

## Current Therapeutic Modalities of Pancreatic Pseudocyst

V. ȘURLIN<sup>1</sup>, E. GEORGESCU<sup>1</sup>, MILENA GEORGESCU<sup>1</sup>,  
D. MARGARITESCU<sup>1</sup>, D. CARTU<sup>1</sup>, LUMINITA CHIUTU<sup>2</sup>,  
S. SANDULESCU<sup>1</sup>, S. RAMBOIU<sup>1</sup>, F. CIOARA<sup>1</sup>,  
A. SĂFTOIU<sup>3</sup>, I. GEORGESCU<sup>1</sup>

<sup>1</sup> 1st Surgery Clinic, University of Medicine and Pharmacy of Craiova

<sup>2</sup> Clinic for Anesthesiology and Intensive Care

<sup>3</sup> Gastroenterology Department, University of Medicine and Pharmacy of Craiova

**ABSTRACT** Pancreatic pseudocyst (PP) is a peripancreatic fluid collection with definite wall, without epithelial lining, occurring lately in the course of severe acute pancreatitis. It is due to the extravasation of pancreatic secretions from disrupted pancreatic ducts. 80% communicate with the pancreatic ducts. Natural course is dominated by resorption in more than 50%. The rest, may persist, enlarge and become symptomatic and/or generating complications. Asymptomatic PP more than 6 cm in diameter and persisting more than 6 weeks are considered for therapy because of fear for complications. Open surgery was the mainstay of therapeutic approach until recently, with good short and long term results. The minimally-invasive approach is actually in full development challenging the place of open surgery. The main objective is the drainage (extern or intern) and very rarely the resection. The external drainage is indicated in PP with thin walls of infected. Percutaneous drainage avoids pancreatic fistula, prolonged hospitalization or infection risk. Endoscopic approach for internal drainage may be the economically better, simpler and safer especially when guided ultrasonographically. Laparoscopic surgery is at the beginning but promising. However, it is expensive and lasts long. Surgical excision is very rarely indicated. In conclusion, PP with indication for therapy, with little exception, should be evaluated for internal endoscopic drainage. Under ultrasonographic guidance it proved feasible, safe and efficient. Open surgery would remain for failures, complications and exclusions from endoscopic approach and the percutaneous approach guided by imagery, for the critical patient with infected PP.

**KEYWORDS** : pancreatic pseudocyst, pancreas, external drainage, internal drainage

### Introduction

Pancreatic pseudocyst (PP) is a peripancreatic fluid collection bounded by a wall composed of fibrous tissue and inflammatory. The name of pseudocyst derives from the absence of epithelial tissue on the inner surface of the cyst wall. It appears in the course of acute pancreatitis, 5-6 weeks from the disease onset and in chronic pancreatitis [1].

It must be differentiated from peripancreatic fluid collections that occur with high frequency - 80% - in the acute phase of acute pancreatitis. Most of them disappear by the 4<sup>th</sup> week of illness, a fraction of these persist and become pseudocysts. PP represents about 75% of pancreatic cystic tumors. These are tumors containing fluid and wall coverings epithelium. Of these 10% are congenital cysts, 5% are benign or malignant neoplasms and 10% are retention cysts [2].

### Physiopathology

Pseudocyst appearance is due to rupture/necrosis of pancreatic ducts in acute pancreatitis with extravasation of pancreatic fluid that

accumulates around the pancreas and developing in time, an inflammatory reaction around and forming a wall of its own. Their formation is late in the disease course, after about 4-6 weeks after onset, which distinguishes them from early peripancreatic fluid collection, without their own wall. PP contains a fluid rich in pancreatic enzymes and may contain necrotic debris but in small quantities. Studies performed by pancreatic retrograde cholangiography revealed in 80% of cases of PP communication with pancreatic ductal system. If PP is injected with contrast, only 25% of cases it enhances the pancreatic ducts. This demonstrates obliteration in time of the communication, by inflammation or fibrosis, resulting in persistent pseudocyst [3]. In chronic pancreatitis, PP appears as a retention cyst caused by pancreatic morphologic changes by the appearance of ductal strictures and calculi.

The incidence reported in the literature is variable: from 1% to 69% (1). It is dependent on the methods used for diagnostic imaging. Thus, previous studies, which used barium upper gastrointestinal series was estimated at 3.1%, while recent studies using computed tomography

or magnetic resonance imaging, the incidence is estimated at about 70%. But even on these studies the actual incidence is difficult to estimate exactly, as in many publications does not make a clear distinction between peripancreatic collections and pseudocysts. Only tracking dynamic imaging of patients with acute pancreatitis can clearly make the difference.

**Natural evolution.** Most pancreatic pseudocysts disappear spontaneously. Imaging observational studies estimates this phenomenon at about 60% (4). This is achieved by self drainage through pancreatic ductal system or by breaking into a hollow viscera of its wall is adjacent to that of the pseudocyst. PP may persist for a longer period of time, can increase in volume and cause complications. Common complications are abdominal pain, duodenal compression with a syndrome of pyloric stenosis, biliary compression with jaundice, intracystic hemorrhage by erosion of a blood vessel and forming a pseudaneurism, breaking into the peritoneal cavity, infection of its content determined in general, by invasive maneuvers [4].

**Absolute indications** are the symptomatic manifestations and complications. In the uncomplicated PP, fear of progression to complications is dominating the decision to treat. There is a postulated therapeutic indication for PP with diameter greater than 6 cm and PP persisting over six weeks since over this period increased incidence of complications and no resorption occurs. [5]. This postulate, however, was contradicted in a recent study published, in which in the pursuit for long-term PP showed a 20% resorption in cases of pseudocysts more than 6 cm in diameter [6] and that after 51 months 63% remained asymptomatic, 9% presented complications and 35% required therapeutic intervention [7]. Before drawing any therapeutic decision is mandatory to exclude a pancreatic cystic neoplasm. For this, consider a history of acute pancreatitis, abdominal trauma and intracystic fluid analysis for the presence of amylase, mucin, tumor markers CEA, CA-125 and CA 19-9.

Open surgery represents a therapeutic method of reference until the end of the last century. The best results were provided by internal drainage of PP by cystgastrostomy, cystduodenostomy and cystjejunostomy on an excluded Roux-en-Y jejunal loop or direct. In recent decades, it has been usurped from more and more by non-surgical intervention, percutaneous or endoscopic and minimally invasive surgery, laparoscopic. Moreover, numerous observational

studies show a rate of spontaneous disappearance of pancreatic pseudocysts of at least 50%.

Current therapeutic modalities for PP can be summarized as follows:

- *External drainage:*

- Percutaneous - directly or guided imaging (ultrasound, CT)

- Surgery - open or laparoscopic,

- *Internal drainage:*

- Surgery - open or laparoscopic,

- Endoscopic - transpapillary directly guided ultrasound

- Mixed - percutaneous and endoscopic

- *Excision:*

- Open surgery / laparoscopic.

The choice of therapeutic modalities is difficult in the current knowledge due to lack of consensus and insufficient therapeutic guidelines and "evidence based medicine", limited number of new procedures, few randomized comparative studies. Endoscopy and laparoscopy technological development creates additional pressure for the introduction of new techniques. On the other hand, in the series published in the literature, new techniques are applied in selected cases, simple, asymptomatic, which normally would not be given treatment indication. They are used for assessing the feasibility, the purpose of training and acquire experience.

*Factors that influence therapeutic decision*

*Pseudocyst size* can influence the choice of approach. In gigantic PP good results are usually obtained with open surgical approach. Lately there have been isolated reports of successful endoscopic drainage.

In PP *located in the pancreatic tail* open surgical approach is safer, hemorrhagic accidents by lesions of the spleen and splenic vessels are easier to control than by endoscopic or percutaneous approach.

*The viscous contents* of the pseudocyst, rich in debris, precludes an effective endoscopic drainage instead, but in open surgery is not a problem.

*Pseudocyst wall thickness* renders the endoscopic or percutaneous puncture difficult. Infected pseudocyst content requires a surgical approach preferably open, excepting critically ill patients who may use percutaneous puncture.

Anatomical changes resulting from local wound healing produced by acute pancreatic inflammation and canalicular strictures should also be taken into account when choosing therapeutic method. They require endoscopic placement of a stent, induce percutaneous

drainage failure, and can be addressed effectively only through surgical or endoscopic internal drainage. Ductal anatomy studies performed by ERCP revealed five possible situations:

- Type I - normal canalicular system - no communication with PP,
- Type II - normal canalicular system - communication with PP,
- Type III - normal canalicular system, stricture - no communication with PP
- Type IV - normal canalicular system, stricture - communication with PP,
- Type V - normal canalicular system - complete obstruction.

Under this classification, the best indication for percutaneous external drainage is represented by type I. Type IV and V are found most frequently among cases of failure of percutaneous external drainage [8].

*Suspicion of malignancy* determines the choice for open approach, to perform biopsies, but this was proved possible also by laparoscopy.

*Critical condition* of the patient determined the choice of a less invasive method performed with minimal local anesthesia or sedation. Failure or complications of non-operative methods automatically lead to a surgical approach usually by open surgery.

## External drainage

Can be achieved by percutaneous or open surgical / laparoscopic. Can be achieved by a simple percutaneous aspiration of cyst content or you can insert a catheter to be left in the remaining cavity with the intention of to prevent fluid accumulation and promote cavity disappearance.

Percutaneous puncture aspiration of PP can be made directly, but with the risk of vascular or visceral injury, and pseudocyst's content infection. Most often there are used ultrasound imaging guide, CT or fluoroscopy to reduce the risk of such injuries by checking needle position and choosing a free path. The way of approach may be transperitoneal or retroperitoneal. Simple puncture aspiration is not sufficient to definitively resolve failures recorded in 54% of cases and relapses in 63% of cases (9). Repeated puncture increases the risk of accidents and complications.

*Percutaneous drainage* involves the insertion of a plastic catheter into the pseudocyst cavity after puncture. Success rate of the method is between 42-92% and is dependent on operator

experience [10] the failure rate is around 16%. Relapse rate is estimated at 7%, complications rate at 18%, and mortality between 0-2%. The drainage period length is on average 2-3 weeks with a range between 7 and 210 days (9). The risk of secondary infection is about 10% (11). Moving towards extinction of the remaining cavity can be followed radiologically by imaging contrast agent injection through the drainage tube. If the catheter or drainage tube is removed too quickly, pseudocysts may form again. A complication of external drainage is the appearance of external pancreatic fistulas because pseudocyst communication with the pancreatic ducts. If there isn't any obstacle in the pancreatic ducts downstream of the orifice of communication, fistula will close spontaneously. Intravenous administration of pancreatic secretion inhibitors, such as for example octreotide, may shorten the period of closure of the fistula. Persistent fistula following an obstruction may lead to surgery. Percutaneous drainage advantages are the simplicity, can be made at the bedside and is not costly. Disadvantages are: long-term hospitalization, the risk of infection, the risk of external pancreatic fistula, repeated hospitalizations, recurrence of the pseudocyst.

*Open external drainage* has the same objective as percutaneous drainage. In practice, is indicated in rare cases: thin walled pseudocyst inadequately to make an anastomosis with the intestine, infected or viscous content, ruptured cyst into the peritoneal cavity. The results are: mortality of 10%, 10% recurrence risk, risk of pancreatic fistula of 10%. External drainage may be done actually by laparoscopic-assisted approach [11].

### *Internal drainage*

Can be performed by open, laparoscopic or endoscopic mixed approach (percutaneous and endoscopic). Internal drainage involves the development of a communication between the cyst cavity and digestive segment: duodenum, stomach, jejunum. This can be achieved through an anastomosis or a plastic tube (stent) so constructed that it can maintain himself in position for a desired period of time.

To achieve a safe anastomosis is required that the present a well individualized and solid wall. The internal drainage of pseudocyst prevents the external discharge of the pancreatic secretions as in a communicating pseudocyst. Over time, this communication is closing itself, because suture of a hollow viscus with an inner surface epithelium with a structure made primarily of granulation tissue, will lead

to the formation of strictures and finally closing communication. Even if there is communication with the pancreatic ducts, pancreatic secretions flow is not sufficient to maintain open communication. Fear of reflux of digestive contents, namely food, into the pseudocyst cavity proved unwarranted because of the relatively short duration of life of the anastomosis and that gastric emptying, duodenal or intestinal is achieved by peristaltic waves. This was demonstrated by performing oral contrast radiography at about 1 week after cystgastrostomy, and no reflux into the PP was identified. [12].

Cystgastrostomy or cystduodenostomy is performed through gastrotomy or duodenotomy. Posterior wall of the duodenum or stomach is incised in the bulging area, communication with pseudocyst is established, a fragment of wall is taken for histopathological examination, the content of the cyst is removed and the communication's edges are sutured for hemostatic purposes to an opening at least equal to the intestinal lumen, ie at least 3 cm [13]. Gastrotomy and duodenotomy are closed afterwards. There is also the possibility of making cystgastrostomy and cystduodenostomy in a side to side manner.

Cystjejunostomy is achieved usually with a Roux en Y excluded jejunal loop. Recent studies on open surgery reported a success rate of 90% with 9% rate of major postoperative complications and 3% of recurrence [14].

Experience in laparoscopic surgery is in the beginnings but the number of published cases is growing. It is possible to perform a safe anastomosis between the PP and digestive tract and the debridement of necrotic material [15]. The most widely used is cystgastrostomy. It can be performed in many ways:

- transgastric, through the anterior wall of the stomach;
- omental bursa, achieving a latero-lateral anastomosis;
- intragastric, by entering the optical trocar and working trocars inside the stomach previously distended by endoscopic insufflation.

Cystjejunostomy can also be done laparoscopically by submesocolic approach in side-to-side isoperistaltic manner or with an excluded Roux-en-Y intestinal loop, but requires more time and more skills. Laparoscopy allows a biopsy of pseudocyst wall before anastomosis. Most authors indicate the use of 3-5 trocars, laparoscopic ultrasound to identify pseudocysts, the ultrasonic scalpel to open the cyst wall and control of hemostasis, the use of staplers to

perform anastomosis in a faster and safer way. Anastomosis can be done manually but is more laborious.

Conversion rate of laparoscopic approach is about 33% [16] at the beginning of the experience and 0% in recent publications (13,17,18,19). Reported complications are postoperative intraperitoneal hemorrhage 1.02% -10% [16,18], 10% residual pseudocyst [17], intra-abdominal abscess from 5.8 to 10% [13,17]. Mortality in recent series of patients is 0% [13,17,18,19]. Average length of stay is between 2 and 10 days (20). Average length of surgery is 105 minutes long for cystjejunostomy, with an average of 150 minutes [21].

Endoscopic internal drainage:

Can be achieved in the following ways:

- Transpapillary introduction of a catheter through the duodenal papilla, retrograde, the main pancreatic duct and then into the pseudocyst cavity.
- Direct: direct drainage through the wall of adjacent hollow viscera - stomach or duodenum,
- Mixed by: endoscopic and percutaneous.

*Transpapillary drainage* is possible when the PP communicates with pancreatic canalicular system. It involves the prior performing of an ERCP to view this communication and any strictures of the pancreatic ducts. It is followed then by the insertion of a guide wire into the cavity of PP, and if necessary, the dilation of the stricture by an endoscopic balloon. On the guide wire is inserted the drainage catheter that can be externalized in the duodenum or better as nasogastric tube because it allows repeated lavage of the cavity. It can also harvest from the stricture, by brushing, cell specimens for cytologic examination, in the purpose of excluding pancreatic cancer. It also presumes the performance of an endoscopic sphincterotomy and papilotomy [22].

*Direct drainage.* Is preceded by endoscopic ultrasound achieving the aims to:

- view the contents of PP, appreciation of homogeneous or inhomogeneous content, clear or with debris, etc. um, debrisappearance appreciation, clear or septa, debris, sfaceluri,
- choosing the area where the wall thickness is the lowest,
- choosing a parietal areas with minimal vascularity with color Doppler mode [22,23,24].

After choosing the optimal location of the puncture, the needle is inserted under ultrasound guidance. Puncture path may be expanded with endoscopic balloon up to 2 cm. This is necessary if there is debris in the cavity to be extracted. Otherwise, it may insert a stent or a nasogastric

catheter. Complications of the method are the perforation of the stomach or duodenum in free peritoneum or retroperitoneal bleeding from a parietal blood vessel parietal or a pseudoaneurysm. Both can lead to emergency surgery. Bleeding complications are more frequent, up to 10% when endoscopic drainage is attempted without endoscopic ultrasound guidance.

Results. Complications (infection, bleeding, perforation) are found in a proportion of up to 20%, recurrence in 15% and mortality less than 1%.

*Endoscopic and percutaneous simultaneous drainage.* This is a drainage procedure published by Sever et al [25] in which a drainage of the PP in the stomach is performed, using a double J catheter, introduced by a direct percutaneous transgastric puncture under assistance of transabdominal ultrasound and endoscopy. Proximal end of the catheter is abandoned in the stomach. Counterindications are:

- complicated pseudocysts (infection, bleeding), multiple, located near inflammatory areas (necrosis, abscess),
- segmental portal hypertension (splenomegaly, upper digestive tract hemorrhage by variceal bleeding) [24].

#### *Surgical excision*

It has the role of a radical and definitive treatment of the pseudocyst. It is possible when the PP is located near the pancreatic tail, the excision requiring a caudal pancreatectomy with or without splenectomy. Because of inflammatory post-acute pancreatitis changes, the intervention is difficult and with high morbidity and mortality.

## Conclusions

Pancreatic pseudocysts with therapeutic indication, with seldom exceptions, should be evaluated first for internal endoscopic drainage. This approach was proven feasible, safe and effective, especially under endoscopic ultrasound guidance. Open surgery would remain reserved to failures, complications and cases excluded from endoscopic approach, and percutaneous drainage for the infected PP in critically ill patients, not fit for a surgical intervention.

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*Corresponding Author: Valeriu Surlin, MD, PhD, Surgery Clinic no.1, Emergency County Hospital of Craiova, Tabaci St. no.1, Craiova, Dolj, e-mail: vsurlin@gmail.com*