Is endoscopic therapy the treatment of choice in all patients with chronic pancreatitis?

Beata Jabłońska

Beata Jabłońska, Department of Digestive Tract Surgery, University Hospital of the Medical University of Silesia, 40-752 Katowice, Poland
Author contributions: Jabłońska B wrote this paper.
Correspondence to: Beata Jabłońska, MD, PhD, Department of Digestive Tract Surgery, University Hospital of the Medical University of Silesia, Medyków 14 Street, 40-752 Katowice, Poland. hjablonska@poczta.onet.pl
Telephone: +48-32-7894251 Fax: +48-32-7894251
Received: September 4, 2012 Revised: October 29, 2012
Accepted: November 11, 2012
Published online: January 7, 2013

Abstract

Chronic pancreatitis (CP) is a progressive inflammatory disease of the pancreas characterized by destruction of the pancreatic parenchyma with subsequent fibrosis that leads to pancreatic exocrine and endocrine insufficiency. Abdominal pain and local complications (bile duct or duodenal stenosis and pancreatic tumor) secondary to CP are indications for therapy. At the beginning, medical therapy is used. More invasive treatment is recommended for patients with pancreatic duct stones (PDS) and pancreatic obstruction in whom standard medical therapy is not sufficient. Recently, Clarke et al assessed the long-term effectiveness of endoscopic therapy (ET) in CP patients. The authors compared ET with medical treatment. They reported that ET was clinically successful in 50% of patients with symptomatic CP. In this commentary, current CP treatment, including indications for ET and surgery in CP patients, is discussed. Recommendations for endoscopic treatment of CP according to the European Society of Gastrointestinal Endoscopy Clinical Guidelines are reviewed. Different surgical methods used in the treatment of CP patients are also discussed. ET is the most useful in patients with large PDS, pancreatic duct obstruction and dilation. It should be the first-line option because it is less invasive than surgery. Surgery should be the first-line option in patients in whom ET has failed or in those with a pancreatic mass with suspicion of malignancy. ET is a very effective and less invasive procedure, but it cannot be recommended as the treatment of choice in all CP patients.

Key words: Chronic pancreatitis; Endoscopic therapy; Surgery; Endoscopic retrograde cholangiopancreatography; Endoscopy

Jabłońska B. Is endoscopic therapy the treatment of choice in all patients with chronic pancreatitis? World J Gastroenterol 2013; 19(1): 12-16 Available from: URL: http://www.wjgnet.com/1007-9327/full/v19/i1/12.htm DOI: http://dx.doi.org/10.3748/wjg.v19.i1.12

INVITED COMMENTARY ON HOT ARTICLES

I have read with great interest the recent article by Clarke et al[1] describing the endoscopic treatment in patients with chronic pancreatitis (CP). I would strongly recommend this article to the readers of World Journal of Gastroenterology. CP is a progressive inflammatory disease of the pancreas characterized by destruction of the pancreatic parenchyma with subsequent fibrosis that leads to pancreatic exocrine and endocrine insufficiency[2,3].

We can distinguish two stages in the natural CP course. At the beginning, recurrent acute pancreatitis is observed in patients. In the later stage, pancreatic exocrine and endocrine insufficiency manifested by maldigestion and malabsorption, loss of weight, steatorrhea and diabetes are reported[4].

Abdominal pain is the most common clinical symptom requiring therapy in patients with CP. It is caused by obstruction of the pancreatic duct either by stones...
or stricture with increasing intraductal pressure and parenchymal ischemia\[^3\]. Therefore, the main aim of CP treatment is to decompress the main pancreatic duct by pancreatic stone removal and pancreatic duct dilation. Different conservative and invasive methods are used in the treatment of CP. At the beginning, medical therapy with analgesics, oral pancreatic enzyme supplements, insulin and a low fat diet is used\[^{10}\]. More invasive treatment is recommended for patients with pancreatic duct stones (PDS) and pancreatic obstruction in whom standard medical therapy is not sufficient. Local complications such as bile duct stenosis and pancreatic tumor are also indications for invasive treatment. Currently, two main invasive (endoscopic and surgical) methods are used in CP treatment. It should be emphasized that surgery is an older treatment method than endoscopic therapy (ET). The first case of surgical removal of PDS was reported in 1883\[^{11}\]. ET as a less invasive treatment has become popular recently. Currently, both treatment methods are used in CP patients\[^{12-26}\].

In their study, Clarke \textit{et al}\[^{10}\] analyzed the use and long-term effectiveness of ET in CP patients. The authors compared ET with medical treatment. They reported that ET was clinically successful in 50% of patients with symptomatic CP. When ET was not successful, surgery had successful outcomes in 50% of patients. Medical therapy was successful only in 31% of symptomatic patients. Based on their study, the authors concluded that ET was an effective treatment method in CP patients. This is a significant study and I agree with the authors’ opinion. However, I would like to precisely define the use of endoscopic methods in CP patients. It is important to know which patients are good candidates for ET. Can we recommend this treatment method for all CP patients? In order to answer this question I would like to cite the most recent (2012) recommendations of the European Society of Gastrointestinal Endoscopy (ESGE) regarding therapeutic intervention in CP patients\[^{26}\].

The ESGE recommends extracorporeal shock wave lithotripsy (ESWL) and endoscopic retrograde cholangiopancreatography (ERCP) as the first-line treatment method. Surgery should be considered in patients with a predicted poor outcome following ET. In patients with stones \(\geq 5\) mm obstructing the main pancreatic duct, the ESGE recommends ESWL as a first step, combined or not with endoscopic extraction of stone fragments depending on the expertise of the center. In CP patients with a main pancreatic duct stricture, the ESGE recommends placement of a single 10-Fr plastic stent, with stent exchange planned within 1 year. If ductal strictures persist after 12 mo of single plastic stenting, the ESGE recommends that endoscopic placement of multiple pancreatic stents or surgery should be discussed by a multidisciplinary team. The ESGE recommends ET as the first-line interventional option in pancreatic pseudocysts in CP patients. In CP-related biliary strictures, endoscopy and surgery should be considered depending on local expertise, patient co-morbidities, and expected patient compliance with repeat endoscopic procedures\[^{8}\].

Some authors\[^{10}\] recommend surgery as an initial treatment in CP patients with pancreatic and bile duct strictures with upstream dilation, and ET as a second-line option in high-risk surgical candidates.

Clarke \textit{et al}\[^{10}\] analyzed a cohort of 146 patients with CP, including 71 (49%) patients receiving ET. The authors analyzed patients following pancreatic and biliary sphincterotomy, pancreatic duct dilation, stone extraction, ESWL pancreatic and bile duct stenting, and transgastric pseudocyst drainage. The pancreatic duct stenting was the most frequent endoscopic procedure. The interesting aspect of this study is the analysis of 8 (11%) so-called bridge patients, in whom ET as the first step was followed by surgery. Another interesting aspect is comparison of the endoscopic with medical treatment.

There are a number of publications comparing endoscopy with surgery in CP patients in the literature. ET is less invasive than surgery. However, according to most authors, surgery is more effective compared to endoscopy\[^{24,26}\]. Hirota \textit{et al}\[^{26}\] compared costs of these two treatment methods. Duration and frequency of hospitalizations, and medical costs were similar between the short-period endoscopic treatment group and surgery group. On the other hand, patients in the long-period endoscopic treatment group required significantly longer and more frequent hospitalizations, and had higher medical costs than both the short-period endoscopic treatment group and the surgery group. According to the authors’ analysis, patients who underwent serial endoscopic stenting for more than 1 year showed no benefit compared with surgical treatment in terms of the frequency of hospital stays and medical costs.

In addition, I would like to describe the role of surgery in CP patients. I agree with Clarke \textit{et al}\[^{10}\] that ET is effective in CP patients, but I would not recommend this treatment method for all patients. In my opinion, patients with multiple strictures and dilation within the pancreatic duct can have more benefits following surgery. It is my belief that patients with a pancreatic mass with suspicion of malignancy and duodenal stricture secondary to CP should also undergo surgery. In the most frequently encountered situation, PDS are treated endoscopically, but in some cases surgery is necessary. In the study of Liu \textit{et al}\[^{9}\], indications for ET were \(\leq 3\) stones, stones confined to the pancreatic head and body, absence of restricted pancreatic duct, PDS diameter \(\leq 10\) mm, and noncompacted stone(s). Surgery was indicated for patients who needed treatment but did not meet the above-mentioned indications, or for whom conservative therapy had failed.

We can distinguish the following types of surgical procedures in CP patients: drainage operations (Puestow, Parvington-Rochelle, Duval procedures), resectional operations (partial and subtotal or total pancreatectomies), resections with extended drainage (Beger, Frey procedures) and neurolysis (celiac plexus block). The most frequently performed surgical procedures are presented in Figure 1. Total pancreatectomy with islet autotransplan-
tation is an alternative surgical option for CP patients. It is important that this procedure can relieve pain and preserve β-cells in patients when other therapies fail\[19,20\]. Sutherland et al\[20\] from the University of Minnesota reported a > 30-year single-center series with good treatment results.

The Frey procedure is a safe and effective procedure with low morbidity and mortality rates in CP patients. It allows effective pain relief in about 90% of patients\[27\]. It is alternative and effective surgery for CP patients with a pancreatic inflammatory mass within the pancreatic head without malignancy\[28\].

According to Palanivelu et al\[23\], the Partington procedure is still the procedure of choice for patients with a dilated main pancreatic duct but without an inflammatory pancreatic head mass because it is simple and associated with a low postoperative morbidity and mortality, preserving pancreatic exocrine and endocrine function. Frey and Beger operations as duodenum-preserving pancreatic head resections (DPPHRs) with extended pancreatic duct drainage are recommended for patients with an inflammatory pancreatic head mass\[29\]. Furthermore, long-term results of two (Beger and Frey) DPPHRs in CP were compared by Keck et al\[30\]. This study revealed a better pain relief following the Frey procedure compared to the Beger operation.

There are some studies comparing DPPHRs and pancreaticoduodenectomy (PD) in treatment of CP patients. According to Zheng et al\[18\], both procedures are effective in relieving pain, but DPPHR is associated with less postoperative morbidity, including pancreatic exocrine and endocrine insufficiency, and better quality of life in patients following operation. Möbius et al\[31\] demonstrated a better quality of life and comparable pain relief and exocrine and endocrine pancreatic function in patients following DPPHR (Beger procedure) compared to patients following PD (Whipple procedure). Also, Witzigmann et al\[32\] revealed a better quality of life in CP patients following DPPHR compared to that experienced by patients following PD.

According to another recent study by Keck et al\[33\], both DPPHR and PD allow the achievement of effective pain relief and good quality of life without differences in endocrine or exocrine function in CP patients. According to Hildebrand et al\[34\], the Frey procedure is an advantageous alternative to the Whipple operation in CP patients. It is comparable to PD in pain relief and is less invasive (with lower morbidity and mortality rates, and a lower rate of newly occurring diabetes mellitus) than PD.

Figure 1 The most frequently performed surgical procedures. A: Partington-Rochelle procedure involving lateral (longitudinal) pancreaticojejunostomy (anastomosis between the longitudinally incised main pancreatic duct and Roux-Y jejunal loop); B: Beger procedure involving resection of the pancreatic head preserving the duodenum. The pancreas is transected at a border between the pancreatic head and body, leaving a thin pancreatic disc between the common bile duct and duodenum. The pancreatic body is drained by end-to-end pancreaticojejunostomy and pancreatic head disc is drained by side-to-side pancreaticojejunostomy using a Roux-Y jejunal loop; C: Frey procedure involving coring out of the pancreatic head overlying the main and accessory pancreatic ducts and uncinate process, keeping at least 5 mm pancreatic tissue posteriorly and medially along with opening the main duct in body and tail. The cored head and opened main duct are drained by lateral pancreaticojejunostomy using a Roux-Y jejunal loop; D: Whipple procedure involving pancreaticoduodenectomy with reconstruction by pancreaticojejunostomy, hepaticojejunostomy and gastrojejunostomy.
Similarly, McClaine et al.\(^{[5]}\) reported that DPPhR was equally as effective as PD in relieving pain and improving quality of life in CP patients; DPPhR was associated with a shorter hospital stay and less blood loss.

The choice of optimal surgery depends on size, number and location of PDS or presence of other complications (pancreatic mass, duodenal or biliary stenosis). In patients with pancreatic ductal stones, the PDS type should firstly be identified. Depending on location, four types of PDS have been established: type I in the head of the pancreas, type II in the body, type III in the tail, and type IV in the whole pancreas. Drainage by pancreatic ductotomy is generally recommended for patients with a dilated pancreatic duct (≥ 6 mm). The Beger procedure and PD are suitable for type I PDS; however, distal pancreatectomy is useful for type III PDS. For patients with type II PDS, the Parving-Rochelle procedure or segmental resection of the pancreas is recommended. For patients with type IV PDS, an alternative to drainage is a Child procedure (subtotal pancreatectomy).\(^{[6,8]}\)

In conclusion, all methods including medical, endoscopic and surgical treatment are used in CP patients. Medical therapy is suitable in patients without complications at the outset of CP. ET is the most useful in patients with large PDS, pancreatic duct obstruction and dilatation. It should be the first-line option because it is less invasive than surgery. The method of ET (pancreatic sphincterotomy or ESWL followed by pancreatic duct stenting) depends on the stone location and the pancreatic duct diameter. Surgery should be the first-line option in patients in whom ET failed or those with pancreatic mass with suspicion of malignancy. Therefore, although ET is a very effective and less invasive procedure, it cannot be recommended as the treatment of choice in all CP patients. In my opinion, surgical treatment without endoscopic treatment should be recommended for patients with duodenal stricture and pancreatic mass with suspicion of malignancy. In these patients, endoscopy should be used only in the diagnosis.

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