

Indications for Endoscopic or Surgical Treatment of Chronic Pancreatitis

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Key Words

Chronic pancreatitis · Endoscopic therapy · Evidence-based surgery

Abstract

In patients suffering from chronic pancreatitis, pain as the predominant symptom remains a therapeutic challenge which often cannot be tackled conservatively. Since pancreatic duct obstruction – frequently within the pancreatic head – is an important etiological factor, treatment in these cases aims at decompressing the duct either endoscopically or surgically. Endoscopic drainage includes sphincterotomy, dilation of strictures, removal of stones, and insertion of a stent; it has a success rate of 30–100%. Surgical treatment may be accomplished by drainage or resection procedures. Drainage procedures (such as the longitudinal opening of the pancreatic duct followed by a pancreaticojejunostomy) can be performed with a low rate of postoperative complications (6–30%) and mortality (0–2%), and can achieve long-term pain relief in 65–85% of the cases. Furthermore, there are a variety of resection procedures such as pancreaticoduodenectomy (Whipple procedure), pylorus-preserving pancreaticoduodenectomy, different types of the duodenum-preserving pancreatic head resection (i.e. Beger, Frey, or Büchler procedures), segmentectomy, and V-shaped excision of the pancreatic duct. However, the surgical procedure of choice is controversially discussed. While it has been shown that parenchyma-preserving surgery is superior to

more extensive resections, it remains unclear which of the modifications of the parenchyma-sparing procedures is suited best for which case. Recently, two randomized controlled trials have demonstrated that surgical treatment is superior to endotherapy in long-term pain reduction, physical health score results, and the number of reinterventions. Thus, in patients with chronic pancreatitis refractory to conservative medical treatment, surgery rather than endotherapy is the standard of care. Parenchyma-preserving resections should preferably be performed because they ensure lower morbidity and mortality, preserve endocrine function, and improve quality of life.

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Introduction

Chronic pancreatitis (CP) is a relatively common disorder of which most of the pathogenesis is not yet well understood. The consequences of this disease are morphologic changes (destruction of acinar and ductal cells, including ductal obstruction, pancreatic stone development, and fibrosis) as well as functional impairments (loss of exocrine and endocrine function). In most of the cases, CP is treated with conservative methods, such as pain management, cessation of alcohol intake, small meals, and pancreatic enzyme supplements. However, pain as the predominant symptom remains a therapeutic challenge which can often not be tackled sufficiently by

conservative treatment. Neurolytic approaches either by percutaneous or endoscopic celiac nerve blocks (with steroids or alcohol) or by surgical denervation procedures meet only with limited success in CP. Since pancreatic duct obstruction – frequently within the pancreatic head – is an important etiologic factor, treatment in these cases aims at decompressing the duct either endoscopically or surgically. However, these invasive treatments cannot heal a late-stage CP, but aim at an improved quality of life.

The treatment options for patients with CP are controversially discussed, particularly the indications for endoscopic vs. surgical therapy (fig. 1). Since pain, the most common indication for intervention, is not a subjective criterion, the decision for or against one of these treatments options is even more complex. The rationale behind treating pain by an intervention is the hypothesis of an underlying pancreatic duct obstruction, which is decompressed by intervention; additionally, it seems that perineural inflammation, which is triggered by the release of toxic substances from the diseased pancreatic tissue, is also an important etiologic factor.

Interventional Treatment Options

Indications for an invasive therapy in CP are (a) chronic upper abdominal pain, which cannot be managed by analgesics, (b) stenosis, for example of the duodenum or the common bile duct or the pancreatic duct, (c) vascular obstructions (e.g. portal vein, superior mesenteric vein) or (d) symptomatic pseudocysts. Importantly, if malignancy is suspected, surgery has to be enforced. Two randomized studies on treatment of CP with either endoscopy (with or without stenting) or surgery have been published so far. Dite et al. [1] reported in 2003 a group of 72 patients that were randomly assigned to undergo either surgery or endoscopic therapy with or without stenting. 80% of the patients in the surgical treatment arm received a resection, while in 20% of the patients, a drainage procedure was performed. 52% of the patients in the group with endoscopic treatment received a sphincterotomy including stent insertion, while in 23% of the patients only a stone extraction was performed. The results after 1 year were almost the same in endoscopic or surgical therapy. 41% vs. 50% (endoscopy vs. surgery) had a pain reduction and 52% vs. 42% of the patients even had a complete pain remission. In both groups, only 8% of the patients did not respond to the therapy at all. However, these clinical outcomes considerably changed after 3 and 5 years: in the

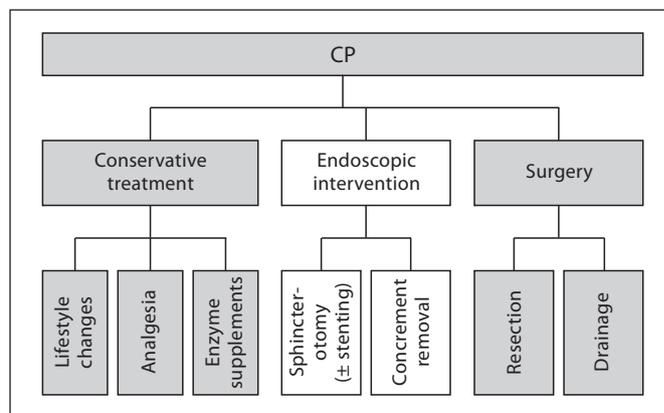


Fig. 1. Different treatment methods for CP. In patients where the symptoms of CP cannot be controlled sufficiently, an interventional treatment is necessary. Recent randomized controlled trials indicate that surgical treatment is superior to endotherapy in long-term pain reduction, physical health score results, and the number of reinterventions.

endoscopic treatment group only 11% (after 3 years) and 14% (after 5 years) of the patients had a complete pain remission. Yet, in the surgical treatment group after 3 and 5 years, 41% and 37% of the patients, respectively, were completely free of pain. Even more interestingly, a similar picture was observed when evaluating the overall response rate to the therapy. The rate of the nonresponders was one third in the endoscopic treatment group, whereas in the surgical treatment group only 12–14% of the patients did not respond at all to the therapy after 3 and 5 years. These differences in long-term pain reduction were statistically significant ($p < 0.05$). Similar results were observed in evolution of the patients' body weight; this evolution is highly relevant since a drop in body weight is an important factor in reducing the patients' quality of life. Analogous to pain reduction, both treatment groups showed a significant gain in body weight in the 1st year in about two thirds of the cases. Evaluating the results after 5 years, only in the surgical treatment group more than half of the patients had a gain in body weight, whereas a weight gain was observed in only 27% of the endoscopically treated patients. At the same time, 42% of the endoscopically treated patients had lost body weight. However, only 29% of all patients in the surgical treatment group had lost body weight 5 years after treatment. These results also were statistically significant and in favor of the surgical treatment. Dite et al. proved in their study that surgical treatment is superior to endotherapy for long-term pain reduction and body weight evolution.

Table 1. Different surgical treatment techniques for CP

Surgical procedure	Eponym	Year of description	Type
Pancreaticoduodenectomy	Kausch-Whipple procedure	1912/1935	resection (pancreatic head, duodenum, pylorus, gastric antrum, gallbladder)
Pylorus-preserving pancreaticoduodenectomy	Traverso-Longmire procedure	1978	resection (pancreatic head, duodenum, gallbladder)
Duodenum-preserving pancreatic head resection	Beger procedure	1972	resection of the pancreatic head, lateral pancreaticojejunostomy decortication of pancreatic head, lateral pancreaticojejunostomy partial resection of the pancreatic head, short-range lateral pancreaticojejunostomy
	Frey procedure	1987	
	Büchler procedure	1995	
Pancreaticojejunostomy	Duval procedure	1954	caudal pancreaticojejunostomy with pancreatic tail resection
	Puestow-Gillesby procedure	1958	longitudinal pancreaticojejunostomy with pancreatic tail resection
	Partington-Rochelle procedure	1960	longitudinal anterior pancreaticojejunostomy
	Izbicki procedure	1998	longitudinal V-shaped excision of the anterior pancreas
Other procedures: segmental resection, left pancreatic resection, total pancreatectomy (depending on pathology and localization).			

Endoscopic therapy with or without stenting could be useful as a first-line treatment since both treatment options show similar results after 1 year.

In 2007, Cahen et al. [2] published another randomized controlled study on the same topic comparing endoscopic vs. surgical drainage of the pancreatic duct in CP. 19 patients were assigned to the endoscopic treatment group and 20 patients received a pancreaticojejunostomy. An interim analysis was performed after 24 months; further randomization of patients into the study had to be stopped since immense differences were observed concerning the outcome. Especially striking was a big difference in the Izbicki pain score comparing the endoscopy vs. the surgical therapy group; the score was significantly lower in the group that had received surgical therapy 6 weeks up to 24 months prior. The statistically highly significant ($p < 0.001$) mean difference in the pain score was 25% in the surgical group vs. 51% in the endoscopic treatment group. Furthermore, at least partial pain reduction was observed in 75% of the surgically treated patients in comparison to only 32% of the endoscopically treated patients; this difference was significant ($p = 0.007$). Also the physical health summary score was significantly improved in the surgical treatment group. The number of reinterventions (endoscopic or surgical intervention) was significantly lower in the surgical treatment group (8 vs. 3). The authors concluded that surgical drainage is significantly more effective in patients with chronic obstructive pancreatitis compared to endoscopic therapy.

In bile duct stenosis, surgical treatment has also shown better results than endoscopic treatment, as Kahl et al. [3] indicated in a study. Stent changes were performed in 3-month intervals over the course of 1 year. 39 patients with and 22 patients without parenchymal calcifications were treated. The failure rate of the endotherapy with stent insertion was 92% in the group of patients with calcifications and 41% in the group of patients without calcifications.

Summing up the results of the randomized controlled studies of Cahen, Dite and Kahl, it can be concluded that in patients with CP, surgical treatment has better long-term results than endoscopic treatment with stent implantation. Patients are benefiting from surgical treatment, and this treatment option is the current standard of care.

Surgical Treatment of CP

Surgery has classically been considered as treatment option for patients who fail conservative therapy. Yet, the timing for surgery is controversial. Some studies suggest that early surgery might delay a progression of CP [4], while others describe a progressive functional loss despite surgery [5]. A firm diagnosis of CP is needed prior to surgery to avoid the discovery of previously unrecognized pancreatic cancer at the time of the procedure. Various surgical techniques have been described for treating CP

Table 2. Randomized controlled trials comparing different interventional methods for the treatment of CP

Publication	Patients	Compared methods	Outcome
Dite et al. [1]	72	Surgery vs. endoscopy	surgery is superior to endotherapy for long-term pain reduction
Cahen et al. [2]	39	Surgery vs. endoscopy	patients with surgery had lower pain scores and better physical health
Klempa et al. [10]	43	Whipple vs. Beger	patients with a Beger procedure had a quicker convalescence and a better postoperative hormonal status
Büchler et al. [11]	40	Traverso-Longmire vs. Beger	patients with a Beger procedure had less pain, greater weight gain and a better hormonal status
Izbicki et al. [12]	61	Traverso-Longmire vs. Frey	equal efficiency for pain relief, but Frey provides better quality of life
Strate et al. [14]	74	Beger vs. Frey	no difference in mortality, quality of life, pain, or exocrine or endocrine function
Köninger et al. [17]	65	Beger vs. Büchler	no long-term differences, but the Büchler procedure can be performed faster and is technically simpler

(table 1). These surgical methods can be classified into drainage operations (e.g. Partington-Rochelle, Puestow-Gillesby) and pancreatic resections. Regarding pancreatic resections there are different methods, for example partial pancreaticoduodenectomy (Whipple procedure), the pylorus-preserving Whipple procedure (also known as Traverso-Longmire procedure), different modifications of the duodenum-preserving pancreatic head resection (i.e. Beger, Frey, or Büchler procedures), the longitudinal V-shaped excision (Izbicki procedure), segmental resection, left pancreatic resection, and total pancreatectomy, depending on the underlying pathology and complications. The duodenum-preserving resection of the pancreatic head was introduced by Hans-Günter Beger in 1972 [6]. The Frey procedure, which is based on the duodenum-preserving resection of the pancreatic head, was first described in 1987 [7]. The Beger procedure includes a transection of the pancreas above the portal vein; the Frey procedure is an extended variation of the Beger procedure, in which instead of a section of the pancreas the pancreatic head is decorticated and the pancreatic duct is opened widely and connected to a loop of the jejunum. Beger et al. [8] published a follow-up study of 504 patients. The safety of the Beger procedure is underlined by an in-hospital mortality of only 0.8%. The follow-up reached a median of 14 years and up to 80% of the patients were pain free; at the same time, 11% of the patients had an improved endocrine function. Even more interestingly, more than two thirds of the patients reached a professional and social rehabilitation, a proof of the success of

this operation method. The quality of life (Karnofsky index of 90–100%) was improved in about three fourths of the patients.

Another parenchyma-preserving operative procedure is the longitudinal V-shaped excision; it was introduced by Izbicki et al. in 1998 [9] and is a contemplable surgical treatment option in a selected group of patients with small duct CP.

When it comes to evidence-based surgery of CP, there are only a few and rather small and monocentric randomized controlled studies comparing the different surgical resecting treatments (table 2). For example, Klempa et al. [10] compared 21 patients treated with a classical Whipple vs. 22 patients treated with a Beger procedure. The duration of the hospital stay was significantly shorter in the group of patients in whom the duodenum was preserved. Also the results with regard to pain reduction, necessity of enzyme substitution, and normal body mass index were better in the group of patients treated with the Beger procedure. Büchler et al. [11] published a similar study in 1995 and also showed better results with a significantly better gain in body weight in the Beger procedure compared to the pylorus-preserving Whipple procedure. Furthermore, in three fourths of the patients with the Beger procedure remission of pain was reached, while this was only the case in 40% of the patients treated with the pylorus-preserving Whipple procedure.

Comparing the Frey procedure with the Whipple procedure, Izbicki et al. [12] were able to prove in several studies that the morbidity in the Whipple procedure was

significantly higher and that the Frey procedure reached a better quality of life. Similar results were published by Riediger et al. [13]: the operating time for the Whipple procedure was much longer than for the Beger procedure. Furthermore, the patients treated with the Beger procedure showed a better gain in body weight postoperatively.

In 2005, Strate et al. [14] demonstrated that the Frey procedure had outcomes similar to the Beger procedure in a 9-year follow-up. They compared the late mortality, quality of life, and pain score as well as exocrine and endocrine function after these procedures and found no difference between the two.

It can be concluded from those studies that in patients with CP the Beger or Frey procedures are superior to the Whipple procedure, while the Beger procedure and the Frey procedure had similar results.

Since the classical duodenum-preserving pancreatic head resection includes a transection of the pancreas above the portal vein and since this is often a critical and dangerous part of the operation, Gloor et al. [15] published a modified technique of the Beger and Frey procedures in patients with CP. This variation of the Beger procedure was established by Büchler in Berne and includes a partial resection of the pancreatic head, while it abstains from a transection of the pancreatic head above the portal vein and also abstains from a wide range pancreaticojejunostomy of the pancreatic body and tail. First clinical results of this new operative procedure were published by Farkas et al. [16]. In this study, all parameters were improved after a median follow-up time of 4.1 years. The observed parameters included pain on the visual pain scale, frequency of pain, pain medication, inability to work, and total pain score. Köninger et al. [17] recently published a study that compared the Beger procedure with its Berne variant (Büchler procedure), and showed that the Büchler procedure is easier to perform (as indicated by a shorter operating time), while it improves the quality of life in the same way as the classical Beger procedure. Müller et al. [18] were further able to show that the Büchler procedure is a surgically safe intervention reaching similar results with regard to the quality of life.

Another organ-preserving surgical treatment is the pancreatic segmental resection [19]. This procedure is suitable for benign and inflammatory processes in the pancreatic body and the pancreatic tail. With an in-hospital mortality of 2.5%, this technique is as safe as the Whipple procedure or the pancreatic left resection. For a comparative analysis, 40 patients with a pancreatic segmental resection were matched with 40 patients with a Whipple procedure or a pancreatic left resection. Blood

loss, duration of hospital stay, mortality and morbidity were similar in all three operative procedures. The advantage of the pancreatic segmental resection was in a significantly lower rate of diabetes mellitus and a significantly better quality of life. Therefore, these operative procedures should be preferred in localized inflammatory processes of the pancreatic body to the Whipple procedure or the pancreatic left resection.

In selected patients with medically intractable pain and complications resulting from CP, duodenum- and spleen-preserving total pancreatectomy also plays a role; due to the subsequent complete endocrine and exocrine pancreatic insufficiency, this procedure is, however, usually reserved for patients with failed previous operations [20].

Summing these studies up, surgical therapy is superior to the endoscopic treatment (with or without stenting) in patients with CP. In the case of a surgical treatment, organ-preserving surgical methods such as the duodenum-preserving pancreatic head resection should be preferred. Today, resections can be performed with low morbidity and mortality, while the endocrine and exocrine function usually can be preserved. Surgical therapy in particular, leads to a sustainable reduction in pain, improvement in quality of life, and for a majority of patients also to social and professional rehabilitation.

Acknowledgements

The authors would like to thank Ms. Susanne Brunnhölzl for her indispensable help in text processing and Ms. Judith Lamb, MA, for language check and spelling correction.

Disclosure Statement

The authors declare that no financial or other conflict of interest exists in relation to the content of the article.

References

- 1 Dite P, Ruzicka M, Zboril V, Novotny I: A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy* 2003;35:553-558.
- 2 Cahen DL, Gouma DJ, Nio Y, Rauws EA, Boermeester MA, Busch OR, Stoker J, Lameris JS, Dijkgraaf MG, Huibregtse K, Bruno MJ: Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med* 2007;356:676-684.

- 3 Kahl S, Zimmermann S, Genz I, Glasbrenner B, Pross M, Schulz HU, Mc Namara D, Schmidt U, Malferteiner P: Risk factors for failure of endoscopic stenting of biliary strictures in chronic pancreatitis: a prospective follow-up study. *Am J Gastroenterol* 2003; 98:2448–2453.
- 4 Nealon WH, Thompson JC: Progressive loss of pancreatic function in chronic pancreatitis is delayed by main pancreatic duct decompression. A longitudinal prospective analysis of the modified Puestow procedure. *Ann Surg* 1993;217:458–466; discussion 466–458.
- 5 Warshaw AL, Popp JW Jr, Schapiro RH: Long-term patency, pancreatic function, and pain relief after lateral pancreaticojejunostomy for chronic pancreatitis. *Gastroenterology* 1980;79:289–293.
- 6 Beger HG: Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis (in German). *Langenbecks Arch Chir* 1987;372:357–362.
- 7 Frey CF, Smith GJ: Description and rationale of a new operation for chronic pancreatitis. *Pancreas* 1987;2:701–707.
- 8 Beger HG, Schlosser W, Friess HM, Büchler MW: Duodenum-preserving head resection in chronic pancreatitis changes the natural course of the disease: a single-center 26-year experience. *Ann Surg* 1999;230:512–519; discussion 519–523.
- 9 Izbicki JR, Bloechle C, Broering DC, Kuechler T, Broelsch CE: Longitudinal V-shaped excision of the ventral pancreas for small duct disease in severe chronic pancreatitis: prospective evaluation of a new surgical procedure. *Ann Surg* 1998;227:213–219.
- 10 Klempa I, Spatny M, Menzel J, Baca I, Nustede R, Stockmann F, Arnold W: Pancreatic function and quality of life after resection of the head of the pancreas in chronic pancreatitis. A prospective, randomized comparative study after duodenum preserving resection of the head of the pancreas versus Whipple's operation (in German). *Chirurg* 1995;66:350–359.
- 11 Büchler MW, Friess H, Müller MW, Wheatley AM, Beger HG: Randomized trial of duodenum-preserving pancreatic head resection versus pylorus-preserving Whipple in chronic pancreatitis. *Am J Surg* 1995;169:65–69; discussion 69–70.
- 12 Izbicki JR, Bloechle C, Broering DC, Knoefel WT, Kuechler T, Broelsch CE: Extended drainage versus resection in surgery for chronic pancreatitis: a prospective randomized trial comparing the longitudinal pancreaticojejunostomy combined with local pancreatic head excision with the pylorus-preserving pancreatoduodenectomy. *Ann Surg* 1998;228:771–779.
- 13 Riediger H, Adam U, Fischer E, Keck T, Pfeffer F, Hopt UT, Makowiec F: Long-term outcome after resection for chronic pancreatitis in 224 patients. *J Gastrointest Surg* 2007;11:949–959; discussion 959–960.
- 14 Strate T, Taherpour Z, Bloechle C, Mann O, Bruhn JP, Schneider C, Kuechler T, Yekebas E, Izbicki JR: Long-term follow-up of a randomized trial comparing the Beger and Frey procedures for patients suffering from chronic pancreatitis. *Ann Surg* 2005;241:591–598.
- 15 Gloor B, Friess H, Uhl W, Buchler MW: A modified technique of the Beger and Frey procedure in patients with chronic pancreatitis. *Dig Surg* 2001;18:21–25.
- 16 Farkas G, Leindler L, Daroczi M, Farkas G Jr: Long-term follow-up after organ-preserving pancreatic head resection in patients with chronic pancreatitis. *J Gastrointest Surg* 2008;12:308–312.
- 17 Königer J, Seiler CM, Sauerland S, Wente MN, Reidel MA, Müller MW, Friess H, Büchler MW: Duodenum-preserving pancreatic head resection – a randomized controlled trial comparing the original Beger procedure with the Berne modification (ISRCTN no. 50638764). *Surgery* 2008; 143:490–498.
- 18 Müller MW, Friess H, Leitzbach S, Michalski CW, Berberat P, Ceyhan GO, Hinz U, Ho CK, Königer J, Kleeff J, Büchler MW: Perioperative and follow-up results after central pancreatic head resection (Berne technique) in a consecutive series of patients with chronic pancreatitis. *Am J Surg* 2008;196:364–372.
- 19 Müller MW, Friess H, Kleeff J, Hinz U, Wente MN, Paramythiotis D, Berberat PO, Ceyhan GO, Büchler MW: Middle segmental pancreatic resection: an option to treat benign pancreatic body lesions. *Ann Surg* 2006;244:909–918; discussion 918–920.
- 20 Müller MW, Friess H, Kleeff J, Dahmen R, Wagner M, Hinz U, Breisch-Girbig D, Ceyhan GO, Büchler MW: Is there still a role for total pancreatectomy? *Ann Surg* 2007;246:966–974; discussion 974–965.