Therapeutical Aspects Regarding Pancreatic Pseudocysts

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Rezumat

Aspecte terapeutice în pseudochistele pancreatice

Frecvent apărute ca și complicații ale pancreatitei, pseudochistele pancreatice sunt entități rare, pentru tratamentul cărora s-au dezvoltat de-a lungul timpului multiple tehnici terapeutice, variind de la metode minim invazive la tehnici complexe de chirurgie clasică. Pseudochistele simptomatice, cele de mari dimensiuni precum și cele ce suferă complicații evolutive de timpul hemoragiei, suprainfecției și rupturii au indicație de drenaj. Alegerea metodei optime de drenaj este deseori o provocare, multiplii factori trebuind să fie luați în considerare, incluzând locația pseudochistului, dimensiunea precum și starea generală a pacientului și comorbiditățile acestuia. Astfel, elaborarea unui algoritm terapeutic ar fi de o utilitate incontestabilă, conferind posibilitatea alegerii unei tehnici fezabile leziunii însă adaptată pacientului.

Cuvinte cheie: pancreas, pseudochist, tratament, drenaj

Abstract

Frequently appearing as a complication of pancreatitis, pancreatic pseudocysts are rare appearances in current medical practice. Multiple therapeutical options are available, from minimum invasive methods to complex open surgical techniques. The indications of drainage include symptomatic pseudocysts, large pseudocysts along with the development of complications such as hemorrhage, secondary infection, and rupture. Choosing the best drainage technique is often a challenge. Multiple factors need to be considered in managing a pseudocyst, including its location, dimension and the patient's

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general state and comorbidities. Thus, a therapeutical algorithm may be of great use in choosing the most feasible technique for the diagnosed lesion that is also patient-adapted.

Key words: pancreas, pseudocyst, treatment, drainage

Introduction

Pancreatic pseudocysts are considered the most frequent complication of acute and chronic pancreatitis, accounting for 75% of all pancreatic cystic lesions (1). When referring to a pancreatic pseudocyst we should consider any fluid collection located in the peripancreatic tissues (occasionally partly or wholly intra-pancreatic located) (2). The location, size and age of the pseudocyst as well as the presence of complications are to be considered when implementing a therapeutical technique (3, 4). The lack of guidelines regarding the optimal treatment of pancreatic pseudocysts and their rather rare appearance are reasons for which continuous dilemmas are raised about their optimal management (3). Thus, comparing the therapeutical methods is mandatory in choosing the best treatment for each case.

Indications of Drainage

According to the latest data, the indications of drainage of a pancreatic pseudocyst are the presence of symptoms like pain attributable to

pseudocyst, discomfort, vomit, along with the development of complications like infection, bleeding or rupture in the adjacent organs (3). Furthermore, biliary, gastric or duodenal obstruction also call for drainage, as does the increasing size of the pseudocyst at follow-up or the imagistic finding on a non-complicated pseudocyst of over 6 cm in diameter (3).

Percutaneous Radiologic Drainage

The main advantages of percutaneous drainage are the relatively low price and the possibility of performing it under local anesthesia. It is often done under radiologic control (5, 6), by using either computer tomographic (*Fig. 1*), ultrasonographic or fluoroscopic guidance or with endoscopic assistance (7-10). The size, location and extent, as well as the disposing of the surrounding viscera, are the main elements to be considered when choosing the approach. Amongst all possible approaches, the transgastric route is most commonly chosen, having the lowest rate of complications (11-14). Other possible paths of access are transperitoneal, retroperitoneal, transduodenal, transhepatic

Figure 1. Pancreatic pseudocyst – CT image

and transsplenic (15). Assessing the completion of the drainage or retained debris as well as the status of the pancreatic duct communication or potentially associated complications as is enteric fistula may be done by performing a sinography (16). The catheter may be removed when the drain output becomes minimal (less than 10 ml/24h) and there is evidence of closure of the pseudocyst-enteric fistula and/or duct communication (16). For infected pancreatic pseudocysts, the percutaneous approach is the best therapeutical option (11-15, 17, 18). It is also useful for aiding definitive diagnosis, when in doubt, allowing amylase dosing from the aspirated fluid, cytologic analysis, and tumor marker dosing (16). It may as well be used when the location of the pseudocyst makes it inaccessible to other drainage methods more routinely used (16).

Having a low rate of mortality, the percutaneous drainage also offers the advantage of not violating the operative field in case surgery will become necessary (11). However, complications may occur, including bleeding (1-2%) (19), lesions of the pleura or other viscera (1-2%) (19), secondary infection (9%) (19). Progression towards pancreatico-cutaneous fistula or recurrence in poorly selected patients having a downstream stricture of the pancreatic duct may also occur (15). These cases will require a rather prolonged period of drainage, of 3 to 6 weeks (15, 20, 21). Yet, often a resulting pancreatico-cutaneous fistula will spontaneously resolve in 60-70% of cases (17). As far as single-step needle drainage is concerned, it is often accompanied by a high rate of recurrence, of over 70%, with a failure rate of more than 50% of cases (6). However, using a catheter for prolonged drainage results in a higher success rate, up to 100% and a low recurrence (22-23%) (22-24).

Endoscopic Drainage

When dealing with pancreatic pseudocysts associated with chronic pancreatitis, the endoscopic approach is of election, whether using transmural or transpapillary route (16, 25).

Transpapillary Drainage

In 40-70% of cases, the pancreatic pseudocyst has a communication with the pancreatic duct, a fact that renders it potentially suitable for transpapillary endoscopic drainage (26-28). When the pseudocyst communicates with the main pancreatic duct or one of its side branches, as seen at ERCP, it may be drained via transpapillary insertion of a stent. The stent is meant to bridge the main pancreatic duct or a disrupted side branch (16). The procedure consists in initial biliary and pancreatic sphincterotomy followed by balloon dilatation of the pancreatic duct stricture and insertion of a stent of 5-7 Fr over the strictured area and beyond (29, 30). The method shows a success rate varying between 60 and 96%. Its predictive factors of success include the presence of strictured areas, the pseudocysts size over 6 cm in diameter, location in the body of the pancreas and an evolution of the pseudocyst of less than 6 months (29). As far as the procedure's safety is concerned, there is a low morbidity and no reported mortality in patients submitted to this maneuver (29, 31-35). Among possible complications, hemorrhage is reported in less than 1% of cases, postprocedural pancreatitis in 5% of cases while stent migration is considered extremely rare (29, 31-35). Some authors reported stent obstruction in secondary infections of the pseudocyst, in which case stent change alone may be the only necessary maneuver (29, 34, 35). The presence of stents in the pancreatic duct is not without consequence, its sole presence leading to strictures similar to those seen in patients suffering from chronic pancreatitis (36, 37). However, these strictures are frequently without functional consequences, being often spontaneously reversible (38).

Transmural Drainage

Depending on the pseudocysts location, the access for transmural endoscopic drainage may be obtained through transgastric or transduodenal approach (16). During the procedure, endoscopic identification of the area of the maximum bulge is performed, using a side-viewing endoscope. Entering the pseudocyst is

done using a needle-knife papillotome with subsequent radiological verification by contrast injection; only then a 7-10 Fr stent may be inserted (35, 39). Concomitant echoendoscopy may be useful for excluding neoplastic lesions or for showing thick-walled pseudocysts or those with marked necrosis (accounting for approximately 50% of patients); it is also able to establish that an endoscopic approach is indeed indicated for the respective lesion (40). Furthermore, echoendoscopy may establish the best point of entry into the pseudocyst, especially when dealing with imprecise intraluminal contour (41). It helps guide the drainage (42-47) thus decreasing the hemorrhage risk by easily avoiding blood vessels and pseudoaneurysms (48, 49). In order to rule out malignant lesions or pancreatic cystadenoma, a biopsy of the wall of the pseudocyst may be performed (50). The stent is maintained for 2-4 months or until radiological proof of pseudocyst resolution and the catheter may be changed if necessary by endoscopic approach (16). The reported cases in the literature reach a success rate between 36-90%, varying with respecting the selection criteria for this particular method (25, 33-36, 40, 44, 49, 51-54). A high rate of success is seen in patients having pseudocysts located in the head and body of the pancreas, pseudocysts with a transmural thickness less than 1 cm as seen on computer tomography or echoendoscopy or complicating chronic pancreatitis rather than an acute necrotizing pancreatitis (25, 32, 35, 53-55). Intra- and postprocedural complications (occurring in under 7% of cases) include bleeding, perforation and sepsis (30), the latest being secondary to infection of necrosis within the pancreatic pseudocyst. In order to minimize the risk of secondary infection, it is important to create a large communication between the cavity of the pseudocyst and the gastric or duodenal lumen, thus favoring an efficient drainage of the content of the pseudocyst (29, 56). Another suggested method for reducing infection rate is performing cyst lavage on an endoscopically placed nasocystic catheter (29, 56). Studies suggest that despite a relatively high rate of complications and recurrence the endoscopic drainage of pancreatic pseudocysts has a signifi-

cantly diminished mortality rate, as compared with open surgical procedures (30)

Laparoscopic Surgery

Traditional methods of drainage of pancreatic pseudocysts were accompanied by a high rate of morbidity and mortality (57, 58). The laparoscopic techniques, once developed, allowed the drainage of pancreatic pseudocysts using the same principles as open surgery, but with a minimally invasive approach. The purpose is to create a large pseudocyst enterostomy and to perform the debridement of the pseudocyst contents. Three types of approaches may be used for internally draining large retrogastric pseudocysts, namely endogastric (57, 59-65), transgastric (57, 64, 66, 67) or extragastric (57, 58, 68) approach. The transgastric approach involves establishing the access to the posterior gastric wall through an anterior gastrectomy. When choosing an endogastric approach, the access is achieved by introducing three ports, including the laparoscope into the gastric lumen. When performing an extragastric approach, we aim to visualize the posterior wall – pseudocyst interface by creating a division in the gastrocolic omentum (16). Ascertaining the location of the pseudocyst is done by inserting an aspiration needle or of a flexible-tip endoscopic ultrasound (63). Often, after creating a large fenestration, a biopsy of the pseudocyst wall is performed, followed by the debridement and lavage of the content, that may be necrotic (16). When dealing with a pseudocyst located in the pancreatic tail, the drainage requires performing a Roux-en-Y pseudocyst-jejunal anastomosis (60, 69, 70) or a loop pseudocyst jejunostomy.

The laparoscopic pseudocyst gastrostomy offers the advantage of a short postoperative stay and of a high success rate, of up to 89% (57, 59, 62, 64). No recurrences were reported for this procedure at follow-up (57, 59, 62, 64). Conversion to open surgery may be required in case of bleeding or other technical difficulties, with a conversion rate of under 7%, (64). Conversion is rarely encountered in well-established pseudocysts (59). The reported

complications include infection of the pseudocysts content as well as recurrence of the pseudocyst, in case of performing an inadequate anastomosis (57, 64). Laparoscopic drainage of acute pseudocysts allow concomitant pancreatic necrosectomy, and, as compared to endoscopic and percutaneous methods (64) it offers the advantage of creating a relatively large pseudocyst enterostomy, thus facilitating more efficient drainage. Furthermore, creating a large cyst-gastric connection decreases the risk of obstruction of the anastomosis as well as the risk of infection and bleeding (16). Despite good short-term results (*Table 1*), the long-term recurrence rate is expected to be similar to open surgery (5-20%) (57, 64, 66, 71-73).

Open Surgical Techniques

Internal drainage of pancreatic pseudocysts, using classical surgical techniques, was historically considered of election for mature, uncomplicated pseudocysts (3). The technical options for internal drainage of a pancreatic pseudocyst include cystogastrostomy, cystoduodenostomy and cystojejunostomy using a Roux-en-Y pseudocyst-jejunal anastomosis. The type of the operation is chosen according to the pseudocysts location and to the nearest by organ pertaining to the gastrointestinal tract (3, 74). For pancreatic pseudocysts densely adherent to the posterior wall of the stomach, cystogastrostomy is of choice (75). On the other side, pseudocysts located in the head and uncinate process of the pancreas are drained by cystiduodenostomy (75). For all remaining pseudocysts, especially for large ones (>15cm in diameter), a cystojejunostomy is considered the appropriate technique (75).

When considering all surgical treatment methods for pancreatic pseudocysts, authors evaluate the morbidity rate somewhere between 10-30% whilst the mortality rate varies between 1-5%. The five years recurrence reaches 20% in some studies (38, 74).

The indications of excision of pseudocysts located in the body or tail of the pancreas through distal pancreatectomy, with or without splenectomy are limited. It is reserved for the treatment of complications such as bleeding from a pseudoaneurysm or for true cysts or cystic neoplasies discovered by biopsy of the cystic wall during surgery (76, 77). Due to the fact that resection is technically more difficult, with higher morbi-mortality and may possibly result in loss of pancreatic function, internal drainage is usually preferred for surgically treating pancreatic pseudocysts (75). Pancreatic resection for pseudocysts is accompanied by a complication rate of 34% and a mortality rate of 8.5% (78). Amongst early complications, pneumonia, intraabdominal infections, hemorrhage and postoperative pancreatitis are the most frequent (76). In the late postoperative period, patients may develop diabetes, chronic pancreatic fistulas or chronic pancreatic insufficiency (76). External surgical drainage, although frequently performed in the past, nowadays has few indications (3, 76). In cases in which anastomotic dehiscence is very likely to occur (because of either unexpectedly infected pseudocyst or unanticipated immature wall, incapable of holding sutures or in case of misdiagnosis) external drainage may still be used (3, 76). The main disadvantage of external drainage is the potential for bleeding due to mechanical abrasion produced by the drainage tube (3, 75, 76). Moreover, the risk of secondary infection is

Table 1. Laparoscopic pseudocyst-gastrostomy

Reference	Technique	Complications	Success rate	Conversion	Recurrence
Smadja et al.(67)	Transgastic	0%	100%	0	N/A
Ammori et al.(59)	Endogastric	0%	100%	0	0
Chowbey et al.(62)	Endogastric	N/A	100%	0	N/A
Park et al.(57)	Exogastric	17%	100%	0	0
Mori et al.(64)	Endogastric	8%	77%	15%	0

high as is the risk of persistent pancreatic fistula (in 10% of patients) requiring subsequent distal pancreatectomy or Roux-en-Y pseudocyst-jejunal anastomosis for drainage (76). External pancreatic drainage, done by classic surgical techniques has a recurrence rate of 18% and a mortality rate of 10% (3, 75, 76). Responsible for the high mortality rate is often the patient's extremely poor condition when submitted to the surgical procedure (76). The cyst wall biopsy is mandatory, regardless of the procedure of surgical drainage elected. Finding any type of endothelium in the wall at histological examination indicates that the lesion is, in fact, a true cyst or a cystic neoplasia, rather than a pancreatic pseudocyst (76). Corroborating all surgical techniques for treating pancreatic pseudocysts, pertaining to classic open surgery we discover a mortality rate of under 1% but with a morbidity of nearly 30% and a recurrence rate of 6% (22, 79).

Thus, the indications for classic open surgical management of pancreatic pseudocysts are limited (76, 80). It is indicated for treating complicated pancreatic pseudocysts that form in the setting of acute pancreatitis, accompanied by extensive pancreatic modifications, inflammation, abscesses and pancreatic necrosis, in which case endoscopic drainage is ineffective (76, 80). Sole pseudocyst drainage is futile, concomitant necrosectomy and debridement being necessary. Another indication is pancreatic pseudocysts associating a pancreatic duct stricture impossible to treat by transpapillary approach (due to the possibility of determining a pancreatic duct dilatation and forming of another pseudocyst behind the stricture). Surgery is performed in order to decompress the duct beyond the stricture, correcting both the pseudocyst and its cause. Only draining the pseudocyst may result in pseudocyst recurrence or in the onset of another episode of pancreatitis (76, 80). For cases in which the etiological diagnosis cannot be certainly established, open surgery is also of choice, sometimes the pancreatic lesion not being able to be differentiated from a neoplastic cyst or benign essential cyst (76). Moreover, for cases of pancreatic pseudocysts connected to the biliary tract, also

associating a bile duct stricture of over 2 cm in length (cases for which endoscopic sphincterotomy cannot be successfully applied) open surgery is of great use (76). Another situation is in cases of intracystic hemorrhage caused by erosion of the pancreatic pseudocyst into the splenic or gastroduodenal artery, with a failed attempt of angiographic hemostasis (76, 80). Moreover, open surgery is useful for cases in which uncontrolled hemorrhage occurs or when minimal invasive treatment fails (76).

Comparative Study of Therapeutical Options

Studies regarding the treatment of pancreatic pseudocysts mention a great variety of results regarding multiple therapeutical alternatives.

Heider et al. prove that patients treated by percutaneous approach have a higher mortality rate as compared to patients treated with open surgery, also having an increased duration of hospitalization (5). Moreover, Morton et al. show that patients treated with surgical drainage have fewer complications, less mortality and diminished hospital stay (81) (*Table 2*).

Akshintala et al. show that percutaneous drainage has higher rates of reintervention despite a similar success rate to endoscopic drainage but patients need a longer hospital stay (82). Two years later, Keane et al. show that endoscopic drainage has higher rates of treatment success, lower rates of reintervention, the patients requiring shorter hospitalization (83) (*Table 3*).

As far as the advantages of transmural echoendoscopic guided drainage are concerned multiple studies showed a higher success rate as compared to classic radiological guided transmural drainage but with similar results and long-term complications (84, 85) (*Table 4*).

Despite similar rates of success, reintervention and complications, echoendoscopic guided transmural drainage is more advantageous as compared to surgical drainage due to requiring less hospital stay and fewer costs (86, 87) (*Table 5*).

Melman et al. show that surgical drainage has a better primary success rate compared to endoscopic drainage, but both have similar

Table 2. Percutaneous drainage vs. surgical drainage

Study		Percutaneous drainage			Surgical drainage		
Name	Type	Morbidity	Mortality	Hospital stay	Morbidity	Mortality	Hospital
Heider et al. (5)	Retrospective	+++	+++	+++	+	+	+
Morton et al. (81)	Retrospective	+	+	+	++	++	++

Table 3. Percutaneous drainage vs. endoscopic drainage

Study		Percutaneous drainage			Endoscopic drainage		
Name	Type	Reintervention rate	Success rate	Hospital stay	Reintervention rate	Success rate	Hospital stay
Akshintala et al. (82)	Retrospective	++	++	++	+	++	+
Keane et al. (83)	Retrospective	++	+	++	+	++	+

Table 4. Classic transmural drainage vs. ecoendoscopic guided transmural drainage

Study		Classic transmural drainage			Ecoendoscopic guided transmural drainage		
Name	Type	Success rate	Complication rate	Reccurance rate	Success rate	Complication rate	Reccurance rate
Varadarajulu et al. (85)	Randomized	+	+	+	++	+	+
Park et al. (84)	Randomized	+	+	+	++	+	+

Table 5. Surgical drainage vs. ecoendoscopic guided transmural drainage

Study		Surgical drainage			Ecoendoscopic guided transmural drainage		
Name	Type	Success rate	Complication and reintervention rate	Hospital stay	Success rate	Complication and reintervention rate	Hospital stay
Varadarajulu et al. (87)	Retrospective	+	+	++	+	+	+
Varadarajulu et al. (86)	Randomized	+	+	++	+	+	+

Table 6. Endoscopic drainage vs. surgical drainage

Study		Endoscopic drainage		Surgical drainage (laparoscopic/open)	
Name	Type	Success rate	Complication rate	Success rate	Complication rate
Melman et al. (88)	Retrospective	+	+	++	+

rates of complications (88) (*Table 6*).

Studies show a great variety of diagnostic and therapeutical techniques. These methods are intensely put under debate as far as indications and advantages are concerned. Often, certain surgical centers show a specific preference in choosing a certain method and their experience usually materializes in exceptional success rates. So, different opinions in

supporting a therapeutical approach, often based on extensive studies, are not uncommon. The curve of learning is nevertheless an important predictive factor for the subsequent results. While taking into account the success and complications rates mentioned by various authors, we find it useful to apply a therapeutical algorithm when drainage is indicated for pancreatic pseudocysts. Thus, we find that

endoscopic drainage, with the two subtypes of approach – transpapillary and transmural should be first considered when needing to drain a pancreatic pseudocyst. Furthermore, the advantages of conventional radiologic methods are incontestable, situating them nevertheless right after the endoscopic techniques in the hierarchy of therapeutical measures. We propose a third method to be considered laparoscopic surgery, followed by open surgical techniques. We see the percutaneous drainage as the last option to be considered due to the potential risks and complications, being nevertheless the only feasible technique for selected cases.

Conclusions

The constant interest in developing new treatment methods for pancreatic pseudocysts and standardizing the treatment indications led, over the years, to a transition from invasive methods to more patient-adapted methods. These therapeutical options are associated with minimum risk of complications and maximum rates of success. Although percutaneous and endoscopic methods possess the advantages of safety, increased efficacy and possibility to be applied to patients with a poor general state, the historical gold standard represented by surgical drainage techniques is still irreplaceable for large pseudocysts or pseudocysts that showed evolutive complications. An overall view of the indications and complications may lead to the development of a therapeutical algorithm of incontestable utility in choosing the most efficient technique for each patient with minimum periprocedural risk.

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