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METHODS OF TREATMENT OF POSTNECROCTIC PANCREATIC CYSTS: MODERN LOOKS OF THE PROBLEM (LITERATURE REVIEW)

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Choosing a surgical method of treatment of postnecrotic pancreatic cysts is an extremely urgent problem these days. With developing technologies and increasing number of minimally invasive methods of treatment, diagnostic capabilities tend to improve. Whereas traditional methods of surgical treatment do not lose their relevance, recent studies optimize the indications for their implementation, which in turn reduces the frequency of the nearest and distant postoperative complications. The article deals with the questions of conservative therapy of postnecrotic cysts, indications and choice of a method of surgical treatment. It covers the methods of minimally invasive surgery, the application of which allows achieving excellent clinical results of treatment The authors pays particular attention to the recent tendency of using several methods of minimally invasive treatment describing that the combination of minimally invasive internal and external drainage has shown its effectiveness. It should be noted that performing intervention data from the position of pathogenetic treatment helps to achieve a good clinical result. The data on the success of combined drainage of postnecrotic cysts are few, which requires confirmation by a large number of publications. Thus, the high incidence of acute pancreatitis, the lack of diagnostic algorithms and clear indications for a wider range of existing methods of surgical treatment of postnecrotic pancreatic cysts leaves a field for subsequent studies and observations.

Key words: *pseudocyst, postnecrotic cyst, minimally invasive technologies*

МЕТОДЫ ЛЕЧЕНИЯ ПОСТНЕКРОТИЧЕСКИХ КИСТ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ: СОВРЕМЕННЫЙ ВЗГЛЯД НА ПРОБЛЕМУ (ОБЗОР ЛИТЕРАТУРЫ)

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Постнекротические кисты поджелудочной железы являются наиболее частым осложнением перенесённого деструктивного панкреатита и травм поджелудочной железы. По данным мировой литературы, частота их формирования составляет 18–92 %. В настоящее время при постнекротических кистах сохраняются на высоком уровне частота летальности и осложнений, таких как нагноение (28–67 %), аррозивные кровотечения (1,6–20 %), перфорация кист в брюшную полость с развитием перитонита (20 %), сдавление различных отделов желудочно-кишечного тракта (3–4 %).

Традиционные методы хирургического лечения постнекротических кист – операции внутреннего и наружного дренирования путём лапаротомии – имеют массу недостатков, связанных с травматичностью операции, высоким риском возникновения интра- и послеоперационных осложнений, продолжительным периодом стационарного и поликлинического периодов лечения, а также с формированием наружного панкреатического свища. Большинство авторов считают наружное дренирование кист поджелудочной железы только вынужденной мерой, когда внутреннее дренирование не представляется возможным. Ряд авторов применяют пункционные и дренирующие методы под ультразвуковым контролем как первый этап лечения, направленный на санацию инфицированной кисты для создания оптимальных условий для последующих радикальных вмешательств.

В настоящее время всё большую актуальность приобретают методы малоинвазивных вмешательств при постнекротических кистах поджелудочной железы: транскутанные пункционно-дренирующие вмешательства под ультразвуковым контролем, выполнение внутреннего эндоскопического транслюминального дренирования, стентирование вирсунгова протока, а также комбинации этих методов малоинвазивной хирургии. Таким образом, проблема выбора тактики лечения постнекротических кист остаётся актуальной до настоящего времени.

Ключевые слова: псевдокиста, постнекротическая киста, малоинвазивные технологии

The topic under consideration is relevant due to an annual increase in the incidence of acute pancreatitis, both in the Russian Federation and in most of the developed world. In the structure of mortality from acute surgical pathology on the Krasnoyarsk Territory in recent years, mortality from acute pancreatitis ranks first and is more than 30 % [7].

One of the complications of acute pancreatitis is postnecrotic pancreatic cyst (pseudocyst) (PNPC).

According to various data, complication of acute pancreatitis and pancreatic necrosis with pseudocysts amounts from 7 % to 80 % [16, 20]. The formation of a pseudocyst should be considered as a favorable outcome in the course of pancreatic necrosis, because compared to extensive forms of destructive pancreatitis it significantly reduces mortality. The second most frequent cause of pseudocyst formation is pancreatic injury, with pseudocysts forming in 10 % of cases [6]. It is worth noting that chronic pancreatitis is complicated by cystic formations in 20–40 % of cases [1, 9, 35].

According to most authors, pseudocyst formation is accompanied by complications, the frequency of which varies from 20 to 70 %, being the main cause of mortality in this pathology. Those include: infection (suppuration) (15–25 %); perforation into the abdominal cavity, into the hollow organs of the abdominal cavity and outwards (5–15 %); internal and external fistulas (5–35 %); obstruction of the abdominal organs due to their compression with the development of gastroduodenal, thin- and colonic obstruction (3–4 %), mechanical jaundice (5–10 %), portal hypertension (4–6 %); carcinogenesis (1.7–3.1 %) and other more rare complications. The most formidable complication of pseudocyst, associated with a high risk of mortality to 60 %, is arrosive hemorrhage in the pseudocyst cavity, abdominal cavity and retroperitoneal tissue [1, 2, 3, 18, 26, 32, 33].

CONSERVATIVE TREATMENT OF PSEUDOCYST

Choosing a surgical method of treatment of postnecrotic pancreatic cysts is an urgent problem nowadays.

Basically, conservative therapy of pseudocyst aims at arresting concomitant inflammation of the pancreas on the background of acute pancreatitis. Such therapy does not specifically targets PNPC, does not take into account the nature of cystic contents, presence or absence of pancreatic ductal leaks, the involvement of surrounding organs in the pathological process. Conservative treatment is based on the principles of antisecretory, infusion, spasmolytic, symptomatic and antibacterial therapy, being non-selective. With this approach, according to many studies, successful conservative treatment is possible in 14–70 % of cases, and complete regression of the cyst occurs only in 15–30 % [2, 6, 20, 31]. According to some authors [19], the best results of conservative treatment are achievable up to 4 weeks after the formation of pseudocysts, up to the so-called acute fluid clusters that do not have a formed connective tissue capsule. Conservative treatment of small sized pseudocyst (up to 4 cm), existing up to 6 weeks from an episode of acute pancreatitis, without signs of complicated course, is also effective [18, 26, 33]. In turn, large pseudocysts and/or existing for more than 6 weeks are not subject to spontaneous regression [1, 14]. Such pseudocysts with prolonged conservative treatment are prone to develop complications.

The use of isolated conservative therapy is a limited and sometimes inadequate option for the treatment of pseudocyst, requiring active surgical tactics.

SURGICAL TREATMENT OF PSEUDOCYST

Currently, there is a wide range of surgical interventions for pseudocyst, which can be divided into 2 groups – traditional surgical treatment and minimally invasive methods of surgical treatment. Traditional surgical methods of treatment include external drainage operations, internal drainage operations, and various options for pancreas resection. Traditional interventions have been popular for many decades due to the lack of modern diagnostic methods and equipment. However, they are still relevant nowadays. Minimally invasive methods of treatment include external puncture and drainage under ultrasound or CT-control; transabdominal transorganic drainage under ultrasound control; laparoscopic operations of external or internal drainage; operations from the mini-access; transluminal (transgastral, transduodenal) endoscopic puncture and drainage; transpapillary endoscopic interventions (stenting of the Virsung duct), etc. Most authors state the necessity of a selective approach to each patient. The choice of surgical treatment option will depend on many factors – the availability of medical facilities; the availability of qualified specialists who have advanced diagnostic and treatment techniques; maturity of pseudocyst capsule; presence or absence of the connection of the PNPC cavity with the Virsung duct; presence of complications and risks of operative intervention [1, 6, 11, 27, 33].

In last decade, the number of minimally invasive interventions for pseudocyst tends to increase. At the same time, the effectiveness of minimally invasive interventions or excessive traumatization of patients decrease due to the lack of a single tactical approach in treatment and diagnostics [5]. First of all, it is caused by inadequate preoperative diagnostics of pseudocyst capsule formation degree; by presence or absence of pseudocyst connection with the Virsung duct; by differential diagnostics with cystic tumors; by the absence of generally accepted terms of intervention, and by inadequate choice of minimally invasive treatment technique [12, 27, 33].

External drainage operations. Many publications argue that the classical laparotomy makes possible a complete revision of the pseudocyst and the pancreas itself, evacuation of pseudocyst contents, necrosequestrectomy, complete sanation, installment of drains in the pseudocyst cavity or drainage system with active aspiration. External pseudocyst drainage is performed in most cases of pseudocyst content contamination. This intervention is an operation of choice for extensive forms of infected pancreatic necrosis complicated with acute pancreatogenic cysts. In some cases, external drainage is performed out of necessity, when infected pseudocyst was detected only after laparotomy, an immature capsule is diagnosed intraoperatively or when a patient's condition prevents more extended volume of intervention. The main advantages of external drainage are the possibilities of intraoperative diagnosis - bacteriological and biochemical examination

of the contents, histological examination of the pseudocyst capsule, sometimes with cyto-histological examination [2, 11, 29]. Nevertheless, external drainage of pseudocyst is associated with the development of serious and sometimes fatal complications. For instance, mortality in case of external pancreatic fistula can reach 30 %, in cases of unrecognized pancreatic ductal leaks – 25 %. The duration of hospital treatment of such patients leaves much to be desired, reaching 35–45 days on average [3, 11, 14, 29].

Internal drainage operations. Internal drainage operations include the formation of cysto-digestive anastomoses – cysto-gastric anastomosis (CGA), cysto-duodenal anastomosis (CDA), cystojejunoanastomosis (CEA). Such interventions are necessary for patients with mature pseudocyst capsule with no suppuration of its contents. According to many authors, the best access for internal drainage operations is a laparotomy, the advantages of which are described above. The performance of cysto-digestive anastomoses, especially in chronic cystic pancreatitis, helps to reduce intraductal hypertension due to drainage of the pseudocyst contents into the cavity of hollow organs involved in the formation of anastomosis. Reduction of pressure in the duct system of the pancreas quickly eliminates pain syndrome and prevents further changes in the pancreatic parenchyma, which can cause excretory and incretory insufficiency [3, 29]. Another important advantage of cysto-digestive anastomoses, noted by some pancreatologists, is the extremely low incidence of pancreatic fistulas [3]. However, many authors indicate a high percentage of other postoperative complications, such as anastomosis failure, peritonitis, pseudocyst suppuration, arrosive hemorrhages, peptic ulcers of the anastomosis, stenosis, suppuration of the postoperative wound, and a high percentage of relapses. The incidence of complications can reach more than 35 % [18, 33]. At the same time, the mortality rate does not exceed 3.1–5.5 % [1, 21].

The choice of type of anastomosis, primarily depends on the anatomical features of a pseudocyst. In case of intraoperative detection of coarse adhesion of pseudocystic wall to posterior wall of stomach the operation of choice will be CGA. If pseudocyst tightly adheres to duodenal wall and is located behind it appropriate procedure is CDA. Most authors claim that when CGA and CDA are formed incidence of complications (especially arrosive hemorrhage) is higher, and mortality is up to 40 %, which is probably caused by gastric and duodenal contents reflux into the pseudocyst cavity [14, 21, 27, 29].

Thus, cysto-digestive anastomoses, mainly CEA, refer to nosotropic methods of surgical treatment of pseudocyst – they have low mortality rate, whilst causing rather large number of postoperative complications.

Variants of resection of the pancreas with pseudocyst. There are many variants of pancreas resection. The most frequently performed options are cystectomy, distal resection of the pancreas together with the pseudocyst, various modifications of Beger's operation, extremely rare ones – pancreatoduodenal resection, pancreatectomy. There are also options for such drainage operations, such as Frey's and pancreatojejunostomy. An indication for resection is indurative cystic pancreatitis of the distal parts of the pancreas, especially in the presence of external pancreatic fistula. An invariable indication for resection is arrosive hemorrhage [13, 14, 27]. Frey's procedure and pancreatojejunostomy are performed for small retention cysts and a serious pathology of the pancreas ductal system (lithiasis, strictures). Pseudotumorous indurative head pancreatitis and pseudocysts in the head of pancreas complicated with mechanical jaundice, portal hypertension call for Beger's operation or pancreatoduodenal resection, depending on the degree of involvement of surrounding organs and tissues in the pathological process [3]. Some authors insist on increasing proportion of resective surgeries, because they are the only radical surgical treatment of cystic pancreatitis. The frequency of complications occurring after these interventions, according to various sources, is in the range of 5.5 % to 40 %, and the mortality – from 2.5 % to 30 %. These data can be explained by the duration and traumatic nature of resective interventions. One should note a high rate of diabetes onset after pancreas resection – 75–95 % [3, 13, 14, 18, 27, 33].

Traditional surgical interventions for pseudocyst are still relevant, and in some situations are the only method of surgical treatment. At the same time, the risk of postoperative complications, mortality rates, financial expenses from long-term inpatient treatment predetermine a search for more effective methods of surgical treatment, which gives opportunities and incentive for the development of minimally invasive surgery.

Minimally invasive methods of treatment of pseudocyst have become widespread in recent decades.

The history of minimally invasive interventions has started in 1976 with the first **transcutaneous (percutaneous) fine-needle pseudocyst puncture** under ultrasound guidance performed by S. Hancke and J.F. Pedersen [4]. Transcutaneous puncture is sufficiently safe, easy to perform, and does not require general anesthesia. Its other important quality is that we can use in patients with severe concomitant pathologies almost without the risk of serious postoperative complications [4, 9, 34, 35, 38]. Recently, there have been limited indications for its implementation, this is associated with a high incidence of pseudocyst relapses, up to 40 % [34, 38]. In any case, many authors agree that this variant of minimally invasive intervention is more focused on its diagnostic capabilities than on the therapeutic effect.

With the development of technology, a number of pancreatologists have introduced a **puncture-draining method** for the treatment of pseudocyst, when small-bore drainage is established in the cavity of the cyst, comparable in diameter with a puncture needle [9, 34]. This method of treatment has become very widespread all over the world, because having the virtues of a fine-needle puncture, it leaves a drainage in the cyst cavity for evacuation of its contents, introduction of various medications, antiseptics, sclerosants and X-ray contrast substances [4, 18, 38]. Using such an option of minimally invasive external drainage in comparison with traditional external drainage operations leads to fewer complications, as evidenced by some publications [38].

Until now, there is no consensus on indications for transcutaneous drainage under ultrasound control [4, 34]. Many authors favor this type of intervention as a starting

treatment for acute pseudocysts against the background of acute pancreatitis, especially with such complications as gastroduodenal obstruction and mechanical jaundice caused by pseudocyst compression of pylorus and common bile duct with large cysts (more 10 cm) and due to ineffectiveness of conservative therapy [18, 33, 34, 38]. When carrying out transcutaneous drainage, as a rule, the degree of pseudocyst wall maturation is not taken into account, neither is the presence of pseudocyst connection with the pancreatic duct. The latter is a direct, although relative, contraindication associated with the risk of forming an external pancreatic fistula. However, in some situations this tactic is possible, being necessary as symptomatic therapy in patients with severe concomitant pathology, or general critical condition [6, 33, 34]. Another important deterrent to the use of transcutaneous drainage is the presence of sequesters in the pseudocyst cavity, especially larger than 4 cm, because the small diameter of the catheter makes their removal impossible [38]. The frequency of complications of transcutaneous drainage is in the range from 8 to 35 %, according to different authors. They include external pancreatic fistulas, bleeding, perforations of the hollow organ of the abdominal cavity. Traumas of the spleen and large vessels are attributed to occasional complications [4, 13, 33, 34, 38]. One should not forget about the technical features of the puncture-drainage method, performed under ultrasound control, because in some situations there is no safe ultrasonic access for puncture.

V.I. Davydkin et al. (2014) have experience of successful application of the **transduodenal US-guided internal pseudocyst drainage** recommended as a necessary intervention when pseudocyst has intricate form and there is no echo window. The effectiveness of this method should yet be confirmed by a larger number of publications [8].

In his studies, A. D'Egidio et al. [37], establish three types of postnecrotic pseudocyst and state indications for **transcutaneous drainage**. To the first type refer postnecrotic cysts that are not connected with pancreas ductal system and that occur after acute pancreatitis. Cysts occurred on the background of chronic pancreatitis and often connected with unchanged major pancreatic duct belong to the second type. The third type includes retention cysts in chronic pancreatitis, formed as a result of obstruction of pancreatic ducts. Transcutaneous drainage can be performed only for cysts of the first group, and is absolutely contraindicated for the third type because it often (in 45–60 %) leads to external pancreatic fistulas [8, 28, 37].

Another important area in development of puncture-drainage methods is the introduction of **large-caliber drainage** of pseudocyst. V.G. Ivshin et al. (2013) have a fairly large experience of using this method in patients with various forms of destructive pancreatitis, both of extensive forms of infected pancreatic necrosis, and localized forms, including postnecrotic cysts. At the same time, the widespread introduction of large-caliber drainage is limited by the capabilities of the medical facility, requiring special X-ray and interventional endoscopic equipment [10].

Hence it follows that transcutaneous puncture-draining methods for the treatment of pseudocyst are often performed not according to indications, and often in the presence of contraindications.

In the last decade, there have been many publications on the use of **laparoscopy in the complex treatment of chronic pancreatitis and pseudocysts** [14, 19, 21], which is connected with mainstreaming of this surgical approach [7]. Laparoscopic operations have a number of advantages over traditional open surgical interventions; they include, first of all, a minor surgical trauma, which is especially important in patients with severe concomitant pathology. In this case, laparoscopy is only one of the surgical approaches allowing to perform such interventions on the pancreas and pseudocyst as external drainage, internal drainage operations, and resection of the pancreas. Another advantage of laparoscopy is the significantly shorter duration of inpatient treatment [28]. The authors emphasize that the use of laparoscopic interventions primarily depends on the experience of the surgeon, which at the same time narrows their potential, as does the presence of expressed adhesion process in the abdominal cavity. Among postoperative complications we can note pancreatic fistulas after external cyst drainage in 28–33 % [21, 28].

A rarer variant of minimally invasive treatment is operations from **minimal access**. There are several options – video assisted omentobursoscopy or operations with the use of "Mini Assistant" set [33, 34, 38]. Literature data indicate a small experience of using this type of operation for pseudocyst, and that makes it difficult to assess the effectiveness.

Endoscopic transluminal drainage. First endoscopic transluminal drainage of pseudocyst was performed in 1975 [36] without any additional visualization technique. In Russia, endoscopic cystogastrostomy was first performed on February 2, 1986 [24]. The method consists in formation of an anastomosis between the cyst and the hollow organ of the abdominal cavity under the control of the endoscope. As a result, the contents of the cyst is drained into the lumen of the stomach or the duodenum [30]. An important point of endoscopic transluminal drainage is the possibility of stage-by-stage sanation of the cyst cavity and removal of sequesters. Subsequently, cysto-nasal drainage was installed for aspiration of cyst contents, administration of antiseptics, and various stents were inserted through the wall of the stomach or duodenum into the lumen of the cyst [15]. This method is technically simple. The number of complications reaches 30 % [24, 36], the most frequent one being suppuration of cyst contents due to reflux of stomach or duodenum contents, bleeding from the puncture site and anastomosis in the process of transmural access, and stenosis of the anastomosis. In addition, transluminal drainage with no visualization can lead to perforation of the hollow organ of the abdominal cavity, and bleeding from large vessels [15, 24, 30, 36]. The frequency of relapses can reach 25 % [24, 36]. The application of this method has been relevant for many years, because of extremely low mortality rate and its less traumatic character. The absence of additional visualization methods did not facilitate wider introduction of transluminal drainage.

Endoscopic transluminal drainage under EUS guidance. In the last decade, there are many publications

related to the use of endoscopic ultrasonography (EUS) in the diagnosis and treatment of gastrointestinal tract diseases. The endoscopic ultrasound method involves an ultrasonic sensor built into the endoscope, which makes it possible not only to examine the hollow organs from the side of the lumen, but also to visualize anatomical formations around them using an ultrasound machine. This area of interventional endoscopy is a promising method for minimally invasive treatment of various gastrointestinal diseases, including pseudocyst. First transluminal drainage of pancreas pseudocysts through the gastric wall exclusively under EUS guidance was performed in 1996. Wiersema et al. [38]. Endo-ultrasound can identify an avascular zone for puncture and subsequent dissection in the wall of the stomach, clearly visualize the cyst, and determine its anatomical features, the distance between the stomach and the cyst. After that, the fine-needle puncture of the cyst is made and a wire string is installed in its lumen, through which the delivering device is inserted. In the presence of X-ray equipment in the cavity of the cyst, it is possible to insert the X-ray contrast material for the purpose of cystography. Then a stent is placed in the cavity of the cyst under visual endoscopic control, and the contents of the cyst is drained into the lumen of the stomach [10, 23]. There are techniques for the formation of anastomosis without stents, when only gastrotomy is produced by an electrocoagulator. Recently, there have been some evidences published of the low effectiveness of this method caused by formation of strictures in cysto-gastric anastomosis. At the same time, small diameter stents are also prone to obturation with pus, detritus or sequesters. Most authors indicate the need to use plastic stents of small diameter in the presence of a uniform content of the cyst. Indications to the choice of metallic stents are the lack of a clear wall of the formation, the presence of sequesters, infection of formation, cysts larger than 6 cm in diameter, tissue thickness between the gastrointestinal wall and the formation of not more than 1 cm [10, 15, 24, 30, 36]. In recent years, there are data on the use of local negative pressure at suppuration of the cyst, when a cysto-nasal vacuum-drainage is set in its cavity [24]. It should be emphasized that the lack of safe access, the distance between the wall of the stomach and the cyst more than 1 cm limit the possibilities of transluminal drainage under EUS guidance. According to different authors, cyst drainage is possible in 95–100 % of cases, and the proportion of complications, especially bleeding, is much lower than with "blind" drainage [10, 20, 36]. According to the literature, the frequency of complications is: for dislocation of drainage, its obturation (ineffective drainage) – 21 %, for suppuration of the cyst – 12 %, relapse – 12 %, bleeding – 0.5–1.5 %, perforation of the hollow organ of the abdominal cavity – 1 % [15, 20, 28].

Analyzing the complications of transluminal drainage under EUS guidance, we can speak about its safety, low-traumatism, which significantly reduces the death rate, shortens the time of staying in the hospital. Currently, transluminal drainage is recommended as first-line therapy for uncomplicated cysts, available for endoscopic manipulation. The use of this technology for the treatment of complicated cysts of the pancreas, including those infected is very relevant.

Endoscopic transpapillary interventions begin their history more than 30 years ago, when stents were first proposed for installation in the Wirsung's duct. Transpapillary stenting is a promising direction of interventional endoscopyю In recent years this type of minimally invasive treatment has become more widely used. A stent installed in the lumen of the pancreatic duct decreases intraductal hypertension, especially if there are strictures or pancreatic edema that compresses the pancreatic duct. On the other hand, in the presence of pseudocyst associated with the Wirsung's duct and intraductal hypertension, the use of transpapillary stenting is promising [22]. According to many authors, the effectiveness of this method of pseudocyst treatment is 72–92 % [22, 25]. However, some authors point to a terrible complication after transpapillary stenting – pancreatonecrosis. According to the literature data pancreonecrosis after this intervention develops in 3–4 % of cases [25].

At the present time, there are no clear indications for transpapillary stenting of the Wirsung's duct in pseudocyst, which requires further research.

The undeniable advantage of all endoscopic methods of pseudocyst treatment is the absence of such complication as external pancreatic fistula, and this makes it possible to expand and optimize the indications for their use.

Another highly promising direction in the treatment of pseudocyst is a combination of minimally invasive interventions. The combined use of transluminal drainage and transpapillary stenting allows rapid evacuation of the cyst and restoration of outflow of pancreatic fluid to the duodenum, which is very important at pancreas duct leak or strictures of the Wirsung's duct. The combination of external and transluminal drainage can be used in infected cysts for their evacuation and preventing external pancreatic fistulas. This direction is still understudied; there are only few data testifying to successful use of this combination of methods [17, 25, 39].

The high incidence of acute pancreatitis, the lack of diagnostic algorithms for pseudocyst treatment and clear indications for a wide range of existing methods of surgical treatment present possibilities for subsequent research and observation.

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