SURGICAL TREATMENT OF CHRONIC PANCREATITIS

ARMIN KOLB, OLIVER STROBEL, MARKUS W. BÜCHLER, JENS WERNER
Department of General Surgery, University of Heidelberg, Germany
Kierownik: prof. dr M.W. Büchler

Chronic pancreatitis (CP) is a benign inflammatory process of the pancreas. Progression of this disease results in structural changes with replacement of functional exocrine and endocrine parenchyma by a fibrotic and inflammatory tissue, often evident as an inflammatory mass. The consequences are diabetes mellitus, exocrine insufficiency, and severe recurrent upper abdominal pain, often resulting in a significant reduction in the quality of life. Additionally, the inflammatory process or the formation of pseudocysts can cause local complications such as obstruction of the pancreatic duct, bile duct or the duodenum. Due to lack of causal therapy, treatment aims at pain relief and substitution of exocrine and endocrine insufficiency. However, many patients require additional therapy for effective pain relief or treatment of local complications. Whereas a lot of these patients undergo repetitive endoscopic interventions, surgical drainage results in better long-term outcome. In patients with an inflammatory mass of the pancreatic head, surgical resection procedures provide good short and long-term results, especially in terms of pain relief.

This article summarizes indications and potential of endoscopic/interventional and surgical therapy and gives an overview of surgical techniques with special focus on organ-sparing procedures such as the duodenum preserving pancreatic head resection and its variants.

Whereas exocrine and endocrine insufficiency may progress, adequate surgical therapy can provide effective long-term pain relief and improvement in the quality of life in patients with CP.

Background, definition and epidemiology

Chronic relapsing pancreatitis was mentioned first as a separate disease in 1946 from Comfort (1). The first classification started in 1963 in Marseille, France initiated by Henri Sarles and separating acute, relapsing acute, chronic relapsing and chronic painless pancreatitis. There was no new classification until 1983 in Cambridge based on imaging and function. The Marseille classification was revised therefore in 1984 again in Marseille and later in Rome 1988 now describing Chronic pancreatitis (CP) as a benign, inflammatory process of the pancreas which leads to progressive and irreversible loss of functional parenchyma and replacement with fibrotic tissue and ductal metaplasia (2). Refined imaging methods increased knowledge of the disease and detailed description of different types of pancreatitis ask for a update or new classification (3).

Incidence and prevalence of CP vary between continents and countries. Most European studies show comparable incidence rates around 7 per 100 000 and prevalence rates around 28 per 100 000, respectively (4, 5, 6). The numbers reported from Asia are markedly higher with a rapidly rising incidence up to 14 per 100 000 (7, 8).

Clinical appearance and etiology of chronic pancreatitis

Clinically, the disease is characterized by recurrent episodes of severe and uncontrollable upper abdominal pain which represents the most common indication for endoscopic and surgical intervention. Additionally, pa-
tients may present with symptoms of endocrine insufficiency (diabetes mellitus) and exocrine insufficiency (diarrhea, steatorrhea, malnutrition and weight loss). In the natural course of CP, as the gland “burns out”, episodes of pain may occur less frequently and be less severe whereas endocrine and exocrine insufficiency frequently increase (9). However, even after 15 years, more than 50% of the patients have pain. Thus, therapeutic nihilism is not an option. CT and MRI scan displays stenoses and dilatations the ductal system. CP can result in either an atrophy of the gland or in the formation of an inflammatory mass, as often observed in European series (10, 11). Furthermore, CP can result in intraductal and/or parenchymal calcifications. Histologically, CP is characterized by inflammatory infiltration, acinar atrophy, formation of metaplastic ductal lesions, extended fibrosis, and in some cases by focal necrosis and cysts (12). Further neural hypertrophy and perineural inflammation can frequently be observed and are the correlate of neuropathic pain (13).

The etiologic factors associated with CP are commonly summarized using the TIGAR-O classification: Toxic-metabolic (alcohol and tobacco are the main reasons in Western countries associated with up to 80-90% of cases), Idiopathic, Genetic (e.g. PRSS1, CFTR, or SPINK1 gene mutations), Autoimmune, Recurrent and severe acute pancreatitis or Obstructive (e.g. pancreas divisum, sphincter oddi dysfunctions or neoplasms) (14). The tropical CP is a common entity in India, southern Africa and parts of South America and typically affects younger patients; tropical CP is often classified as idiopathic but may in fact have a mixed etiology, including nutritional, metabolic and genetic factors (15).

Diagnosis

The diagnosis of chronic pancreatitis is based on a thorough history and physical examination, laboratory data, and imaging studies, which reflect the imaging abnormalities as well as functional impairments of the pancreas. Chronic pancreatitis is a well-defined disease on histopathologic grounds, but histology is rarely available for diagnosis. The correct diagnosis of chronic pancreatitis is easy in the late stages but difficult in early stages of the disease. There are several imaging methods for patients with known or suspected chronic pancreatitis. In early stages of the disease, both endoscopic retrograde pancreatography (ERP) and endoscopic ultrasonography (EUS) are methods with reliable diagnostic accuracy. Initial studies have shown superiority of EUS (in experienced centers) over ERP for the diagnosis of chronic pancreatitis in its early stages. Transabdominal ultrasonography (US) is less sensitive for the diagnosis of chronic pancreatitis and should be limited generally to patients with advanced stages. In patients with early stages, we believe that the combination of ERP and CT provide the most reliable morphologic information. An alternative diagnostic method is EUS. Among all imaging methods, MRI (magnetic resonance imaging) and MRCP (magnetic resonance cholangiopancreatography) is the method with the most rapid development over the last years. With further improvement of hardware and software, it is likely that these methods will be able to visualize even the early stages of the disease in the near future.

The most common pancreatic function tests do not detect mild to moderate exocrine pancreatic insufficiency with adequate accuracy. Therefore, pancreatic function tests play only a complementary role in the routine clinical evaluation of chronic pancreatitis; however, these tests are important methods used in clinical research or specialized pancreatic disease centers.

Treatment

The treatment of chronic pancreatitis is complex and should involve conservative, endoscopic, and operative therapeutic approaches.

Conservative treatment

Conservative treatment is the basis of any adequate management of CP and includes reduction of etiologic risk factors, including abstinence from alcohol and nicotine consumption, substitution for exocrine and endocrine insufficiency and nutritional supplements, as well as pain therapy. Extracorporal shockwave lithotripsy (ESWL) can be used in painful, chronic, calcified pancreatitis. The median delay to pain relief was 1.1 years, but 38% had pain relapse after 2 years. With a combination
of ESWL and endoscopy (sphincterotomy and fragment extraction after ESWL), the rate increased to 45%. The mortality was 0, and the morbidity in the endoscopy group was 3% (16).

Endoscopic treatment

However, many patients require additional therapy for effective pain relief or treatment of local complications. Most of these patients are primarily referred to gastroenterologists and undergo endoscopic treatment. Endoscopic treatment options and their possible indications are effective therapy of pseudocyst, pancreatic ductal obstruction by stenoses and/or calculi to decompress and drain the pancreatic ductal system. Additionally percutaneous catheter drainage is available as a temporizing measure in poor surgical patients with complicated or infected pancreatic pseudocysts. For pain control, endosonography guided or percutaneous celiac nerve block with alcohol or steroids and thoracoscopic splanchnicectomy are described.

However, in almost all patients endoscopic treatments, have to be repeated on a regularly basis. In consequence, the patients have to remain in endoscopic therapy and are frequently re-hospitalized. Two recent randomized controlled trails demonstrated the superiority of surgical versus endoscopic therapy in primary success rate, pain relief and quality of life in patients with proximal duct obstruction (17,18). A large multicentre study in 1018 patients reports a success rate of endoscopic therapy (multiple sessions) in 65% and necessity of surgery in 24% of those patients within 2 years (19). A study on 61 patients with bile duct stenosis due to CP reported a 1-year success-rate of 59% of endoscopic stenting with stent replacement every three months, but failure of endoscopic therapy in the majority of cases with presence of calcifications (7.7% success rate) (20). Moreover, 49% of patients without successful therapy after one year finally underwent surgery. In patients with symptomatic pseudocysts without ductal obstruction, endoscopic drainage procedures may be equally safe and effective as surgical drainage and superior to external drainage, as reported in a recent retrospective study (21). However, this remains to be confirmed in larger scale randomized trials.

These data allow the following recommendations concerning endoscopic vs. surgical treatment of CP:

- Patients with proximal stenosis without calcifications and without inflammatory mass may be treated endoscopically first. If repetitive endoscopic treatment fails, the option of surgery has to be evaluated.
- In patients with distal obstruction, calcifications or inflammatory mass surgery is superior to endoscopic treatment and patients should thus undergo surgery early in the course of the disease.
- Pancreatic pseudocysts can be treated endoscopically. If endoscopic treatment fails, a surgical drainage procedure should be performed.

If endoscopic treatment does not result in effective pain relief, patients should undergo surgical therapy early, because persistent pancreatic pain may become pancreas-independent over time.

Appropriate management requires individualization in almost every patient. A complication of chronic pancreatitis managed medically in one patient may be best handled by operative intervention in another patient because of confounding factors. Thus, treatment of chronic pancreatitis requires a cooperative, multidisciplinary team.

Surgical treatment of chronic pancreatitis

There are different concepts for the surgical treatment of chronic pancreatitis. The concept of preservation of tissue (drainage operations) would be the goal for protection against further loss of pancreatic function. The second main concept is based on resective procedures in case of an undilated pancreatic duct, if the pancreatic head is enlarged or if a pancreatic carcinoma has to be suspected in chronic pancreatitis. These two concepts are leading to different surgical procedures, drainage procedures and pancreatic resections.

Drainage procedures

Sphincterotomy of the pancreatic duct was one of the first operative procedures proposed for patients with a dilated pancreatic duct in chronic pancreatitis with presumed obstruction or stenosis of the papilla Vater. Unfortunately, this procedure was associated with
minimal lasting success for the amelioration of pain, indicating that a stenosis at the papilla Vater is neither the cause of pain in chronic pancreatitis nor the cause of ductal dilation. In patients with isolated pancreatic pseudocysts, often in patients with a history of a severe episode of acute pancreatitis, a drainage procedure in form of a cysto-jejunostomy with Roux-en-y reconstruction is still the surgical procedure of choice. However, a pancreatic left resection may be a good alternative in cases with large cysts in the pancreatic tail.

In contrast, direct ductal-enteric drainage by the original Puestow procedure or its modification by Partington and Rochelle is initially successful in patients with chronic pancreatitis and a dilated pancreatic duct. The original Puestow procedure included resection of the tail of the pancreas with filleting open the pancreatic duct proximally along the body of the pancreas with anastomosis to a Roux-en-Y loop of jejunum. Partington and Rochelle modified the Puestow procedure by eliminating the resection of the pancreatic tail. The preservation of functional tissue and reduction of operative mortality to less than 1% and morbidity to less than 10% are the goals and benefits of this operation (tab. 1). Unfortunately, large series have reported persistence of long-term (>5 year) relief of pain in only 30-50% of patients; in addition, patients with a dominant mass in the head of the pancreas and a nondilated pancreatic duct do not appear to profit from a drainage procedure at all. Thus, the sole drainage procedures are rarely indicated in chronic pancreatitis.

Pancreatic resections

The partial pancreatoduodenectomy (Kausch-Whipple-procedure), in its classical or pylorus-preserving variant, has been the procedure of choice for pancreatic head resection in CP for many years and is indicated in a vast majority of patients presenting with a ductal obstruction located in the pancreatic head, frequently associated with an inflammatory mass (22, 23). The duodenum-preserving pancreatic head resections in its variants Beger-procedure (24, 25), Frey-procedure (26, 27), and Bern-procedure (28) represent less invasive, organ-sparing techniques with equal long-term results (tab. 2).

Independent of the technique of DPPHR, an intraoperative frozen section has to be obtained to rule out pancreatic adenocarcinoma. If the frozen section is suspicious for malignancy or if a cancer is suspected already preoperatively, a PD represents the oncologically adequate approach. Irrespective of the technique, if carried out by experienced hands pancreatic head resection is a safe and effective therapy with good short- and long-term results in patients with CP and an inflammatory mass in the head of the pancreas (23, 25, 26, 31-34).

In patients without circumscript mass in the pancreatic head and small duct disease (diameter of the pancreatic duct <3 mm) a V-shaped excision of the anterior aspect of the pancreas is a safe approach with effective pain management (29). In the rare cases in which a patient presents with segmental CP in the pancreatic body or tail, e.g. due to posttraumatic ductal stenosis, a middle segment pancreatectomy or a pancreatic left resection can represent the best approach. Similarly, a total pancreatectomy may be necessary in very selected cases with severe inflammation involving the entire pancreas and has to evaluated especially in patients with pre-existing insulin-dependent diabetes mellitus (30). However, these three options are very rarely indicated in patients with chronic pancreatitis.

Partial pancreatoduodenectomy: Kausch-Whipple-procedure

The extent of resection in the Kausch-Whipple pancreatoduodenectomy (PD) includes pancreatic head with duodenum and

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<td>Cystojejunostomie</td>
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<td>Laterolateral pancreaticojejunostomy: Partington-Rochelle procedure</td>
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<td>Caudal drainage: Puestow procedure</td>
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the lower third of the stomach. PD was initially designed for malignancies in the pancreatic head and associated with high morbidity and mortality. With increasing safety the procedure has also been used for patients with CP (35). With the pylorus-preserving pancreatoduodenectomy (ppPD) a less invasive procedure for resection of cancer or CP was introduced, in which the stomach is preserved (fig. 1) (36). PD and ppPD in experienced hands are safe and effective procedures with an operative mortality of 2-5% and lasting pain relief in about 80% of patients (22, 37). Furthermore, PD provides the benefit of adequate resection of an unrecognized pancreatic adenocarcinoma, which may arise and presents a differential diagnosis is some patients with CP (37). However, in contrast to patients with pancreatic cancer, resection of the duodenum is not necessary in the majority of patients with CP.

Duodenum-preserving pancreatic head resection: Beger-procedure

Beger et al. introduced the duodenum-preserving pancreatic head resection (DPPHR) as a less radical and organ-sparing procedure designed specifically for patients with CP and an inflammatory mass in the head of the pan-

Fig. 1. Pylorus-preserving pancreaticoduodenectomy. Partial pancreaticoduodenectomy (here shown as pylorus-preserving procedure). The pancreatic head is removed with the duodenum. The reconstruction is performed by a pancreaticojunostomy, hepaticojejunostomy and a duodenojejunostomy.
creas (fig. 2) (10, 24, 25, 31). Similar to PD the pancreas is divided at the level of the portal vein. However, in contrast to PD, the pancreatic head is excavated with preservation of the duodenal and a layer of pancreatic tissue. The reconstruction is performed by two anastomoses with a jejunal loop to drain the pancreatic remnant and to cover and drain the defect in the pancreatic head. During this procedure the common bile duct can be opened and drained with an internal anastomosis to treat bile duct obstruction. The DPPHR has gained wide acceptance and has become the procedure of choice for most patients with CP in Europe. However, maybe because the technique is technically more demanding than PD, it is not commonly used outside Europe, for example in the USA.

Duodenum-preserving pancreatic head resection: Frey-procedure

A different approach of a duodenum-preserving pancreatic head resection Procedure is the Frey procedure. Frey et al. developed a modification of the DPPHR which represents a hybrid technique between the Beger- and Partington-Rochelle procedures (fig. 3) (26, 27, 38). Compared to the Beger-procedure the resection in the pancreatic head in the Frey-modification is smaller and combined with a laterolateral pancreaticojejunostomy to drain the entire pancreatic duct towards the tail. In contrast to the Beger-procedure reconstruction can be performed with one single anastomosis. This procedure is not suitable in patients with a large inflammatory mass in the pancreas without stenosis of the left-sided pancreatic duct, as often observed in the European collectives. However, it appears advantageous in patients with less severe inflammation in the head combined with an obstruction in the left-sided pancreatic duct. In our own patient collective, the Frey procedure is only rarely indicated (1-2%), since the left part of the pancreatic duct is rarely obstructed.
Duodenum-preserving pancreatic head resection: Bern modification

The Bern modification of the DPPHR represents a technical simplification of the Beger-procedure with equal outcome (28, 33, 34, 39). The excavation of the pancreatic head can be performed with identical extent compared to the Berger-procedure. However, in contrast to the Beger-procedure the pancreas is not divided at the level of the portal vein, which is often difficult because of inflammation and portal hypertension. The reconstruction can be performed by one single anastomosis between a jejunal loop and the continuous pancreatic resection rim (28) (fig. 4). As in the Beger-procedure, a bile duct obstruction can be managed by internal bile duct anastomosis. The Bern-modification of DPPHR appears thus ideal for patients with an inflammatory mass and without stenosis in the left-sided duct. Adequate drainage of the pancreatic duct has to be verified by probing. If a stenosis is discovered, the resection can be extended towards the left similar to the Frey/Partington-Rochelle procedures until adequate drainage is achieved. However, in our collective this is necessary in only 2-3% of cases (34).

The above-mentioned techniques of pancreatic head resection were compared in several randomized-controlled trials (RCTs), in which their safety and efficacy was confirmed. The RCTs comparing PD and DPPHR (33, 40-44) as well as a recent metaanalysis (45) demonstrate comparable mortality and efficacy in terms of pain relief as well as endocrine insufficiency; however, the less invasive DPPHR was superior in hospital stay, exocrine insufficiency, weight gain and quality of life in medium-term follow-up. In even more recent studies with long-term follow-up these metabolic advantages appear to be lost over time and long-term results of PD and DPPHR are equal in terms of pain management and quality of life as well as endocrine and exocrine function (compare results reported in the initial trials and the latest follow-ups in tab. 3). Of interest, the resection techniques remain effective in terms of pain relief and quality of life but cannot stop the progress of exocrine and endocrine insufficiency on the long term (33, 44). One explanation may be that resection effectively treats the obstruction and hypertension, but does not completely stop continued cellular damage and parenchymal loss (37). Certainly these observations stress the importance of continued conservative treatment by reducing etiologic factors, substitution for exocrine and endocrine insufficiency and probably antioxidant therapy (46).

The RCTs comparing different techniques of DPPHR demonstrate equal outcome in both pain control/quality of life and metabolic parameters after Beger vs. Frey and Beger vs. Bern technique (39, 47, 48, 49). However, the latter trial demonstrated that, with equal outcome, the Bern modification of DPPHR represents a technically simpler alternative, as reflected by a significantly (by 46 minutes) operative time as well as a significantly shorter hospital stay (11 vs 15 days) (39). Recent reports confirm that that the Bern modification of DPPHR can be performed without severe complications or mortality in smaller series.

![Fig. 4. Bern modification of the Duodenum-preserving pancreatic head resection. The Bern modification is a technical simplification of the Beger-procedure. The extent of resection of the pancreatic head is comparable to the Beger-procedure. The pancreas is not dissected on the level of the portal vein. Thus, reconstruction can be performed with one single anastomosis of the pancreas with a Roux-en-Y jejunal loop. The bile duct can be opened and an internal anastomosis can be performed (as shown). The pancreatic duct towards the tail has to be probed and an internal anastomosis has to be performed to prevent stenosis](image-url)
Thus, the Bern technique represents a modification of DPPHR which may find broader acceptance due to technical and economic advantages (tab. 4).

**CONCLUSIONS**

The adequate therapy of chronic pancreatitis is adjusted to the symptoms of the patient, the stage of the disease and the morphology of the pathological changes of the pancreas. Conservative therapy is the basis of treatment in all patients and has to accompany both interventional and surgical therapy. Endoscopic therapy appears to be effective for internal drainage of pseudocysts and in proximal ductal stenoses in patients without calcifications. However, endoscopic therapy requires frequent reinterventions and if it is not sufficiently effective after one year, the patient should be referred to surgery. The surgical technique has to be adjusted to the pathomorphological changes of the pancreas. Recent data proposes that regional and intercontinental differences in the surgical strategy and preference for one of the surgical techniques for pancreatic head resection may in fact be based on differences in the anatomic pathology between patient collectives. For patients with CP and an inflammatory mass in the head of the pancreas the DPPHR is less invasive than a PD with comparable long term results and should thus be considered the treatment of choice. The Bern modification of DPPHR represents a technical variation which is equally effective but technically less demanding. Whereas surgical therapy provides effective long-term pain-relief and improvement of quality of life, it does not stop a decrease in both endocrine and exocrine function. Thus, endocrine and exocrine function should currently not be considered to define a successful therapy in CP. Instead, strategies for improvement or maintenance of endocrine and exocrine function remain an interesting field of research.

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<th>Procedure</th>
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<td></td>
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<td>mniejsza niewydolność zewnątrzwydzielnicza, mniejsze zużycie leków przeciwbólowych / less exocrine insufficiency, less need of analgesics</td>
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<td>Büchler (1995) (40)</td>
<td>20</td>
<td>less impaired glucose metabolism</td>
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<td></td>
<td>20</td>
<td>higher gain of weight</td>
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<td>more frequent pain relief</td>
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<td>Müller (1997) (43)</td>
<td>10</td>
<td>more frequent delayed gastric emptying</td>
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<td>more frequent pathologic secretion of enteral hormones</td>
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<td>Müller (2008) (33)</td>
<td>20</td>
<td>equal in pain relief, exocrine and endocrine function</td>
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<td>Izbicki (1998) (41)</td>
<td>31</td>
<td>better professional rehabilitation</td>
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PD: pancreatoduodenectomy, ppPD: pylorus-preserving pancreatoduodenectomy, DPPHR: duodenum-preserving pancreatic head resection, QoL: Quality of life
REFERENCES


