

Pancreatic Pseudocysts Dilemma; Cumulative Multicenter experience in Management using Endoscopy, Laparoscopy, and open surgery

By

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Running title: treatment of pancreatic pseudocysts

Abstract

Introduction and aim of the work: Pancreatic pseudocyst is the commonest cystic lesion of the pancreas. When interference is indicated, open surgical therapy is the standard therapy with which other therapeutic modalities should be compared. Recently, endoscopic and laparoscopic approaches were reported for management of these cases. We aimed at exploring the minimally invasive techniques in treatment of pancreatic pseudocysts, namely endoscopic and laparoscopic, and comparing them to the open surgical therapy.

Patients and methods: Fifty nine patients with pancreatic pseudocyst assigned for interference were included in this study. Thirty five patients were treated endoscopically, two laparoscopically and twenty two by open surgery. The endoscopic techniques used were cystogastrostomy in thirty cases, cystoduodenostomy in three cases, and trans-ampullary drainage in two patients. In the laparoscopic cases, a loop-sutured cystojejunostomy was done. The open surgical techniques were cystogastrostomy in fifteen patients and cystojejunostomy in seven patients.

Results: The endoscopic therapy had the shortest procedure time (30 min) in comparison to 110 and 105 min for the laparoscopic and open surgical groups respectively. No mortality was reported in any of the groups. Postoperative complications represent 14%, 40% for the endoscopic and the open surgical groups respectively. The hospital stay was shorter for both endoscopic and laparoscopic cases than open surgical cases.

Conclusion: Minimally invasive therapeutic techniques, whether endoscopic or laparoscopic for treatment pancreatic pseudocyst could be considered valuable, competitive and promising alternatives for open surgery. Moreover, it is less invasive, less costly, with less hospitalization and rapid return to work. Large scale comparative studies are highly recommended in the future.

Key words: pancreatic pseudocyst, cystogastrostomy, cystojejunostomy.

Introduction:

Pancreatic pseudocyst is a localized fluid collection that is rich in amylase and other pancreatic enzymes and is surrounded by a wall of fibrous tissue without epithelium lining communicated with pancreatic duct system in 22-57 % of cases, either directly or indirectly via pancreatic parenchyma that can be located almost everywhere in the abdominal cavity. In most of the time, however, they are found in the lesser sac behind the stomach^{1,2,3}. An acute pseudocyst is a collection of pancreatic juice enclosed by a wall of fibrous or granulation tissue, which arises as a consequence of acute pancreatitis or pancreatic trauma, whereas a chronic pseudocyst is a collection of pancreatic juice enclosed by a wall of fibrous or granulation tissue, which arises as a consequence of chronic pancreatitis and lack an antecedent episode of acute pancreatitis⁴.

Initial diagnosis is accomplished most often by cross-sectional imaging, however EUS with fine needle aspiration has become the preferred test to help distinguish pseudocyst from other cystic lesions⁵. More than 50% of pseudocyst cases resolve spontaneously. The two main factors determining spontaneous regression of pancreatic pseudocysts are size and time of evolution after diagnosis¹, but larger cysts are more likely to be symptomatic or cause complications. The indications for drainage procedure are persistent symptoms or complications as infection, gastric outlet or biliary obstruction, and bleeding⁶.

Three strategies for pseudocysts drainage are available: endoscopic (transpapillary or transmural), percutaneous, or open surgery. As a result, the management varies based on local expertise, and feasibility, however endoscopic drainage is becoming the preferred approach because it is less invasive than surgery, avoids the need for external drain, and has a high long-term success rate. A tailored therapeutic approach taking into consideration patient preferences and involving multi-disciplinary team of therapeutic endoscopist, interventional radiologist and pancreatic surgeon should be considered in all cases^{5,7}.

The Cyst fluid obtained by FNA should be examined for tumor marker values. Results showed that carbohydrate antigen 19-9 levels of >50 000 U/mL had 75% sensitivity and 90% specificity for distinguishing mucinous tumors from other cystic lesions. CEA levels of <5 ng/mL had 100% sensitivity and an 86% specificity for distinguishing serous cystadenoma from other cystic lesion. Amylase levels of >5000 U/mL had 94% sensitivity and 74% specificity to pseudocysts from other cystic lesions. So high Ca 19-9, low CEA, and high amylase in cyst fluid are very indicative of mucinous tumors, serous cystadenoma, and pseudocysts, respectively⁵. Endoscopic drainage of pseudocysts is becoming the preferred therapeutic approach because it is less invasive than surgery, avoids the need for external drain and has a high long-term success rate. Drainage is accomplished with either a transpapillary rout or direct drainage across the stomach or duodenal wall^{3,7}. A transpapillary ERCP approach is used when the pseudocyst communicates with the main pancreatic duct, usually in the genu of the pancreatic duct, and proved successfulness in duct disruption^{1,2}. A transgastric or transduodenal approach is used when the pseudocyst is directly adjacent to the gastroduodenal wall. The endoscopic approach is dependent upon the presence of a bulge into the lumen of the stomach or duodenum in order to determine the entry site for catheterization. This approach has several risks as missing the cavity, injuring intervening vessels, and sub-optimal placement of the drainage catheter³. Therapeutic echoendoscopes now make it possible to treat pseudocysts with EUS-guided transmural stenting^{3,7,8}. The pseudocyst is punctured with a diathermy needle and then the stoma is extended to 10-15 mm incision using over-wire sphincterotome. For the possibility of infection, stenosis or obstruction of the stoma, an endoprosthesis (stent) may be applied either double pigtail plastic, or self-expanded mesh metallic stent if feasible as it is more efficient especially used if the contents of the collection are thick, necrotic, or infected, as these collections may not adequately drain through plastic stents^{3,7,9}. This

maneuver is done by expert pancreaticobiliary endoscopist with sound clinical judgment regarding the appropriate indication, aided by EUS access, and expert surgical and interventional radiologic support for complication^{9,10}.

Laparoscopy on the other hand was used by several authors for drainage of pancreatic pseudocysts, whether to the stomach or to the jejunum, laparoscopic cystogastrostomy is either through intraluminal or an extraluminal approach. Laparoscopic cystojejunostomy appears to be more appropriate because of the excellent results obtained by the same technique in open surgery using simple loop cystojejunostomy without enteroenterostomy. Laparoscopic surgery has been recommended as a safe, reliable, and minimally invasive treatment as advances in the technique and instrumentation improve the ability to perform more complex procedures avoiding the greater morbidity and longer recovery from open surgery¹¹. Gastro-pseudocystostomy and jejuno-pseudocystostomy, both achieved adequate internal drainage that facilitate concomitant debridement of necrotic tissue within the acute type of pseudocyst, and achieved good results with minimal morbidity¹².

Patients and methods:

Fifty nine patients with pancreatic pseudocyst assigned for interference were included in this study. Thirty five patients were treated endoscopically, two laparoscopically and twenty two by open surgery.

Criteria that should be applied in selecting patients for surgical intervention include persistence of the pseudocyst for more than 6 weeks and ultrasonography evidence of reasonable wall thickness. Other parameters include size of greater than 7.5 cm in diameter, additionally, maturity of the pseudocyst should be allowed for 4-6 weeks to have a cyst wall thick enough to facilitate its drainage. The site of the cyst is another factor that may dictate certain operative decision. Retro-gastric cysts which are enlarging anteriorly can be treated by a posterior cystogastrostomy. This is appropriate only if the stomach is closely applied to the front of the cyst. On the other hand, cysts around the head of the pancreas close to the duodenum can easily be drained by cystoduodenostomy. Large cysts, which enlarge and bulge inferiorly through the transverse mesocolon, are best drained by cystojejunostomy. In general, the most preferable approach is cystojejunostomy Roux-en-Y because the Roux loop can be anastomosed to the lower part of the cyst. Resection is preserved for those pseudocysts largely replaced the tail or body of the pancreas. In this study, endoscopic techniques used were cystogastrostomy in thirty cases, cystoduodenostomy in three cases, and trans-ampullary in two cases. On the other hand; laparoscopy was done in two cases by loop-sutured cystojejunostomy, versus open surgery doing cystogastrostomy in fifteen, and cystojejunostomy in seven patients.

Data of the patients were categorized with comparison between the three approaches as regards the invasiveness of the procedure, the time needed, morbidity and mortality encountered, and patient hospital stay

Results:

Fifty nine patients with pancreatic pseudocyst assigned for interference were included in this study, age and sex incidence of our patients were shown in **table (1)**.

Management of pseudocysts was randomly assigned for one of three approaches accordingly:

Group I included thirty five patients, treated endoscopically, group II included two patients treated laparoscopically, versus twenty two patients were treated by open surgery as shown in **table (2)**.

Endoscopic approaches were the treatment of choice in our tertiary center as convenient, effective, feasible, minimally invasive, treatment option with very low if any morbidity and mortality rate, short hospitalization period, low cost, with high patient acceptance and satisfaction. Technique of

endoscopic maneuvers included cysto-gastrosyomy, cysto-duodenostomy, and trans-ampullary drainage as shown in **table (3)**.

Laparoscopic drainage of pseudocyst was done in two patients by loop-sutured cystojejunostomy; on the other hand, open surgery drainage was done in twenty two cases by cystogastrostomy in fifteen patients and cystojejunostomy in seven patients.

Data of our cases were collected and comparison between the three groups was done considering the invasiveness of the procedure, the mean time of the procedure (minutes), post-operative morbidity incidence, mortality incidence, and the mean hospital stay in days as shown in **table (4)**.

Discussion:

Surgery has been the gold standard for the treatment of pancreatic pseudocysts, by decompression and drainage procedure³. The aim of internal drainage is the production of a communication between the cyst and the lumen to drain the contents; however, this option is typically reserved for uncomplicated pseudocysts, and several sites can be used for drainage including stomach, duodenum or a Roux loop of jejunum^{5,13}.

The surgical stoma should be placed in the most dependent portion of the cystic cavity in order to maximize the chances of complete drainage. The stoma usually remains patent and functional for several months⁵.

Controversy surrounds the question of which viscus should be used for pseudocyst drainage: stomach, duodenum or a Roux loop of jejunum. Some favors gastropseudocystostomy, and others favors jejunopseudocystostomy. There are also advocates of individualized approach when operation is chosen according to the particular anatomy and condition of the patient. Some modifications were adopted to the technique as oversewing the gastropseudocystostomy stoma to reduce the incidence of post-operative bleeding, place multiple mattress sutures of permanent material circumferentially around the anastomosis in the area of fusion, and the use of disposable stapler for creation of gastropseudocystostomy stoma⁴.

In our study, open surgical treatment was resold to in twenty two patients (37.3%), by cystogastrostomy in fifteen patients and cystojejunostomy in seven patients. The mean time of the procedure was 105 minutes, mortality was zero percent, post operative morbidity incidence was 14.3%, and the mean hospital stay in days was 7 days. This was comparable to other reported data documented that surgery was associated with significantly higher mortality and morbidity rate (9%) than with other less invasive therapy (1%) ($P < 0.05$)⁵. Others document morbidity rate of 10-30%, and a 10-20 recurrence rate³; however cumulative data shows a success rates from 70% - 100%, morbidity of 9-30% and a cyst recurrence was observed in 0-20%^{11,14}.

In our study, laparoscopic surgical treatment was resold to in two patients (3.4%), by cystojejunostomy. Unfortunately; this is a small number of patients to comment on but the mean time of the procedure was 110 minutes, zero mortality, overall morbidity incidence was 22% and the mean hospital stay in days was 3 days. This was acceptable as laparoscopic surgery has been recommended as a safe, reliable, and minimally invasive treatment for pancreatic pseudocyst^{15,16}, as advances in laparoscopic surgical technique and instrumentation have furthered our ability to perform more complex laparoscopic procedures¹⁷. Laparoscopy has contributed enormously in the management of pseudocysts. Many series have reported excellent outcomes with the laparoscopic procedure¹⁸. It offers all of the benefits of minimally invasive surgery to the patient while maintaining all of the principles of PP surgery^{16,19}.

The minimally invasive approach to gastropseudocystostomy allows for wide drainage of the pancreatic pseudocysts and might avoid the greater morbidity and longer recovery from an open surgical procedure. Laparoscopic gastropseudocystostomy and jejunopseudocystostomy achieve adequate internal drainage, facilitate concomitant debridement of necrotic tissue within the

pseudocysts, and achieve good results with minimal morbidity, with excellent outcomes^{4,16,20}, and it should be considered a choice of treatment in the management of pancreatic pseudocyst¹⁹. However, the role of surgery in treatment of pancreatic pseudocysts has changed for several reasons, first of all endoscopic drainage techniques have become refined and universally available, and the natural history of pseudocysts has disclosed that most asymptomatic pseudocysts need no treatment⁴.

Endoscopic drainage of pseudocysts is becoming the preferred therapeutic approach because it is less invasive than surgery, avoids the need for external drain and has a high long-term success rate³. In our study, endoscopic treatment was resorted to in thirty five patients (59.3%), by cystogastrostomy in thirty patients, cystoduodenostomy in three patients, and trans-ampullary drainage in two patients, by deployment of two stents in most of cases, with success rate of 95%, and complete resolution of the cysts within a month. The crucial anatomic fact that makes endoscopic drainage of pseudocysts feasible is that a pseudocyst does not have its own structure; rather, it is a space delineated by the normal anatomic structures adjacent to the inflammatory process namely the stomach, intestine, liver, spleen, or transverse mesocolon (and part of the pancreas). The wall of the stomach or the duodenum is often common wall of the pseudocyst between which a thick inflammatory peel forms a poorly defined interface. This allows an enterostomy to be performed without concern for a potential space between the pseudocyst and the stomach and duodenum, which could develop if the pseudocyst and digestive walls were simply in close apposition⁴, that results in transgastric or transduodenal deployment of 10 F 2 or 3 cm plastic stent, usually patients required two stents placed into the cyst with a technical success rate for stent placement 94%. Interestingly 82% had complete resolution with a partial resolution in 12% of the patients, and complications encountered are perforation and bleeding²¹. Another study underwent EUS-guided transmural drainage showed an overall success rate of 94%^{22,23}, as only EUS provides the ability to evaluate the distance between the fluid collection and the bowel wall, to detect the presence of wall adherence, and to identify vessels that may be interposed between the 2 lumens. It is necessary to see into and beyond the wall to perform this procedure safely and effectively^{2,9}. So, by adopting this approach, more complicated cases of pancreatic pseudocyst can successfully be treated with much lower morbidity and mortality rate compared to surgical drainage with a lower overall recurrence rate^{2,3}. Endoscopic cystogastrostomy is an excellent alternative to surgery as it provides immediate symptomatic relief for the patient. Furthermore necrosectomy can also be performed by deployment of self-expandable metal stent (SEMS)^{2,24,25,26,27,28}. However; there is no data to prove that metal stents are superior to plastic stents in terms of treatment efficacy, complications, recurrence rates or cost-effectiveness^{7,29}.

Endoscopic approach has resulted in a success rate of more than 90% in patients with chronic pseudocysts. The recurrence rate after endoscopic drainage is low, 4%, technical success rate of the drainage procedure was 97% and the mortality rate was 1%, and the complication rate is less than 16%. Endoscopy is also capable of guiding the drainage of infected pseudocysts using naso-cystic drains. It may even be possible to drain infected necrotic pancreatic tissue using this techniques⁵. The addition of nasocystic catheter for irrigation/drainage is very beneficial for necrosectomy process, vigorous irrigation of necrosis with several liters of saline, followed by 3% hydrogen peroxide, which helps break up necrotic tissue and drainage of debris and thick cystic content⁹.

In our study, this maneuver was adopted in 14 patients (23%), in whom the content of the pseudocyst after puncture was thick infected debris; so beside stent deployment, a nasocystic catheter was inserted within the cavity with continuous wash for 2 days then extracted before discharge. This approach allows rapid debridement of the pseudocyst that remarkably shortens patient's stay, especially in patients with sepsis. Patient can be started on a regular diet within 24 h

of the procedure; also the risks involved with surgery as infection are virtually eliminated. Patient can be discharged from the hospital sooner without the need for special care instructions. Moreover, the procedure is much less invasive compared to surgery, patient's overall hospital stay is reduced, which not only saves on healthcare costs and prevent in-hospital complications, but also improves patient's overall satisfaction³⁰.

the current trend in managing pancreatic pseudocysts with minimally invasive therapeutic and endoscopic procedures is superior to surgical procedures in terms of morbidity and mortality rates, however these procedures cannot always be performed and feasible. In making decisions about the treatment of pancreatic pseudocyst it is important to note that about 50% do not require intervention and resolve spontaneously with observation and clinical follow-up¹⁰. The selection of a technique for pseudocyst drainage depends on the experience of the treating group. However, transpapillary drainage is a safe and highly efficient option when the lesion is less than 6 cm, and it is connected to the pancreatic duct¹.

Resolution rates after surgical and non-surgical methods are comparable, but clinical and technical aspects may mandate either method, as any of types of management have the same possibility of a good outcome. Therefore, today we have to rely on best clinical practice, consequently; each patient requires an individual, multidisciplinary approach, thereby obtaining optimal treatment outcome⁴.

Conclusion:

In conclusion, treatment of pancreatic pseudocyst is in an era of re-evaluation. Relatively new and minimally invasive techniques have been introduced as alternatives to the standard conventional open surgical management. Endoscopic procedures have been increasingly used with excellent results. Laparoscopic approach, although difficult, appears to be promising. However, large-scale comparative studies of the three different therapeutic modalities are highly recommended.

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