgery significantly exceeds the possible risks [89]. The advantage of closing defects with local tissues is also the absence of the need for intensive postoperative control of the flap. In such cases postoperative therapy, in particular the use of anticoagulants, may be more sparing. In other situations the advancement of local flaps can be technically a more complex and risky manipulation as compared to using a free microvascular flap, the practice technique of which has become more accessible and significantly simplified thanks to modern technologies [1].

In some cases a more detailed preoperative planning of the operation with a clear assessment of the width of resection margins is necessary. The base of the defects after removal of neoplasms can be tendons and articular surfaces, which significantly worsens wound healing, leading to delayed radiation or chemotherapy. In this situation it is necessary to apply a combination of plastic reconstructive surgery methods to close the surgical defect and to prevent infection of the wound and nearby structures - tendons, bones, and muscle tissue. The use of a free microvascular flap pertains to high-tech medical care; despite the more sophisticated technique of execution, this variant of reconstruction can be considered the only correct tactic for a particular patient.

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## IN VIVO EVALUATION OF XENOGENEIC ACELLULAR BOVINE FASCIA GRAFTS IN THE RECONSTRUCTION OF ABDOMINAL WALL DEFECTS IN SWINE EXPERIMENTAL MODEL

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## ABSTRACT

In this study autor purpose to evaluate the feasibility of using bovine fascia in the experimental substitution of the fascial plan for the reconstruction of major anterior abdominal wall defects in the experimental model.

Plastic reconstruction of the surgically induced abdominal wall defect using decellularized bovine fascia grafts was performed on 5-week-old Landrace pigs (3 animals) in which the abdominal wall defect of 10x5.0 cm was surgically induced with the involvement of all layers, including the peritoneum. The animals were subsequently euthanized 90 days after the intervention. For decellularization, sterile 0.5% SDS solution (HiMedia) was used in volume required to obtain acellular tissues. The solution was changed every 24 hours for 72 hours.

The preventive results of the histopathological examination allowed the author to conclude that the use of decellularized bovine fascia grafts in the experimental model is characterized by the dominance of active regenerative processes with tissue remodeling and host cell invasion, the xenogeneic implant tissues being subjected to gradual degradation and substituted with the neoformed host connective tissue, the rationale of the usefulness of this biological material requiring additional comparative and clinical immunological studies.

The results of this experimental study allow us to conclude the following that the usage of bovine fascia acellular grafts as an alternative xenogeneic biological implant in reconstructive surgery of abdominal wall defects, this option requiring additional comparative and clinical immunological studies.

Key words: bioimplant, acellular grafts, bovine fascia, reconstructive surgery

## **INTRODUCTION**

The use of biological implants is a new and alternative approach to the reconstruction and regeneration of soft tissues with promising results. The purpose of the study was to evaluate the feasibility of bovine fascia use in the substitution of the fascial plan for the reconstruction of the anterior abdominal wall defects in the swine experimental model.

Several approaches to the reconstruction of abdominal wall defects, including the components separation technique, pedicle and free flap reconstructions, the use of synthetic and biological implants, etc., are described in the literature. These methods have as main objective the protection of the abdominal contents and the restoration of the functional support [27]. Although synthetic surgical implants are capable of providing the necessary biocompatibility and acceptable resistance in supporting abdominal cavity organs, their use is associated with the development of some adverse effects, including fibrous encapsulation, infection, erosion, net expulsion, fistula, intestinal obstruction, etc. [7, 23]. Reconstructive surgical interventions using remote musculofascial tissues are associated with

postoperative morbidity, functional disturbances and volume deficiencies in the donor region. The use of biological implants is a new and alternative approach to the reconstruction and regeneration of soft tissues with promising results, which could provide an accessible source of tissues with appropriate properties [17, 22, 24]. In order to avoid the adverse inflammatory response present in cases of the use of organ transplants, it is necessary to effectively remove cellular components and antigenic structures, efficient decellularization being extremely important, whether the source is allogeneic or xenogeneic. In this context, currently several decellularized grafts (extracellular matrices) of both human (allogeneic) and animal (xenogeneic) origin are available in the reconstruction of the abdominal wall [8, 12]; testing of the properties and efficacy of these biomaterials being under constant attention [11, 16].

The purpose of this study was to evaluate the feasibility of using bovine fascia in the experimental substitution of the fascial plan for the reconstruction of major anterior abdominal wall defects in the experimental model.

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## **MATERIAL AND METHODS**

Plastic reconstruction of the abdominal wall defect using decellularized bovine fascia grafts was performed on 5-week-old Landrace pigs (3 animals) in which the abdominal wall defect of 10x5.0 cm was surgically induced with the involvement of all layers, including the peritoneum; the animals being subsequently euthanized 90 days after the intervention. The process of decellularization of bovine fascia allografts was preceded by decontamination for 6 hours in the antibiotic cocktail (gentamicin (KRKA), lincomycin (World Medicine), amphotericin B (World Medicine) with RPMI (HiMedia). For decellulariza-tion a sterile 0.5% SDS solution (HiMedia) was used in volume required to obtain acellular tissues. The solution was changed every 24 hours for 72 hours. After decellularization under sterile conditions, the membrane was washed thoroughly with 0.9% NaCl solution, after which it was repeatedly decontaminated for 24 hours in the antibiotic cocktail, the efficiency of decellularization being histologically confirmed (fig. 1).



Fig. 1. Histological appearance of the bovine pericardium before decellularization (A), with preserved differentiated fibrillary connective structure of different density with an obvious marked nuclear-cellular component. ×100 VG Colouration and after decellularization (B) highlighting arranged acellular connective tissue bundles among which the extracellular matrix appearance is attested. ×25. H-E Staining.

For bacteriological examination to determine sterility, the solution was collected in which SDS tissues were washed, 2 ml of transport fluid and 3-4 small portions of 5x5 mm tissue from different graft sections in Thioglycolate Medium (HiMedia) and Sabouraud Dextroze Broth (HiMedia). The incubation was performed for 7-10 days to get final results. Tissues for storage at -86°C were placed in 50% Glycerol (Alchimia) solution with **RPMI** (HiMedia) and stored in the freezer at -80°C. Before use, the tissues were thoroughly washed with 0.9% NaCl solution.

## **RESULTS AND DISCUSSION**

No postoperative complications or cases of ventral incisional hernia were found in the experimental animals group. In all cases, the postoperative wound scarred primarily. In the mobilization process, a dense fibrous tissue area covered with adipose tissue (fig. 2A) was detected in the abdominal wall defect region with a decellularized bovine fascia graft. Weak areas or suture line dehiscence were not found. At the abdominal cavity opening, the adherence of the omentum to the internal surface of the implant was determined (fig. 2B, C), which could easily be detached (fig. 2D). The macroscopic examination of the resected piece laterally excised within 2 cm of the suture line (fig. 3A) allowed finding a connective tissue area covered by fat tissue with musculature pretension at the periphery. The internal surface had a pale, uneven yellowish tint, in rows, with fine adhesions of the fatty tissue of the omentum (fig. 3B). In the section perpendicular to the surface, a thickness of 2.4 - 2.7 cm of the connective area could be attested (fig. 3C). The histological examination of the pieces taken at the border line between the implant and host tissues revealed a varied picture manifested by the presence of the fascia graft partially embedded in the neoformed connective tissue and in cellular-adipose tissue seconded by the presence of a polymorpho-cellular inflammatory process, with predilection a lymphocytic one with the neoformation of lymphoid pseudo-follicular structures. At the level of the connective tissue, implant calcinosis (fig. 4A) was observed, contralaterally signs of implant slipping being found, fibrotic processes being revealed in these areas, and the presence of a mature neoformed cellular connective tissue layer could be noticed (fig. 4B). At insignificant distances from the border there was found the presence of implant residues encrusted in the neoformed hypercellularized connective tissue, which contained fibroblasts, monocytic-macrophagic and symplastic elements, these being directed to the implant residues and having a significant contribution to their destruction (fig. 4C). At the level of neoformed tissue, a collagenised tissue area was observed (fig. 4D).

In some areas, the implant was encapsulated in the neoformed connective tissue mass, which was more fibrosing on the external surface compared to the internal areas directed to the peritoneal cavity. The winding appearance of the implant could be often observed, which may be due to the disruption of the implant in the central and eccentric areas (fig. 5A).



Fig. 2. Macroscopic appearance of the external surface of the reconstruction abdominal wall defect area with decellularized bovine fascia graft: A - before the abdominal cavity opening; B, C - aeration of the omentum on the internal surface of the implant; D - macroscopic appearance of the internal surface of the implant after the omentum detachment



Fig. 3. Macroscopic appearance of the external surface of the implant (A), internal surface (B) and cross-section surface (C): 1 - connective-fibrous area with graft elements; 2 - fat tissue; 3 - muscle tissue.

In all the investigated samples, at different levels, on the implant projection in the neoformed tissue mass there were revealed implant residues attacked by the polymorphic-cellular component and polynuclear cellular symplasts, which pleads for a varied inflammatory cellular reactivity with the development of a latent and periodic fibrogenesis (fig. 5B, C, D). Adjacently, pseudofollicular and lymphoid follicular structures were present in the connective tissue area. These changes had a mosaic and chaotic appearance, including the whole area. In one case, on areas oriented towards the inner surface there were observed areas of adherence to the liver surface and implant calcinosis areas (fig. 5E).

The basic role of the biomaterials used in reconstructive surgery is to provide temporary mechanical support and the development of regenerative tissue of controlled size and form [5]. Ideally, the biological material should have mechanical properties appropriate for the desired applicability, resistance to infection after implantation, it should have remodeling properties in the host tissue with mechanical and biological properties identical to those of the missing tissue, it should have revascularization and cell infiltration properties, as well as elasticity, etc. [26].



Fig. 4. A - border area with the implant graft presence in the neoformed connective tissue area (1); 2 - graft sheets in the neoformed adipose tissue area; 3 - lymphoid pseudofollicular structures; B - border area with absent implant elements: 1 - neoformed connective tissue; 2 - small lymphocyte infiltrates in the neoformed tissue area; C - implant residues embedded in the neoformed connective tissue: 1 - implant residues attacked by polynuclear cellular symplasts; 2 - neoformed connective tissue with collagen fiber area; 3 - connective tissue of the peritoneal area with polymorphic cellular elements; D - external connective area with the presence of collagenized fibers (1) and internal area of neoformed connective tissue rich in cellular elements.



Fig. 5. A - histological appearance of the border area an undulating implant appearance in the neoformed connective tissue area, hypercellularized by the polymorphic-cellular population; B - implant residues attacked by polymorphic-cellular macrophagal cell symplasts; C - implant residues in disjunction on account of progressive cellular polymorphic-cellular activity; D - graft residues in disjunction penetrated by fibroblasts, lymphocytes, solitary leukocytes surrounded by polymorphic-cellular cells; E - implant sheet on the peritoneal surface - granulomatous structures with giant cells in the connective tissue layer; F - implant residues between the liver capsule and the neoformed peritoneal fibrous connective tissue layer.

Several studies have found that biological implants from different sources contribute to improved tissue regeneration by revascularization, leukocyte migration and cellular repopulation, thus having a beneficial role in the abdominal wall reconstruction, theoretically minimizing the complications associated with the use of synthetic materials [2, 4].

In the literature, there are multiple reports describing the effectiveness of biological materials derived from different sources: human, swine or cattle [10, 21]. Among the biological materials of human origin, the use of human acellular dermal matrix (AlloDerm) is the most widespread option in the reconstruction of abdominal wall defects [14, 18], including congenital ones [1, 19].

Certain performances have also been found in cases of use of xenogeneic biological grafts, including: dermic swine collagen (Permacol) [9], swine intestinal submucosa matrix (Surgisis) [3], swine acellular dermal matrix [20], bovine acellular pericardium [15], acellular dermal bovine matrix, etc. [25].

In the literature, there are few studies showing the results of the use of fascia grafts as a potential biological material in reconstructive surgery, more commonly human autologous fascia lata material [6] being evaluated. Bovine fascia xenografts are not widely described as potential biological material.

There are unique experimental studies that have reported their use in the reconstruction of experimentally induced muscular and peritoneal defects, finding that this biological material has good tolerance, long resorption time, and can be used for clinical purposes [13]. In this context, the up-to-dateness of this study is undisputed.

Thus, the results of this experimental study allow us to conclude the following:

- The decellularized bovine fascia implant is characterized by a polymorphic inflammatory response, the predominance of cellular spectrum indicating the dominance of active regeneration processes with tissue remodeling and invasion of host cells, the xenogeneic implant tissues being subjected to gradual degradation and substituted by the host's neoformed connective tissue.
- The results of the experimental study justify the utility of bovine fascia acellular grafts as an alternative xenogeneic biological implant in reconstructive surgery of abdominal wall defects, this option requiring additional comparative and clinical immunological studies.

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## PARTICULARITIES OF TISSUE REGENERATION OF DECELLULARIZED BOVINE PERICARDIUM XENOGRAFTS USED IN THE RECONSTRUCTION OF THE ANTE-RIOR ABDOMINAL WALL DEFECTS IN THE EXPERIMENTAL MODEL

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## ABSTRACT

The purpose of this study was to evaluate the regeneration potential of decellularized bovine pericardium grafts used as an option to close the abdominal wall defects in the experimental model.

The study group consisted of pigs subjected to reconstructive surgery of congenital abdominal wall defects (group 1 - 3 animals) (fig. 1) and total defect of the abdominal wall created surgically (involving all layers, including the peritoneum) with decellularized bovine pericardium (group 2 - 3 animals). Animals were sacrificed and investigated 30 days (3 animals) and 90 days after surgery (3 animals).

he results of this experimental study have allowed us to conclude the following:

- The acellular bovine pericardium graft is characterized by strength and durability, favorable for the reconstruction of major abdominal wall defects.
- In the regenerative-reparative processes of the acellular bovine pericardium grafts used in the reconstruction of the abdominal wall defects together with fibrogenesis processes, there are also processes of metaplasia with differentiation in chondroblasts which induce the neoformation of cartilage foci in the biological implant, which, then functions as an enchondral ossification factor with the formation of trabecular osteogenesis and ossification foci.
- The results obtained imply the need for further studies to clarify the role of these changes in the development of potential follow-up postoperative complications.

Key words: abdominal wall defects; biological grafts; extracellular matrix; bovine pericardium; biocompatibility

## INTRODUCTION

Bovine pericardium is a collagen-rich biological tissue widely used as a natural biomaterial in the modeling of a variety of bioprostheses in cardio-vascular surgery [4, 6] in reconstructive surgery of soft tissue defects [9] and complex defects of the abdominal wall [2, 5].

The removal of cellular components from the biological grafts while preserving the extracellular matrix allows for better tissue remodeling due to reduced antigenicity, graft degradation processes, host cell recellularization, formation of a new extracellular matrix and neovascularization [7]. Although the use of decellularized biological implants represents a performance in reconstructive surgery, the long-term interaction of these xenogeneic biomaterials with the local tissues and physiological systems of the patient as well as the regeneration processes induced by them are not elucidated. The possibility of predicting biocompatibility and undesirable consequences of these biological grafts can minimize patient's risk, which determined the up-to-dateness and novelty of the topic being addressed [7, 10].

The purpose of this study was to evaluate the regeneration potential of decellularized bovine pericardium grafts used as an option to close the abdominal wall defects in the experimental model.

## **MATERIAL AND METHODS**

The study group consisted of pigs subjected to reconstructive surgery of congenital abdominal wall defects (group 1 - 3 animals) (fig. 1) and total defect of the abdominal wall created surgically (involving all layers, including the peritoneum) with decellularized bovine pericardium (group 2 - 3 animals). Animals were sacrificed and investigated 30 days (3 animals) and 90 days after surgery (3 animals). To decellularize the bovine pericardium, sterile SDS solution 0.5% (HiMedia) was used, the decellularization efficiency being histologically confirmed. The decellularized grafts were stored in 50% Glycerol (Alchimia) solution with RPMI (HiMedia) at -80  $^{\circ}$  C (fig. 2).



Fig. 1. Stages of experimental surgical reconstruction of the congenital defect of the abdominal wall with decellularized bovine pericardium graft: A - intraoperative aspect of the defect after mobilization; B - excision of membranes; C - closure of the abdominal cavity; D - fixing the implant to the marginal fibrous ring of the defect.



Fig. 2. Histological aspect of the bovine pericardium before decellularization (A), with the preserved differentiated fibrillary connective structure of various density with a marked nuclear-cellular component × 100. VG coloration, and after decellularization (B) with marked bundles of orderly acellular connective tissue among which the elements of the extracellular matrix are revealed. × 25. HE coloration

## **RESULTS AND DISCUSSION**

In study group 1 there were neither postoperative complications, nor incisional hernias of the anterior abdominal wall. In all 3 cases postoperative wounds were primarily scarred (fig. 3A). After the mobilization of the external surface of the bovine pericardium graft area, no lumps were found, the area being fairly compact in the account of the fibrous tissue on which adipose tissue developed (fig. 3B). There were no adhesions at the opening of the abdominal cavity (fig. 3C). At macroscopic examination, the graft presented as a deformed and corrugated flap of pale brown color, more accentuated at the margins, comprised by connective tissue, which is more pronounced from the peritoneal part (fig. 3D).

In study group 2 complications were not recorded either, the postoperative wound healing primarily (fig. 4A, B). At the opening of the abdominal cavity, the left lobe of the liver was adhered to the operative incision region (2 cases), in all 3 cases the omentum was adhered intimately to the internal surface of the implant. No inter-intestinal adhesions were observed in the abdominal cavity (fig. 4C). After the omentum detachment from the
internal surface of the implant, some hemorrhage dots were observed (ig. 4D).









Fig. 3. A - appearance of the postoperative scar; B - macroscopic appearance of the external area of the bovine pericardium implant region; C - macroscopic aspect of the peritoneal surface of the bovine pericardium implant region; D - implant region (macropreparate): 1 - implant graft; 2 - internal peritoneal connective area; 3 - external cellular-adipose connective tissue.









Fig. 4. Macroscopic appearance of the acellular bovine pericardium graft area during animal's sacrifice (explanations in the text)

After the circular resection of the implant application area, the macroscopic examination revealed that the external surface was dominated by elastic hard fibrous tissue (fig. 5A). The internal surface of the implant represented a tough, trabecular plate, with small hemosiderosis foci. At the periphery there was an incomplete bead of variable thickness (0.2-0.6 cm) and hard (bone) consistency corresponding to the suture line boundaries, 0.5-1.3 cm wide (2 cases), or even 2.3 cm (1 case) (fig. 5 B). In section, the implant area was 1.7 to 2.5 cm thick at the bead level it had sponge-like appearance (fig. 5 C).



Fig. 5. Macroscopic aspect of the resection piece of the acellular bovine pericardium graft area; A - external surface: 1 - fibrous-connective plate; 2 - muscle tissue; B - the ossified bead-like internal surface; C - implant in perpendicular section: 1- fibrous-connective plate; 2 - osteogenic area in the bead; 3 - osteocartilaginous area in the plate; 4 - muscle tissue.

The results of the histological examination in study group 1 allowed to find that the graft ends were invaded by vascularized fibrous connective tissue. At the boundary between the graft and the proper tissue, the presence of an invasive focal or zonal fibrillar-cellular reaction, with the predominance of fibroblasts of the neoformed connective tissue and penetration in different ratio at the edges of the graft, is observed (fig. 6A). At this level, granulomatous changes, especially of the peritoneal area, of various dimensions, with polynuclear cellular symplasts, some with necrosis in the center, and others with calcinosis, were also revealed. Frequently, there were graft-like tissue fragments in the granuloma area (fig. 6 B, C).



Fig. 6. A - border region: 1 - implant graft; 2 - internal peritoneal connective area; 3 - external connective cellular-adipose area; B - marginal region: 1 - implant graft; 2 - granulomas of polynuclear giant cellular symplasts, with calcinosis; 3 - neoformedfibrillary connective tissue; 4 - proliferative penetration zone of the cellular-fibrillary component of the implant; C - granuloma structure: 1 - necrotizing elements in the granuloma area; 2 - granulomatous tissue of giant cellular symplasts, macrophagic-lymphocytic and fibrillary-connective component.

At the level of active interaction of the neoformed host tissue with the implant graft degeneration area such as hyaline drop-like dystrophy was attested on the graft region, associated with necrolytic degeneration and invasion of the fibroblastic cellular component (fig. 7).



Fig. 7. A - aspects of tissue interaction: 1 - implant graft; 2 - fibrillary cellular connective tissue penetrating into the graft area. B - A sequence at higher magnification: 1 - implant graft; 2 - fibroblastic fibrillary-cellular connective tissue strips penetrating into the graft; 3 - dystrophy; C - interaction area between the graft and the neoformed connective tissue: 1-implant graft; dystrophy zone in the hyaline drop; 2 - invasion of cellular fibrillary connective tissue; D - aspects of degeneration in the hyaline drops of the graft with fibroblasts penetration: 1 - degeneration in graft hyaline drops; 2 - penetration of fibroblasts into the area of degeneration

Concomitantly with the fibroblastic proliferative activity, the presence of lymphocytic and monocytic elements, macrophages, including proliferation of the vascular endotheliocytic component, was attested. The implant fibers underwent intumescent changes (fig. 8 A). At this level, in some areas, a varying intensity of the polymorphic cell component was observed, with the presence in different ratio of polynuclear giant cellular symplasts with phagocytic embedding aspects of the hyaline droplets (fig. 8 B, C, D)



Fig. 8. A - graft-host tissue interaction: 1 - intumescent graft and hyaline degeneration; 2 – fibro-cellular and mixed cellular fibrillary proliferative penetrating processes; B – giant cellular reaction at the tissue intersection line; C - hyaline degeneration foci invaded by polymorphic cellular component with the formation of giant cellular symplasts of macrophagic origin with hyaline incorporation; D - macrophagicsymplasts with polynuclear giants lined with hyaline droplets.

The results of the histological examination, performed in all three cases of the decellularized bovine pericardium graft use in the reconstruction of total abdominal wall defects, including the peritoneal wall (lot 2), revealed that the inflammatory cells practically disappeared 90 days after surgery. At the same time, marked proliferative processes of fibrous tissue with chaotic orientation, with or orientation in connective cords were revealed.

In all three cases, there could be revealed characteristic foci of cartilaginous and bone metaplasia manifested by hypercellularized sections with the presence of fibroblasts and some islets of immature chondric and trabecular tissue, trabecular bone tissue patches in different proportions in the area between the graft and host tissues, sometimes they could also be observed in central areas (fig. 9).

At the bead level and in the underlying area of the bovine pericardium graft, in one case, there were osteogenic mature osteoid plates with random trabecular appearance with diminution of osteoblasts at the trabecular and peri-insular level, where the connective tissue became denser, forming a periosteal strip (fig. 10A). In 2 cases, pathological neoformed tissue was present in some places as an osteo-cartilaginous component (fig. 10B) or some-



Fig. 9. A - immature mesenchymal cartilage islet in fibroblastic connective tissue mass located 2.5 cm from the border between tissues; B - immature mesenchymal cartilage islet in the connective tissue mass (1) and immature trabecular bone plate (2) in the adjacent area of the bead at the borderline; C - 1.2 cm area from the bead where immature trabecular bone plates are located at the border with the host tissue; D - immature trabecular osteogenic island partially surrounded by cells of osteoblastic (1) and fibroblastic (2) origin.

times as a trabecular osteogenic plate that could reach in different ratio the central area of the xenogeneic implant (fig. 10C), the intertrabecular fields being lined with acellular adipose tissue. In the central areas of the implant, connective tissue platelets with chaotically oriented cords of collagen bundles in combination with mesenchymal tissue (fig. 10 D, E, F) were frequently observed.



Fig. 10. A - ossified bead area with diminished osteoblasts activity; B - mature osteocartilaginous structures located in the mass of the neoformed connective tissue; C - osteogenic plate in the medial area with periosteum and cellular-adipose tissue; D - neoformed connective plate with chaotically oriented collagen fibers in various ratio; E - neoformed connective tissue cords with active and proliferative aspects of fibroblasts; F - neoformed connective tissue cords with collagen fibers in combination with mesenchymal tissue.

In 2 cases, hemosiderosis foci were observed in the biopsies taken from the central areas towards the internal (peritoneal) surface (fig. 11A). In some sectors, corresponding to the lacunar aspect, a stratification of the connective tissue from the peritoneum was noted, marking a lax aspect with spaced neurovascular bundles, while on the external surface it was much denser with proliferative aspects of fibroblasts (fig. 11B).

In some samples from the central area, lax connective tissue plates were observed in the dense area, at the periphery with lymphocyte infiltrate, sometimes with the neoformed pseudofollicular structures and the presence of hemosiderosis (fig. 11C). In all cases, at a distance of up to 2.2 cm from the borderline, the peritoneal tissue consisted of mature connective tissue, limited in various ratio by fatty tissue. (fig. 11D).



Fig. 11. A - medial area with micro-macrofocal hemosiderosis; B - connective tissue towards the peritoneal and compact area towards the external surface, spaced neurovascular bundles; C – lax mesenchymal connective tissue plates penetrated by vascular network; D - structural aspect of the peritoneum at distance. In spite of the relevant developments in the use of decellularized bovine pericardium grafts, some complications such as biological matrix deterioration and tissue degeneration due to implant calcification have been identified [3]. Our findings are consistent with the data published by some authors who found the development of osteocartilaginous metaplasia foci in the late postoperative period when using decellularized bovine pericardium xenografts preserved in glutaraldehyde in reconstructive surgery of the major vessels in experimental animal studies [1, 8]. Chondroid and / or bone metaplasia is considered by some authors to be a reversible change involving fibroblasts and myofibroblasts, ischemia being one of the causes [1].

Thus, the results of this experimental study have allowed us to conclude the following:

- The acellular bovine pericardium graft is characterized by strength and durability, favorable for the reconstruction of major abdominal wall defects.
- In the regenerative-reparative processes of the acellular bovine pericardium grafts used in the reconstruction of the abdominal wall defects together with fibrogenesis processes, there are also processes of metaplasia with differentiation in chondroblasts which induce the neoformation of cartilage foci in the biological implant, which, then functions as an enchondral ossification factor with the formation of trabecular osteogenesis and ossification foci.
- The results obtained imply the need for further studies to clarify the role of these changes in the development of potential follow-up postoperative complications.

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## RECONSTRUCTIVE OPERATIONS OF SERIOUS SCOLIOTIC DEFORMATION AT CHILDREN

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#### ABSTRACT

In Clinic of Vertebrology, Orthopedics and Traumotology of the "N.Georgiu" Scientifically-Practical Center of Children's Surgery 58 children with scoliosis (>70°) of different etiology, have been pre- and post-operatively examined with a follow-up of 1 to 5 years. The comparative analysis of the quality of the life of patients with severe spine deformations (according to a questionnaire "EQ-5D"), before and after surgical intervention, has shown that quality of the life of patients in postoperative period essentially improved, in comparison with the preoperative period, from 12,7±0,3 points to 7,02 ± 0,1. The distant results of surgical treatment were: good – 39 (68,4%), satisfactory – 12 (21,1%), unsatisfactory – 7 (12,3%). The differential election of treatment option in spine deformation management depends on the age of patient, extent of deformation, spine mobility and neurological impairment. Application of high technologies allows achieving good results in these patients.

Key words: scoliosis; spine deformations; high technologies, children

#### **INTRODUCTION**

Irrespective of etiology, spine deformations in adolescents represent the cause that influences the main peculiarities of the spinal column: its safety and stability; initially it is manifesting by pains, static's infringements, and internals' dysfunction, subsequently it leads to severe decrease of quality of the life [1, 8, 9, 11]. The choice of surgical and therapeutic options in the management of spine deformations at children is still controversial [2, 5, 6, 11].

**Problems and contradictions**. At the present moment at scoliotic illness' treatment, surgical tactics remains discussed in the following aspects:

- At what age is it better to operate?
- What surgical technique will be more effective?
- Whether surgical intervention at the level of zones of growth and intervertebral disks will be expedient?

Data of epidemiological research, conducted Scientifically-Practical Center of Children's Surgery by randomization method, showed that in 2011 the frequency of scoliotic illness of RM reached on 7,8% at children and teenagers (till 18 years), from which 0,26% – the deformation angle was > 70°. They make 5,2% in structure of diseases of a locomotorium apparatus. [10].

**Work's goal:** rising of quality of the life of children with spine deformations, by working out of surgical treatment algorithm.

#### **MATERIAL AND METHODS**

In Clinic of Vertebrology, Orthopedics and Traumotology of the "N.Georgiu" Scientifically-Practical Center of Children's Surgery 58 children with scoliosis (>70°) of different etiology, for correction of deformation at which was used polysegmentary constructions, have been pre- and post-operatively examined with a follow-up of 1 to 5 years (2008 – 2012). The evaluation included collecting of anamnesis data, clinical examination, labs and imaging (standard radiography/ with functional tests, magnetic resonance). Children were aged between 5 and 17 years; they were predominantly girls – 61(56%).

Patients were parted, on 3 categories: I category – 26 patients with complete growth (14-16 years) (medium – 14,8 years) and idiopathic mobile spine deformations, curvature angle to 70-85°, coefficient of Harrington >5; II category – 18 patients with complete growth (14-17 years) and idiopathic rigid forms of deformation (medium – 15,9 years), curvature angle is more than 85-90° and coefficient of Harrington < 5; III category – 16 patients with juvenile idiopathic and congenital deformations (5-12 years).

The main goals of surgical interventions were: elimination of deformation and disbalance correction and spine stabilization. Surgery allowed obtaining the following results: reconstruction of forward and average spine columns, restoration of physiological spine profiles (frontal and sagittal); restoration of normal anatomy of the vertebral channel; stabilization of the spine-impellent segment.

#### **RESULTS AND DISCUSSION**

Tactics of surgical interventions, depending on category was following:

The I category – 26 patients with complete body growth (14-16 years) and idiopathic plentiful spine deformations was carry out one-stage dorsal correction (Fig 1).



# Fig 1. Before operation the angle of deformation was 70° (A) and after operation - 0 °, correction of deformation is 100% (B)

The II category – 18 patients with complete body growth (14-16 years) and idiopathic rigid forms of deformation by the first stage was executed forward spine mobilization (a multilevel discectomy), the second – dorsal correction of deformation by C-D system (Fig 2.).



# Fig 2. Before operation the angle of deformation was 127 $^{\circ}$ (A) and after operation - 29 $^{\circ}$ , correction of deformation is 98 $^{\circ}$ (B)

The III category–16 patients with juvenile idiopathic and congenital deformations (5-12 years) was carried out "blocking spondylosyndesis" at curvature top with the following dorsal correction by "a growing construction". In process of children growth through minimum invasive access the phased system's distraction is carried out. One step of a distraction equals 1 cm. Intervals of stage-by-stage correction depend on age growth activity and rates of deformation advance: from 6 months to 1,5 years.



Fig. 3. Before operation (A) and after operation of "blocking spondylosyndesis" at curvature top with the following dorsal correction by "a growing construction" (B)

The comparative analysis of the quality of the life of patients with severe spine deformations (according to a questionnaire "EQ-5D"), before and after surgical intervention, has shown that the quality of the life of patients in postoperative period essentially improved, in comparison with the preoperative period, from 12,7±0,3 points to 6,7±0,1. The distant results of surgical treatment were good: (correction > 55%) –39 (68,4%), satisfactory (55%-40%) –12 (21,1%), and unsatisfactory (< 40%) –7 (12,3%). Complications took place in 9(15,8%) cases.

#### **CONCLUSIONS:**

The tactics of surgical treatment of spine deformations and further forecast depend on the type of neurological infringements and the character of bones' damages.

Optimum method of correction of difficult rigid scoliotic spine deformations were: forward spine release; dorsal correction and backbone fixation by a metal construction.

Surgical treatment of difficult juvenile scolioses began at 10-12 years old, and combined forward spine release with the following dorsal correction without posterior spine fusion execution.

In cases of congenital deformations primary operative defect's correction was carried out at children at the age of 3-7 years – "blocking spondylosyndesis" at curvature top with the following dorsal correction by "a growing construction" without posterior spine fusion execution.

Final correction of deformation, posterior spine spondylosyndesis and thoracoplasty are carried out on the end of spine growth.

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