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**ҚАЗАҚСТАН ХИРУРГИЯСЫНЫҢ  
ХАБАРШЫСЫ**

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**ВЕСТНИК ХИРУРГИИ  
КАЗАХСТАНА**

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**BULLETIN OF SURGERY  
IN KAZAKHSTAN**

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**ХИРУРГИЯ**

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## Abstract

The purpose of research is to determine the feasibility of laparoscopic pancreatoduodenectomy in tumors of the periampullary zone.

**Material and methods.** In the period from 2016 to 2022 at the Syzganov National Scientific Center of Surgery, 193 patients underwent PD with a diagnosis of a tumor of the periampullary zone. Of these, 6 patients were performed laparoscopically. All patients who underwent LPD were female. The age of the patients ranged from 15 to 77 years (average age – 55,7 years).

**Results.** In 4 (66.7%) patients, cancer of Ampulla of Vater was detected, in 2 (33.3%) pancreatic head cancer. According to the final histology data, adenocarcinoma and the degree of differentiation G2 were detected in all cases. Data on the histology and size of the tumor are summarized in Table 1. The average age of patients was 55.7 years. All patients had a clinic of mechanical jaundice before surgery; the average levels of bilirubin in the blood were 121.3 mmol/l. Accordingly, all patients underwent drainage of the biliary tract. Of these, 5 (83.3%) patients underwent percutaneous stenting and 1 (16.7%) endobiliary stenting.

**Conclusion.** Thus, we presented our initial experience of performing laparoscopic PD. Our results shows the feasibility of laparoscopic PD safely and radically for tumors of the periampullary zone in certain cases. The accumulation of experience in such interventions leads to an improvement in immediate results and a reduction in postoperative complications, the operative time.

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## Conflict of interest:

The authors declare that they have no conflicts of interest

## Keywords:

pancreatoduodenectomy, laparoscopic, pancreaticojejunostomy, consistency of pancreas, diameter of pancreatic duct

## Периампулярлық аймақ ісіктерінің лапароскопиялық гастропанкреатодуоденалды резекция жасау тәжірибеміз

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## Тұжырым

**Жұмыстың мақсаты.** периапулярлық аймақ ісіктері үшін лапароскопиялық ГПДР орындылығын анықтау.

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## Түйінді сөздер:

гастропанкреатодуоденалдық резекция, лапароскопиялық, панкреатикојејуноанастомоз, ұйқы безінің консистенциясы, ұйқы безі түтігінің диаметрі



пациентке ГПДР жасалды. Оның ішінде 6 науқасқа лапароскопиялық жолмен жасалды. Лапароскопиялық ГПДР жасалған барлық науқастар әйелдер болды. Науқастардың жасы 15-тен 77 жас аралығында болды (орташа жасы – 55,7 жас).

**Нәтижелер.** Науқастардың 4-де (66,7%) үлкен емізікшесінің қатерлі ісігі, 2-де (33,3%) ұйқы безі басының қатерлі ісігі анықталды. Гистологияның соңғы деректеріне сәйкес, барлық жағдайларда аденокарцинома және G2 дифференциация дәрежесі анықталды. Ісіктің гистологиясы мен мөлшері туралы мәліметтер 1-кестеде келтірілген. Пациенттердің орташа жасы 55,7 жасты құрады. Операцияға дейін барлық науқастарда механикалық сарғаю клиникасы байқалды; қандағы билирубиннің орташа деңгейі 121,3 мкмоль/л құрады. Бүкіл науқастарға өт жолдарын дренаждау операциялары жасалды. Оның ішінде 5 (83,3%) науқасқа тері-бауыр арқылы холангиостомия және 1 (16,7%) науқасқа эндобилиарлы стенттеу жүргізілді.

**Қорытынды.** Осылайша, біз лапароскопиялық ГПДР бойынша алғашқы тәжірибемізді ұсындық. Біздің нәтижелеріміз белгілі бір жағдайларда периапулярлық аймақ ісіктерінде лапароскопиялық ГПДР-дің қауіпсіз және түбегейлі орындылығын көрсетеді. Мұндай оталарды жасауда тәжірибені арттыру, нәтижелердің жақсаруына және операциядан кейінгі асқынулардың, операцияның ұзақтығының төмендеуіне әкеледі.

## Наш опыт лапароскопической гастропанкреатодуоденальной резекции при опухолях периапулярной зоны

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### Аннотация

**Цель работы:** определить целесообразность лапароскопической ГПДР при опухолях периапулярной зоны.

**Материалы и методы.** В период с 2016 по 2022 г. в Национальном научном центре хирургии им. А.Н. Сызганова 193 пациентам была выполнена ГПДР с диагнозом – опухоль периапулярной зоны. Из них 6 пациентам операция была выполнена лапароскопическим путем. Все пациенты, перенесшие ЛГПДР были женского пола. Возраст больных варьировал от 15 до 77 лет (средний возраст – 55,7 лет).

**Результаты.** У 4 (66,7%) пациентов был выявлен рак БДС, у 2 (33,3%) - рак головки поджелудочной железы. Согласно окончательным данным гистологии, во всех случаях была выявлена аденокарцинома со степенью дифференцировки G2. Данные о гистологии и размере опухоли сведены в таблицу 1. Средний возраст пациентов составил 55,7 лет. У всех пациентов до операции наблюдалась клиника механической желтухи; средние уровни билирубина в крови составляли 121,3 мкмоль/л. Соответственно всем пациентам было выполнено дренирование желчных путей. Из них 5 (83,3%) пациентам дренирование было выполнено чрескожным путем и 1 (16,7%) - эндобилиарное стентирование.

**Заключение.** Таким образом, мы представили наш первичный опыт выполнения лапароскопической ГПДР. Наши результаты подтверждают тезис об осуществимости лапароскопической ГПДР безопасно и радикально при опухолях периапулярной зоны при определенных случаях. Накопление опыта таких вмешательств приводит к улучшению непосредственных результатов и уменьшению послеоперационных осложнений, длительности операции.

**Ключевые слова:**  
гастропанкреатодуоденальная  
резекция, лапароскопическая,  
панкреатикоеноанастомоз,  
консистенция  
поджелудочной железы,  
диаметр панкреатического  
протока

## Introduction

Pancreatic cancer (PC) is one of the most aggressive cancers, with about 9% of an overall 5-year survival rate. In 2020, more than 57,000 new cases are expected in the United States, which is estimated to lead to more than 47,000 deaths [1]. In recent years, the incidence of PC has increased, and it is expected that by 2030, PC will be one of the leading causes of cancer mortality [2, 3]. Unfortunately, due to the late manifestation, only 15-20% of patients are candidates for surgery [1]. Approximately 60-70% of pancreatic adenocarcinomas occur in the head of the pancreas, and the rest is found in the body (15%) and tail (15%) [4].

Pancreatoduodenectomy (PD) is a classical surgical procedure for the treatment of benign and malignant tumors in the pancreatic head, terminal part of the common bile duct, duodenum and the ampulla of Vater [5, 6]. For the first time, successful PD was reported by Whipple in 1935 for the treatment of a periampullary tumors [7], however, this procedure became widely used only since 1990 due to previously high mortality. Despite the ongoing development of treatment, PC remains one of the most difficult tumors for treatment and the five-year survival rate reveals less than 10% [8].

The minimally invasive method, after two decades of its introduction into clinical practice, is becoming increasingly popular in pancreatic surgery, mainly due to increased experience in this field and the availability of new technologies [9-12]. Minimally invasive surgery is used more often than conventional surgical operations due to the achievement of comparative satisfactory oncological results, reduction of postoperative pain, decrease usage of narcotic analgesics and decrease hospital stay [13].

The world's first laparoscopic PD (LPD) experience was described in 1994 by Gagner M, Pomp A. [14]. LPD has become increasingly popular among surgeons in the last decade [15-18]. Despite the breakthrough in this field and the positive aspects of laparoscopic surgery, most centers and surgeons try not to apply this method of surgical treatment, due to possible complications, technical difficulties, the need for experienced surgeons in laparoscopic interventions [19]. Several studies have been published, including three randomized controlled trials (RCTs) with inconclusive results of the relative advantage of LPD over open PD (OPD) [20-22].

A long operation time is one of the disadvantages of the laparoscopic method, which was revealed in a number of comparative analyses of OPD and LPD [23]. In general, the increased experience in LPD, standardization of operational procedures and mutual understanding between the surgical team, contributes to reducing the operation time after 10 cases of LPD [24]. Wang

et al. reported that the duration of the operation before 50th case was 8.1 hours, after 50th case was 5.4 hours and after 250th case was 4.7 hours [25]. Kenrick et al. in their observations reported that the operation time decreased on average from 7.7 hours in the first 10 patients to 5.3 hours in the last 10 [26].

The use of a full laparoscopic approach to PD has recently become widespread all over the world, and it is beginning to be considered largely applicable [27,28]. It has been shown that a total LPD is feasible and safe and provides a number of potential benefits, including lesser blood loss, need for blood transfusion, stay in the intensive care unit and hospital stay compared to OPD [29].

In Kazakhstan, the first PD was performed in 1980 in the Syzganov National Scientific Center of Surgery by Professor Aliyev M.A. and Seisembaev M.A. Over the past 5 years (2016-2022), 193 PD have been performed at the Syzganov's National Scientific Center of Surgery. The first LPD was performed in 2019 at the Syzganov's National Scientific Center of Surgery (Professor Baimakhanov B.B.).

The main purpose of this article is to determine the feasibility of laparoscopic PD in tumors of the periampullary zone.

## Materials and methods

In the period from 2016 to 2022 at the Syzganov National scientific center of surgery, 193 patients underwent PD with a diagnosis of a tumor of the periampullary zone. LPD was performed in 6 patients. All patients who underwent LPD were female. The age of the patients ranged from 15 to 77 years (mean age – 55.7 years).

We analyzed the clinical characteristics of patients (age, gender, tumor localization, CA 19-9, pancreatic consistency, pancreatic duct diameter and histopathological diagnosis), intraoperative data (operation time, number of removed lymph nodes and intraoperative blood loss) and postoperative data (postoperative pancreatic fistula, bleeding and relaparotomy, hospital stay).

Preoperatively, all patients underwent a laboratory, instrumental methods of examination and abdominal contrast enhanced computed tomography.

Indications for LPD were the following: tumor size less than 2.5 cm without metastasis and invasion into superior mesenteric and portal vein. Patients with hard gland and a dilated pancreatic duct were also included to indications for LPD, which are considered as good conditions for reconstruction. Exclusion for LPD were: severe pancreatitis of the body and tail, the presence of a concomitant disease in the patient (cardio-respiratory), age above 70 years, the history of open abdominal surgery, a soft gland and a small diameter of the pancreatic duct, which complicate reconstruction. Preoperatively, all patients had undergone drainage of the bileduct.

**Table 1.**  
Preoperative characteristics,  
intraoperative and  
histopathological data of patients  
who underwent LPD

Preoperative characteristics	Number of patients n=6
<b>Gender</b>	
Male	-
Female	6 (100%)
Age	55,7 (15-77)
<b>Localization of tumors</b>	
Head of pancreas	2 (33,3%)
Ampulla of Vater	4 (66,7%)
<b>Preoperative drainage of the biliary tract</b>	
PTBD	5 (83,3%)
Endobiliary stenting	1 (16,7%)
CA 19-9, U/ml	198±987
<b>Texture of pancreas</b>	
Hard	5 (83,3%)
Soft	1 (16,7%)
Tumor size, cm	1,9 (1,4 – 2,7)
<b>Diameter of pancreatic duct, mm</b>	
≤5	2 (33,3%)
>5	4 (66,7%)
Number of removed lymph nodes	19 (16-21)
<b>Type of tumor</b>	
Adenocarcinoma	6 (100%)
Others	-

*Surgical technique and  
postoperative management*

The position of the patient on the operating table on his back with legs spread by 40 degrees with the head end lifted. The position of the operator is between the legs, assistants are on the sides. First of all, under the umbilicus, a Veress needle is used to insufflate CO<sub>2</sub> into the abdominal cavity. The location and number of trocars are the key principles of the operation (Figure 1). An optical trocar (C) with a diameter of 10 mm is inserted along the middle line, 2 cm below the umbilicus. 2 trocars (B, D) are placed in the mesogastric region at the umbilicus level along the mid-clavicular line, one 12-millimeter trocar in the left side and the second 10-millimeter trocar in the right side, which are used by the operating

surgeon. The remaining 2 trocars (A, E) are installed in the mesogastric region 2 cm above the umbilicus level along the anterior-axillary line, 5 mm trocars in the right and left sides, which are used by assistants. A 30-degree tilt was used for the optical system. The changing positions of the trocars varied depending on the stage of the operation. During the mobilization, ports A, B, D are mainly used by the surgeon. When mobilizing the duodenum by Kocher maneuver, the surgeon use ports A, B. When performing pancreaticojejunostomy, the optical port is C, the surgeon use ports B, D. During hepaticojejunostomy, the optics is changed to port D, and the surgeon use ports E, C, as shown in Figure. 1.





Figure 1.  
Placement of trocars for  
laparoscopic PD

After the introduction of the first port, an examination of the abdominal cavity and liver is carried out to exclude any metastases. The lesser sac is opened with excision of the gastrocolic ligament using ultrasonic scissors. The left gastro-omentum vessels are preserved, while the right ones are intersected. Then the common hepatic artery (CHA) is mobilized by removing the lymph nodes that are located around the artery (8a and 8p group lymph nodes). The gastroduodenal artery (GDA) is isolated, which is also cleared from lymphatic tissues, then clipped (usually 2 clips are left on the stump of the GDA) and intersected. At this stage of the procedure, the anterior surface of the portal vein (PV) is mobilized and exposed, just above the neck of the pancreas. Next, lymph dissection is performed in the area of the hepatoduodenal ligament (group 12) and along its proper hepatic artery (group 12a).

Then a cholecystectomy is performed and lymph nodes along the common bile duct (group 12b) are removed. The common hepatic duct is dissected with scissors just above the site of the introduction of the cystic duct. After that, lifting the portal vein, lymph node dissection is performed behind the portal vein (group 12p). Then the duodenum is mobilized by Kocher to the

level of the horizontal part with the exposure of the inferior vena cava (IVC) and to the beginning of the superior mesenteric artery (SMA). Then the superior mesenteric vein (SMV) is identified along the lower edge of the pancreas and a tunnel is formed between the posterior surface of the pancreas and the PV, SMV. The duodenum is pulled back to release the horizontal part from the Treitz ligament. Then, pulling the duodenum, lymph node dissection is performed behind the head of the pancreas (group 13) and the upper mesenteric vessels (group 14). Then the small intestine is mobilized, the mesentery vessels are coagulated and intersected before the ligament. Further, at a distance of 25 cm from the Treitz ligament, the jejunum is intersected with a laparoscopic stapler (Endo Gia 40, purple cartridge).

Then the stomach is intersected at the level of the antrum with a laparoscopic stapler (Endo Gia 60, purple cartridge). The pancreas in the isthmus is dissected with ultrasound scissors and the main pancreatic duct is dissected with scissors, as shown in Figure 2. The specimen is placed in a container for further removal. Then the specimen is removed through an infraumbilical trocar with an expansion of the incision to 3-4 cm.

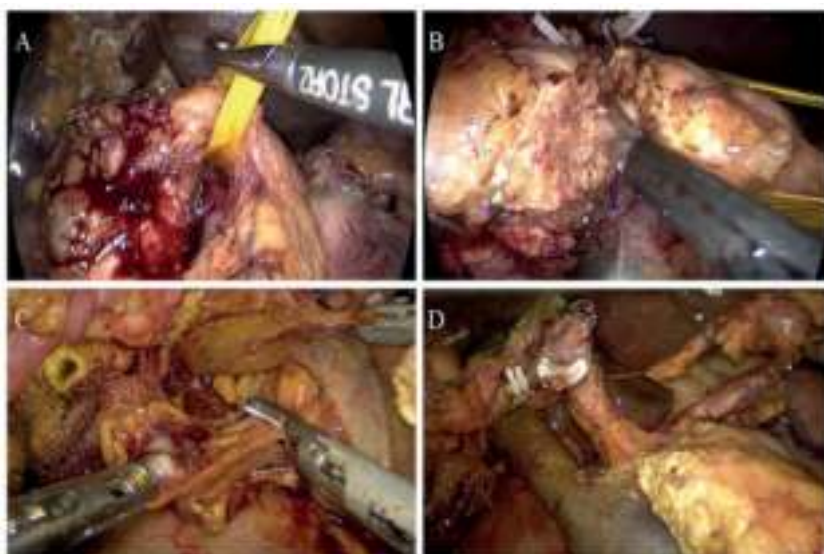


Figure 2.  
Stages of the operation: A - The  
formation of a tunnel between  
the pancreas and the portal  
vein; B - The transection of the  
main pancreatic duct and the  
pancreatic parenchyma; C - The  
stage of lymph node dissection; D  
- The final view after lymph node  
dissection

*Reconstructive phase:*

Anastomoses are formed sequentially on one loop of the small intestine: pancreaticojejunostomy (PJA), hepaticojejunostomy (HJA) and gastroenterostomy (GEA). In PJA with a diameter of the main pancreatic duct less than 5.0 mm, stent drainage is left.

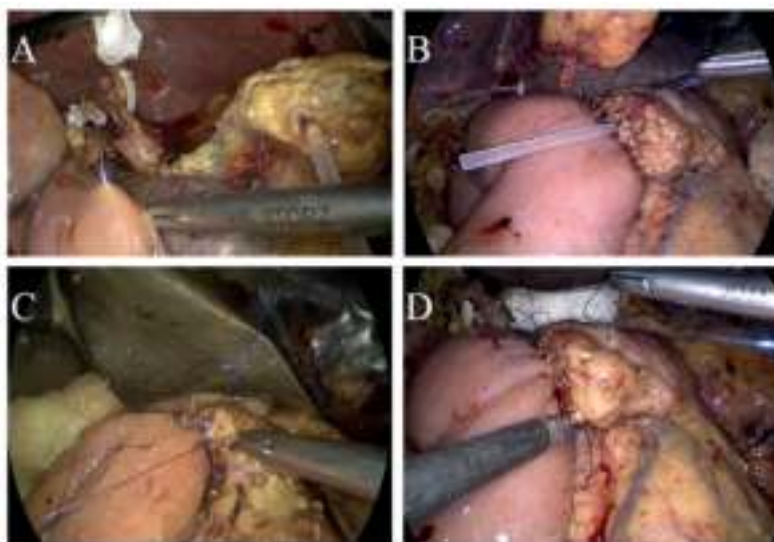
In laparoscopic PJA, as in open PJA method, a double-row anastomosis of the "end to side" type between the pancreatic duct and the mucous membrane of the small intestine is formed.

In modified Blumgart PJA, our technique is begun with the imposition of a transpancreatic U-shaped suture. The first suture is located higher in the upper edge of the pancreas. The suture is applied to the

entire thickness through the pancreas from the front to the back wall. Then a suture is applied to the small intestine through the serous-muscular layer, followed by transfixation of the pancreas to the entire thickness from the posterior to the anterior in a U-shaped form. Then, nodular sutures are applied separately between the posterior wall of the pancreas and small intestine in the amount of 2-3 sutures. After that, a second transpancreatic U-shaped suture is applied to the lower edge of the pancreas, as indicated above. Then a small enterotomy is performed opposite the pancreatic duct and a stent is inserted into the jejunum through it. Ductal-mucosal PJA is created in the same way as with traditional Blumgart anastomosis (Figure 3).

**Figure 3.**

Laparoscopic ductal-mucosal pancreaticojejunostomy "end to side" with the stent drainage: A - The suture of the posterior wall of the anastomosis with U-shaped sutures; B - The formation of the posterior wall of the anastomosis and the installation of a stent into the pancreatic duct; C - The suture of an anastomosis between the pancreatic duct and the mucosa of the small intestine; D - The final type of superposition of PJA

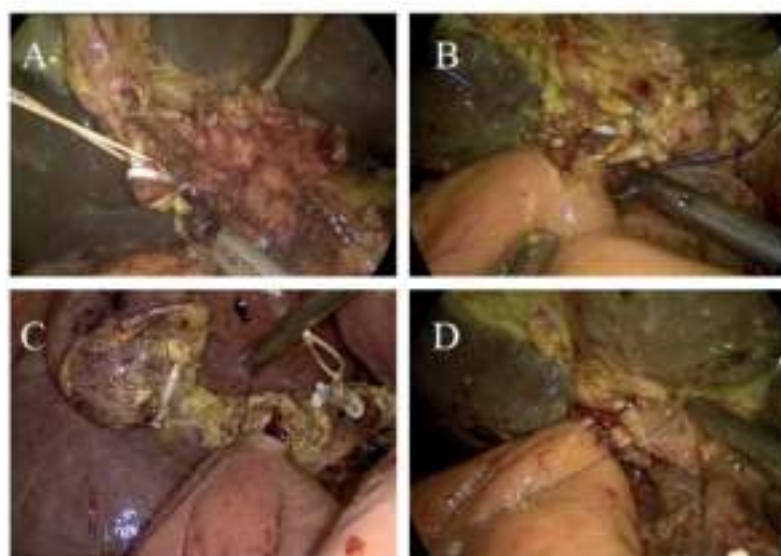


The end-to-side HJA is performed with a continuous running 5-0 PDS suture at a distance of about 15-20 cm from the PJA, as shown in Figure 4. The posterior and anterior walls of the anastomosis are stitched with continuous sutures

according to the principle of vascular technique. During the application of a continuous suture on the front wall, the sutures are not stretched. After application, continuous suture are carefully stretched and tied.

**Figure 4.**

The stage of laparoscopic hepaticojejunostomy "end to side" with a continuous running suture: A - The transection of common hepatic duct; B - The suture of the posterior wall of the anastomosis; C - The suture of the anterior wall of the anastomosis; D - The final type of HJA overlay

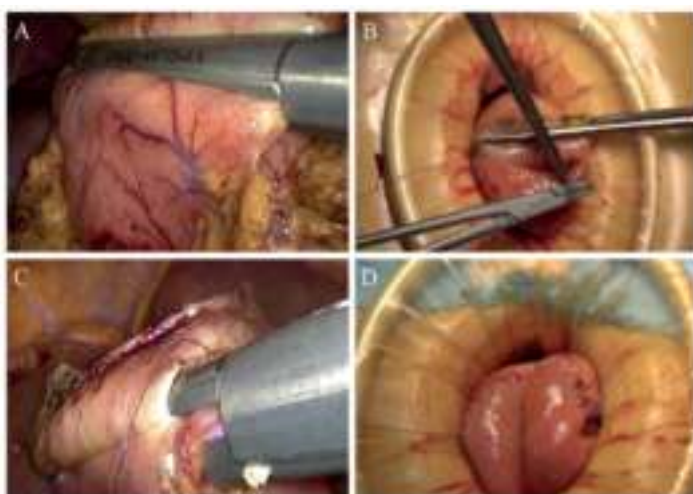


At the stage of formation of GEA "side by side" anastomoses, we use two methods: manual method through mini-laparotomy access and intracorporeal in total LPD.

1. When performing an anastomosis by manual method, the anastomosis is performed through a mini-laparotomy access. A small incision is made in the epigastric region with a length of 4-5 cm, from where the specimen is removed and

anastomosis is applied by the traditional method, as shown in Figure 5.

2. When performing a total LPD, the anastomosis is performed by the intracorporeal method. First, holes for a laparoscopic linear stapler are made on the wall of the stomach and small intestine. Then, using a linear stapler with a diameter of 60 mm (Covidien) with a purple cartridge, an anastomosis is performed by the post-rim method, as shown in Figure 5.



**Figure 5.** The stage of applying gastroenteroanastomosis: A - Dividing the stomach with a stitching device; B - The imposition of GEA by manual method through mini-laparotomy access; C - The imposition of laparoscopic intracorporeal GEA with a linear stapler; D - The final type of GEA by manual method via mini-laparotomy access

In the postoperative period, nasogastric and urinary catheters were removed from all patients on the 2nd postoperative day, unless additional problems arose. Oral alimentation was started on the 3rd day under normal conditions. The level of drainage amylase was measured on the 3rd and 5th postoperative days. Prophylactic octreotide was administered subcutaneously and continued regularly for three days after surgery.

**Statistical analysis**

Statistical analysis was carried out using the Microsoft Excel 2010 package (Microsoft, USA). Arithmetic mean and standard deviations (M±SD) were calculated to describe quantitative data. Absolute and relative (%) values were calculated for the analysis of qualitative data.

**Results**

In 4 (66.7%) patients, cancer of Ampulla of Vater was detected, in 2 (33.3%) pancreatic head cancer. According to the final histology data, adenocarcinoma

with the degree of differentiation G2 was detected in all cases. Data on the histology and size of the tumor are summarized in Table 1. The mean age of patients was 55.7 years. All patients had a clinic of mechanical jaundice before surgery; the mean levels of bilirubin in the blood were 121.3 mmol/l. Accordingly, all patients underwent drainage of the biliary tract. Of these, 5 (83.3%) patients underwent percutaneous stenting and 1 (16.7%) endobiliary stenting. All LPD were performed using standard surgical techniques. Intraoperative data are shown in Table 2.

Mean operative time was 480 minutes. Depending on the consistency of the pancreas, the hard gland mainly prevailed in 5 (83.3%) patients and soft in 1 (16.7%). In 4 cases GEA was performed by mini-laparotomy access and in 2 cases was completed total laparoscopically. No additional trocars were required to complete the operation. No intraoperative transfusions were performed.

Intraoperative data and complications	OPD (n = 187)	LPD (n = 6)	p-value
Operation time (min.)	380 (260 – 600)	480 (390 – 660)	ns
Hospital stay (days)	17 (11–34)	11 (8–17)	ns
Blood loss (ml)	240 (180 - 1500)	130 (40 - 350)	ns
Pancreatic fistula	6 (3.2%)	1 (16,7%)	ns
Delayed gastric emptying	9 (4.8%)	-	-
Bleeding	8 (4.2%)	1 (16.7%)	ns
Re-operation	6 (3.2%)	1 (16.7%)	ns
Wound infection	11 (5.9%)	-	-
Hospital mortality	5 (2.7%)	-	-

**Table 2.** Comparison of intraoperative data and complications of patients who underwent PD, n=193, from 2016 to 2022



Mean blood loss was 130 ml. Mean hospital stay was 11 days. Conversion to open surgery was required for only 1 patient, where there was a significant inflammatory process in the area of the head of the pancreas. In all cases, R0 resection was achieved. Number of removed lymph nodes was 19.

A postoperative complication was observed in 1 (14.3%) patient in the form of intra-abdominal erosive bleeding, which required repeated surgery. Hospital mortality was not observed.

#### Discussion

Laparoscopic PD is considered one of the most difficult surgical interventions, which is associated with the imposition of multiple and complex anastomoses [23]. A long operative time is one of the disadvantages of the laparoscopic method, which was revealed in a number of comparative analyses of OPD and LPD [23]. Gagner M, Pomp A. described the world's first LPD experience in their work [14]. It has also been shown that LPD has the following problems: long operative time and increased postoperative morbidity compared to open surgery [14]. In general, the increased experience of working in the LPD, standardization of operational procedures and mutual understanding between the surgical team, contributes to reduction in operation time [24]. Wang et al. and Kendrick et al. in their observations reported that, with the accumulation of experience, the operative time was reduced [25, 26].

Over the past few years, there has been an opinion that laparoscopic approaches can be safely used for almost all typical operations when they are performed by highly qualified surgeons [30]. A comparison of the results of OPD and LPD showed the advantage of the laparoscopic method associated with a decrease in blood loss; the frequency of wound complications and a shorter hospital stay [31]. Historically, the first LPD was performed in 1994 by Gagner M. et al. [14]. They published a series of 10 cases in which the average work time was 8.5 hours and the conversion rate was 40%, and concluded that the benefits of LPD are questionable [32].

The emergence in recent years of robotic surgery for pancreatomectomies has provided a viable alternative to open and laparoscopic methods [33]. It has been shown that robotic PD provides advantages over laparoscopy, such as reduced blood loss and shorter hospital stay in the postoperative period [34], and also provides greater stability and accuracy of handling the instrument [35]. The operation of robotic laparoscopy is less physically stressful, avoids prolonged fixation of the position and provides an ergonomic position [36]. The potential advantages of robotic assistance, such as additional maneuverability and precision of movements, can be offset by the disadvantage of the lack of tactile feedback, especially in patients with a soft, loose pancreas or a thin anastomosis [37]. Buchs et al. studied 44 patients with RPD and 39 patients with OPD and found significantly shorter operative time (444 minutes compared to 559 minutes,  $p = 0.0001$ ) and reduced blood loss (387 ml compared to 827 ml,  $p = 0.0001$ ) in the robotic group compared to the open group [38].

World experience shows that there is no significant effectiveness of LPD, but some indicators are improving, such as: no wound complications, less blood loss, reduced average hospital stay, reduced postoperative pain, improved quality of life. The long operative time decreases with the accumulation of experience and large numbers of performed LPD. In our work, we also did not reveal the effectiveness of LPD, the statistical difference between LPD and OPD. This may be due to a small amount of cases. In the future, with an increase in the number of operations, especially laparoscopic, perhaps then we will determine the data on the effectiveness of LPD.

For the first time, Dokmak et al. [39] showed a high incidence of complications with the laparoscopic approach with poor selection of patients, a significant increase in grade C pancreatic fistulas and postoperative bleeding. For the author, the selection of patients is mandatory, especially for obese patients and for patients with a high risk of developing pancreatic fistula [39].

Based on this, we also believe that a good selection of patients is needed for the laparoscopic approach, adhering to the following factors: the tumor size is less than 2.5 cm without signs of metastases, without invasion in the superior mesenteric vein and portal vein. Also, indications were considered as a hard gland and a wide pancreatic duct, which are considered to be good conditions for reconstruction.

Pancreatic fistulas are the most common complication that leads to high morbidity and mortality after both open and laparoscopic PD [40-42].

Adhering to the clear indications for the implementation of LPD in our work, the hard gland mainly prevailed in 5 (83.3%) patients and soft in 1 (16.7%). One patient who had a soft gland developed a pancreatic fistula of class C in the postoperative period. After that, this patient had postoperative bleeding, which required a relaparotomy. According to literature data, pancreatic fistulas after pancreatoduodenal resection occur in up to 5-30% of cases in world practice [44].

To reduce the frequency and complications of anastomosis, several techniques have been studied, including pancreatogastrostomy, ductal-mucosal anastomosis, invagination pancreatojejunostomy or the use of octreotide. However, none of them showed a clear advantage [45-48].

To date, in world practice, the long operative time for LPD is considered the most discussed issue. In the initial stages, during the LPD, a long operative time is revealed, associated with the complexity of the operation itself and in the imposition of several anastomoses. But world experience shows that with the accumulation of experience and an increase in the number of LPD, the operative time decreases. Wang et al. reported that the operative time before the 50th case was 8.1 hours, after the 50th case 5.4 hours and after the 250th case was 4.7 hours [25]. In our work, the operative time averaged 8 hours. We believe that with an increase in the number of LPD, operative time will be decreased.

### Conclusion

We presented our initial experience of performing laparoscopic PD. Our results show the feasibility of LPD for tumors of the periampullary zone in certain cases.

The accumulation of experience in such interventions leads to improvement in immediate results and reduction in both postoperative complications and operative time.

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# MYCOTIC ANEURYSM OF THE SUPRARENAL AORTA, CELIAC TRUNK AND SUPERIOR MESENTERIC ARTERY. CASE STUDY

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## Abstract

The article presents a rather rare clinical observation and literature review of surgical interference for mycotic (infectious) aneurysm of the suprarenal aorta with damage to paired and unpaired branches (celiac trunk, superior mesenteric and renal arteries). The authors note the features of the clinical course of aortic lesions (chronic ischemia of the digestive system, cardiorenal hypertension), the mechanisms of the disease development, and indicate the need for open repair of the thoracoabdominal aorta.

**Қолқаның супраренальды бөлігінің, целиак діңінің және жоғарғы шажырқай артериясының микотикалық аневризмасы. Клиникалық бақылау**

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## Тұжырым

Мақалада сирек кездесетін клиникалық бақылау, жұптасқан және жұпталмаған бұтақтардың (целиакия діңі, жоғарғы шажырқай және бүйрек артериялары) қатысуымен қолқаның супраренальды бөлігінің микотикалық (инфекциялық) аневризмасына хирургиялық араласудың әдеби шолуы келтірілген. Авторлар аорта зақымдануының клиникалық ағымының

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**Conflict of interest:**

The authors declare that they have no conflicts of interest

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**Түйінді сөздер:**

микотикалық аневризма,

висцеральды тармақтар

ерекшеліктерін (ас қорыту жүйесінің созылмалы ишемиясы, вазоренальды гипертензия), аурудың даму механизмдерін атап өтеді және қолқаның торакоабдоминальды бөлігін ашық қалпына келтіру қажеттілігін көрсетеді.

## Микотическая аневризма супраренального отдела аорты, чревного ствола и верхней брыжеечной артерии. Клиническое наблюдение

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### Аннотация

В статье представлено достаточно редкое клиническое наблюдение и литературный обзор оперативного вмешательства по поводу микотической (инфекционной) аневризмы супраренальной части аорты с поражением парных и непарных ветвей (чревный ствол, верхняя брыжеечная и почечная артерии). Авторы отмечают особенности клинического течения поражения аорты (хроническая ишемия органов пищеварения, вазоренальная гипертензия), механизмы развития заболевания и указывают на необходимость открытой реконструкции торакоабдоминальной части аорты.

### Relevance

Numerous publications and whole chapters in monographs are devoted to aortic aneurysms and main arteries. Aneurysms are often referred to as "time bombs" because the patient is constantly under the threat of rupture and development of complications, up to a fatal outcome. The frequency of aneurysms of different localization is different. So, at present, the frequency of abdominal aortic aneurysms (AAA) in the Russian Federation is 10-40 cases per 100,000 population, in the USA - 36.2. It has been noted that over the past 20 years, the prevalence of AAA has decreased [1, 2]. According to pathoanatomical data, aneurysms are detected in 0.16–1% of all autopsies, i.e., the disease was not recognized in-life [3]. The true prevalence of aneurysms of the splanchnic arteries remains unclear due to the asymptomatic course. It is generally accepted that it does not exceed 0.1–2% [4, 5]. Most often, among the aneurysms of this localization, there are aneurysms of the

splenic artery - 60-70%, less often of the hepatic artery - about 20%. Aneurysms of the celiac trunk (CT) and mesenteric arteries (MA) total about 10%. According to various data, the prevalence of aneurysms of the superior mesenteric artery (SMA) is 3.2-8% in the structure of aneurysms of the splanchnic arteries [6, 7]. The incidence of SMA aneurysms is no more than one in 12,000-19,000 autopsies.

The increase in the detection rate of SMA aneurysms in recent years is due to the widespread use of instrumental examination techniques in patients with nonspecific abdominal complaints: ultrasound (US) diagnostic methods, computed tomography, magnetic resonance imaging (MRI) [8]. Also, the growth in the number of aneurysms is facilitated by the development of methods for invasive diagnostics and treatment, which leads to the development of iatrogenic pseudoaneurysms [9, 10]. A somewhat independent group consists of aneurysms of the extracranial branches of

the aortic arch, which are less common than aneurysms of other localizations. More often, aneurysms of such localization have a traumatic etiology, while the frequency of true aneurysms of the arteria carotis, according to various sources, ranges from 0.4 to 4% of all aneurysms of peripheral arteries, surgeries for which in practice are performed only in 0.1-2% of cases [11, 12]. We have encountered a dissecting aneurysm of the common carotid artery (CCA) with the transition of the dissection to the internal carotid artery with its subsequent thrombosis [13]. The most common are atherosclerotic aneurysms, while mycotic aneurysms are a fairly rare lesion of the aorta and main arteries. According to statistics in Europe, the total number of mycotic aneurysms is 0.65% to 2%. It is believed that the first description of a septic aneurysm belongs to Osler W., who in 1885 presented a clinical observation of a 30-year-old patient with malignant endocarditis who died from rupture of the aortic arch. Autopsy revealed 4 "mushroom-shaped protrusions" on the aortic arch, which the author called "mycotic aneurysms" [14].

The term "mycotic aneurysm", introduced by Osler W, is still used today. It should be noted that the author had in mind only a morphological feature - a "mushroom-like" type of aneurysm, but not an etiological factor. In fact, 93% of these aneurysms have a sac-like structure on imaging [14]. The actual mycotic lesion as an infectious agent that causes destruction of the vascular wall is very rarely described in the literature. The most common pathological microorganisms are Salmonella (predominant in Asia) and Staphylococcus aureus (predominant in European and North American patient populations), which account for about 40% of lesions [15]. According to Hsu R.B. et al. (2005), systemic Salmonella infection causes damage to the vascular wall in 16.2–19.8% of patients [16].

The pathogenesis of arterial infectious lesions obviously suggests the presence of a primary intimal lesion. Therefore, atherosclerosis is the most important predictor of mycotic aneurysms. It is possible that such difficult-to-diagnose lesions as a penetrating aortic ulcer and intramural hematoma may also become the focus of a primary infectious lesion. Cases of secondary infection of pre-existing aneurysms have been described. Fourneau L., et al. (1996) of 176 patients with a clinically unsuspected infected abdominal aortic aneurysm, 14.2% were cultured from the aneurysm wall. However, the authors did not note any influence on the frequency of prosthesis infection in the long-term period [17].

The increase in the number of patients with mycotic aneurysms in the second half of the 20th century is explained by the increase in the number

of people infected with immunodeficiency (primarily HIV-infected and intravenous drug users). Bacterial endocarditis as a risk factor at the end of the 20th century was detected in 17% of patients [18]. Localization of aortic lesions: ascending aorta and arch – 6%, thoracic aorta – 42%, visceral aorta – 13%, infrarenal – 32% [19].

There is currently no international consensus on the optimum treatment of mycotic (infected) aneurysms. The Russian national guidelines only state the need for surgical treatment and recommend tactics similar to the treatment of aortoenteric fistulas. We have also observed this complication recently. At the same time, the prospect of endovascular treatment is evaluated with caution. The North American guidelines (2018), as well as the recommendations of the European Society of Cardiology for the treatment of aortic diseases (2014) and the Russian guidelines for the diagnosis and treatment of aortic diseases (2017), "bypass" these types of aneurysms [20, 21, 22].

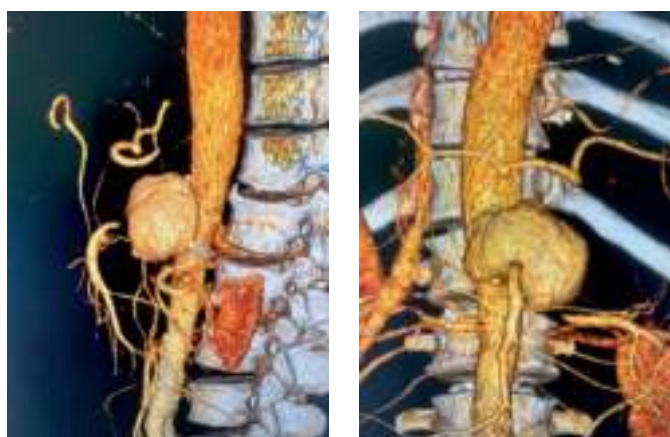
We came across an interesting case that fully confirms the above assumption, a combination of atherosclerotic lesions of the aorta with the formation of a combined atherosclerotic and mycotic aortic aneurysm, TC and SMA. We devoted our publication to the analysis of this observation.

Patient G., aged 52 (Medical history sheet No. 4161). Was admitted to the Department of Vascular Surgery of the Atyrau Regional Cardiology Center of the Health Department of the Atyrau Region in a planned manner on December 19, 2022.

Complaints at admission to pain in the left side of the abdomen, stool retention and poor passage of flatus, periodic chills, weakness. According to the patient, he fell ill acutely about 18 days ago, when pains suddenly appeared in the left side of the abdomen and there was a general weakness. He associates his disease with a sudden increase in blood pressure to 230/120 mm Hg (obvious vasorenal genesis of hypertension). There were no injuries. In blood tests, there was an increase in the level of procalcitonin, leukocytosis and an increase in C-reactive protein (CRP). CT scan of the abdominal organs with contrast (before admission to our clinic) dated November 28, 2022: Conclusion: CT signs of a penetrating ulcer of the anterior wall of the suprarenal abdominal aorta with the formation of a saccular aneurysm, with moderate para-aortic infiltration, and edema of the aortic walls. Occlusion at the mouth of the celiac trunk and superior mesenteric artery. Hepatomegaly. Diffuse changes in the liver parenchyma, chronic calculous cholecystitis, chronic pancreatitis. Adenoma of the left adrenal gland. Figure 1 a, b.



Figure 1.  
a, b. MSCT 3D reconstruction  
(volumetric rendering mode,  
arterial phase)



He was referred to our hospital after consulting a vascular surgeon with a diagnosis of atherosclerosis. Aneurysm of the supraceliac abdominal aorta with a penetrating ulcer of the anterior wall without rupture and dissection, subacute course. Syndrome of chronic ischemia of the digestive system (CIDS). Occlusion at the mouth of the celiac trunk and superior mesenteric artery.

Epidemiological anamnesis: denies infectious hepatitis, sexually transmitted diseases, malaria, typhoid and tuberculosis. Over the past six months, the blood was not transfused, has not been under the treatment with the dentist, injections were not made. Bad habits: denies. Allergies to drugs and food are not noted. On regular medical check-up with a cardiologist with a diagnosis of arterial hypertension of the III-degree, risk 4. Surgery: appendectomy in 1986.

Objective data at admission: overall health status of medium severity, due to the underlying disease. Normosthenic body build, supernutrition. Vesicular breathing in the lungs, there were no crackles. Respiration rate - 17 in min. Heart tones are muffled, rhythmic. Arterial pressure - 190/120 mm Hg, pulse 112 per minute, rhythmic. The moist tongue. The abdomen is symmetrical, not swollen. On palpation, the abdomen is soft and painless. There are no peritoneal signs. The liver at the edge of the costal arch, painless. The spleen is not non-palpable. Intestinal peristalsis is auscultated. The kidney punch is negative on both sides. The unimpeded urination, painless. The gases are released. According to

the words, the stool was formed after taking laxatives.

Status localis: Symptoms of Homans, Moses is negative. The pulsation of the arteries in the upper and lower extremities is determined throughout. There are no noise symptoms on auscultation over the main arteries.

CT scan of the chest dated 12.11.2022: CT signs of chronic bronchitis. Pulmonary fibrosis of S5, S6, S8, S9 and S10 segments of the right lung and S5 and S8 segments of the left lung. Fibrogastroduodenoscopy dated 22.11.2022: Conclusion: Erosive antral gastritis. Video colonoscopy dated 18.18.2022: Conclusion: Mixed hemorrhoids. CT scan of the abdominal cavity organs dated 12.11.2022: In addition to the above data. Hyperplasia of both adrenal glands. Formation of (cyst?) and a single parapelvic cyst of the left kidney. Moderate calicopyeloectasia of both kidneys. Circular thickening of the walls of the sigmoid and rectum. Dolichosigmoid. Atherosclerosis of the abdominal aorta and iliac arteries. Hernia of the anterior abdominal wall. MRI of the abdominal cavity organs and retroperitoneal space with contrast, dated November 29, 2022: Conclusion: MRI shows signs of a penetrating ulcer of the anterior wall of the supraceliac abdominal aorta with the formation of a saccular aneurysm, with moderate para-aortic infiltration, and edema of the aortic walls. Occlusion at the mouth of the celiac trunk and superior mesenteric artery. Hepatomegaly. Diffuse changes in the liver parenchyma, chronic calculous cholecystitis, chronic pancreatitis. Adenoma of the left adrenal gland. Figure 2, 3, 4.

Figure 2.  
Frontal view







Figure 3,4.  
Lateral view

In the lateral view, especially when magnified, it is clear that the aorta and the aneurysm itself are, as it were, wrapped in a "cloak" of altered tissues. Apparently, these are the consequences of an infected hematoma formed as a result of a defect in the aortic wall.

Aortography dated 02.12.2022: Conclusion: In the suprarenal abdominal aorta, a saccular aneurysm measuring 40 mm x 35 mm with smooth round edges is contrasted. Figure 5.



Figure 5.  
Radiopaque aortography

With hypertension, it is seen that all lumbar arteries are contrasted, i.e. there are no thrombotic overlays, which is typical for atherosclerotic aortic aneurysms.

EchoCG dated 29.11.2022: Conclusion: EF-54%. The study was conducted against the background of tachycardia, slight dilatation of the LA. Relative mitral insufficiency 0-1 degree. Concentric (moderate) hypertrophy of the left ventricle. Systolic function of the left ventricle is satisfactory. Diastolic dysfunction of the left ventricle type 1. Ultrasonography of the BCT dated 01.12.2022: Conclusion: Atherosclerosis of the BCA.

Stenosis in CMPR of both CCA is 35-40%. Small diameter of the vertebral artery on the left. Non-rectilinear course of the vertebral arteries in the CV. Ultrasonography of the kidneys dated 01.12.2022: Conclusion: The abdominal aorta and renal arteries are patent. Hemodynamic abnormalities were not revealed.

Ultrasound of the aorta, renal and visceral arteries dated December 1, 2022: Conclusion: Atherosclerosis. Saccular aneurysm of the suprarenal abdominal aorta (d-45 mm, length 5 cm). Figure 6 a, b, c, d

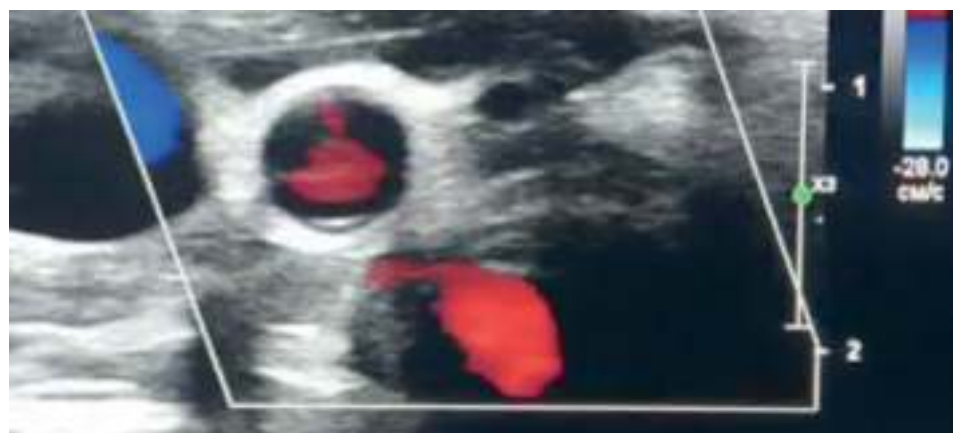


Figure 6. a

Figure 6. b



Figure 6. c

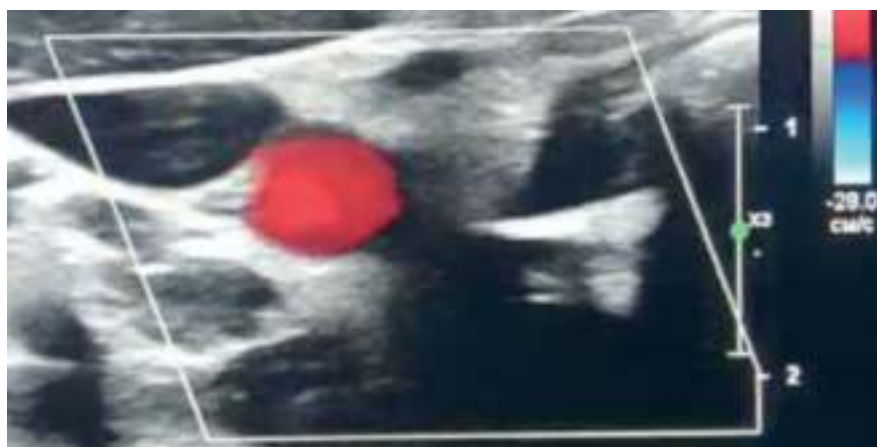
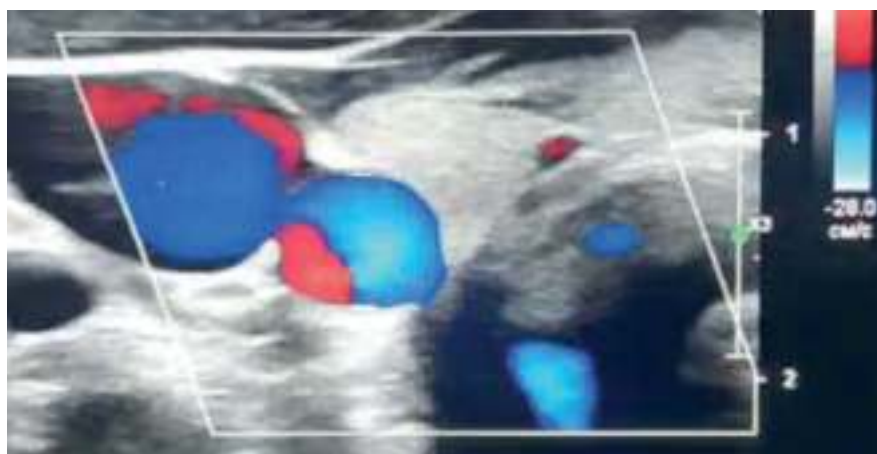


Figure 6. d



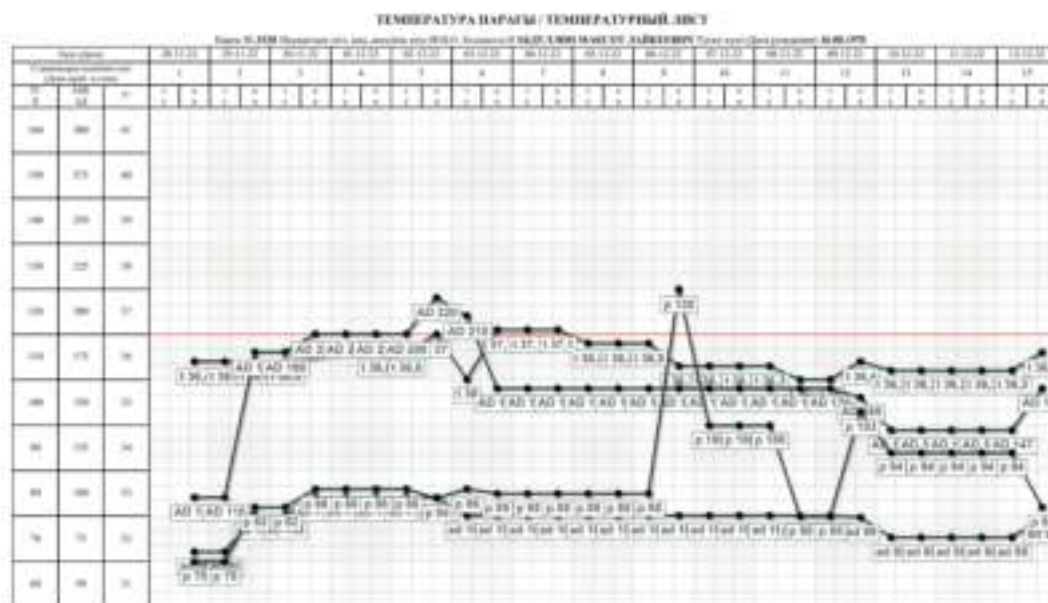
A series of sonograms shows that initially there is no defect in the aortic wall (Figure 6 a), and in Figure 6 b, the minimum blood flow appears only in systole. When the aortic wall is stretched, the shunt increases.

In order to prepare for the surgery, all

consultations of specialists were carried out: a cardiologist, an endocrinologist

Unlike other authors [23], we did not observe any clinically significant temperature fluctuations during the entire period of observation of the patient. What is shown in Figure 7.

Figure 7.  
Medical card



After additional examination and preparation on 20.12.21, the surgery was performed - Left-sided thoracophrenolombotomy, subdiaphragmatic splanchnicoganglionectomy. Resection of an aneurysm of the celiac trunk and superior mesenteric artery with bifurcation alloprosthesis of the celiac trunk and superior mesenteric artery (Prosthesis Polymaille C 16x8x8 mm). Decompression of the left renal artery. Drainage of the pleural cavity and retroperitoneal space.

Surgical report: Under general endotracheal anesthesia after treatment of the surgical area with a solution of betadine, a layer-by-layer incision along the 9th intercostal space on the left with dissection of the costal arch and pararectally to the navel, thoracophrenolombotomy was performed. The diaphragm is crossed at the base with the intersection of the medial crura. The abdominal muscles were crossed pararectally with the release of the retroperitoneal space with the separation of the peritoneum and the left kidney medially. The aorta was mobilized in the descending section, the abdominal aorta to the bifurcation. Subphrenic splanchnicoganglionectomy. During the revision, there is a saccular aneurysm of the celiac trunk and superior mesenteric artery along the anterior surface of the suprarenal section with a diameter of up to 5.0 cm, pulsating. Non-productive hemostasis. There is no fluid in the pleural cavity on the left. The lungs are pale pink. The thoracic aorta was isolated above the diaphragm and aneurysm with dissection of the para-aortic tissue, d-22 mm, taken on a holder. The abdominal aorta was mobilized below the aneurysm between the outlets of the superior mesenteric artery and the renal arteries, d-18 cm, taken on a holder. The lumbar branches were taken on capron - 3.0. In view of the periproces and a pronounced adhesive process, the aneurysmal sac was mobilized along all walls with technical difficulties. The celiac trunk and bifurcations were mobilized, the superior mesenteric artery within healthy tissues, d-8 mm. The left renal artery and vein are mobilized to

the opening, not dilated d- 8 mm, compressed at the opening by an aneurysmal sac (LVA decompression). The aorta above and below the aneurysm was taken with aortic clamps. Opened aneurysm. The lumen of the aneurysm is free. The revision revealed an aneurysm of the celiac trunk and superior mesenteric artery. There was a resection of the aneurysmal sac at the neck. It was decided to perform alloprosthetics of the celiac trunk and superior mesenteric artery with Polymaille alloprosthesis (16x8x8 cm). There was an imposition of the anastomosis between the aorta and the prosthesis type end of the prosthesis on the side of the aorta continuous suture Prolene 3.0. Embolism prevention. Gradually removed the clamp from the aorta. The seam line is hermetic. Aortic clamping time is 30 min. A clamp is placed on the prosthesis. Intraoperatively, autohemotransfusion using the Sorin Xtra apparatus was used, 350 ml of blood poured into the wound was transfused. Vascular clamps were placed on the celiac trunk. An arteriotomy 1.5 cm long was made, a thrombus in the lumen, 1.0 cm in size, was removed. A good counterpulsation was obtained. The anastomosis of the upper branch of the prosthesis with the celiac trunk was made end-to-side with a continuous suture with Prolene 6.0. Embolism prevention. Clamps were removed. The anastomosis line is hermetic. Vascular clamps on the superior mesenteric artery were imposed. An arteriotomy 1.5 cm long was made, the bright lumen. A good counterpulsation was obtained. An anastomosis was made between the lower branch of the prosthesis with the superior mesenteric artery end-to-side with a continuous suture with Prolene 6.0. Embolism prevention. Clamps were removed. The anastomosis line is hermetic. Hemostasis. Non-productive. The separation of drainage into the pleural cavity and retroperitoneal space. The diaphragm is sutured with a continuous stitch with Mercil No.1. The ribs and costal arch are connected X-shaped with nylon 5.0. Layered wound closure. Type of surgery in Figure 8.

**Figure 8.**  
Aortogastric and superior mesenteric prosthetics.  
General view of the completed reconstruction



Histological examination of biopsy material of the 2nd category of complexity (No. 15768-70), the number of pieces is 3, stained with hematoxylin-eosin. The sectioned slide is represented by the growth of connective tissue with hemorrhages and full-blooded vessels. Pathological and histological conclusion: In the preparation, the material is represented by the growth of fibrous tissue among adipose tissue and inflammatory infiltration and purulent- fibrinous pellicle, the vessels are dilated in the lumen of the stasis of erythrocytes.

The bacteriologic examination: the growth of pathogenic flora was not detected. Sensitivity to antibiotics dated 22.12.2022: Staphylococcus saprophyticus - 105 (Azithromycin /S/, Cefotaxime /R/, Cefazolin /R/, Levofloxacin /S/, Cefaclor /R/, Ciprofloxacin /S/).

In the post-surgical period, the phenomena of acute renal failure in the stage of polyuria were observed, treatment was carried out by a nephrologist. There is no edema. Natural urination, the volume of excreted urine is 5800.0 ml. Creatinine is 484  $\mu\text{mol/l}$ . Urea is 20.5  $\mu\text{mol/l}$ . Potassium is 3.5  $\mu\text{mol/l}$ . Diagnosis: OPP in the polyuric

stage. After the treatment, the effect of the treatment was noted and the patient was discharged (06.01.23). At discharge, the general condition is satisfactory. Medical and labor recommendations and observation and treatment by a vascular surgeon, a cardiologist and an endocrinologist, a control CT scan after 3 months were given. Antibacterial therapy for a period of 1 year.

Diagnosis at discharge: Polyvascular disease. Aneurysm of the celiac trunk, superior mesenteric artery. Occlusion at the opening of the celiac trunk. Critical stenosis of the superior mesenteric artery. Extravasal compression of the left renal artery. Syndrome of chronic ischemia артериальная гипертензия III др, риск 4of the digestive system. Cardiorenal hypertension. BCA atherosclerosis. Stenosis in CMPR of both CCA is 35-40%. Chronic cerebrovascular insufficiency I deg. Background: Arterial hypertension III deg, risk 4. Concomitant: Diabetes mellitus type 2, newly diagnosed. Erosive antral gastritis. Umbilical hernia. Combined hemorrhoid. Anemia of mild severity.

The control study 3 months after the surgery is shown in Figure 9 (a, b).

**Figure 9 (a, b).**  
Control CT angiography 3 months after surgery





In this case, the classical onset of the disease was observed. Diagnosis is based on the clinical picture (pain, fever, sepsis), laboratory tests (inflammatory markers) and characteristic morphological features (saccular, sometimes multi-chamber protrusion of the arterial wall, perivascular edema, hematoma and/or fibrous tissue). The presence of gas in the perivascular area and the rapid growth of the aneurysm are pathognomonic symptoms [23, 24].

It can be assumed that an infectious agent joined the site of the greatest atherosclerotic lesion, which caused a penetrating ulcer of the anterior wall of the suprarenal abdominal aorta with the formation of a saccular aneurysm, which is confirmed by the opinion of other authors [17].

The tactics we chose was based on the analysis of literature data. So, in the work of Maksimov A.V. et al. 2 cases were analyzed, in the first case direct intervention

was performed, in the second case endovascular intervention was performed. In the second case after 3 months there was a manifestation of a local infectious process with the development of a fatal complication - aortoduodenal fistula and the patient died [23].

#### Conclusion

An analysis of the results of examinations suggests that the evolution of this aneurysm occurred as follows: initially, the infection joined the aortic wall (this corresponds to the period of the onset of the disease: pain, fever, increased procalcitonin), after the formation of a defect in the aortic wall, a slight blood supply began under the adventitia and para-aortic fiber with infection in this area. The expansion of the aortic wall defect zone led to the formation of a false aneurysm, and after the active infectious process subsided, an aneurysmal sac lined with thrombotic masses was formed.

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transplantation

# TREATMENT OF INOPERABLE LIVER ALVEOCOCCOSIS

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## Abstract

A systematic review of the publication, on the topic of diagnosis and treatment of inoperable alveolar echinococcosis of the liver over the past 30 years, to study the effectiveness of various methods of treatment of inoperable alveococcosis of the liver.

We conducted a systematic search of literary data and selected sources from Google Scholar, PubMed, as well as research papers and online educational publications in English and Russian.

Our literature review included 120 papers in which, according to the authors with inoperable liver alveococcosis, 883 patients were described, out of 120 articles: 29 full articles, 23 literary reviews, 68 clinical cases described. The authors of the articles were from various countries, such as Turkey (26%), France (24%), Germany (20%), China (18%), England (6%), Japan (5%) and other countries in Europe and Asia.

## Бауырдың ота жасауға келмейтін альвеококкозын емдеу

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## Тұжырым

Соңғы 30 жылдағы бауырдың отаға жасауға келмейтін альвеолярлы эхинококкозын анықтау және емдеу тақырыбындағы басылымға жүйелі шолу, ота жасауға келмейтін бауыр альвеококкозын емдеудің әртүрлі әдістерінің тиімділігін зерттеу.

Біз әдебиет деректерді жүйелі түрде іздестірдік және Google Scholar, PubMed дереккөздерін, сондай-ақ ағылшын және орыс тілдеріндегі зерттеу жұмыстары мен онлайн оқу басылымдарын таңдадық.

Біздің әдебиет шолуымызға 120 жұмыс енгізілді, онда жұмыс істемейтін бауыр альвеококкозы бар авторлардың мәліметтері бойынша 883 пациент сипатталған, 120 мақаланың ішінен: толық мақалалар - 29, әдеби шолулар - 23, клиникалық жағдайларды сипаттау-68. Мақала авторлары Түркия (26%), Франция (24%), Германия (20%), Қытай (18%), Англия (6%), Жапония (5%) және Еуропа мен Азияның басқа елдерінен болды.

## Лечение неоперабельного альвеококкоза печени

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**Аннотация**

*Систематический обзор публикации, по теме диагностики и лечения неоперабельного альвеолярного эхинококкоза печени за последние 30 лет, изучить эффективность различных методов лечения неоперабельного альвеококкоза печени.*

*Мы провели систематический поиск литературных данных и отобрали источники из Google Scholar, PubMed, а также исследовательские работы и учебные онлайн-издания на английском и русском языках.*

*В наш литературный обзор было включено 120 работ, в которых по данным авторов с неоперабельным альвеококкозом печени было описано 883 пациентов, из 120 статей: полных статей - 29, литературных обзоров - 23, описание клинических случаев – 68. Авторы статей были из различных стран, таких как: Турция (26%), Франция (24%), Германия (20%), Китай (18%), Англия (6%), Япония (5%) и другие страны Европы и Азии.*

**Конфликт интересов:**  
Авторы заявляют об отсутствии конфликта интересов

**Ключевые слова:**  
альвеококкоз, неоперабельный альвеококкоз печени, альбендазол, трансплантация печени

**Introduction**

Alveococcosis - (Latin Alveococcosis; alveolar echinococcosis, multicameral echinococcosis) – helminthiasis from the group of cestodoses. The disease is common in Switzerland, Turkey, Japan, France, Russia, Central Asian countries, northwestern Canada and Alaska [1]. Alveococcosis of the liver is a parasitic liver cancer, due to its infiltrative growth, the ability to metastasize, as well as the high frequency of relapses after surgical treatment [2, 3]. Liver infection caused by *E. multilocularis* (alveococcosis) is a particularly difficult clinical problem, since their biology mimics that of slow-growing cancers [3].

In alveococcosis of the liver, due to direct spread, the diaphragm, peritoneum, hepatoduodenal ligament, pericardial sac, pleura, lungs, adrenal glands, kidneys, hepatic veins and inferior vena cava are most often affected. Distant metastases are usually localized in the lungs, brain, bones and spleen. Patients with alveococcosis of the liver may develop severe hepatobiliary complications, such as recurrent cholangitis, secondary biliary cirrhosis after prolonged cholestasis or Budd-Chiari syndrome [4-6].

Alveolar echinococcosis lesions are most often localized in the right lobe of the liver, and in advanced cases they germinate into large bile ducts and vascular structures (portal vein, hepatic veins and inferior vena cava), extensive liver surgery is often required with the risk of death as a result of uncontrolled bleeding or liver failure [7].

Due to infiltrating growth and the ability to metastasize, the course of the disease can be complicated by such complications as: the development of mechanical jaundice, portal hypertension, perforation of the decay cavity, germination into neighboring organs, ascites [2, 8-10]. Complications of the underlying disease, in turn, significantly limits the possibilities of treatment [11]. Extrahepatic localization of alveococcus is extremely rare, and damage to other organs in the presence of a focus in the liver is regarded as distant metastasis [12].

It should be noted that for the successful care of patients with alveococcosis in surgical hospitals, the following are important: a well-defined algorithm of diagnostic methods that determine the choice of surgical treatment tactics; classification that allows optimizing surgical treatment algorithms and routing of patients; a set of techniques for performing

liver resections that make it possible to perform such operations in more patients and accordingly, reduce the proportion of patients requiring liver transplantation. Unfortunately, the diagnosis of alveococcosis is mainly established in the late stages of the disease with the manifestation of complications [3, 13, 15].

The epidemiological history includes the collection of information about the epidemiological environment, staying in endemic areas, food culture, and the profession of the patient. Most often, infection occurs when cutting carcasses, skins of infected animals, when non-compliance with the rules of personal hygiene and keeping animals (hunting dogs), when eating the liver of infected intermediate hosts [15-17].

Less often there are cases of infection when eating wild berries and herbs contaminated with animal feces. Also, risk factors include close contact with agricultural or domestic animals [15].

A group of WHO experts in 1996 proposed the classification of alveococcosis (PNM), which is currently used. It resembles the oncological classification (TNM) and allows a fairly objective assessment of the prevalence of a parasitic focus in the liver (P), taking into account the involvement of nearby organs (N) and the presence of distant metastases (M) [19, 20].

According to epidemiologic monitoring data from Europe and Asian countries, due to the asymptomatic course of the disease, at the time of diagnosis, more than 60-70% of patients are unresectable and it is impossible to perform radical surgery [21, 22].

Currently, WHO still recommends considering transplantation if all of the following signs are present: 1) severe hepatic insufficiency (secondary biliary cirrhosis or Budd-Chiari syndrome) or recurrent life-threatening cholangitis; 2) inability to perform radical liver resection; 3) absence of extrahepatic localization of alveococcosis. However, immunosuppression promotes the re-growth of larval remains and the formation or increase in the size of metastases [23]. Antiparasitic therapy should be administered orally at a dose of 10– 15 mg / kg / day, in 2 takes, with a fat-rich diet. In practice, adults are prescribed a daily dose of 800 mg divided into two takes for at least 2 years and follow these patients for at least 10 years [23].

According to various sources and authors, the

five-year survival rate after cytoreductive resection and liver transplantation was 40.0% and 66.7% [24, 25].

Continuous use of antiparasitic treatment in comparison with periodic administration of antiparasitic drugs according to the scheme can prevent the growth of metastases after liver transplantation, the survival rate after liver transplantation is 71% in 5 years, with a relapse-free survival rate of 58% [26]. Overall survival after liver transplantation is quite low: 85% after 1 year, 71% after 5 years and 49% after 10 years due to relapse of the disease [27].

A systematic review of the publication, on the topic of diagnosis and treatment of inoperable alveolar echinococcosis of the liver over the past 30 years, to study the effectiveness of various methods of treatment of inoperable alveococcosis of the liver.

We conducted a systematic search of literature data and selected sources from Google Scholar, PubMed, as well as research papers and online educational publications in English and Russian.

*Inclusion criteria*

We included sources that met our inclusion criteria: research papers in which studies were conducted in patients with inoperable liver alveococcosis. After reviewing a lot of literature reviews about Echinococcosismultilocularis, we can say that this topic is very relevant all over the world, but over the past 10 years there have been very few publications on inoperable liver alveococcosis, in connection with which we took sources for a period of more than 30 years.

We aspired to evaluate a sample from sources in which attention was paid to the treatment of this pathology

in the late stages. We evaluated the articles in random order. Based on the key aspects. The data elements taken for this article included: study design, sampling method, number of patients and operations performed, determination of the result, randomized controlled trial.

Our literature review included 120 papers in which, according to the authors with inoperable liver alveococcosis, 883 patients were described, out of 120 articles: 29 full articles, 23 literary reviews, 68 clinical cases described. The authors of the articles were from various countries, such as Turkey (26%), France (24%), Germany (20%), China (18%), England (6%), Japan (5%) and other countries in Europe and Asia.

*Classification*

For the first time in 1996, a group of WHO experts proposed the classification of alveococcosis (PNM), which is currently used. It resembles the Oncological Classification (TNM). The PNM staging system for liver alveococcosis was proposed in 2006 by the European Network for Coordinated Surveillance of Liver Alveococcosis [20, 26].

According to this classification, surgical treatment is justified in the group of patients with peripheral or mono-lobar localization without involvement of the main vascular structures, P1N0M0 and P2N0M0, which indicate I-II stage of the disease, respectively. Patients with P3 and P4 with any N and M, who belong to the III and IV stages of the disease, due to the progression of the disease, radical surgery is not indicated (known as R0) [28].

According to the WHO classification, the following principles should be followed in the treatment of patients with liver alveococcosis (Table 1).

**Table 1.**  
A stage-by-stage approach  
to the treatment of alveolar  
echinococcosis

WHO Classification	Operation (R0)	Palliativecare	Drugtherapy	Recommendations	
P1N0M0	++		+	Radical resection (R0) BMZ for 2 years PET / CT control	Maximum
				Radical resection (R0) BMZ for 3 months	Minimum
P2N0M0	++		+	Radical resection (R0) BMZ for 2 years	Maximum
				Radical resection (R0) BMZ for 3 months	Minimum
P3N0M0			+	BMZ continuously PET/CT/MRI initially and 2 years apart	Maximum
				BMZ continuously	Minimum
P3N1M0		++	+	BMZ continuously + PET/CT/MRI initially and 2 years apart	Maximum
				Surgical intervention ifindicated	Minimum
P4N0M0		++	+	BMZ continuously + PET/CT/MRI initially and at 2-year intervals	Maximum
				Surgical intervention ifindicated	Minimally
P4N1M1		++	+	BMZ continuously + PET / CT/MRI initially and at 2-year intervals	Maximum
				Surgical intervention ifindicated	minimally

## Discussion

According to the above table, WHO recommends the management of patients with liver alveococcosis as follows:

1) Antiparasitic drugs are mandatory for all patients, temporarily after complete resection of lesions and for life in all other cases;

2) Minimally invasive treatments should be preferred over cytoreductive resection whenever possible;

3) Radical resection is the first choice in all cases where it is possible [22].

In our opinion, the above-mentioned WHO classification does not make it possible to determine the extent of liver damage, the presence of the prevalence of the process in the main vessels and bile ducts, an assessment of the state of the liver parenchyma, the volume of the presumed non-affected part of the liver, which affect the further tactics of treatment of patients.

Of course, this classification is not an alternative, but it is necessary to revise the classification in the future or possibly supplement it to determine the optimal tactics and routing of patients among medical institutions, which will certainly lead to an increase in the resectability and radicality of surgical interventions, and improve treatment results.

### *Drug treatment of inoperable liver alveococcosis*

Long-term drug treatment with benzimidazoles can actually be considered as the basis for the complex treatment of human alveolar echinococcosis [29]. Mebendazole (MBZ), a benzimidazole derivative, was the first successfully used drug [30, 31].

Mebendazole (MBZ) is a highly effective broad-spectrum anthelmintic widely used for the treatment of nematode, cestode and even protozoal infections. After its use began in 1970, MBZ was the first drug in the BMZ group that was found to have a lethal effect on metacystodes in infected patients [32].

Mebendazole is insoluble in water, and therefore it is believed that the drug is not readily available for the treatment of liver alveococcosis in humans, since MBZ is absorbed at the intestinal level, reaching the liver there is very little active substance left. In this regard, it is believed that it is not inactive for the treatment of liver alveococcosis [33]. In patients with alveococcosis of the liver, MBZ should be prescribed for at least 2 years after radical surgery or permanently in inoperable cases, as well as in patients who have undergone incomplete resection or liver transplantation [29]. Long-term MBZ therapy is usually well tolerated, in some patients it has been used for more than 20 years [34].

However, from 5 to 40% of patients treated with MBZ with liver alveococcosis, adverse reactions were described [35-38]. In the treatment of patients, there were side effects such as gastrointestinal disorders, hair loss, neutropenia, anaphylactic reactions, glomerulonephritis, dizziness, headache, mental visibility, hematotoxic effects and abnormal

serum transaminase levels, notably most of these reactions occurred during the first month of taking the drug [39, 40].

In recent years, few studies have been aimed at improving the chemotherapeutic activity of MBZ. This is largely due to the gradual replacement of MBZ with albendazole [47].

Albendazole (ABZ) is a derivative of BMZ with a wide spectrum of activity, including in helminthiasis and protozoal infections. First introduced for human use in 1982, ABZ has now replaced MBZ as the drug of choice for the treatment of *E. multilocularis*, mainly due to its improved bioavailability, superior efficacy, ease of administration and fewer undesirable effects [38, 44, 48, 49]. In addition, ABZ is 40% cheaper than MBZ [40].

Nevertheless, the availability and/or cost of ABZ continues to be a problem in many socio-economically disadvantaged countries and even in high-income countries [50].

Oral administration of ABZ is currently recommended at a dose of 10-15 mg per kg of body weight per day - in two takes for the treatment of *E. multilocularis* [29].

Brunetti E and his co-authors [29], at the consensus of WHO and the Informal Working Group on Echinococcosis, focused on the issue of continuous use of ABZ at a dose of 10-12 mg/kg/day. Serum levels of the drug should be measured at regular intervals. Toxic hepatitis, hematological diseases, alopecia may occur in a group of patients treated with ABZ, requiring regular further medical supervision [29]. ABZ should be prescribed for at least 2 years, and these patients should be monitored for at least 10 years for possible relapses [29].

Continuous antiparasitic treatment should not be interrupted because it can be dangerous due to the spread of the process and the frequency of relapses [48-50].

Since ABZ is currently considered a relatively safe drug, continuous therapy is preferable to schematic monthly receptions. Recent descriptive studies based on a series of cases have shown that the frequency of undesirable side effects associated with ABZ ranges from 3 to 5% [40,45,46], and some studies have not reported their absence [47]. The most frequently described adverse reactions were jaundice, severe headache, cough, hemoptysis, changes in serum transaminase levels, dizziness, hair loss and itching [40, 45, 46].

The healing effect of a patient with an inoperable lesion has not yet been established, but should include a negative PET/CT result, a calcified component of alveolar echinococcosis lesion of more than 50%, as well as the disappearance of specific antibodies [51, 52].

Also, in the treatment of liver alveococcosis, such drugs as broad-spectrum nitazoxanide [54, 55] and Thiazolidines [53], or the antifungal drug amphotericin-B-deoxycholate [56, 57] were studied. Genistein and genistein derivatives are active



against metacestode in vitro [58].

The transition to clinical use was carried out only in relation to several drugs: conventional and liposomal amphotericin B was used as a life-saving treatment in several patients who did not tolerate ABZ [59]. Nitazoxanide, a broad-spectrum anti-infective drug, demonstrated remarkable efficacy in an experimental model [54], but could not demonstrate efficacy alone and in combination with ABZ or amphotericin B [60, 61].

The goal of treating inoperable liver alveococcosis with Albendazole is tumor regression, absence of disease progression, which is considered a success, since increasing formation can cause serious problems such as blockage or compression of the bile ducts, cholangitis, abscess, cirrhosis and portal hypertension [62].

Despite the successful long-term use of the drug, there are late complications, such as bleeding from varicose veins of the esophagus or cholestatic complications [31]. Hepatotoxicity and myelotoxicity are the most serious side effects of albendazole, discontinuation of treatment may be required in up to 4% of cases [29].

Long-term treatment with benzimidazole stabilizes the disease in 55-100% of patients [63]. A very important unique conclusion is that a noticeable regression of giant lesions (> 15 cm) is possible in 15-20% of patients with inoperable liver alveococcosis. Many clinical studies show that the correct treatment with albendazole is indicated in patients with inoperable liver alveococcosis, with the exception of patients with end-stage liver disease. For inoperable patients who are indicated for liver transplantation, some authors recommend taking antiparasitic therapy with benzimidazole before transplantation in 60-70% of cases [64, 65].

In conclusion, it should be noted that all patients with inoperable liver alveococcosis should be prescribed long-term treatment with albendazole. It may be reasonable to prepare a living donor for possible transplantation in the event of a severe complication, such as recurrent cholangitis, acute portal vein thrombosis or albendazole hepatotoxicity. Dilution may be a sign of a reaction to Albendazole. [66].

Some reports reported a 10-year survival rate of 80-90% of cases, which was achieved by improving conservative treatment with correction of complications during conservative treatment with minimally invasive methods [67, 68].

All inoperable patients with liver alveococcosis in the treatment of conservative therapy should be monitored by ultrasound, CT and/or MRI at intervals of 3-6 months for the effectiveness or progression of the disease [29].

The availability of ABZ is hampered by limited distribution and increased cost not only in socially and economically disadvantaged areas, but also in a number of developed countries. In addition, this compound appears to have a parasitostatic rather

than a parasitocidal effect, and there is no alternative drug for patients with *E. multilocularis* [70].

#### *Minimally invasive methods of treatment of inoperable liver alveococcosis*

Patients with inoperable liver alveococcosis and the presence of symptomatic complications: obstruction of the bile ducts, cholangitis and bacterial infection of the necrotic cavity, which develops in the foci of neglected lesions, symptomatic palliative treatment is used [71-73]. Non-surgical procedures, such as drainage of the biliary tract under ultrasound control or drainage of an abscess, were not performed until 1982 [74]. With compression or germination of the formation into the bile ducts and the development of mechanical jaundice, with hepatic insufficiency, Percutaneous-transhepaticcholecystocholangiostomy or ERCP, EPST with endobiliary stenting is used to reduce biliary hypertension, hepatic insufficiency [76].

#### *Percutaneous-transhepatic methods of decompression of the biliary tract*

With compression of the biliary tract or the germination of liver alveococcosis, many complications develop for the patient, such as mechanical jaundice followed by liver failure, the development of cholangitis, which threaten the patient's life [76].

Percutaneous-transhepatic methods of decompression of the biliary tract are currently a minimally-invasive first step in the treatment of patients with mechanical jaundice, cholangitis and liver failure. But there are also disadvantages of percutaneous-transhepatic methods of decompression of the biliary tract, as a rule, drainage is installed for a long time, and requires regular replacement to prevent obstruction. And also a big disadvantage of external drainage of the biliary tract is that it significantly contributed to the deterioration of the quality of life of patients [75].

#### *Endoscopic methods*

Endoscopic bile duct stenting currently almost completely replaces surgical palliative surgery and percutaneous drainage of the biliary tract for the treatment of biliary complications in patients with alveolar echinococcosis, as endoscopic dilation of bile duct strictures followed by the installation of several plastic stents provides internal drainage of bile into the patient's body [76].

A review of endoscopic procedures (ERCP) for the treatment of biliary complications of alveolar echinococcosis in several dozen clinical centers has shown that such procedures are currently used routinely and, as a rule, successfully alleviate symptoms and maintain long-term permeability of biliary strictures [75, 76].

Endoscopic bile duct stenting currently almost completely replaces surgical palliative surgery and percutaneous drainage of the biliary tract for the treatment of biliary complications in patients with alveolar echinococcosis. Although no specific studies have been conducted to assess the quality

of life of patients receiving such treatment, many authors suggest that this significantly contributed to improving the quality of life of patients with chronic biliary obstruction and multiple episodes of cholangitis [75].

#### *Drainage of the decay cavity*

Drainage of the decay cavity can be useful to reduce the risk of bacterial infection and relieve symptoms caused by large masses. A sharp regression with proper treatment with albendazole is possible in 15-20% of patients with inoperable liver tumors [74]. Later, mini-invasive procedures were used to treat jaundice and abscess in patients with alveolar liver damage, and the average frequency of laparotomies per patient with cytoreductive surgery decreased from 2.8 to 1.4% [74].

After reviewing a lot of literature reviews, we did not find a lot of material about percutaneous drainage of the decay cavity for the treatment of patients with inoperable alveolar echinococcosis of the liver, perhaps in our opinion, when the decay cavity is drained and oxygen enters the alveococcus cavity, a possible death of the parasite metacystodes occurs. However, the evidence and conducted experiments on this fact are not described at the moment. We hope that in the near future, perhaps, some research will be carried out on this matter.

#### *Cytoreductive liver resections in inoperable liver alveococcosis*

Many authors describe that R1 resection led to a higher rate of disease progression than R0, and the frequency of complications associated with parasitism was similar to that observed only with benzimidazole therapy. Thus, surgery to remove R1 does not seem to offer any advantages over benzimidazole-only therapy in the treatment of alveolar echinococcosis, and it should be avoided [77].

At the time of diagnosis, the parasitic process in most cases passed into an incurable stage of the disease. On the one hand, it was recommended to perform resections, even if they are incomplete, in order to decompress bile ducts or remove the decay cavity [78]. The causes of incomplete resections were extensive liver damage, distant metastases or direct invasion into the vascular structures of the liver, vena cava and diaphragm or retroperitoneal space [79]. There are even cases of liver transplants that are considered cytoreductive due to non-radical removal of alveococcosis from the abdominal cavity or spread into the pleural cavity and lungs [80].

Many authors have reported a case of cytoreductive resection due to invasion of the vena cava and good long-term results in the early and late postoperative period [81]. With the appearance of a suppurated cavity and persistent septic status, not effective conservative treatment, the elimination of the parasitic focus is the principle of treatment, preferably by resection of R1 or even R2, if resection of R0 is impossible [82]. Thus, cytoreductive operations should be limited due to a variety of complications,

such as: the risk of anesthetic benefits, the risk of uncontrolled bleeding, the risk of surgical infections and repeated operations and death [83].

Against this background, the value of cytoreductive operations in the data of many authors is considered doubtful [82]. In this connection, the frequency of cytoreductive resections began to decrease with the advent of mini-invasive and transplantation technologies [84].

In our opinion, during the surgical intervention, when the spread of the process into the surrounding tissues was detected and it was not possible to perform surgery in the amount of R0, cytoreductive resection was performed, or taking into account the development of various complications in the patient, the patient was prepared for cytoreductive resection to eliminate complications. Previously, cytoreductive surgery was considered the gold standard in the treatment of patients with inoperable liver alveococcosis. In our opinion, to date, mini-invasive methods with additional antiparasitic therapy have become the first link in the treatment of inoperable liver alveococcosis compared to cytoreductive surgery.

#### *Transplantation methods*

Liver transplantation, the most extensive liver resection, has been proposed as an alternative approach for unresectable alveolar echinococcal liver [85]. To date, various authors have reported about 100 liver transplants. [86-91]. Despite the negative picture of *E. multilocularis* infection, liver transplantation was associated with excellent long-term results, characterized by a 5-year survival rate of 85% [92].

Thus, the presented data seem to convincingly confirm liver transplantation as a surgical method of treating individual patients with unresectable alveolar echinococcosis of the liver. It is noteworthy that the results presented by other authors also confirm its effectiveness. A multicenter European-based study conducted by Koch and his co-authors reported a 5-year survival rate of 71% [93]. Similarly, in another transplant center, a corresponding 5-year survival rate of 77.8% was reported by Aydinli and his co-authors in a recent analysis of the results [94].

#### *Autotransplantation*

Due to the shortage of donor organs, an ex-vivo method was developed with subsequent autotransplantation of liver segments free of alveococcosis. This method, developed by Rudolf Pichlmayr and his team in Germany for the treatment of "inoperable" liver tumors in the 1990s, this method may represent itself as an alternative to liver allotransplantation in liver alveococcosis, especially interesting for such a chronic tumor-like infectious disease, extremely sensitive to immunosuppressive therapy [95, 96].

To date, liver allotransplantation is still used in advanced cases, especially when hepatic veins and vena cava are included in the parasitic lesion, when life-threatening complications occur, but a

shortage of donors and lifelong administration of immunosuppressants, accompanied by increased susceptibility to disease recurrence, prevented the use of this approach [97].

#### *Allotransplantation*

The high level of postoperative morbidity and mortality (30% during the first 6 months after transplantation), as well as the frequency of relapses (10% local and 20% with distant metastases) raise an ethical question, especially when the liver is obtained from living donors [98].

Liver allotransplantation, initiated for the treatment of liver alveococcosis in the mid-1980s, is associated with the risk of recurrence or progression of extrahepatic lesions of alveococcosis, especially brain metastases, due to suppression of immunity [99, 100].

In Europe, in addition to the recommendations of the Expert Consensus 2010, the shortage of donors, as well as the tendency to promote ABZ treatment in combination with minimally invasive methods of treatment in cases with advanced liver alveococcosis, contributed to a decrease in the number of patients-candidates for liver allotransplantation [101,102].

Contrary to this attitude, the beginning of the 21st century was marked by the publication of several clinical cases and a series of patients with liver alveococcosis who received liver allotransplantation, including transplantation from a living donor, from China, Turkey and the USA [103-114]. Carrying out liver transplantation against the international recommendation may be due to the clinical conditions of patients in these countries, due to late diagnosis in very advanced and complex

cases, as was observed in Western Europe in the early 1980s. Earlier diagnosis, a reduction in the number of palliative surgeries, improved management of ABZ and non-surgical interventions and, possibly, resection *ex vivo* plus autotransplantation are likely to contribute to a reduction in the number of liver allotransplantations in alveococcosis in the future. The overall results suggest that liver transplantation should remain a "life-saving therapy" in very advanced cases.

Liver transplantation from a posthumous donor may benefit patients with progressive liver failure, with Budd-Chiari parasitic syndrome or when resection methods are exhausted, as well as patients with end-stage functional disorders caused by secondary biliary cirrhosis, secondary sclerosing cholangitis and postnecrotic cirrhosis [115-119].

#### **Conclusion**

The management of patients with inoperable liver alveococcosis requires an individual approach to each patient. Accurate diagnosis plays an important role in determining treatment tactics and affects the outcome of the disease. Various methods of basic (resection of the liver R0 and liver transplantation), mini-invasive (PTBD, ERCP, drainage of the decay cavity), drug (antiparasitic) treatment are used only for certain indications, with the right treatment tactics, good long-term results can be obtained. Liver transplantation is the last treatment option for patients with inoperable liver alveococcosis with severe hepatic cell insufficiency, portal hypertension with signs of bleeding from varicose veins of the stomach and esophagus, and intolerance to antiparasitic therapy.

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The authors declare that they have no conflicts of interest

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## TROCAR SITE INCISIONAL HERNIAS

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### Abstract

**Objective:** to analyse the incidence of trocar site hernias among patients admitted to the surgical clinic on an emergency basis with a diagnosis of an incarcerated hernia.

**Materials and methods.** The retrospective and prospective study; the follow-up period is 10 years. A statistical analysis of patients with incarcerated hernias had been performed. A total of 1,448 subjects was selected for the study. Of these, 825 (57.0%) patients were diagnosed with incarcerated hernias of various localizations. The diagnosis of incarceration among 623 (43.0%) subjects proved to be false, and the hernias of these patients were classified as "reducible" and "irreducible" hernias.

**Results.** An analysis of the operations revealed 34 patients with trocar site hernias, representing 2.34% of the total number of patients admitted to hospital with hernias and 4.93% of those operated on an emergency basis.

**Conclusion.** The rare, partial incarceration of the omentum and small intestine, the so-called Richter's hernia, after using 5-mm-diameter trocars was revealed in 4 people operated on previously (3 to 5 years). Moreover, the hernial orifice (abdominal wall defect) at the time of our operation turned out to be significantly larger than after puncture with a 5-mm trocar. A direct correlation was found between the incidence of trocar site hernia and the degree of obesity, body mass index.

## Отадан кейінгі троакарлы жарықтар

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**Түйінді сөздер:**

қысылған жарықтар, троакарлы жарықтар, Рихтер қысылуы, дене салмағының индексі

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### Тұжырым

**Мақсаты:** троакарлы жарықтардың пайда болу жиілігіне хирургия бөлімшелеріне жедел түрде қысылған жарық диагнозымен жеткізілген науқастарға анализ жасау.

**Материалдары мен әдістері.** Ретроспективті және проспективті зерттеу. Бақылау уақыты 10 жыл. Қысылған жарық диагнозымен науқастарға статистикалық анализ жүргізілді. Науқастар 1448 адам арасынан іріктеп алынды. Олардың 825 (57,0%) қысылған жарықтар диагностикаланды, ал 623 (43,0%) науқаста қысылған жарық диагнозы дәлелденбеді. Бұл науқастарда жарықтар қайтадан кіретін және қайтадан кірмейтін жарықтар деп анықталды.

**Нәтижелер.** Троакарлы жарықпен 34 науқасқа ота жасалды. Стационарға түскен жалпы науқастар санының 2,34% және де жедел түрде ота жасаған науқастардың 4,93% құрайды.

**Қорытынды.** 4 адамда диаметрі 5 мм троакарларды қолданумен операция жасалған (3 жылдан 5 жылға дейін), сирек шарбы майының және жіңішке ішектің жартылай қысылуы (қабырғалық қысылу) - Рихтер жарығы анықталды. Операция барысында жарық қақпасы (іш қабырғасының ақауы) 5 мм троакармен тескеннен кейінгіге қарағанда айтарлықтай үлкен болып шықты. Троакар жарығының пайда болу жиілігі мен семіздік дәрежесі мен дене салмағының индексі арасында тікелей корреляция анықталды.

## Послеоперационные троакарные грыжи

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#### Аннотация

**Цель исследования** - провести анализ частоты образования троакарных грыж среди больных доставленных в хирургическую клинику в экстренном порядке с диагнозом ущемленной грыжи.

**Материалы и методы.** Исследование ретроспективное и проспективное, период наблюдения 10 лет. Проведен статистический анализ больных с ущемленными грыжами. Отбор пациентов проведен среди 1448 человек. Из них у 825 (57,0%) больных диагностированы ущемленные грыжи различной локализации. У 623 (43,0) - диагноз ущемления не подтвердился, грыжи у таких лиц были квалифицированы как «вправимые» и «невправимые» грыжи.

**Результаты.** Анализ операций показал, что с троакарными грыжами было 34 человека, что составило 2,34% от общего количества доставленных пациентов с грыжами в стационар и 4,93% от количества прооперированных в экстренном порядке.

**Выводы.** У 4 человек оперированных ранее (от 3 до 5 лет) с после применения троакаров диаметром 5 мм выявлены редкие, частичные ущемления сальника и тонкого кишечника – так называемые ущемления Рихтера. При чем грыжевые ворота (дефект брюшной стенки) на момент нашей операции оказались значительно большими чем после прокола троакаром 5 мм. Выявлена прямая корреляция частоты образования троакарных грыж от степени ожирения, индекса массы тела.

#### Конфликт интересов:

Авторы заявляют об отсутствии конфликта интересов

#### Ключевые слова:

ущемленные грыжи,  
троакарные грыжи, ущемление  
Рихтера, индекс массы тела

#### Relevance

Hernias attributed to laparoscopic surgery have recently become more common [1]. In the early days of the development of laparoscopic surgery, these complications were scarcely focused on. An analysis of literary sources during the period of widespread introduction of endoscopic operations indicates that the main emphasis was placed on the search and testing of new operational techniques associated with the implementation of new technologies, tools and equipment followed by pooling of experience and the publication of scientific materials that proved out the successful results of treatment. In this respect, the significant advantages of minimally invasive endoscopic techniques and the lack of postoperative complications inherent in the traditional surgical techniques were evidenced [1, 2].

Therefore, for a long time it was thought that postoperative hernias were secondary and that they could only occur after open laparotomies. Because the cause of hernial defects of the anterior abdominal wall after abdominal surgery was considered to be: a) large incisions; b) extensive tissue trauma; c) tissue infection; d) insufficient anatomical comparability of the edges when suturing the abdominal cavity; e) inadequate (inaccurate) comparability of different tissue structures; f) cutting or loosening of surgical sutures, etc.

However, the lack of the above risk factors in those operated on with laparoscopic instruments did not save patients from surgical complications [3, 4].

The accumulated global experience testifies to cases of new, strictly endoscopic surgery-specific complications (trocar injuries of internal organs, vessels, burns due to high frequency currents, subcutaneous emphysema, pneumomediastinum, etc.) [5-10].

Among the complications, the incarcerated hernias after laparoscopic surgery or so-called trocar site hernias

are quite common.

It could not be denied that the introduction of laparoscopic technologies has led to a decrease in the number of so-called "traditional" surgical complications after abdominal surgery, which primarily included incisional hernias. However, as time has passed, it has become clear that postoperative defects of the anterior abdominal wall often occur in laparoscopically operated patients as well. The increasing incidence of such complications is now a growing concern among practicing surgeons.

Incisional hernias in such cases have been associated with insufficient closure and healing of the so-called trocar wound (puncture site and instrument placement). Moreover, many surgeons do not close the remaining defects of the anterior abdominal wall after removal of laparoscopic ports from the abdominal cavity, if these defects are minor. This excludes the use of laparoscopic ports with a diameter of 10 mm or more.

In the international literature, such postoperative defects are referred to as TSIH (Trocar site incisional hernia) [1]. Moreover, few studies describe the incidence or risk factors contributing to hernias at present.

There are insufficient data on studies results in the medical literature examining the mechanism or causes of so-called trocar site hernias in patients admitted to the emergency department with surgical complications, including those with a high body mass index (BMI) and obesity.

**Objective:** to determine the prevalence of TSIH in patients admitted to the surgical department on an emergency and elective basis and to identify risk factors for hernia after laparoscopic surgery.

#### Materials and methods

Retrospective and prospective methods of analysis were used in the study. Patients who underwent laparoscopic surgery for various abdominal pathologies



over a ten-year period (2011 - 2020) were studied and the case-records were reviewed in the study.

All patients were assessed using the criteria and parameters as below: history of laparoscopic access during surgery, diagnosis of anterior abdominal wall hernia, overweight, obesity, diabetes, concomitant cardiac and pulmonary pathology, age, gender, etc. Clinical examination, radiography (-scopy), computed tomography (CT), and ultrasound of the abdomen and anterior abdominal wall were analysed to confirm the existence of a trocar site hernia.

Statistical analysis, tabulation and plotting were carried out using the software Statistica 10.0. Statistical analysis took into account that the main variable studied was the incidence of TSIH. Other results of clinical and instrumental examinations represented the additional criteria. A multivariate analysis was aimed at the identification of risk factors. The terms after the operation were taken into account for the above ten-year period starting from the second day after the surgery. Particular attention is paid to the observation of patients with overweight, obesity (body mass index over  $>25 \text{ kg/m}^2$ ) of varying severity (stages I-IV).

#### Results

In total, the cohort with trocar site hernias included 34 subjects who were selected from 1448 patients admitted to the surgical clinic with a diagnosis of incarcerated hernia. All patients (1448) were admitted to the hospital on an emergency basis; the diagnoses were verified after examining by the surgeons. Of these, 825 (57.0%) patients were diagnosed with incarcerated hernias of

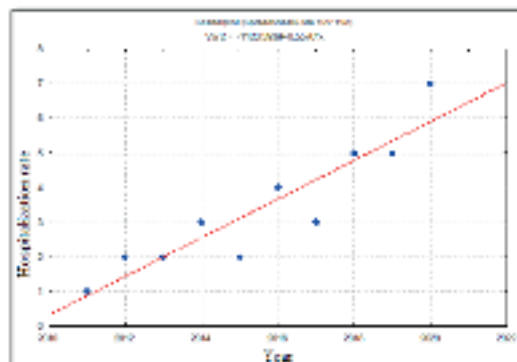
anterior abdominal wall of various localizations. The diagnosis of incarceration among 623 (43.0%) patients proved to be false, and the hernias of these subjects were classified as "reducible" and "irreducible" hernias.

Of the group of patients (825 people) with signs of incarceration, an emergency surgery was performed for 689 (83.5% of 825) patients. The remaining 136 (16.5% of 825) patients had a hernia removal at the time of examination in the diagnostic department. Therefore, one part of the patients refused hospitalization for surgery, the other part was transferred to other clinics for surgical treatment.

The analysis of the operations revealed 34 patients with trocar site hernias, representing 2.34% of the total number of patients admitted to hospital with hernias and 4.93% of those operated on with hernias. This observation group included 11 men and 23 women who met the prerequisite selection criteria. From the anamnesis it was found that all of them had been operated on previously between 2 and 15 years ago. But in 75% of the cases, laparoscopic surgery was performed in the period of 3-5 years ago.

The mean annual hospitalization rate with strangulated TSIH was as follows  $M(3.4)$ ;  $MD(3)$ ;  $(SD)\pm 1.8$ . Where, M is the mean of the number of patients hospitalized and treated, MD is the median, SD is the standard deviation. It has been revealed a definite upward trend in the number of persons hospitalised in the surgical department with postoperative trocar site hernias. The calculations are shown graphically in the Figure 1.

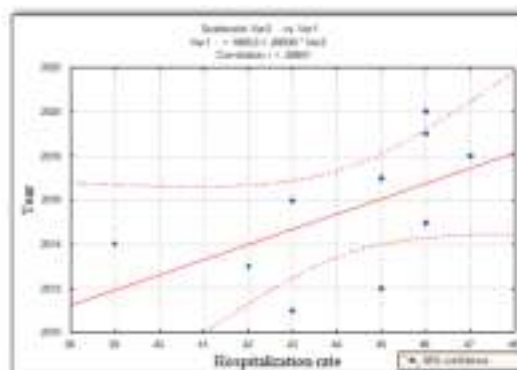
**Figure 1.**  
Hospitalization rates for trocar site hernias  
Where, (●) – values of the average rate  $M\pm$ ; ( / ) - trend line indicating an increase in the hospitalization of patients with TSIH



In addition, it should be noted that the correlation indices by years of observation have a rather moderate than strong correlation (Pearson,  $r = 0.55$ ). However, according to our calculations, the probability of this trend

to be maintained in subsequent years is positive. The probability of this correlation persisting in subsequent years after our study is well evidenced in the graph in the Figure 2.

**Figure 2.**  
Probability of increasing correlation between hospitalisation rate and follow-up years. Where, (●) are the values of the average  $M\pm$ ; ( / ) - trend line indicating an increase in the hospitalization of patients with TSIH



In addition, based on the analysis we have done for the previous ten-year period, we can assume an intensification of the correlation for the coming years. This includes the so-called cumulative effect. This is not unrealistic given the principle – the more patients

operated on with the use of trocars, the more trocar complications expected. The probability increase plot with the empirical and theoretical cumulative distribution is shown in the Figure 3.

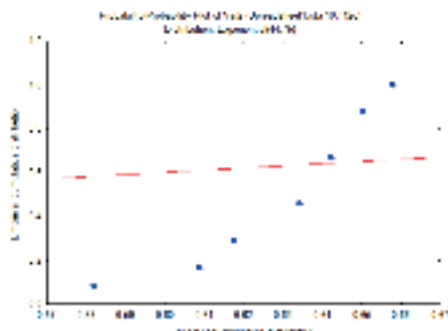


Figure 3. Probability of cumulative and empirical distribution of cases. Where, distribution: exponential (=44,75)

The analysis of the location of trocar site hernias revealed that paraumbilical hernias were more common (19 cases) than the other localizations (15 cases). This amounted to 1.3% and 1.0%, respectively, of all hernias hospitalised on an emergency basis. If we consider the percentage of the number of patients operated on, then these figures will be higher - 2.3% and 1.8%. It should be noted 4 cases of lateral localization of a trocar site hernia, all of which occurred after puncture with a 5-mm trocar. When clarifying the anamnesis, two patients had drainage tubes in these places. It turned out that these cases are the incarceration of the omentum and intestines. In the remaining 2 cases, incomplete

or partial incarceration of the intestine (the so-called "Richter's hernia") was observed. These strangulated hernias were reported in obese individuals with a high body mass index (BMI over 26.5). Moreover, the diameter of the hernial opening was significantly larger than the diameter of the 5-mm trocar, which was used during the first surgery. Among those with trocar site hernias, the vast majority of patients were overweight and had a high body mass index. A graphical picture (3D graphics) of the intercorrelation between the quantitative growth of trocar site hernias over time and a large body weight of patients with excess fatty tissue on the anterior abdominal wall is shown in the Figure 4.

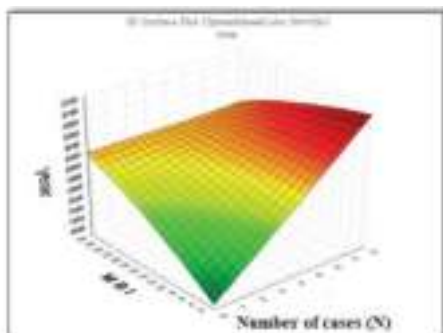


Figure 4. Interdependence between the increase in cases of trocar site hernias and length of follow-up (years) and body mass index (MBI)

#### Discussion

It is believed that Dr. Fear R.E. (USA) first reported a hernia TSH (Trocar Site Hernia) after a puncture of the anterior abdominal wall with a trocar. He published his observations in the Journal "Obstetrics & Gynaecology" in March 1968. The article studied the historical and contemporary views at that time on the role of laparoscopy in gynaecological diagnostics [11]. Subsequently, many authors recognized this as the first report of trocar site hernias [12-15].

Then in 1991 Maio Angela and Ruchman Richard B. reported a trocar site hernia with small intestinal obstruction occurring immediately after cholecystectomy [16]; this was the first report of trocar site hernias in digestive surgery. Since then, many similar reports have been published after cholecystectomy and, more recently, after many gastrointestinal surgeries. Published reports show extremely wide variation in the clinical aspects of trocar site hernias. They are so significant that many authors began to delve into the terminology, classification, and the meaning of the medical term "hernia of the trocar section" or "trocar

site hernia", which is not clearly defined today [12-16].

However, the main point is that trocar site hernias after laparoscopic surgery are, according to international authors, rare complications in laparoscopic surgery [17]. Hernias are more common after the use of trocars with a diameter  $\geq 10$  mm. However, there are rare cases of such hernias where a laparoscopic instrument with a 5 mm diameter has been inserted into the abdominal cavity. Such cases can lead to serious postoperative complications. In 2016, Pereira N, Hutchinson AP, Irani M and co-authors conducted a systematic review of publications, which analysed 295 cases of the formation of defects in the anterior abdominal wall after laparoscopic surgery. Of these, in 5.76%, the hernia was associated with a defect in the area of 5 mm. Moreover, the incidence of umbilical and non-umbilical (lateral) localization is slightly different (56% and 44%) [17].

Considering the results of our study, it can be noted that they are mostly consistent with the data presented by the above authors in their publications and articles. It should be said that in our case, the main localization of postoperative trocar site hernias coincides with the

incidence indicated by many authors. However, there are some differences between our results and those published in international papers. Thus, the majority of incarcerations in the lateral localisation are associated with appendectomy, laparoscopic diagnosis and gynaecological surgery rather than cholecystectomy. There are almost no reports of trocar site hernias after the use of a 5-mm trocar in the global literature. In our opinion, it is very difficult to make any comparison and obtain reliable statistics. This also applies to descriptions of the strangulated gut according to the Richter type, which are very scarce in the literature. This requires significant large-scale multicentre studies, not just at the level of one region or a single clinic.

Many surgeons, when determining the kind of the incarceration, adhere to the previously proposed classification of trocar site hernias, which divides them into 3 types:

- Early-onset type: An early type that occurs immediately after surgery, with frequent small intestinal obstruction, especially Richter's hernia.

- The late-onset type: A type of late onset that occurred a few months after surgery, mainly with local protrusion of the abdomen without development of small intestinal obstruction.

- The special type: The special type indicated protrusion of the bowel and/or omentum. Trocar -site hernias with fascial defects of 10 mm or more should be closed, including of the peritoneum [18].

According to Abe Fukumitsu and his co-authors, the so-called Richter's hernias are characteristic only in the early postoperative period. However, in our case, we trace the result of the trocar incarceration at a much later stage.

The submitted study result on the diameter of the hernial orifice (orifice after trocar puncture), which we observed, is a contribution to this scientific field. Moreover, we find a significant increase in the defect of the anterior abdominal wall after a trocar hole of 5 mm, made 3-5 years or more ago. The escalation of trocar site hernias rate is associated with rise in the number of operations, including an increase in the number of overweight and obese patients operated on, which is accompanied by the effect of stretching the anterior abdominal wall and weakness of the muscle aponeurosis.

#### Conclusion

In the last decade, there has been an increase in the incisional hernias after laparoscopic surgery. A statistical trend line indicates a projected increase in this pathology. One of the most dangerous complications for the patient is a trocar site hernia. The share of trocar site hernia among all incarcerated hernias operated on an emergency basis is 2.34%. There is a correlation between the incidence of incarcerated hernia and the age of surgery, trocar diameter, overweight and obesity. The rarest complication of a trocar site hernia is Richter-type intestinal incarceration (Richter's hernia).

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# RADIOWAVE SURGERY OF TUMORS AND DYSPLASTIC NEOPLASMS OF THE MAXILLOFACIAL AND RELATED AREAS IN CHILDREN AND ADULTS

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## Abstract

The purpose of this investigation is to show the effectiveness of the use of radiofrequency resection of tumors of various anatomical locations in children and adults.

**Materials and methods.** 599 patients with masses and dysplastic changes of maxillofacial and other areas were treated by RF resection. Total 706 lesions were resected. Patients were treated in hospital and outpatient settings.

**Results.** Clinical diagnosis and pathology report were congruent in 100% cases. No post-operative complications, short post-operative rehabilitation. Radiofrequency surgery is a preferred treatment of choice in treatment of masses and dysplastic lesions.

**Conclusion.** Radiofrequency surgery of tumor or other lesions is minimally invasive surgery with satisfactory cosmetic results. The majority of patients undergo RF surgery without complication or long-term post-operative care.

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## Conflict of interest:

The authors declare that they  
have no conflicts of interest

## Keywords:

tumors, neoplasms, dysplastic  
lesions, radiofrequency surgery,  
maxillofacial region

## Балалар мен ересектердегі бет-жақ және іргелес аймақтардағы ісіктер мен диспластикалық процестердің радиотолқынды хирургиясы

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## Тұжырым

**Жұмыстың мақсаты** – балалар мен ересектердегі түрлі локализациядағы ісіктерді емдеу кезінде радиотолқынды хирургияны пайдаланудың тиімділігін көрсету.

**Материалдар мен әдістер.** Бет-жақ және басқа аймақтарда ісіктері және диспластикалық өзгерістері бар 599 науқасқа ем жүргізілді, 706 жаңа түзілім жойылды. Науқастың жасына, жаңа түзілімнің өлшемі мен орналасуына байланысты ем стационарда және амбулаториялық жағдайда жүргізілді.

**Нәтижелер.** Клиникалық диагноз бен морфологиялық зерттеудің нәтижелері 100% сәйкес келеді. Интраоперациялық асқынулар жоқ, операциядан кейінгі қалыпқа келу қысқа мерзімді қамтиды.

**Қорытынды.** Ісіктерді және диспластикалық процестерді емдеудегі радиотолқынды хирургия әдісінің тиімділігі жоғары әрі таңдау әдісі болып табылады.

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ісіктер, жаңа түзілімдер,  
диспластикалық процестер,  
радиотолқынды хирургия,  
бет-жақ облысы

## Радиоволновая хирургия опухолей и диспластических процессов челюстно-лицевой и смежных областей детей и взрослых

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**Конфликт интересов:**  
Авторы заявляют об отсутствии  
конфликта интересов

**Аннотация**

**Цель работы** - показать эффективность использования радиоволновой хирургии при лечении опухолей различной локализации у детей и взрослых.

**Материалы и методы.** Проведено лечение 599 пациентов с опухолями и диспластическими изменениями челюстно-лицевой и других областей, удалено 706 образований. В зависимости от возраста пациента, размера, локализации новообразования лечение проводилось в стационаре и в амбулаторных условиях.

**Результаты.** Совпадение клинического диагноза и результата морфологического исследования в 100%. Отсутствие интраоперационных осложнений, короткий срок послеоперационного восстановления.

**Заключение.** Метод радиоволновой хирургии в лечении опухолей и диспластических процессов высокоэффективен и является методом выбора.

**Ключевые слова:**  
опухоли, новообразования,  
диспластические процессы,  
радиоволновая хирургия,  
челюстно-лицевая область

**Introduction**

The mainstream treatment of various masses/tumors/lesions is surgical. Radiofrequency surgery has the advantages:

Does not damage healthy surrounding tissues on the periphery as well as in depth of the skin.

Coagulation effect at the same time of the excision  
Incision is effortless without any pressure on the tissue which helps consequent healing.

No burn injury compared to laser or electrocoagulation

The Radiofrequency device was invented and applied into practice by NASA (USA) in the late 1980s. We started using RF Surgitron in Kazakhstan in 1999.

**Material and methods**

During 1999-2021 we operated 599 patients (101 children and 498 adults). The majority of patients had benign nevi (38.7%) and warts (28.3%) of head and neck areas which caused patients' aesthetic distress. The number of these masses fluctuated between 1-2 and 25 in various topographic locations. (Table 1, 2)

In women, the triggers for increasing in size and

number of benign neoplasms were: hormonal changes (pregnancy, menopause), excessive exposure to sun, stress. In men, main reasons for changing in number and character of growth were trauma, sun exposure, metabolic disorders, mainly obesity. In people over 50 years of age the formation of xanthomas of the eyelids and atheromas of face, neck and body were mainly associated with obesity and age-related hormonal changes (hypothyroidism, menopause etc.) Accelerated growth of angiofibroma and spread to the adjacent paranasal sinuses increased during pregnancy.

Patients with periorbital masses were allocated in a distinct group due to specific anatomical features: proximity of eyeball and muscles of facial expressions, eyelids and rich vascular supply. A particular care should be taken of eyelash follicles when surgically excising pigmented nevi of the ciliary margin (palpebra) due to risk of damage to the follicles. The same precautions apply to the eyelid hemangioma which often involves conjunctiva. Therefore, the eye guard was used to prevent an injury to the eye.

**Table 1.**  
Distribution of patient by  
age and gender

Children (0-16 y.o.)		Adults (17-83 y.o.)
Male	Female	Male
42	59	159
41.8%	58.2%	31.9%

**Table 2.**  
Distribution of patients by  
pathology type

Pathology	Quantity (%)
Hemangioma	83 (11.8%)
Benign Nevus	273 (38.7%)
Papilloma	200 (28.3%)
Epidermoid cyst	15 (2.1%)
Keratoma	59 (8.3%)
Angiofibroma	16 (2.3%)
Lipoma	5 (0.7%)
Atheroma	29 (4.1%)
Neurofibroma	3 (0.4%)
Fibromixoma	3 (0.4%)
Chondroma	2 (0.3%)
Keloid	9 (1.3%)
Basal cell carcinoma	2 (0.3%)
Adenocarcinoma	2 (0.3%)
Xanthelasma	5 (0.7%)
Total	706 (100%)

## Results

Treatment of mixed hemangioma in children 1-7 were carried out in the hospital. 2 stages of treatment were identified:

Sclerotherapy with Lauromacrogol 400 (20mg/ml) ("etoxysclerol") under sedation.

Fulguration of capillary hemangioma or skin hyperpigmentation.

Capillary small size cavernous hemangiomas (up to 5 mm in diameter) in older children 8-16yo were resected using fulguration under local anesthesia. In adults the surgery was done under local anesthesia with concurrent antiseptic irrigation (furacillin). Postoperative instructions include Solcoseryl gel (Switzerland) on the wound for 3 days and Solcoseryl cream afterwards for 4 days. Wound was not covered. Treatment of hairy nevi comprised of resection of the mass with the subsequent RF coagulation

of each hair follicle to prevent recurrence. Repeat coagulation was performed in particularly persistent lesions. (Figure 1, 2, 3)

After the resection of Basal cell carcinoma (BCC) and adenocarcinoma using RF Surgitron the wound in the first 48 hours post-surgery was covered either with Solcoseryl gel (healing agent) or raw egg white. After 2 days all wounds were treated by using Solcoseryl gel for 14 days.

Treatment of the extensive angiofibroma of the ethmoid and maxillary sinuses included 2 stages.

Sclerotherapy injection via foramina alveolaris in the tuber maxillaris under direct

Rhinoscopy with good hemostasis.

RF resection of the tumor without carotid ligation with minimal bleeding. Wound healing by primary intention.

All specimens were sent for pathology confirmation.



Figure 1.  
Removal of the pigmented nevus of the skin: before and after



Figure 2.  
Removal of forehead atheroma: before and after



Figure 3.  
Removal of a large papilloma: before and after

## Conclusion

Radiofrequency surgery of tumor or other lesions is minimally invasive surgery with satisfactory cosmetic

results. The majority of patients undergo RF surgery without complication or long-term post-operative care.

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# INTRAMEDULLARY BLOCKING IMPLANTS ARE NEW POSSIBILITIES IN THE TREATMENT OF PATIENTS WITH FRACTURES OF TUBULAR BONES

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**Conflict of interest:**

The authors declare that they

have no conflicts of interest

**Keywords:**

tubular bones, treatment

## Abstract

We have produced 49 shoulder, femur and tibia osteosynthesis by blocking internal fixation in 47 patients with multiple and combined trauma. Paraarticular and diaphyseal femur fractures were predominated and found in 18 patients (39%), humerus fractures were detected in 9 (20%) of victims of diaphyseal shin fractures were observed in 22 (47%) patients. Multiple injuries of two or three segments were identified in 6 (13%) patients. We have applied the primary dynamic blocking concerning the stabilization of the transverse and oblique diaphyseal fractures, and we have performed static blocking fragments with comminuted fractures. Postoperative complications were observed in 8 (17%) patients patients. Outcomes were followed up in 39 patients in terms of 8 to 18 months. Favorable anatomical and functional results were stated in 32 (68%) patients.

## Интрамедуллярлық блоктаушы имплантаттар – түтік тәрізді сүйектердің сынуы бар науқастарды емдеудегі жаңа мүмкіндіктер

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**Түйінді сөздер:**

түтік тәрізді сүйектер, емдеу

## Тұжырым

Барлығы 49 ота иық, жамбас және жіліншік сүйектерінің интрамедуллярлық остеосинтез блоктау әдісімен көптеген біріктірілген жарақаттары бар 47 науқасқа жасалынды. Сан сүйегінің периартикулярлық және диафиздік сынықтары басым болды және 18 науқаста (39%) анықталды, 9 (20%) иық сүйегінде зардап шеккендерде анықталды, 22 (47%) пациенттерде балтыр сүйектерінің диафиздік сынықтары байқалды. Екі және үш сегменттердің бірнеше зақымдануы 6 (13%) науқастарда анықталды. Көлденең және қиғаш көлденең диафиздік сынықтарды тұрақтандыру кезінде бастапқы динамикалық блоктау қолданылды, ал сынған сынықтар кезінде сынықтарды статикалық блоктау орындалды. Отадан кейінгі кезеңде науқастардың 8-де (17%) асқынулар байқалды. Ұзақ мерзімді нәтижелер 39 пациентте 8 айдан 18 айға дейінгі мерзімде байқалды. 32 (68%) пациентте қолайлы анатомиялық-функционалдық нәтижелер анықталды.

## Интрамедуллярные блокирующие имплантаты – новые возможности в лечении больных с переломами трубчатых костей

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### Аннотация

Произведено 49 операции остеосинтеза плечевой, бедренной и большеберцовой костей методом блокирующего интрамедуллярного остеосинтеза у 47 больных с множественной и сочетанной травмой. Околосуставные и диафизарные переломы бедренной кости преобладали и констатированы у 18 больных (39%), плечевой кости выявлены у 9 (20%) пострадавших, диафизарные переломы костей голени отмечены у 22 (47%) пациентов. Множественные повреждения двух и трех сегментов были определены у 6 (13%) больных. При стабилизации поперечных и косопоперечных диафизарных переломов применялось первичное динамическое блокирование, а при оскольчатых переломах выполнено статическое блокирование отломков. В послеоперационном периоде наблюдались осложнения у 8 (17%) пациентов. Отдаленные результаты прослежены у 39 пациентов в сроках от 8 до 18 месяцев. Благоприятные анатомо-функциональные результаты констатированы у 32 (68%) пациентов.

### Конфликт интересов:

Авторы заявляют об отсутствии конфликта интересов

### Ключевые слова:

трубчатые кости, лечение

### Relevance

The existing trend of increasing the number of severe skeletal injuries dictates the need to improve the tactics and methods of treatment of combined and multiple injuries, which is an urgent problem in modern traumatology.

The main principles in the treatment of diaphyseal fractures of the lower extremities in patients with concomitant and multiple trauma remain stable surgical fixation, the timing of surgical intervention. Pathogenetic justification is the early stabilization of damaged segments in order to prevent complications of traumatic disease, as well as in a complex of anti-shock measures [1, 2]. Numerous injuries of various organs and systems lead to the effect of the syndrome of mutual burdening and the development of traumatic disease [1, 3]. Fixation of fractures of the lower extremities in the acute period of traumatic disease with external fixation devices in severe concomitant trauma is an alternative method, however, in 57-71% of cases, osteosynthesis with devices is not final, the treatment of fractures often takes a two-stage character, inflammation of the soft tissues around the pins and rods often occurs [3, 4, 5]. In the countries of near and far abroad, for more than two decades, intramedullary locking rods have been used in the treatment of diaphyseal and periarticular fractures.

The undoubted advantage of the technique is low trauma, which is associated with extra-focal antegrade insertion of the pin and the absence of the need for reaming the medullary canal. Minimally invasive implantation of a metal construct causes minimal disruption of periosteal

vascularization, which subsequently contributes to the consolidation of bone tissue. The insertion of a nail into the medullary canal away from the fracture site minimizes the risk of postoperative infectious complications - 2.3-4.1% [2, 4, 6, 7, 8, 9, 10].

### Material and methods

Over the past two years, 2020-2022, 49 operations of osteosynthesis of the humerus, femur and tibia using the method of blocking intramedullary osteosynthesis were performed in 47 patients with multiple and combined trauma in the traumatology departments of the CEH (City emergency hospital) in Almaty. There were 26 (56%) men and 21 (45%) women. By age categories, patients were distributed by the following: 20 years - 9 (20%) patients, 22 (47%) patients in the group of 20-40 years, 12 (26%) victims were noted from 40 to 60 years, over 60 years - 4 (9%). The majority of 35 (75%) patients were admitted within the first three days after the injury, 10 (22%) patients came in from 3 to 10 days, and only 2 (5%) injured were admitted later than 10 days. Among the skeletal injuries, periarticular and diaphyseal fractures of the femur prevailed and were diagnosed in 18 patients (39%), the humerus was found in 9 (20%) victims, diaphyseal fractures of the tibia were noted in 22 (47%) patients. Multiple injuries of two and three segments were identified in 6 (13%) patients. The dominant place among comorbidities is occupied by closed craniocerebral injury, noted in 51% of cases (24 patients), chest trauma was detected in 34% (16 patients), abdominal trauma only in 15% (7 victims) (Figure 1, 2, 3).



Figure 1. Before and after operation



Figure 2.  
Before operation



Figure 3.  
After operation



Surgical interventions were performed at various time from the moment of injury. The majority of 29 (60%) patients were operated on within 3 to 10 days from the moment of injury, in the early period on days 1-3, osteosynthesis was performed in 11 (23%) patients, and in the later period after 10 days or more in 7 (15%) of patients.

The choice of optimal terms for surgical intervention and the method of primary fixation of fractures was carried out based on the severity of the patient's general condition.

We used this method of osteosynthesis for fixation of periarticular and diaphyseal fractures of different localization. In 30 cases, the fractures were transverse or oblique transverse according to AO classification A2, A3. In other cases, the fractures were comminuted: type B1-3 in 12 patients, C1-3 in 7 cases.

Metal structures manufactured by ChM were used - a system of lockable intramedullary rods CHARFIX®system, including femoral rods - universal, trochanteric and telescopic, tibial rods - reconstructive and retrograde, shoulder rod reconstructive and compression. When stabilizing transverse and oblique diaphyseal fractures (type A), primary dynamic blocking was used, and for comminuted fractures (type B and type C), static blocking of fragments was used with intraoperative correction of the length of the damaged segments. Insertion of nails is carried out by a closed antegrade method under the control of an electron-optical converter. The correct determination of the point for the introduction of a metal construct is essential, which determines the non-traumatic insertion of the rod through the medullary canal and the success of closed reposition of bone fragments, especially in comminuted and fragmentary fractures. As stabilizing comminuted

diaphyseal fractures, an important point is preoperative planning, selection of a nail of the appropriate size, and intraoperative restoration of the length of the damaged segment after distal blocking. In these cases, static blocking was used, which prevented the possibility of secondary displacement of fragments along the length.

#### Results and discussion

In the postoperative period, additional plaster immobilization was not used, and active movements in the adjacent joints of the damaged segment were performed from the second day after the operation. Walking with a partial load on the injured limb was allowed from 3–5 days for diaphyseal fractures of the femur and tibia, depending on the general condition of the patients, for periarticular fractures at 4–5 weeks after X-ray control. Dynamic X-ray and clinical observation had been performed in 38 patients. Consolidation of fractures and restoration of the support function of the injured limbs had been achieved in 30 patients 6–8 months after the operation. Of this group of patients, in 18 cases, the removal of fixators had been performed 14-16 months after the operation. 20 patients with different stages of fracture consolidation are being monitored as outpatients. In 6 patients with comminuted and fragmentary fractures of the tibia, the nail had been dynamized 2-3 months after the operation by removing the static blocking screws, which can make it possible to create physiological compression in the fracture area without the risk of shortening the damaged segment. Postoperative complications had been observed in 8 (17%) patients. Suppuration of soft tissues in the area of the postoperative wound had been detected in 1 patient. In this case, it is possible to stop the infectious process without removing the metal structure. In 1 patient, after osteosynthesis

of a diaphyseal fracture of the femur, angular deformity had been detected within 7-9 degrees. In 1 patient with an injury, a fracture of the distal screws had occurred 1.5 months after osteosynthesis of diaphyseal fractures of both tibia due to repeated trauma. Broken screws had been removed. In 1 patient with a periarticular fracture of the distal humerus, a nail fracture had occurred against the background of delayed consolidation. The rod had been removed and osteosynthesis had been performed with a plate with bone grafting. In 3 cases, there had been a delayed consolidation of comminuted fractures of the tibia, in which the nail had been dynamized. In 1 patient with delayed consolidation of a fragmentary fracture of the humerus, after 3.5 months, the nail had been removed, and osteosynthesis with a locking nail with reaming of the medullary canal. Long-term results had been followed up in 39 patients within 8 to 18 months. Favorable anatomical and functional results had been

observed in 32 (68%) patients.

#### Conclusions

Our chosen tactics of blocking intramedullary osteosynthesis of diaphyseal and periarticular fractures of tubular bones without reaming the medullary canal in patients with polytrauma is a modern and low-traumatic method. Blocking metal constructions allows to create a strong stabilization in the early stages after surgery, preserve the endosteal blood supply to bone fragments and thereby create optimal conditions for reparative osteogenesis. Early painless rehabilitation (exclusion of bed rest in the postoperative period, active restoration of movements in adjacent joints, walking with a dosed load, no need for external immobilization). The usage of this treatment approach in patients with polytrauma significantly expands the capabilities of the surgeon, significantly reduce the period of disability and recovery, and often save patients' lives..

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hernias, neonatal surgery, diagnosis

# CONGENITAL DIAPHRAGMATIC HERNIA IN NEWBORNS

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## Abstract

*Congenital diaphragmatic hernia is a congenital developmental defect that can be diagnosed during the prenatal period. Diaphragmatic hernias are common diseases and, although they can often be incidental, they must be recognized as a congenital defect of the diaphragm that is dangerous for the life of the newborn. Congenital diaphragmatic hernias are characterized by traumatic tears of the herniated diaphragm (Bochdalek, Morgagni). This condition is strictly treated by surgery. In such cases, children with this disease require diagnosis and preoperative preparation according to the protocol of the Ministry of Health of the Republic of Kazakhstan for at least two days. Surgical treatment is performed after hemodynamic stabilization. During the pre- and postoperative periods, all children require active intensive therapy. This article describes the key aspects of surgical treatment. Despite the fact that congenital diaphragmatic hernia is a severe congenital defect, sometimes accompanied by the pathology of several systems or organs, the stabilization and further surgical treatment of such patients have made significant progress. Modern foreign surgery has shifted towards endoscopic surgery. The data from foreign articles and studies in the field of congenital diaphragmatic hernia allow us to expand the range of possible methods for prenatal diagnosis and treatment.*

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## Тұжырым

Көкет жарығы бұл антенатальді кезеңде анықталатын туа біткен даму ақауы. Көкет жарығы жиі кездесетін аурулар қатарына кіреді және бұл аурулар жиі кездейсоқ болғанымен, көкеттің туа біткен ақауы ретінде саналуы керек және жаңа туған нәрестенің өміріне қауіп төндіреді. Туа біткен көкет жарығы көкеттің травмалық жыртылумен сипатталады (Бохдалека, Морганья). Бұл ауру тек хирургиялық емделеді. Мұндай жағдайларда ауруға шалдыққан балаларға диагностика, ота алдындағы дайындық Қазақстан Республикасы Денсаулық сақтау министрлігінің хаттамасы бойынша кемінде екі тәулік жүргізілуі қажет. Хирургиялық ем гемодинамиканы тұрақтандырғаннан кейін жүргізіледі. Операцияға дейінгі және кейінгі кезеңде барлық балалар белсенді қарқынды терапияны қажет етеді. Бұл мақалада хирургиялық емдеудің негізгі сәттері көрсетілген. Туа біткен көкет жарығы бір ағза даму ақауы болғанымен, кейде бірнеше ағза біріктірілген патологиясы болуы мүмкін, мұндай науқастарды тұрақтандыру және одан әрі хирургиялық емдеу айтарлықтай өзгерістерге алып келеді. Көкет жарығы туа біткен ақау болуына қарамастан, кейде бұл ақауға бірнеше жүйе немесе ағзалардың туа біткен даму ақаулары қосарлануы мүмкін, науқас жағдайы тұрақтануы мен әрі қарай хирургиялық емнің біршама алға жылжуы байқалады. Заманауи шетелдік хирургия, эндоскопиялық хирургияға бет бұруда. Туа біткен көкет жарығы тақырыбындағы шетелдік мақалалар мен зерттеу деректері бізге антенатальды диагностика мен емдеудің мүмкін әдістерінің ауқымын кеңейтуге мүмкіндік береді.

## Врожденная диафрагмальная грыжа у новорожденных

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#### Аннотация

Диафрагмальная грыжа - врожденный порок развития, который диагностируются антенатальном периоде. Диафрагмальные грыжи - достаточно распространенное заболевание, и нередко являются случайной находкой, опасной для жизни новорожденного. Врожденные диафрагмальные грыжи характеризуются травматическими разрывами диафрагмы (Бохдалека, Морганьи). Данное заболевание лечится хирургическим путем. При таких случаях детям необходимо должная диагностика, предоперационная подготовка согласно протоколу Министерства Здравоохранения Республики Казахстан в течении не менее двух суток. Оперативное лечение проводится после стабилизации гемодинамики. В пред- и послеоперационном периодах все дети нуждаются в активной интенсивной терапии. В данной статье указаны ключевые моменты хирургического лечения диафрагмальных грыж. Несмотря на то, что врожденная диафрагмальная грыжа является тяжелым врожденным пороком, порой в сочетании с врожденными пороками развития других систем или органов, стабилизация и дальнейшее хирургическое лечение таких пациентов имеет значительные успехи, в частности эндоскопической хирургии. Данные зарубежных статей и исследований в области врожденной диафрагмальной грыжи позволяют нам расширить спектр возможных методов антенатальной диагностики и лечения.

Конфликт интересов:  
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Ключевые слова:  
врожденная  
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новорожденные, типы  
диафрагмальных грыж,  
неонатальная хирургия,  
диагностика

#### Relevance

Congenital diaphragmatic hernia is a condition that results from the stretching and absence of chest muscles that normally separate the abdominal and chest cavities. It causes the displacement of organs such as the stomach, spleen, intestines, and liver into the chest cavity. According to a study by Eimear Kirby in 2020, diaphragmatic hernia affects 2.3-2.8% of live newborns. This condition is common among newborns, and despite treatment, 30-70% of infants have an unfavorable prognosis and complications. The treatment of diaphragmatic hernia has developed significantly in recent years, moving from postnatal stabilization to prenatal optimizations. Congenital pathology of diaphragmatic hernia is localized and often occurs alongside other organ and system defects.

The purpose of the study: to analyze the outcomes

of surgical treatment of newborns diagnosed with a hernia of the diaphragm.

#### Materials and methods

In the neonatology and neonatal surgery department, 40 newborns with diaphragmatic hernia were treated between 2017 and 2021. Of these, 30 (75%) were boys and 10 (25%) were girls. During the antenatal period, all pregnant women underwent screening ultrasound examinations (USE). However, diaphragmatic hernia was diagnosed in 38 (95%) pregnant women. This pathology was not diagnosed in two pregnant women (5%). The time of detection of these defects coincided with the interval between 21 and 34 weeks of pregnancy. In pregnant women, congenital heart defects were detected in 8 (2%), one (2.5%) had omphalocele, and additional developmental defects were identified (Figure 1).

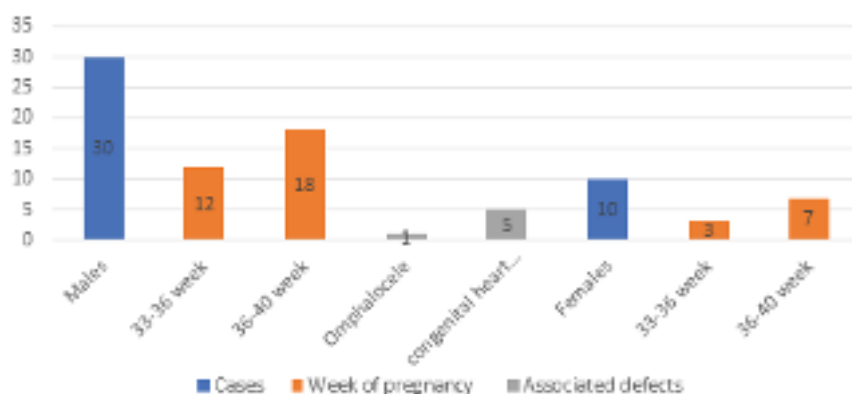


Figure 1.  
Cases and gestational age (week)

In the maternity ward, cases of newborns were evaluated, a general X-ray of the chest and abdominal cavity was performed, and 90% of infants were assisted with a mechanical ventilation machine. 10% of children were resuscitated without receiving initial care, and it should be noted that 10% of children did not become ill at all. In all cases, nasogastric tubes were installed. After stabilizing the newborns' condition, they were transferred to the neonatal surgery department of the

scientific center for pediatrics and pediatric surgery within 24 hours after birth. Chest X-rays (Figure 2.) and ultrasound examinations of the abdominal cavity, clinical and laboratory studies were conducted. Prenatal screening is the gold standard for diagnosis: most often prenatal ultrasound, chest X-ray after birth, the method of ultrasound of the thoracic and abdominal cavity, EchoCG, FEGDS, computed tomography, therapeutic bronchoscopy.



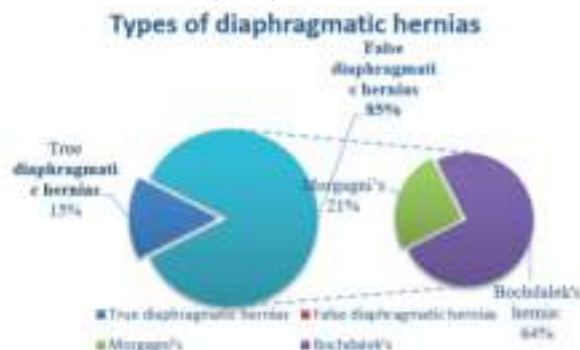
Figure 2.  
After and before X-Ray



It should be noted that of these 40 (100%) newborns, 33 children (82.5%) were treated with a diagnosis of false left-sided diaphragmatic hernia. Of these, 30 (90.9%)

were children with Bochdalek hernia. Morgagni hernia was found in 9.1% of cases (Figure 3).

Figure 3.  
Types of diaphragmatic hernias



#### Results and discussion

And the remaining 7 (17.5%) infants received treatment for true diaphragmatic hernia. Over these 5 years, no other types of diaphragmatic hernia were encountered. According to the statistics of the surgical waiting list, 7 (17.5%) children underwent thoracoscopic normalization for true diaphragmatic hernia. Of the 33 (82.5%) infants, 31 (93.9%) underwent surgery on the abdominal cavity. The remaining 2 children (6.1%) underwent thoracotomy. Of these 33 (82.5%) infants, 27 infants (81.8%) underwent diaphragm autoplasty

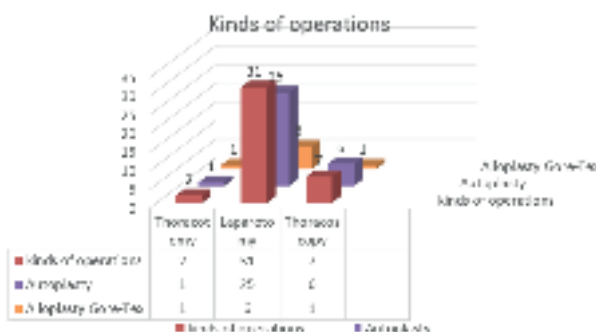
during the operation, and 6 (8.2%) infants underwent alloplasty (Figure 5) with synthetic material (Gore-Tex). In cases of double defect (omphalocele), during the operation, the omphalocele defect was introduced into the left diaphragm, an operation was performed on the diaphragm, and then the abdominal organs were placed in a Schuster bag due to incompatibility with the abdominal cavity. The second stage was performed after 7 days.

According to this 5-year statistic, 5 (12.5%) infants died in our hospital. The cause of death is often persistent pulmonary hypertension and congenital heart disease.

Figure 4.  
Intraoperation laparotomy view



Figure 5.  
Kinds of operations



Overall, this study provides valuable information on the treatment of diaphragmatic hernia in newborns and highlights the importance of prenatal screening for this condition. The findings of the study suggest that false left-sided diaphragmatic hernia is more common than true diaphragmatic hernia, and that surgery on the abdominal cavity is more frequently performed than thoracotomy. The study also highlights the importance of early diagnosis and prompt treatment in improving outcomes for newborns with diaphragmatic hernia.

#### Conclusion

Based on the information presented, it can be

concluded that there is a need to increase the level of perinatal care, particularly in the area of prenatal screening for diaphragmatic hernia. Pregnant women should be hospitalized at the 3rd or 4th degree of pregnancy to ensure early detection of any potential health issues in the fetus. In addition, the medical team should follow the protocol of the Republic of Kazakhstan to provide appropriate first aid to newborns and avoid any unfavorable conditions during transportation. These measures can help reduce the mortality rate of infants with diaphragmatic hernia and improve their chances of successful treatment.

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**Keywords:**

Stenosis of the carotid artery, extracranial carotid artery, ischemic stroke, acute disorders of cerebral circulation, diagnostics

# MODERN ORGANIZATION ASPECTS OF THE PREVENTION OF ISCHEMIC STROKE IN PATIENTS WITH EXTRACRANIAL CAROTID STENOSIS

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## Abstract

Stroke is the second leading cause of death and the third leading cause of disability globally. This literature review described risk factors and diagnostic aspects of ischemic stroke prevention. Carotid stenosis and occlusion is a treatable cause of ischemic stroke, which can be diagnosed by duplex scanning of the brachiocephalic arteries. The reasons for the low effectiveness of preventive measures for ischemic stroke are the incomplete collection of anamnesis for risk factors that affect the clinical prognosis, the low use of modern diagnostic methods by primary health care general practitioners in the screening of patients.

## Ұйқы артериясының экстракраниалды стенозы бар науқастардағы ишемиялық инсультты алдын алуды ұйымдастырудың заманауи шаралары

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## Тұжырым

Инсульт дүние жүзінде өлімнің екінші себебі және мүгедектіктің үшінші себебі болып табылады. Бұл әдебиет шолуында ишемиялық инсульттің алдын алудың қауіп факторлары мен диагностикалық аспектілері сипатталған. Ұйқы артериясының стенозы және окклюзиясы ишемиялық инсульттің емделуге болатын себебі болып табылады, оны брахиоцефалиялық артерияларды дуплексті сканерлеу арқылы анықтауға болады. Ишемиялық инсульттің алдын алу шараларының төмен тиімділігінің себептері клиникалық болжамға әсер ететін қауіп факторлары бойынша анамнездің толық жиналмауы, жалпы тәжірибелік дәрігерлердің заманауи диагностикалық әдістерді аз қолдануы болып табылады.

## Современные аспекты организации профилактики ишемического инсульта у больных с экстракраниальными стенозами сонных артерий

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## Аннотация

Инсульт является второй ведущей причиной смерти и третьей ведущей причиной инвалидности в глобальном

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Авторы заявляют об отсутствии конфликта интересов

масштабе. В данном литературном обзоре были описаны факторы риска и диагностические аспекты профилактики ишемического инсульта. Стеноз и окклюзия сонных артерий являются излечимой причиной ишемического инсульта, который может быть диагностирован с помощью дуплексного сканирования брахиоцефальных артерий. Причинами малой эффективности профилактических мер ишемического инсульта, являются не полный сбор анамнеза по факторам риска, которые влияют на клинический прогноз, низкое использование современных методов диагностики врачами общей практики ПМСП в скрининговом обследовании пациентов.

**Ключевые слова:**  
стеноз сонной артерии,  
экстракраниальный стеноз,  
ишемический инсульт,  
острые нарушения мозгового  
кровообращения, диагностика

## Introduction

Ischemic stroke is an acute cerebrovascular disorder and is leading cause of long-term disability in developed countries. Mortality from stroke ranges from 25 to 30%, and survivors remain at high risk of developing recurrent ischemic episode such as heart attack, recurrent stroke, and death [1]. Atherosclerosis is the cause of about a third of all strokes, especially the bifurcation of the common carotid artery, is the main cause of ischemic stroke, accounting for approximately 20% of all strokes; while 80% of these events may occur without prior symptoms, emphasizing the need of preventive examination in patients at risk [2]. The rate of progression of carotid stenosis is unpredictable. The disease can develop rapidly, slowly or remain stable for many years. Modern treatments aim to slow down the progression of the disease and protect the patient from the development of a stroke [3].

According to the World Health Organization (WHO), from 1990 to 2019 there were 101 million cases of stroke - this figure is called the "prevalence" of the disease in the study. At the same time, in 2019 alone, 12.2 million cases of the disease were registered, 6.55 million people died. Every year the morbidity and mortality from cardiovascular diseases is increasing rapidly [1].

There are more than 2 million people who are suffering from cardiovascular diseases (CVD) in Kazakhstan. Every year, 40,000 Kazakhstans have a stroke. Of these, 5 thousand die within 10 days after a stroke [4].

The high human and high economic costs highlight the need to reduce the burden of cardio-vascular diseases in Kazakhstan. WHO notes that the risk of developing cardiovascular diseases can be reduced by changing four behavioral risk factors (tobacco use, harmful use of alcohol, unhealthy diet and lack of physical activity), as well as metabolic risk factors such as high blood pressure or high cholesterol (WHO, 2013) [5].

Measures aimed at preventing CVD in Kazakhstan are relatively low-cost and economically beneficial. Intervention cost analyses were conducted for four prevention packages which are targeting tobacco control, the harmful use of alcohol, lack of physical activity and excess salt intake, as well as for a package of clinical interventions, for the treatment of cardiovascular disease and diabetes. Implementation costs policy packages to reduce tobacco, alcohol, salt, and increase physical activity for the period 2018-2022 are estimated at 5.0 billion tenge, 10.2 billion tenge, 4.5 billion tenge and 4.7 billion tenge, respectively. The cost of clinical interventions, aimed at the treatment of cardiovascular diseases and diabetes, were the highest, they will amount to 140.7 billion tenge [6].

Smoking is a major CVD risk factor. This is because it causes endothelial injury and dysfunction in both coronary and peripheral arteries and an increased risk of thrombosis [7]. According to the WHO Report on the Global Tobacco Epidemic, about one-fifth (22%) of the adult population in Kazakhstan currently use tobacco, and almost everyone daily (WHO, 2017d) [7].

Alcohol-related mortality in Kazakhstan is one of the highest in the European Region. In 2016, almost 74% of male deaths from cirrhosis of the liver and 34% of injuries were attributable to alcohol use for women, these indicators were 45% and 31%, respectively [8].

Physical activity levels are not monitored in Kazakhstan on an ongoing basis. IN 2010, 21% of adults did not recommendations regarding the level of physical activity; estimated by 2016 this year. More recent estimates show that the prevalence of under-reporting physical activity in 2016 was 26% (95% CI 19-34%) for men and 29% (95% CI 20-39%) for women [9].

According to the latest ranking of 187 countries, in 2010 the standardized by age, the average daily salt intake of the population in aged 20 years and older was 15 g per day in Kazakhstan (6.0 g sodium per day) [10]. In 2010, in the 20-69 age group, 32% of cardiovascular deaths were attributable to consumption of more 5 g salt per day (more than 2 g sodium per day) [11].

Elevated levels of any metabolic factor may increase the risk of cardiovascular events; the risk is exacerbated in people with multiple risk factors. In Kazakhstan in 2016, the age-standardized prevalence of overweight (BMI  $\geq 25$  kg/m<sup>2</sup>) was 54% for men and 53% for women. In addition, 19% of men and 23% of women are obese (BMI  $\geq 30$  kg/m<sup>2</sup>) [12].

According to the World Health Organization (WHO 2020), Clinical interventions for cardiovascular disease and diabetes were the most expensive, costing 140.7 billion tenge over a five-year period [13].

Recognizing the significant impact of cardiovascular disease on the health of the population and the economy of Kazakhstan, this review suggests that there is potential for further implementation of prevention measures both at the level of the entire population and at the individual level.

The reasons for the low efficiency of the existing system of stroke prevention are associated with ideological, organizational and technological problems. Among them, the most significant are: the inconsistency of the concept of risk factors for assessing an individual prognosis, the lack of organizational solutions that allow qualified screening of the population to detect cerebrovascular pathology, the insufficient use of new diagnostic methods by general practitioners in screening patients, as well as the rigidity of thinking of some doctors, considering invasive surgery as a cause of disability. The identification of patients with carotid stenosis has crucial role in the prevention of ischemic stroke. Safe and informative methods of ultrasound diagnostics characterized the brain vessels conditions, it also timely detected danger of atherosclerotic plaques, critical narrowing of the arteries which can lead to ischemic stroke.

### *Extracranial carotid artery diseases state*

Carotid disease studies have historically classified patients into two groups: symptomatic (patients who have had a stroke, transient ischemic attack (TIA), or fugax amaurosis due to cerebral ischemia) and asymptomatic (no neurological events but only clinical signs of atherosclerosis).

With asymptomatic carotid stenosis, the risk of stroke



in the next year increases by more than 3% (the relative risk increases by more than 50%) [14]. According to most studies, the risk of ipsilateral stroke increases with increasing degree of stenosis: less than 1% per year with stenosis; less than 50% - from 1% to 5% per year with stenosis of more than 50% [15, 16].

In symptomatic patients, there is a clear correlation between the degree of stenosis and the risk of stroke. According to NASCET (North American Symptomatic Carotid Endarterectomy Trial), the incidence of stroke after 18 months of medical therapy without revascularization was 19% in patients with 70–79% stenosis, 28% in patients with 80–89% stenosis, and 33% in patients with 70–70% stenosis, 79% patients with 90–99% stenosis [17]. This correlation is less clear in asymptomatic patients. In the ACAS and ACST study, asymptomatic patients with 60–80% stenosis had a higher incidence of stroke than patients [18]. The annual incidence of stroke in asymptomatic individuals with carotid stenosis of more than 60% receiving drug treatment is 2.5% [19].

Two mechanisms contribute to the high risk of stroke in carotid stenosis: hypoperfusion and arterial embolism. The main difference between symptomatic and asymptomatic stenosis, perioperative risk and patient life expectancy is determined by therapy [20]. Stroke associated with atherosclerotic lesions of the extracranial carotid arteries can occur through several mechanisms [22]: atheroembolism of cholesterol crystals; arterial embolism; structural disintegration of the wall (dissection); acute thrombotic occlusion; decreased cerebral perfusion with plaque growth.

Worldwide, cerebrovascular disease accounts for more than five million deaths per year (1 in 10) and approximately 3% of total health care spending. In 2003, about 21 billion euros were spent in the European Union on the treatment of cerebral ischemia. From 2005 to 2050, the estimated cost of a stroke to the US economy is \$2.2 trillion. In the face of a global health problem, with significant associated costs, advances in stroke prevention and its consequences are needed [22].

Screening for asymptomatic carotid stenosis:

A. Screening of symptomatic patients;

B. Potential "high risk groups" who may benefit from screening for asymptomatic stenosis.

To choose the imaging techniques to evaluate carotid arteries: duplex ultrasound examination of the carotid arteries; magnetic resonance imaging and angiography; computed tomography angiography; catheter digital subtraction arteriography [23].

Carotid ultrasound is widely available and is associated with little risk and discomfort. Medical and economic studies have not shown the feasibility of mass screening of the adult population using ultrasound duplex scanning. However, there is evidence of the advisability of screening in risk groups for prophylactic surgical treatment in order to reduce the incidence of strokes, total population screening for asymptomatic carotid stenosis not recommended due to lack of cost-effectiveness, as well as the potentially harmful effects of false positive and false negative results in the general population, and the small absolute benefit of various types of invasive interventions [24]. They recommend to screening the adults over 65 who have three or more risk factors for cardiovascular disease, and screen asymptomatic patients with carotid murmur who are potential candidates for carotid revascularization and

screen those who are scheduled for coronary bypass surgery. However, many authors suggest that screening for CS among high-risk individuals will allow timely drug therapy to prevent stroke and cardiovascular events [25].

*Management of patients with extracranial stenosis of the carotid arteries at the level of primary health care and hospital*

Management of patients with atherosclerotic carotid stenosis should include both consistent modification of risk factors, including lifestyle changes (smoking cessation, healthy, balanced nutrition, exercise), and, in the presence of arterial hypertension and / or diabetes mellitus, treatment in accordance with the principles. The recommended medication is 100 mg aspirin daily for asymptomatic stenosis and 100 mg aspirin or 75 mg clopidogrel for symptomatic stenosis. Statins should be taken for long-term prevention of cardiovascular disease. Current guidelines recommend lowering LDL cholesterol to < 70 mg% or < 50 mg% in patients at high risk for atherosclerosis [26]. Currently, the aim of medical treatment of symptomatic extracranial stenosis of the internal carotid artery is to reduce the likelihood of further embolic events originating from the plaque of the internal carotid artery. Medical management aims to prevent further events until carotid disease is healed and, secondly, to manage the risk factors that are common to cardiac atherosclerotic disease, thus reducing the risk of future ischemic events. A 2016 meta-analysis showed that early initiation of acetylsalicylic acid monotherapy after TIA or ischemic stroke reduced the rate of subsequent events by 60% [27].

"Surgery" includes carotid endarterectomy and carotid stenting. Decades ago, intervention for secondary prevention after extracranial embolic stroke from the internal carotid artery was delayed by 4–8 weeks to allow the brain to "recover". This was done in the hope of avoiding the consequences of early reperfusion such as cerebral edema and hemorrhage. However, excessive delay in intervention resulted in an excessively high number of recurrent strokes [28]. Large-scale randomized prospective multicenter studies in America and Europe (NASCET, ECST, ACAS) have proven the advantages and high efficiency of surgical treatment of patients with symptomatic and asymptomatic disease with severe ICA stenosis compared with conservative therapy. The results of these studies have made carotid endarterectomy the procedure of choice, subject to standards developed by the Stroke Council and American Heart Association in 1989 [29]. New Canadian guidelines recommend intervention on the carotid arteries during the first few days after a non-disabling stroke or TIA. Dual antiplatelet therapy is warranted immediately but should be limited to a short period (less than 21 days) due to the risk of bleeding. Statin therapy should be considered as secondary prevention; however, its benefit in reducing early relapses is not clear [30].

#### Conclusion

Screening for carotid stenosis being costly for routine carotid ultrasound in the population remains controversial. At the same time, it must be recognized that ultrasound is important not only for everyday clinical conditions, but also for the introduction of patients with acute ischemic stroke. Visual assessment and dynamic changes using carotid ultrasound can provide valuable information for primary health care. This strengthens the interaction between the hospital and primary health care.

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The authors declare that they

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pancreas, Atlant classification

# MODERN METHODS OF DIAGNOSIS AND TREATMENT OF ACUTE PANCREATITIS. LITERATURE REVIEW

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## Abstract

**Purpose.** Differentiation of modern methods of diagnosis and treatment of acute pancreatitis in clinical practice.

A literature review of foreign randomized clinical trials and meta-analysis, international clinical recommendations of the PubMed electronic database for the period from 2002 to 2022 was conducted. 28 relevant articles on the topic of the review were selected from them.

**Conclusions.** Thus, using one method or one scale, it is impossible to predict the severity of acute pancreatitis in the first hospitalization hours. This days the treatment of acute pancreatitis is based on the latest international recommendations developed by the International Association of Pancreatology (IAP) and the American Pancreatic Association (APA). According to this guide, we believe that acute pancreatitis needs to be diagnosed and treated, also there is a need a number of randomized large-scale surgical trials of acute pancreatitis which have to be conducted.

## Жедел панкреатиттің диагностикасы мен емінің заманауи әдістері. Әдебиет шолуы

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## Тұжырым

**Мақсаты.** Клиникалық тәжірибеде жедел панкреатиттің диагностикасы мен емінің заманауи әдістерін саралау.

2002-2022 жылдар аралығындағы PubMed электрондық дерекқорының шетелдік рандомизацияланған клиникалық зерттеулері мен мета-талдауларына, халықаралық клиникалық ұсыныстарына әдебиет шолуы жүргізілді. Олардың ішінен шолу тақырыбына арналған 28 өзекті мақала таңдалды.

**Қорытынды.** Осылайша, бір әдісті немесе бір шкаланы қолдана отырып, ауруханаға түскен алғашқы сағаттарда жедел панкреатиттің ауырлығын болжау мүмкін емес. Бүгінгі күнге дейін жедел панкреатитті емдеу Халықаралық панкреатология қауымдастығы (IAP) және Американдық ұйқы безі қауымдастығы (APA) әзірлеген соңғы халықаралық нұсқауларға негізделген. Осы нұсқаулықтың

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мәлімдейді

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жедел панкреатит,

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классификациясы

негізінде жедел панкреатитті диагностикалау, ем жүргізу қажет және әлі де жедел панкреатиттің хирургиялық емінде бірқатар рандомизацияланған ауқымды зерттеулер керек деп есептейміз.

## Современные методы диагностики и лечения острого панкреатита. Обзор литературы

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### Аннотация

**Цель исследования** - дифференциация современных методов диагностики и лечения острого панкреатита в клинической практике.

Был проведен литературный обзор зарубежных рандомизированных клинических исследований и метаанализа, международных клинических рекомендаций электронной базы данных PubMed за период с 2002 по 2022 год. Из них отобраны 12 актуальных статей, посвященных теме обзора.

**Заключение.** Таким образом, с помощью одного метода или одной шкалы невозможно предсказать тяжесть острого панкреатита в первые часы госпитализации. На сегодняшний день Лечение острого панкреатита основано на последних международных рекомендациях, разработанных международной ассоциацией панкреатологии (IAP) и Американской ассоциацией поджелудочной железы (APA). На основании этого руководства мы считаем, что необходимо диагностировать острый панкреатит, провести лечение и еще предстоит провести ряд рандомизированных крупномасштабных исследований хирургического лечения острого панкреатита.

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**Ключевые слова:** острый панкреатит, панкреонекроз, поджелудочная железа, классификация Атланти

### Relevance

Acute pancreatitis is a polyetiological is demarcation type acute aseptic inflammation of the pancreas based on pancreatic necrobiosis and enzyme autoaggression, necrosis and dystrophy of the gland with the addition of a secondary purulent infection. About 20-30% of patients suffer from a severe form of acute pancreatitis, and the mortality rate in the hospital is 15% [4]. Among the causes of high mortality, one of the most important places is occupied by late diagnosis of destructive forms and various complications of the disease, an insufficient choice of conservative and surgical tactics. The solution to these problems can be achieved by examining the patient, collecting a detailed anamnesis

and the ability to make the correct diagnosis of the disease by providing first aid and sending the patient to a surgical hospital. Most of the generally accepted methods of treatment are aimed at eliminating the complications of the disease, among which are such common methods of treatment as organ failure and infection. Here we will consider in practice the modern therapy of acute pancreatitis, emphasize the importance of diagnostics in determining the etiology and identifying complications that have a sharp impact on the body and during control.

About 140 causes of acute pancreatitis are known. Of these, the most basic features are shown in table 1 below [5].

Etiological factors	Explanation
I. Disorders of the biliary tract	1. Gallstone diseases
II. Toxic condition	1. Alcohol

Table 1. The most common causes of acute pancreatitis [4]

The most widely used classification system for acute pancreatitis is based on international consensus Atlanta classification, which is considered and revised in 2012. [4]. Based on this classification, it was achieved to characterize the standardized clinical and X-ray nomenclature of acute pancreatitis and associated complications, based on the scientific

advances achieved over the past two decades. Thus, the use of the terms "acute pseudocyst" and "pancreatic abscess" is currently not recommended. Instead, the four classification types are determined based on the presence of pancreonecrosis and the time elapsed since the onset of pancreatitis [4].

According to the Atlantic classification (2012),



at least two of the following three symptoms are required to diagnose acute pancreatitis: abdominal pain (constant, severe pain in the epigastric region, transmission to the back, with a very acute onset); serum lipase (amylase) values must be at least 3 times higher than the normal upper limit; detection of the characteristic symptoms of acute pancreatitis in contrast-enhanced CT or, more rarely, magnetic resonance imaging (MRI) or transabdominal ultrasound.

In the Atlantic classification, the following morphological types of acute pancreatitis are distinguished:

- interstitial edema pancreatitis
- necrotic pancreatitis, which in turn is divided into several types: parenchymal necrosis of the pancreas, peripancreatic necrosis, parenchymal pancreatic necrosis (the most common) combined with peripancreatic necrosis.

According to the 2014 classification proposed by V.S. Savelyeva, there are three main forms of acute pancreatitis [5]:

- I. Edematous pancreatitis;

II. Sterile pancreatic necrosis: - by prevalence: limited and spreading;

- depending on the type of lesion: fatty, hemorrhagic, combined.

III. Infected pancreatic necrosis

To determine the severity of the process, it is necessary to take into account the presence of local and general complications (Table 3). Local complications: peripancreatic accumulation of septic phlegmon; pancreatic pseudocyst; acute pancreatitis and limited necrosis; fibrosic-purulent peritonitis (local inflammation); gastric evacuation disorders, thrombosis of the spleen and portal veins and necrosis of the large intestine; formation of internal and external pancreatic, gastric and intestinal Eels; arrosive bleeding.

Common complications are transient (can be detected within 48 hours) or chronic. To determine polyorgan insufficiency, three organ systems must be evaluated: respiratory, cardiovascular and renal. For this purpose, a modified Marshall scale [4] is used (Table 2). If there are 2 or more points on this scale-it means that there is organ failure.

Table 2. Modified Marshall assessment system to assess organ dysfunction [4]

Organ system	Score				
	0	1	2	3	4
Respiratory (PaO <sub>2</sub> /FIO <sub>2</sub> )	>400	301-400	201-300	101-200	<=101
Renal (serum creatinine, mg/dL)	<1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
Cardiovascular (systolic blood pressure, mmHg)	>90	<90	<90	<90	<90

By clinical picture and severity:

Acute mild pancreatitis has a rapid positive effect with the effect of infusion therapy, usually within 3-7 days. There is no need for resuscitation measures and surgical treatment. Frequency-80-85%. Morphologically, interstitial edema corresponds to pancreatitis, microscopic necrosis of the parenchyma is rare detected (Table 3).

Acute pancreatitis of moderate severity is characterized by transient polyorgan dysfunction,

which can be stopped within 48 hours with appropriate infusion therapy. Morphologically, there is a necrosis of peripancreatic tissues of different distribution and location.

Severe acute pancreatitis is accompanied by persistent or progressive polyorgan dysfunction, which is not stopped by infusion therapy for more than 48 hours. Morphologically, necrosis of the pancreatic parenchyma and the appearance of other local complications of acute pancreatitis. Severe pancreatitis occurs in about 15-20% of patients [4].

Table 3. The main complications of acute pancreatitis (Banks P.A. Classification of acute pancreatitis—2012 y. [4])

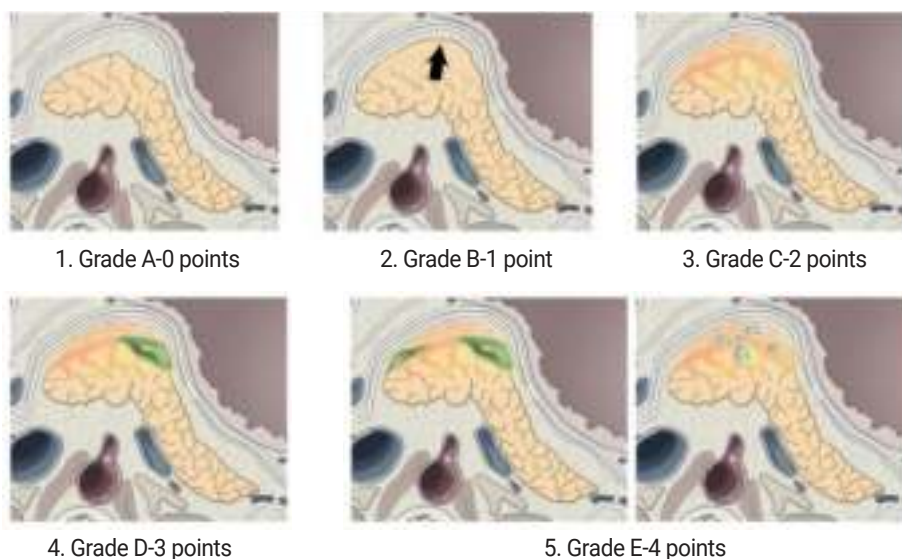
Local complications of acute pancreatitis	Non-pancreatic manifestations and systemic complications
<ol style="list-style-type: none"> <li>1. Accumulation of acute fluid in the abdominal cavity</li> <li>2. Acute pancreatitis - sterile/infective</li> <li>3. Acute peripancreonecrosis - sterile/infective</li> <li>4. Acute extrapancreonecrosis - sterile/infective</li> <li>5. Pancreatic pseudocyst - sterile/infective</li> </ol>	<ol style="list-style-type: none"> <li>1. Cholecystolithiasis</li> <li>2. Choledocholithiasis</li> <li>3. Expansion of the bile ducts outside the liver</li> <li>4. Thrombosis of the portal vein</li> <li>5. Varicose veins of the esophageal and gastric veins</li> <li>6. Arterial pseudoaneurysm</li> <li>7. Hydrothorax</li> <li>8. Ascites</li> <li>9. Spread of inflammation to the stomach, duodenum, colon, kidneys</li> <li>10. Necrosis of the colon wall</li> </ol>

Balthazar E.J. and other authors proposed [6] a complex CT severity index (CT Severity Index-CTSI) to assess the severity of pancreatic parenchymal necrosis (score from 0 to 6) and extraglandular inflammatory process (Grade A – E, Score 0-4) (Figure 1, 2). Determines the clinical severity, complications

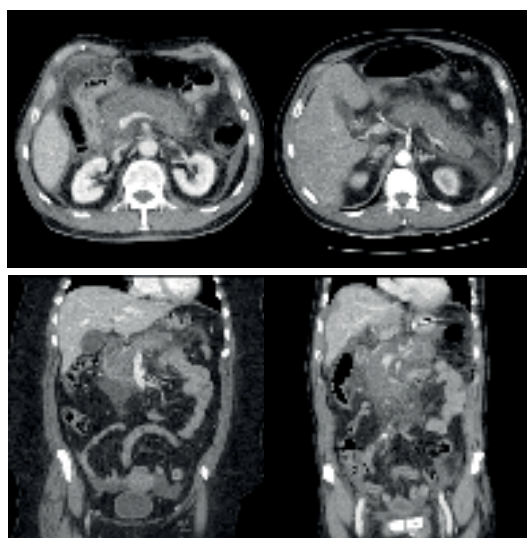
and mortality rate through a CT range of 0 to 10 (Table 4). Patients with CTSI from 0 to 1 do not have mortality and complications, while patients with index 2 have 4% of cases of complications, and with index 7-10, 17% of deaths occur and 92% of cases develop complications [6].

<p><i>Degree A.</i> Normal type of pancreas-0 points (Figure 1)  <i>Degree B.</i> Increase in pancreatic Volume - 1 point  <i>Degree C.</i> Signs of inflammation in the area of the pancreatic parenchyma-2 points  <i>Degree D.</i> Enlargement of the pancreas and the presence of fluid in the anterior paranephral space-3 points  <i>Degree E.</i> Fluid retention in at least 2 areas-4 points</p>	<p><i>According to the indicators of the prevalence of necrosis:</i>                  Damage to &lt;30% of the pancreatic parenchyma — 2 points                  Damage to the parenchyma of the pancreas in the range of 30-50% - 4 points                  Damage to the parenchyma of the pancreas &gt;more than 50% - 6 points</p>
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**Table 4.** Balthazar E.J. the main criteria for the severity of acute pancreatitis on the scale in CT [6]



**Figure 1.** Balthazar E.J. assessment of acute pancreatitis on the scale [6]



**Figure 2.** Patient A., 60 years old, as a result, due to the development of acute pancreatitis in the pancreas, which coincides with tomographic signs of necrosis of Grade E on the Balthazar scale

There are various clinical and scoring acute pancreatitis severity determination systems have been developed, such as Ranson, BISAP, APACHE II, etc. for assess the severity of the disease and identify the patients who requiring intensive care or aggressive treatment [7, 8].

The most common for an objective assessment of the severity of patients with acute pancreatitis is the Ranson scale (Table 5), proposed in 1974 [7]. It includes 11 criteria that are evaluated during the patient's admission and within the first 48 hours after the onset of the disease.

At the reception	After 48 hours
<ol style="list-style-type: none"> <li>1. Age &gt;55 years</li> <li>2. Leukocytosis &gt;16,000/ml</li> <li>3. Glucose level &gt;11.1 mmol/l</li> <li>4. LDG &gt;350 ED/l</li> <li>5. AST &gt;250 ED l</li> </ol>	<ol style="list-style-type: none"> <li>1. HT reduction &gt;10%</li> <li>2. Urea level rise &gt;1.8 mmol/l</li> <li>3. Plasma calcium level &lt;2 mmol/l</li> <li>4. PaO<sub>2</sub> &lt;60 mm Hg</li> <li>5. BE &gt; 4 mmol/l</li> <li>6. Estimated sequester of liquid &gt;6 L</li> </ol>

**Table 5.** Prognostic criteria for acute pancreatitis on the Ranson scale [7]

The presence of each sign is estimated at 1 point, the absence – at 0 points. The prognostic value of the Ranson scale is as follows: with a score of 2 or less, the mortality rate is less than 1% (mild severity of pancreatitis), from 3 to 5 points-the mortality rate is up to 15% (moderate severity of pancreatitis), from 6 to 8 points - the mortality rate is up to 40% and from 9 or higher – the mortality rate is up to 100% (6 or more points-severe pancreatitis).

In 2008 Wu B.U. et al. proposed a new predictive assessment system for early determination of the

severity of acute pancreatitis, which they called BISAP (Bedside Seex of Severity in Acute Pancreatitis-an indicator of the severity index of acute pancreatitis) [8]. If one of the listed criteria is present, one point is awarded. Based on the studies carried out, it can be concluded that using the BISAP scale (Table 6, 7), even before the onset of complications on the first day of the patient's stay in the hospital, it is possible to identify a group at high risk. The BISAP scale more accurately predicts organ failure at an early stage of the disease, which increases the advantage of this scoring system [8, 9].

**Table 6.**  
Criteria for early detection of acute pancreatitis on the BISAP scale [8]

Clinical signs	Point
Blood urea nitrogen (BUN) >25 mg/dl	1
Impairment of status	1
Systemic inflammatory response syndrome (SIRS)	1
Age >60 years	1
Presence of a pleural effusion	1

3 points correspond to 5-8% of mortality, 5 points or higher correspond to 25% of mortality.

**Table 7.**  
Criteria for the severity of acute pancreatitis [8]

Mild pancreatitis	Severe pancreatitis
Minimal functional disorders and absence of serious complications	Polyorgan deficiency and local complications
By relieving symptoms and normalizing indications, there is a rapid clinical effect of conservative therapy;	<ol style="list-style-type: none"> <li>9 points or higher on the APACHE – II scale or shock.</li> <li>Respiratory failure (<math>PaO_2 &lt; 60</math> mm Hg)</li> <li>Renal failure (creatinine level above <math>&gt;177</math> mmol/l)</li> <li>Gastrointestinal bleeding (more than <math>&gt; 500</math> ml/day)</li> <li>Coagulopathy (PLT level <math>&lt;100 - 109</math>/l, fibrinogen <math>&lt;1.0</math> g/l)</li> <li>Metabolic disorders (hypocalcemia <math>&lt;1.87</math> mmol/l)</li> </ol>

To date, the treatment of acute pancreatitis is based on the latest international guidelines developed by the International Association of pancreatology (IAP) and the American pancreatic Association (APA). Modern recommendations provide for the use of evidence-based medicine-based methods in the treatment of acute pancreatitis [10].

The main diagnostic criteria for acute pancreatitis [11]: pain; vomiting; flatulence (Mondor triad); subfebrile body temperature; cyanosis of the face and limbs.

Cyanosis in the form of purple spots on the face is called Mondor's symptom, cyanosis spots on the lateral walls of the abdomen ("pericoplastic ecchymoses") - Gray-Turner symptom, pericoplastic cyanosis - known as Grunwald symptom [12]. The presence of hyperesthesia of the skin in the area of the navel and the parotid area on the left at the level of ThVIII-IX is a symptom of Makhov and Kach.

The diagnostic algorithm for acute pancreatitis consists of a step-by-step approach. The first stage is the initial diagnosis at the reception, the second is the enzymatic-reactive phase of pancreatitis-the first two weeks of the disease, the third stage is the stage of infective pancreatitis.

At the first stage of diagnostics at the reception, the main task is to be able to carry out differential diagnostics with urgent surgical pathology of the abdominal cavity [12]. Comprehensive diagnostics is carried out with a thorough analysis of the cause, history of the disease, clinical-laboratory and instrumental methods (ultrasound examination, laparocentesis, videolaparoscopy). Clinical leading signs of acute pancreatitis are characterized by

acute onset, pronounced pain in the upper half of the abdomen, irrationality, nausea, vomiting that does not bring relief, dry mouth, thirst, and a brownish coating on the tongue [11].

A laboratory sign of acute pancreatitis is hyperfermentemia (usually serum amylase and urine diastase are examined). Normal indicators of the level of amylase in the blood in the apparent clinic of pancreatitis and hypoamylasemia indicate a violation of the pancreas and loss of its excretory function. It has been found that with acute pancreatitis, the concentration of trypsinogen-2 in the urine increases. Determining the level of this protein in the urine is a more reliable test than a diastasis test. Trypsinogen-2 levels increase rapidly and increase for several days or even weeks after the seizure, and amylase concentration decreases after 1-3 days [11].

Ultrasound examination is one of the informative methods of instrumental diagnostics. In acute pancreatitis with ultrasound, you can see an increase in the volume of the pancreas, infiltration of surrounding tissues, accumulation of fluid around the gland, in the fatty sac. The main difficulties in conducting ultrasound in acute pancreatitis are associated with intestinal pneumatosis, difficulties in scanning with pronounced obesity. When conducting an ultrasound examination, the following parameters are assessed: the shape, dimensions, contours, structure and echogenicity of the pancreas, the quality of visualization of the pancreatic duct and its diameter, the presence or absence of focal changes in the gland, the condition of the gland and tissues around the pancreas, as well as the presence or

absence of fluid in the abdominal cavity [12, 13].

The main changes that can be detected on ultrasound are as follows: increase in the size of the pancreas in 88% of cases (normal size of the pancreas: head 3-4. 5 cm; body 2.5-3 cm; tail 3-4 cm); blur of contours-in 90.6% of cases; exceeding 3 mm of distance

between the posterior wall of the stomach and the anterior surface of the pancreas and reaching 10-20 mm, which characterizes the edema of parapancreatic tissues in 53% of cases; changes in the echogenicity of the gland (Figure 3-4): increase - in 85.6% of cases; (normal - in 8.6% of cases) decrease-in 5.8% of cases [14].



**Figure 3.** Acute pancreatitis, destructive type. An increase in the volume of the pancreas, blurring of the contours, an increase in the distance between the stomach and the back wall of the pancreas are detected

**Figure 4.** Acute pancreatitis, increased echogenicity of the pancreas (compared to echogenicity of the liver)

So, in the 70s of the last century, methods of treating acute pancreatitis with hypothermia, peridural anesthesia, forced diuresis were introduced into practice [15]. Knowledge has been accumulated about the enzymatic-toxic pathogenesis of acute pancreatitis, extracorporeal detoxification methods have been actively introduced into clinical practice: hemosorption [16], lymphosorption [17] or a combination of them. Intravenous anti-enzyme therapy with drugs trasilol, kontrikal, gordox, etc. they began to replace intra-arterial, including local and intrauterine administration [18]. Considering the connection of acute pancreatitis with arterial hypoxemia and respiratory insufficiency, many authors recommended including hyperbaric oxygen saturation procedures daily in the complex of therapeutic measures, and in more severe cases - twice a day [19].

In the 80s, a fundamentally new method of treating acute pancreatitis was developed with 5-fluorouracil and fluorofur, which were administered intravenously, endolymphatically, intraductally and topically [20].

Treatment of acute pancreatitis should be general pathogenetic, according to the accepted classification, it should also begin with complex conservative therapy, and the following basic principles: elimination and prevention of hypertension in the bile and pancreas, suppression of secretion of the pancreas, stomach and duodenum, elimination and reduction of enzyme toxemia, elimination of hypovolemia, prevention of water-electrolyte and protein disorders, analgesic therapy, the fight against intestinal paresis. The severity of acute interstitial (edema) pancreatitis allows patients to be admitted to the surgical department for treatment, while treatment with pancreonecrosis should be carried out only in the intensive care unit and intensive care unit [10].

Relief of pain syndrome in many patients can be achieved with the use of analgesics, antispasmodics,

a glucose-novocaine mixture. In the absence of an analgesic effect, it is necessary to resort to injections of narcotic analgesics, the performance of various novocaine blockages (round liver ligament, etc.), although preference is given to peridural anesthesia, including the fight against intestinal paresis [21].

Detoxification methods (forceful diuresis), including extracorporeal (plasmapheresis, blood ultrafiltration, hemosorption, lymphosorption) and enterosorption are only used for subtotal pancreonecrosis or in severe cases of patients infected with pancreonecrosis, bacterial peritonitis or septic phlegmon [16, 17].

In case of edematous pancreatitis, antibacterial prophylaxis is not indicated, and for pancreatitis it is necessary. In addition, it is difficult to strictly distinguish between the therapeutic or prophylactic purpose of prescribing antibiotics. Of course, one point should be taken into account: when empirically choosing antibiotics, their selective penetration into the pancreatic tissue and the spectrum of their action should spread to Gram-negative and Gram-positive aerobic and anaerobic bacteria. In this regard, carbapenems, fluoroquinolones (especially Pefloxacin)+metronidazole, Generation III-IV cephalosporins, penicillins with a  $\beta$ -lactam ring (piperacillin/ tazobactam, ticarcillin/clavulanate) are considered the drugs of choice today [22].

The use and effectiveness of preventive antibiotic therapy in acute pancreatitis has long been disputed. Although early studies have shown that the administration of antibiotics can prevent infectious complications in patients with sterile necrosis [22], subsequent studies have not revealed benefits. Thus, recent data have shown that the preventive use of antibiotics in patients with acute pancreatitis is less associated with a significant reduction in mortality or morbidity [23]. Thus, conventional prophylactic antibiotics are not



recommended for all patients with acute pancreatitis [3].

Aminoglycoside antibiotics (for example, gentamicin and tobramycin) do not enter the pancreatic parenchyma in standard intravenous doses. Acyl-ureidopenicillins and cephalosporins penetrate into pancreatic tissues and are effective against gram-negative microorganisms [24]. Ciprofloxacin, moxifloxacin and carbapenems penetrate the pancreatic tissue well, however, due to the high level of tolerance to quinolones worldwide, the use of quinolones should be limited as much as possible and used in patients with allergies to antibiotic drugs with a  $\beta$ -lactam ring [25].

Metronidazole, which has a bactericidal spectrum directed only against anaerobes, also penetrates well into the pancreas. The pathogenesis of secondary bacterial infection of the pancreas is still being discussed. Pathogens can enter the pancreas hematogenously, through the biliary system, from the duodenum through the main pancreatic duct, or through transmural migration of the large intestine through the translocation of colon bacteria [26]. Most of the causative agents of pancreatic infection are Gram-negative bacteria of the gastrointestinal tract (*Escherichia coli*, *Proteus*, *Klebsiella pneumoniae*), which are caused by a violation of the intestinal flora and damage to the intestinal mucosa. Fungal infection is a serious complication of acute pancreatitis, accompanied by morbidity and mortality [27]. *Candida albicans* is the most common organism, followed by *Candida tropicalis* and *Candida krusei*. Although fungal infections that complicate acute pancreatitis usually occur in proportion to the degree of pancreatic necrosis, there is not enough data to support the prevention of fungal infections, so it is not recommended. The expediency of introducing antifungal drugs (fluconazole, etc.) into complex treatment 7-10 days after the start of antibacterial therapy is beyond doubt [22].

The introduction of a nasogastric probe and its regular aspiration for at least 2-3 days in order to create functional rest of the pancreas, stomach and duodenum 12, the same period is prescribed to the diet №0, the epigastric region is provided with an ice [15, 20]. Enteral nutrition maintains the barrier of the intestinal mucosa, prevents destruction and prevents the movement of bacteria that cause pancreatic necrosis. Compared to parenteral nutrition in general, enteral nutrition reduces infectious complications, organ failure, and mortality [28].

The list of absolutely useless drugs in the treatment of acute pancreatitis can be found in the latest international guidelines developed by the International Association of pancreatology (IAP) and the American pancreatic Association [10].

They are: atropine, protease inhibitors (aprotinin, cordox, kontrikal); antisecretory drugs, (octreotide); anti-inflammatory drugs; glucocorticoids; antioxidants, etc.

In accordance with the indicated recommendations of the above organization [10], procedures that lead to a deterioration in the patient's condition in acute pancreatitis: starvation, gastric lavage with cold water, plasmapheresis.

On June 3, 2019, the World Society of Emergency Surgery published guidelines for the treatment of patients with severe acute pancreatitis [29]. Based on the instructions, all patients with severe acute pancreatitis should undergo contrast CT or MRI. It is stated that 72-96

hours after the appearance of clinical manifestations is the optimal time to conduct CT with contrast.

Also known as: as laboratory parameters: that the limit values of serum amylase and lipase usually increase by 3 times the upper limit of the norm; that the level of C-reactive protein  $\geq 150$  mg/L on the 3rd day of the disease can be used as a predictive factor for severe acute pancreatitis; hematocrit  $>44\%$  is an independent risk factor for pancreatitis and urea level  $> 20$  mg/l is an independent predictive factor for death; procalcitonin is the most sensitive laboratory test to detect pancreatic infection and the fact that low serum levels are a strong negative predictive sign of infected necrosis; it has been shown that mortality decreases when surgical interventions are postponed for more than 4 weeks after the onset of the disease [29].

In the first 12-24 hours, aggressive infusion therapy reliably reduces mortality. Infusion therapy with maximum effect in the first 12-24 hours of the disease, however, less active infusion therapy is used in patients with heart, kidney failure or ARDS [10].

In acute pancreatitis, the prophylactic use of antibiotics is not recommended to prevent infectious complications. Due to the fact that more than 24 hours after the onset of the disease, almost 60% of patients are admitted to the hospital, conservative treatment they can be considered conditionally late, so it should begin with the first hour of hospitalization and be carried out in parallel with the examination carried out [11].

In the journal *Gastroenterology* on February 04, 2018, the American Gastroenterological Association's guidelines for the initial treatment of patients with acute pancreatitis were published [31]. The instructions recommend the use of targeted infusion therapy for patients with acute pancreatitis. Targeted infusion therapy is defined as titration of intravenous solutions for specific clinical and biochemical perfusion purposes (e.g. heart rate, mean blood pressure, CVD, diuresis, blood urea concentration and hematocrit). The American Gastroenterological Association does not advise whether salt or Ringer's solution should be used. The use of hydroxyethylcrachmal solutions in patients with acute pancreatitis is not recommended and there is no need for prophylactic use of antibiotics in patients with suspected severe acute pancreatitis and necrotic pancreatitis [31]. In patients with predictive severe acute pancreatitis or necrotic pancreatitis requiring enteral tube feeding, a nasogastric or nasojejunal tube is recommended [31].

Acute ERHPG ( $<24$  hours) is required in patients with acute cholangitis. Currently, there is no evidence of optimal timing of ERHPG in patients with biliary pancreatitis without cholangitis [10].

There are many surgical interventions used in the treatment of acute pancreatitis: laparoscopic abdominal drainage and sanation; omentobursopancreatostomy; pancreatic resection; pancreatectomy; pancreatonecrosequestrectomy; pancreatic cryodestruction; drainage of purulent foci, laparotomy, etc.

Pancreatic (enzymatic, non-bacterial) peritonitis is the main indication for laparoscopic sanation and abdominal drainage [32]. The use of minimally invasive (endoscopic) methods for drainage, sanation and necrectomy is recommended [10, 29]. As a rule, Patients with clinical manifestations of septic complications are operated on an average of 14 days

before the onset of the disease, which coincides with the development of complications after necrosis. Ideally, the intervention should be delayed as much as possible (usually 4 weeks), as this reduces complications[10]. In the case of surgical decompression, the retroperitoneal space must be maintained to reduce the risk of infecting the pancreas and peripancreatic space.

#### Conclusion

Based on the study, we came to the conclusion that using one method or one scale is inaccurate to

predict the severity of acute pancreatitis in the first hours of hospitalization. To date, the treatment of acute pancreatitis is based on the latest international guidelines developed by the International Association of Pancreatology and the American pancreatic Association. Based on this guide, we believe that it is necessary to diagnose acute pancreatitis, conduct treatment, and there is a still need a number of randomized large-scale surgical trials of acute pancreatitis which have to be conducted.

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## DRUG-INDUCED AUTOIMMUNE HEPATITIS: SYSTEMATIC REVIEW AND CASE STUDY

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### Abstract

Drug-induced liver injury (DILI) is one of the types of adverse reactions to drugs that occur as a result of their hepatotoxic effect. The pathogenesis of drug-induced autoimmune hepatitis (LIAH) is based on the production of autoantibodies to neoantigens, which are proteins of the cytochrome P450 system, which are the result of the reaction of drug metabolites. A clinically relevant problem, such as drug-induced liver damage, affects 1-1.5 million patients almost every year. The annual incidence of DILI ranges from 2.3-13.9 per 100,000 population in population studies from Europe. The Icelandic population study recorded the highest rates of 19.1 per 100,000 population per year. And in the only study based on the US population, it was found that DILI is approximately 3 per 100,000 population. Acute hepatitis is currently a well-known manifestation, and accounts for more than 90% of liver damage caused by medications. According to studies, 2.9 - 8.8% of DILI and 2 - 18% of AIH are associated with drug-induced autoimmune hepatitis. The incidence of drug-induced liver damage with the presence of antibodies (antibodies to nuclear antigen, smooth muscle and soluble liver antigen) to AIH is 83% for nitrofurantoin, 74% for minocycline, 60% for methyl dopa and 43% for hydralazine.

## Дәрімен шақырылған аутоиммунды гепатит: жүйелік шолу және клиникалық жағдай

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### Тұжырым

Дәрімен шақырылған бауырдың зақымдануы – бұл гепатотоксикалық әсерінің нәтижесінде пайда болатын дәрілік препараттардың жағымсыз реакциялардың бір түрі. Дәрімен шақырылған аутоиммунды гепатиттің патогенезінде дәрілік зат метаболиттерінің реакциясының нәтижесі болып табылатын P450 цитохромы жүйесінің ақуыздары- неоантигендерге аутоантиденелердің өндірілуіне негізделген.

Дәрімен индуцирленген бауырдың зақымдануы, жыл сайын 1-1,5 миллион пациенттерді қамтитын клиникалық маңызды мәселе.

Бауырдың дәрі салдарынан зақымдалуының жыл сайынғы жиілігі Еуропадағы популяциялық зерттеулерде 100 000 халыққа шаққанда 2,3-13,9 санын құрайды. Исландия бойынша популяциялық зерттеу жылына 100 000 халыққа шаққанда ең жоғарғы көрсеткіш - 19,1 көрсетті. Ал АҚШ популяциясына негізделген жалғыз зерттеуде «бауырдың дәрі салдарынан зақымдалуы» шамамен 100 000 халыққа 3 көрсеткішін құрайтыны анықталды. Жедел гепатит бүгінгі таңда дәрінің салдарынан, бауырдың зақымдалуының 90%-н құрайтындығының айқын көрінісі болып табылады. Зерттеулерге сәйкес, бауырдың дәрі салдарынан зақымдалуы 2,9-8,8% және аутоиммунды гепатит 2-18%, дәрілік аутоиммунды гепатитпен байланысты. Бауырдың дәрі әсерінен зақымдалуы антиденелердің болуының (ядролық антигенге, тегіс бұлшық етке және бауырдың еритін антигеніне) жиілігі аутоиммундық гепатитке 83%, нитрофурантоинға 74%, моноциклинге 60%, метилдопаға 43% және гидразалинге 43% құрайды.

## Лекарственно-индуцированный аутоиммунный гепатит: систематический обзор и клинический случай

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### Аннотация

Лекарственно-индуцированное повреждение печени – это один из видов нежелательных реакций на лекарственные препараты, которые проявляются в результате их гепатотоксического влияния. В основе патогенеза лекарственно-индуцированного аутоиммунного гепатита лежит выработка аутоантител к неоантигенам, представляющим собой белки системы цитохрома P450, которые являются результатом реакции метаболитов лекарственных средств.

Клинически актуальная проблема, как лекарственно-индуцированное поражение печени, затрагивает 1–1,5 миллиона пациентов почти каждый год.

Ежегодная заболеваемость лекарственно-индуцированным повреждением печени колеблется от 2.3-13.9 на 100 000 населения в популяционных исследованиях из Европы. В исландском популяционном исследовании были зарегистрированы самые высокие показатели 19.1 на 100 000 населения в год. А в единственном исследовании, основанном на населении США, было установлено, что лекарственно-индуцированное повреждение печени составляет примерно 3 на 100 000 населения. Острый гепатит в настоящее время является широко известным проявлением, и составляет более 90% повреждений печени, вызванных лекарствами. По данным исследований 2.9-8.8% лекарственно-индуцированного повреждения печени и 2-18% АИГ связаны с лекарственно-индуцированным аутоиммунным гепатитом. Встречаемость лекарственно-индуцированного повреждения печени с наличием антител (антитела к ядерному антигену, гладким мышцам и растворимому антигену печени) к АИГ, составляет 83% для нитрофурантоина, 74%, для миноциклина, 60% для метилдопы и 43% для гидралазина.

### Introduction

The authors of the article from the Netherlands found that about 40% of people with medical drug induced liver damage had elevated levels of immunoglobulin G, in 60-70% of cases there were positive antibodies to nuclear antigen (ANA) and smooth muscle (SMA) [3]. Autoimmune hepatitis, developed as a result of drug damage to the liver, accounts for approximately 9% of all cases of AIH [3]. According to the results of a study in Colombia, drug-induced autoimmune hepatitis makes up an insignificant part of AIH [4]. Even if the clinical and histological characteristics may be similar, but patients with LIAH are more likely to suspend treatment with a low risk of relapse, progression to cirrhosis or the need for liver transplantation [4]. We studied the epidemiology of drug-induced autoimmune hepatitis in the PubMed and Science Direct databases.

### Material and methods

We conducted a literature review on databases such as PubMed and Science Direct for the period from 2010 to 2022 in English by keywords: drug induced liver injury, drug induced liver injury clinical case, RUCAM, drug-

induced autoimmune hepatitis. Next, filters were used by publication date, research design and access to the article. Articles with no clinical significance were excluded. A total of 29 articles were included that met the criteria.

At the second stage, the analysis of a clinical case was taken from the Central Municipal Clinical Hospital, department of gastroenterology, with an established diagnosis of drug-induced autoimmune hepatitis was carried out. A retrospective research method was used.

### Results and discussion

The RUCAM scale is used to determine the causal relationship of drug-induced liver injury [8]. There are 3 main types of drug-induced liver injury based on the ratio of serum enzymes: hepatocellular, mixed and cholestatic [1].

Classification of drug-induced liver injury (DILI) according to the AASLD Practice Guide for Liver Damage Caused by Drugs, Herbs and Dietary Supplements from 2022:

By mechanism, DILI can be classified as either direct (i.e., dose-dependent, internal, and predictable) or idiosyncratic (largely dose-dependent, idiosyncratic and unpredictable) (Table 1) [9].

Mechanistic classification	Direct hepatotoxicity	Idiosyncratic hepatotoxicity	Indirect hepatotoxicity
Incidence	Common	Rare	Intermediate
Dose relatedness	Yes	No	No
Predictable	Yes	No	Partially

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печени, клинический случай,  
RUCAM, лекарственный  
аутоиммунный гепатит

Table 1.  
Classification of drug-induced  
liver injury [9]



Reproduced in animal models	Yes	No	Not usually
Latency	Rapid (days)	Variable (days to years)	Delayed (months)
Phenotypes of injury	Serum AST, ALT, or ALP elevations, hepatic necrosis, acute fatty liver, nodular regeneration	Mixed or cholestatic hepatitis, bland cholestasis, chronic hepatitis	Immune-mediated hepatitis, fatty liver, chronic hepatitis
Examples	Acetaminophen, niacin, intravenous methotrexate	Amoxicillin-clavulanate, cephalosporins, isoniazid, nitrofurantoin	Immune checkpoint inhibitors, anti-CD20 monoclonal Ab, protein kinase inhibitors
Mechanism of injury	Intrinsic hepatotoxicity that is dose-dependent	Idiosyncratic host metabolic or immune reaction	Indirect effect on liver or host immunity

The third mechanism of hepatotoxicity is called indirect drug-induced liver injury, which occurs when the biological action of the drug affects the host's immune system, which leads to a secondary form of liver damage [9]. The advantage for studying the molecular mechanisms of liver damage caused by medications and herbs is that the antigen (drug, its metabolite) is known, which remains unknown for autoimmune hepatitis [10]. In order to choose the right therapy and distinguish drug-induced autoimmune hepatitis from drug-induced liver damage without autoimmune hepatitis (AIH), it is necessary to perform a liver biopsy [7]. According to the results of a retrospective cohort study conducted from January 2010 to January 2020 among patients in one of the medical centers in China, it was found that with each relapse, the latency period decreased, and laboratory tests decreased [11]. In patients with chronic drug-induced liver injury, the risk was high after the second episode [11]. A group of persons with a possible predisposition to AIH were postmenopausal female patients with elevated levels of serum immunoglobulin IgG [11].

A study conducted at the University Hospital of Brighton and Sussex, UK, found that the natural course of drug-induced autoimmune hepatitis is similar to AIH, especially in terms of the presence of severe fibrosis on admission and the inability to maintain remission when immunosuppression is withdrawn [12]. After carefully reviewing the data at the Mayo Clinic in Rochester, Minnesota, researchers concluded that a significant proportion of patients with AIH have drug-induced AIH, mainly due to nitrofurantoin and minocycline [13]. Department of Gastroenterology and Hepatology, Faculty of Medicine, Mie University, Japan, studied seven cases of autoimmune hepatitis that developed after drug-induced liver injury, in which it was found that a wide range of drugs can cause AIH [14]. Given that AIH can develop even after normalization of liver enzymes, careful follow-up is required in all cases of drug-induced liver injury [14].

Based on the results obtained in the Department of Surgical Gastroenterology in China, it should be noted that the differences in ALT, AST and CD4 + Foxp3 + CD25 - Treg between patients with drug-induced autoimmune hepatitis and patients with AIH are clinically useful for differentiating these two diseases on their early stage [15].

A study conducted in Japan revealed clinical characteristics of drug-induced liver injury, which

showed histological findings similar to AIH [16]. In such patients, a liver biopsy is recommended to determine the appropriate treatment tactics [16]. A study conducted at the Department of Anesthesiology and Critical Care at Johns Hopkins University showed that drug-induced autoimmune hepatitis is the most common process of drug-induced liver hypersensitization, which is observed in approximately 9–12% of patients with autoimmune hepatitis [17]. According to an article published in the Department of Gastroenterology, Kyoto Okamoto Memorial Hospital (Japan), a clinical case of a patient diagnosed with IgG4-associated AIH with an etiology presumably caused by drugs is presented [18]. Oral prednisolone was started and discontinued after achieving biochemical remission. Autoimmune hepatitis recurred after discontinuation of steroids; however, remission was achieved with ursodeoxycholic acid [18].

According to a search on the Medline database, since 1966 there are 14 registered cases of AIH caused by statins [19]. The article by E. Kawasaki et al. describes 2 clinical cases, which report on patients with type 1 diabetes who developed autoimmune hepatitis (AIH) after taking statins [19]. Most cases of AIH were diagnosed within 1 year of statin use, with a mean age of  $56.7 \pm 11.0$  years [19]. The article by A. Villamil and others reported 2 cases of acute autoimmune hepatitis in patients with multiple sclerosis treated with IFN-beta 1a [20]. One of the complications of alpha-IFN treatment in patients with chronic viral hepatitis is the development of autoimmune hepatitis [20]. An article published in Canada found that transient liver enzyme disorders are relatively common in children receiving anti-TNF treatment [21]. Anti-TNF-associated drug-induced liver injury with autoimmune features is rare but must be recognized before therapy can be discontinued [21]. A study in Iceland showed that when assessing clinical use and safety risk, TNF- $\alpha$  inhibitors were more likely to cause liver damage compared to other biologics [22]. A study conducted at the Walter Reed National Military Medical Center (USA) showed a case of infliximab-induced seronegative AIH responding to budesonide therapy, with a successful change in the treatment regimen for inflammatory bowel disease to vedolizumab [23]. A review conducted at the Institute for Liver Research, King's College Hospital, London (UK) proposes a structured practical approach to the diagnosis and treatment of a group of patients with autoimmune hepatitis [24]. In studies conducted at Hasetepe University, Department of Gastroenterology, in Turkey, it was shown that after the use of tumor necrosis

factor- $\alpha$  (anti-TNF- $\alpha$ ) blockers, including infliximab, etanercept and adalimumab, mild to moderate increased activity of liver enzymes, cases of severe hepatitis were rare [25]. For this reason, TNF- $\alpha$  blockers are considered as a potential cause of drug-induced autoimmune hepatitis [25]. According to a review conducted in the Department of Gastroenterology, Belgrade Children's University Hospital, immune-mediated hepatotoxicity of albendazole was found to be one of the possible mechanisms of liver damage [26]. The use of albendazole in the treatment of parasitic infections, especially in children, requires careful monitoring [26]. This article, conducted at the Department of Medicine and Pediatrics, Rush University Medical Center, Chicago (USA), describes a clinical case of a male adolescent who developed autoimmune hepatitis induced by minocycline [27]. A study by the Department of Gastroenterology and Hepatology, Rutgers School of Medicine, New Jersey, showed that drug-induced liver injury remains the most common cause of acute liver injury in the United States [28]. Drug-induced liver injury is one of the most challenging diseases faced by hepatologists due to the

variety of drugs used in clinical practice, available herbs and nutritional supplements with hepatotoxic potential, the ability of the disease to present with a variety of clinical and pathological phenotypes, and also due to the current lack of specific biomarkers [29].

**Case study**

Patient K., 52 years old, complained about severe weakness, headaches, dizziness, shortness of breath during physical activity, fatigue. From the anamnesis of the disease: she has been ill for 2 years the history of disease about 2 years, when AIH was first diagnosed. Concomitant diseases: Autoimmune thyroiditis. She took dietary supplements for a long time. The diagnosis was made. The diagnosis is: Drug-induced liver injury, mixed variant (requires dynamic monitoring for possible drug-induced autoimmune hepatitis) with pronounced biochemical activity at the onset of the disease (126 ULN ALT dated 11.04.2020) and moderate biochemical activity at the time of examination (5.9 ULN ALT) (Figure 2, 3, 4). Autoimmune thyroiditis, subclinical hypothyroidism. Dyslipidemia. The results of laboratory studies are presented in Figures 1, 2, 3, 4 5.

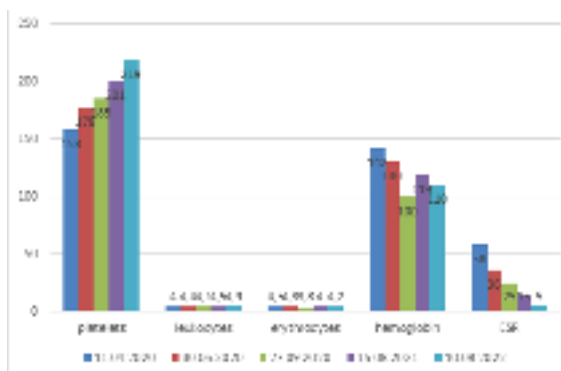


Figure 1. Results of Complete blood count

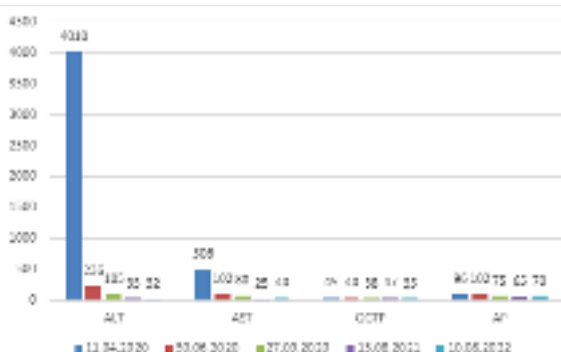


Figure 2. Results of a biochemical blood test

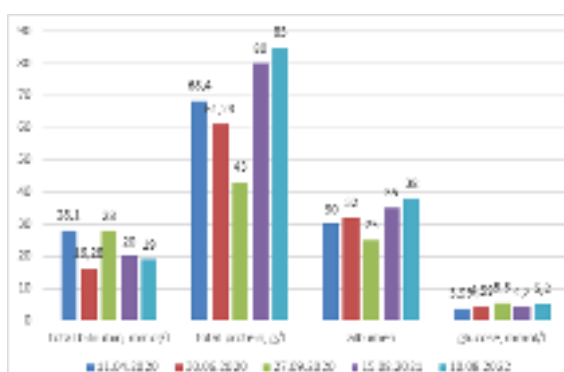


Figure 3. Results of a biochemical blood test

Figure 4. Results of a biochemical blood test

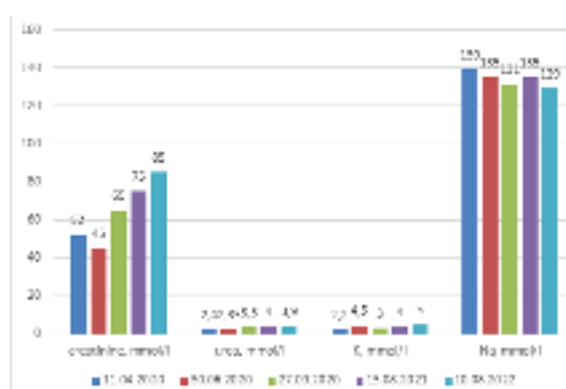
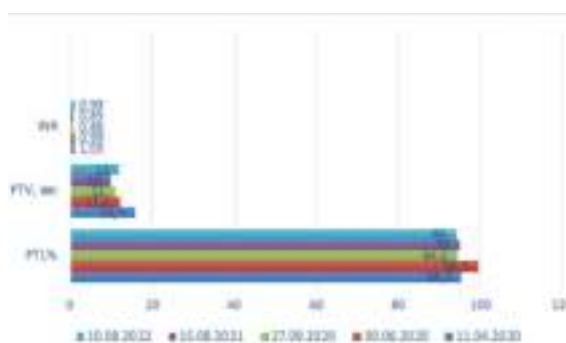


Figure 5. Coagulation test



The patient was prescribed standard immunosuppressive therapy with Prednisolone 60 mg in 2-3 times a daily, Ursodeoxycholic acid 500 mg 2 times a day before breakfast and at night for a long time. When re-examined about 3 months after, there was a biochemical response to immunosuppressive therapy (minimum biochemical activity). In this regard, it was recommended to reduce the dose of Prednisolone from 20 mg to 5 mg per week to 10 mg / day orally daily until 11 am - for a long time;

alternative option - Budesonide (Budenofalk) 3 mg 3 times a day before meals - long-term. Azathioprine or 6-mercaptopurine 50 mg/day. At the moment, the patient is under our careful dynamic observation.

**Conclusions**

Drug-induced liver injury and drug-induced autoimmune hepatitis may be similar in clinical laboratory findings. The final role in the differential diagnosis is played by a liver biopsy, which is necessary for further treatment.

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## К 120-летию профессора Брякина М.И.

Брякин Михаил Иванович родился 18 ноября 1902 г. в с. Долганка Алтайского края, в 1921 г. закончил среднюю школу. В 1921-1922 гг. работал учителем школы 1 ступени. С 1922 г. в течение 5 лет - студент медицинского факультета Томского государственного университета, получил звание «врача» в 1927 г.

В 1927-1928 гг. работал заведующим районной больницы, а последние 5 лет врачом-ординатором хирургического отделения областной больницы г. Петропавловска. Брякин М.И. с 1934 г. работает в г. Алма-Ате в системе КазМинздрава, а в 1935-1941 гг. совмещает эту работу ассистентом кафедры госпитальной, затем факультетской хирургии Алма-Атинского государственного медицинского института.

С началом Великой Отечественной войны Брякин М.И. призван в ряды Советской армии, где прослужил в должности начальника хирургического отделения и хирургического полевого подвижного госпиталя до 1947 г., был демобилизован в звании майора медицинской службы. В годы войны он становится поливалентным военно-полевым хирургом. С 1947 г. начинается педагогическая деятельность в стенах АГМИ в должности доцента на кафедре факультетской хирургии.

С 1954 по 1958 г. заведует кафедрой факультетской хирургии, а в 1959-1980 гг. - кафедрой госпитальной хирургии. В течение 10 лет с 1954 по 1964 г., Брякин М.И. по совместительству главный хирург МЗ Казахской ССР. Благодаря организационному таланту, за эти годы, он внес большую лепту в организации и становлении Института хирургии, специализированных отделений травматологического, урологического, нейрохирургического профиля и челюстно-лицевой хирургии.

Во время службы в рядах Советской Армии защитил кандидатскую диссертацию на тему: «О стимулирующем действии 2% раствора молочной кислоты на регенерацию костной ткани». Докторская диссертация, посвященная актуальной проблеме хирургической гастроэнтерологии, была успешно защищена в 1953 г. на тему: «О некоторых последствиях перерезки блуждающих нервов в эксперименте и при хирургических вмешательствах в клинике». Звание профессора получил в 1955 г. За заслуги в подготовке практических хирургов и научно-педагогических кадров Брякину М.И. в 1947 г. присвоено звание - «Заслуженный врач», в 1957 г. - «Заслуженный деятель науки» Казахской ССР.

Научная и практическая деятельность профессора Брякина М.И. была многогранной. Он основоположник хирургии пищевода в Казахстане, одним из первых в республике начал выполнять резекции легких при раке и бронхоэктатической болезни, много сделал для развития хирургии легочного туберкулеза, сосудистой хирургии, впервые

в республике наложил спленоренальный анастомоз при портальной гипертензии, в числе первых начал выполнять митральную комиссуротомию и оперировать больных с незаращением Боталлова протока, после консультации и по направлению профессора Сатпаевой Р.А. Под его руководством разрабатывались вопросы анестезиологии и реаниматологии, внедрялись в практику современные виды общей анестезии, потенцированной спинномозговой анестезии, много внимания уделялось вопросам травматологии.

Под руководством Брякина М.И. защищено 34 кандидатских и докторских диссертаций. Диссертации посвящены проблеме шока, травматологии, хирургической гастроэнтерологии, сердечно-сосудистой, торакальной хирургии. Вышедшие из хирургической школы профессора Брякина М.И., академик Ормантаев К.С., профессора Денягина Т.П., Забозлаев С.С., Кукеев Т.Г., Андреев Г.Н., Кушекбаев М.Н., Ибадильдин А.С., доценты - Заморская Е.В., Симонянс Э.С., Трипольская Г.И., Маткаримов М.Т., Урашев С.Т. и многие другие возглавляли, продолжают руководить кафедрами, работать в научно-практических учреждениях Республики Казахстан, и, практически, во всех странах СНГ.

В течение 26 лет профессор Брякин М.И. был председателем и членом правления республиканского, городского и областного научных хирургических обществ Казахстана. Его участие в организации и проведении пленумов, съездов, заседаний хирургических обществ, выступления с программными докладами по актуальным вопросам хирургии привлекало внимание практических врачей, ученых-медиков. В 1957-1959 гг. он участвовал в работе международного Конгресса онкологов (г. Лондон) и сердечно-сосудистых хирургов (г. Мюнхен). Научная публикация Брякина М.И. составила более 120 статей в республиканских и союзных изданиях, в материалах пленумов, съездов РК, СССР, 3 монографии и ряд учебных пособий для студентов и врачей-интернов.

Профессор Брякин М.И. был человеком большого врачебного долга, опытным клиницистом, прекрасным диагностом, в совершенстве владел хирургическим мастерством. Он был принципиальным и требовательным педагогом, прекрасным лектором. Его милосердие к больным, доброжелательность к ученикам и коллегам снискали ему заслуженный авторитет у широкой медицинской общественности и населения.

Врачебная, педагогическая и общественная деятельность Брякина М.И. была высоко оценена. Ему были присвоены почетные звания - «Заслуженный врач», «Заслуженный деятель науки Казахской ССР». За заслуги перед Родиной в военные и мирные годы он был награжден орденом «Красной Звезды», двумя орденами «Трудового Красного Знамени» и орденом «Знак почета», многими медалями и Почетными грамотами Верховного Совета Казахской ССР, Министерства здравоохранения.

Профессор Брякин М.И. умер 20 января 1985 г., на 83 году жизни.

*Профессор Ибадильдин А.С.,  
доцент Бердаuletов Б.А., доцент Кушекбаев М.Н.*