Challenging dogmas in pancreatic surgery: biliary drainage, outcome and beyond
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Citation for published version (APA):

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Review Article: Surgical Management of Chronic Pancreatitis

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Alimentary Pharmacology & Therapeutics
2007 Dec;26 Suppl 2:221-32
SUMMARY

Background
The therapeutic approach to patients with chronic pancreatitis (CP) is complicated by the fact that patients are presented to the physician at different stages of disease and in the presence of varying clinical symptoms. Generally, an expectant approach is justified for patients with asymptomatic CP. At present, patients with symptoms related to gland destruction are initially treated by endoscopic means, while surgical treatment of CP is usually reserved for intractable abdominal pain, suspicion of cancer, and complications such as persistent pseudocysts.

Aim
To review the studies currently available evaluating surgical and/or endoscopic management of CP.

Results
Improvements in imaging techniques, as well as a better understanding of the pathophysiology of CP and mechanisms causing pain, have led to a more conscious selection of patients for surgery. Type of surgery depends on whether the pancreatic duct is dilated, presence of an inflammatory mass and occurrence of complications (pseudocysts, gastric outlet obstruction). Eventually, after initial endoscopic treatment, a substantial number of patients still need surgery for persistent complaints.

Conclusions
For patients with symptomatic CP, a multidisciplinary approach is indicated with low threshold to surgical intervention, since long-term pain relief is accomplished more often after surgical treatment than after endoscopic treatment.
INTRODUCTION

Chronic pancreatitis (CP) is a benign, progressive inflammatory condition causing histological damage of pancreatic parenchymal tissue. In an advanced stage of disease, gland atrophy occurs with or without calcifications. In contrast to acute pancreatitis, in which after removing the causative factor morphological changes of the gland resolve, the changes in CP are thought to be irreversible. After a subclinical phase of variable duration, clinical symptoms become apparent and, ultimately, patients are found to suffer from pancreatic exocrine and endocrine insufficiency as a result of destruction of the gland. The estimated incidence and prevalence of CP are 6–8 and 25–75 per 100,000 individuals, respectively, depending on the geographical area. The rising prevalence of CP, a decreasing male–female ratio as well as a younger age of onset are suggestive of phenomena pointing to changing patterns in alcohol consumption.

Compared to the general population, patients with CP have an increased mortality rate of which 15–20% is directly related to the disease and local complications. The remaining deaths are due to indirect causes, such as infection, smoking, malnutrition, liver failure and trauma. The risk for patients with CP to develop pancreatic cancer in the course of their illness is estimated to be 4–6% per 20 years.

The possibility to treat CP surgically is still not fully acknowledged by many (referring) doctors. This explains why patients are presented relatively late in the course of their disease. In the past decades however, available surgical procedures for treatment of CP have witnessed some major advances. Especially for the appropriate indication in a multidisciplinary decisional approach and surgery in a professionally competent way, surgical intervention offers a long-term relief of symptoms in more than 90% of patients with CP.

ETIOLOGY AND PATHOPHYSIOLOGY

The TIGAR-0 classification defines causes of CP in several major categories: toxic-metabolic, genetic, recurrent and severe acute pancreatitis, obstructive morphological and idiopathic. In the light of recently identified genetic predispositions for pancreatitis as well as a better understanding of pathophysiologic mechanisms, development of CP is likely to be multifactorial. A complex interrelationship of the distinct factors listed in the TIGAR-0 might be necessary for the final development of CP. The most dominant cause of CP is since long considered to be toxic-metabolic. An excessive use of alcohol should account for up to 85% of the cases of CP, whereas recent in vitro and in vivo experiments also demonstrate a significant role of cigarette smoking.

Morphologically, CP is characterized by pancreatic main duct and side branch duct alterations, resulting in the ‘chain of lakes’ appearance on a pancreaticogram (multiple strictures and dilatations of the pancreatic duct). The most dramatic histo-
logical change in CP comprises the irreversible destruction of functional glandular parenchyma and subsequent replacement by fibrous tissue. Generally, fibrosis is the accumulation of excessive amounts of extracellular matrix proteins in a tissue. Pancreatic stellate cells (PSCs) are responsible for synthesis of these matrix components. In the ongoing process of inflammation, cytokines, oxidant stress as well as ethanol and metabolites activate PSCs, resulting in an increased endogenous production of cytokines by PSCs themselves which gives a perpetuation of activation of PSCs. Ultimately this leads to an excessive production of matrix components. Although CP is well defined on histopathological grounds, the clinical diagnosis in the early course of disease is not based on histology.

Figure 1  Stones in proximal as well distal part of the pancreatic duct on reconstructive computed tomography imaging. In the left upper panel a line is drawn through the liver, gallbladder and pancreatic duct and a large intraductal concrement. The right upper panel shows a coronal view of the pancreatic head and body area with the venous confluens. The lower left panel is a sagittal view of the pancreatic body and venous confluens. In the right lower panel a coronal cross section is seen of multiple stones in the dilated pancreatic duct in longitudinal view. R, right; A, anterior.

The principle symptom in CP is episodic or intractable pain, being the main complaint in the majority of patients. The pathophysiology of pain in CP is still incompletely understood and likely to be multifactorial. An increased intraductal pressure and/or intraparenchymal pressure, as a result of strictures, calculi or distal inflammatory process, is since long thought to be a cause of pain, especially when a dilated pancreatic duct is present (Figure 1). The fact that endoscopic or surgical treatment of
the obstruction relieves pain supports this hypothesis. Several other causes of pain in CP have been suggested: hypersecretion of the pancreas due to impaired exocrine function, pancreatic ischemia and perineural inflammation. The last theory is gaining ground as studies have shown an increased presence of several neurotransmitters in afferent pancreatic nerves in CP. Finally, the pancreatic inflammatory process can induce duodenal and/or common bile duct stenosis contributing to the development of pain, although the hypothesis for the latter is disputed.14-16

Local complications of CP can cause additional symptomatology. Pseudocysts or an inflammatory process in the pancreatic head causes local compression which might result in common bile duct stenosis, causing obstructive jaundice, cholestasis and cholangitis and obstruction of the pancreatic duct. Compression of the portal and/or splenic vein might occur, as well as portal / splenic venous thrombosis and (segmental) portal hypertension. Splenic vein thrombosis occurs in 2–4% of patients with CP. This event leads to isolated gastric varices with resulting gastrointestinal hemorrhage. In the course of CP vascular (venous or arterial) complications could arise and although rare, they imply potentially lethal hemorrhagic events. Also duodenal obstruction, leading to motility disorders and vomiting, may occur.

Bile Duct Obstruction

Another category of indications for surgery are caused by local complications of CP, which might affect adjacent structures. A frequent complication of CP is stricture of the distal bile duct, due to fibrotic stricturing or compression of the inflammatory process. Its incidence is reported to be 6% (3–23%) in patients hospitalized for CP; the incidence increased to 35% (15–60%) for those patients who required surgical intervention for CP.17 Especially patients with an inflammatory process in the head of the pancreas are at risk for development of biliary obstruction. Although fibrotic biliary strictures might be managed initially with endoscopic therapy, the long-term success rate is disappointing. Surgical correction by a choledochoduodenostomy or hepatico-jejunostomy should be considered in case stricture resolution has not occurred after 1 year of endoscopic treatment.18;19 Cholecystoenterostomy seems to be associated with a higher incidence of cholangitis and should be avoided whenever possible.

Duodenal Obstruction

Duodenal obstruction caused by CP is a less common complication with an incidence of 1.2% (0.5–13%) among hospitalized patients, increasing to 12% (2–36%) in patients requiring surgical intervention for CP.17 Two types of duodenal obstruction are to be distinguished: an acute temporary narrowing by the inflammatory process, pseudocyst or mesentery which might be treated conservatively, and a persistent stenosis resulting from fibrosis, requiring surgical treatment by a gastroenterostomy.

Pseudocysts

Pseudocyst formation is a common complication in acute as well as CP; in the latter, the incidence is 20–40%.20 Large, symptomatic pseudocysts can be treated effec-
Part III Chronic Pancreatitis and its Surgical Treatment

Surgical treatment (i.e. cyst-gastrostomy or cystenterostomy) is indicated in case of endoscopic failure, infection or when an pancreatic abscess has developed. A high morbidity rate of a duodenum-preserving pancreatic head resection (HR) with its considerable learning curve renders this procedure less favorable. Nealon and Walser suggested that for the treatment of CP (pancreatic duct >7 mm) with a concomitant pancreatic pseudocyst, drainage by a pancreaticojejunostomy (PJ) without simultaneous cyst drainage is sufficient and would lead to resolution of the pseudocyst.21

Vascular Complications

Major vascular complications pose a rare but acute and potentially lethal complication in CP and are caused by erosion of an artery in the pseudocyst wall. Presentation of the bleeding is either from the papilla of Vater or as a bleed into the abdominal cavity. Balachandra and Siriwardena demonstrated in a recent review that mesenteric angiography detects the source of bleeding, mostly from splenic, gastroduodenal, superior and inferior pancreaticoduodenal artery, or a false aneurysm in 94% of the cases.24 Concomitant embolization, either for spontaneous hemorrhage or in patients postoperatively, resulted in successful hemostasis in three quarters of the cases. Mortality was remarkably low, especially when angiography was undertaken as first intervention for bleeding instead of surgery. Therefore, surgical intervention for vascular complications should be reserved as a last resort and performed only if embolization has failed and bleeding persists.

Pancreatic Cancer in CP

The differentiation between CP and pancreatic cancer poses a diagnostic dilemma. Usually both diseases are easy to distinguish on clinical investigation and imaging studies; however, they may present with same symptoms and may display similar findings during imaging. Furthermore, pancreatic cancer is associated with secondary inflammatory changes and patients with CP are known to have an increased risk for the development of cancer, especially in hereditary pancreatitis.2,3,5,25 Misdiagnosing pancreatic cancer for CP prevents a patient from being adequately treated for a potentially curable pancreatic cancer. Clearly, for patients without a clear clinical picture of CP and in whom pancreatic cancer cannot be ruled out on the basis of radiological findings, histological testing is obligatory. Analysis demonstrated that in a small subgroup of patients who underwent a pancreatoduodenectomy (PD) for suspicion of having a periampullary tumor without conclusive preoperative diagnosis on imaging (no hypodense lesion), more than half of these patients were diagnosed with a (pre)malignancy on histological grounds after resection.26 Furthermore, van Gulik et al. have described a series of 42 patients who were previously diagnosed with CP, but appeared to have (unresectable) pancreatic cancer within 3 years of follow-up.25 A study of Sakorafas and Sarr supports these findings: 14 of 484 patients (2.9%) who underwent surgery for CP had developed pancreatic cancer after a mean of 3.4 years.27 Pancreatic malignancy should be suspected in patients who have had
surgery for CP when symptoms (such as recurrent pain, jaundice, weight loss or anorexia) recur. It is justified therefore to perform resection when differentiation between (focal) pancreatitis and pancreatic cancer is difficult. This approach is still followed in the Academic Medical Centre (AMC) in Amsterdam considering the fact that the number of patients who underwent a PD for suspected carcinoma but were finally diagnosed with (focal) CP increased from 6.4% to 10.3% after 1996. Especially, with low surgery-related morbidity and mortality rates of 1–3% PD is a relatively safe procedure now, offering also adequate pain relief in CP. In our series of 644 patients after PD (January 1992–January 2006), performed under the suspicion of pancreatic cancer, 65 patients (10.1%) were diagnosed with CP instead of cancer on histopathological grounds after resection. Overall mortality was 1.4%, being 1.6% for pancreatic cancer and 0% for those patients who turned out to have CP.

SURGICAL TREATMENT FOR PAIN

Different surgical options in the management of CP for treatment of pain exist: (i) drainage by a PJ, (ii) combined drainage and resection; Frey procedure (core resection of the head region) and Beger procedure (duodenum-preserving pancreatic HR), (iii) resection procedures; such as PD, distal (or left-sided) and total pancreatectomy (TP). Once the indication is established for surgical intervention for CP, morphological features of the pancreas have to be evaluated in order to determine the most optimal surgical procedure. Crucial factors to consider are the presence and location of an inflammatory mass, dilatation and strictures of the pancreatic duct and/or common bile duct and duodenal stenosis on contrast-enhanced (helical) computer tomography and magnetic resonance cholangiopancreatography.

Pancreatic Duct Drainage

To achieve pain relief for patients with dilatation of the main pancreatic duct (>5–7 mm) without an inflammatory mass, draining the dilated main pancreatic duct by creation of a longitudinal PJ is the treatment of choice. Initially reported in 1958 by Puestow and Gillesby this operation underwent a modification by Partington and Rochelle with respect to omitting resection of the tail. A Roux-en-Y jejunal loop is anastomosed side-to-side to the whole length of the pancreas, achieving a complete drainage of the Wirsung and Santorini ducts (Figure 2).

The procedure is associated with low morbidity and perioperative mortality rates (0–5%, mean 1.1 ± 1.7%; Table 1). In our series of PJ for CP (n=136) mortality was 0.7%. Another advantage of PJ is complete preservation of exocrine and endocrine functions of the pancreas. A substantial relief of abdominal pain is achieved, according to many different studies, in 42–100% of patients (mean 80.1 ± 14.8% Table 1).
Figure 2  Performing a pancreaticojejunostomy (PJ). (a) Opening of the omental sac and view on the pancreas, the middle colic vein, the right gastroepiploic vessels (arrow). (b) Opened pancreatic duct with multiple intraductal stones, soon to be removed. (c) Posterior layer of the longitudinal PJ from tail to head. A rim of longitudinal opened pancreatic tissue (arrow), where the anterior layer will be sutured next, and ductal mucosa is visible (arrowhead). (d) Complete longitudinal [lateral or side-to-side] PJ (arrows). Stapled end of jejunal loop visible (arrowhead). Downstream a jejunoojejunostomy is performed to complete the Roux-en-Y construction.

Besides relieving chronic pain in the majority of patients, PJ also prevents recurrent acute pain exacerbations. Nevertheless, in spite of these results, a number of patients have to cope up with clinically relevant recurrences of pain or have failed to obtain pain relief at all. This could be due to inappropriate selection of patients for this procedure. Patients with CP might present with an inflammatory mass in the pancreatic head and as well have strictures of the main pancreatic duct or side branches in the head region. These features might not have been properly dealt with when performing a PJ, possibly explaining eventual treatment failure. Performing a combined drainage and resection, such as a Frey procedure, may be more appropriate in such cases. Importantly, recurrent pain after PJ is also significantly associated with persistent alcohol abuse. In case of recurrence of pain after PJ and presence of an inflammatory mass, performing a more extensive secondary surgical procedure is justified by involving a resectional procedure.
**Table 1** Longitudinal/lateral pancreaticojejunostomy for chronic pancreatitis in studies >20 pts, excluding caudal PJ.

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of patients</th>
<th>Complete or partial pain relief (%)</th>
<th>Mortality (%)</th>
<th>Mean follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarles</td>
<td>69</td>
<td>85</td>
<td>4</td>
<td>60</td>
</tr>
<tr>
<td>Warshaw</td>
<td>33</td>
<td>83</td>
<td>3</td>
<td>43</td>
</tr>
<tr>
<td>Morrow et al.</td>
<td>46</td>
<td>80</td>
<td>0</td>
<td>72</td>
</tr>
<tr>
<td>Sato et al.</td>
<td>43</td>
<td>100</td>
<td>0</td>
<td>110</td>
</tr>
<tr>
<td>Bradley et al.</td>
<td>48</td>
<td>66</td>
<td>0</td>
<td>69</td>
</tr>
<tr>
<td>Nealon et al.</td>
<td>41</td>
<td>93</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Drake et al.</td>
<td>23</td>
<td>90</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>Greenlee et al.</td>
<td>86‡</td>
<td>80</td>
<td>3</td>
<td>95</td>
</tr>
<tr>
<td>Adloff et al.</td>
<td>105</td>
<td>93</td>
<td>2</td>
<td>65</td>
</tr>
<tr>
<td>Wilson et al.</td>
<td>20</td>
<td>76</td>
<td>5</td>
<td>60</td>
</tr>
<tr>
<td>Delcore et al.</td>
<td>28</td>
<td>86</td>
<td>0</td>
<td>42</td>
</tr>
<tr>
<td>Adams et al.</td>
<td>85</td>
<td>55</td>
<td>0</td>
<td>76</td>
</tr>
<tr>
<td>Bühler et al.</td>
<td>35</td>
<td>42</td>
<td>0</td>
<td>48</td>
</tr>
<tr>
<td>Sielezneff et al.</td>
<td>57</td>
<td>84</td>
<td>0</td>
<td>65</td>
</tr>
<tr>
<td>Sakorafas et al.</td>
<td>120</td>
<td>81</td>
<td>0</td>
<td>96</td>
</tr>
<tr>
<td>Boerma et al.</td>
<td>50</td>
<td>88</td>
<td>0</td>
<td>27</td>
</tr>
<tr>
<td><strong>Mean results (± SD)</strong></td>
<td><strong>889</strong></td>
<td><strong>80.1 ± 14.8</strong></td>
<td><strong>1.1 ± 1.7</strong></td>
<td><strong>62.7 ± 24.9</strong></td>
</tr>
</tbody>
</table>

* 88% of the patients without dilated pancreatic ducts.
† Either ductal or cyst drainage.
‡ Study consisted of 91 pts, 5 omitted who underwent a caudal PJ.

It is likely that pancreatic calculi aggravate the clinical course of CP and are not merely the inevitable sequelae of an ongoing gland destruction. The rationale for intervention is increased intraductal pressure by ductal stones leading to increased parenchymal pressure, resulting in pancreatic ischemia and pain. Although CP is a progressive disease, animal experiments showed a normalization of the pancreas after an 'early' surgical drainage procedure, both morphologically and functionally. A study of our group, comparing results of early and late surgical drainage in an experimental porcine model of chronic obstructive pancreatitis, supports these findings. Early surgical drainage resulted in a marked improvement in histopathology grades and pancreatic exocrine function as opposed to the late drainage group. Clinical studies, however, have reported contrasting results: some authors described a progressive deterioration in exocrine and endocrine function after surgical drainage, whereas others saw a postponement of both exocrine and endocrine insufficiency after successful early surgical drainage. One study demonstrated that in 87% of patients who underwent drainage by a PJ, pancreatic endocrine and exocrine insufficiency stabilized during complete follow-up (mean: 49.2 months) compared to 22% for those who were not operated upon (mean follow-up: 46.7 months). A study by Maartense et al. evaluated in a prospective study the effect of resection procedures for CP vs. surgical drainage on both endocrine and exocrine pancreatic function.
significant improvement of endocrine function after drainage by a PJ was found, as measured by blood glucose levels preoperatively and postoperatively, whereas clinical exocrine function was not influenced after either procedure.

In the AMC mostly a PJ is performed when surgical treatment of CP is indicated (in the absence of an inflammatory mass), making up for almost two-thirds of all surgical procedures for CP (Table 2).

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Drainage procedures (longitudinal PJ)</td>
<td>136 (63)</td>
</tr>
<tr>
<td>Combined drainage and resection (Frey or Beger)</td>
<td>42 (20)</td>
</tr>
<tr>
<td>(PP)PD</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Left-sided resection</td>
<td>30 (14)</td>
</tr>
</tbody>
</table>

HR: (duodenum-preserving pancreatic) head resection; Frey: core resection of the head and pancreaticojejunostomy; PD: pancreatoduodenectomy; PPPD: pylorus preserving pancreatoduodenectomy.

Surgery-related morbidity of a PJ is 22%, mortality 0.7% in 136 patients in 12 years. Morbidity of any surgical procedure for CP, being either PJ, complete or core HR, or PD, was 18% in our series of 216 patients, and mortality 1.4%. Bleeding complications were most often managed conservatively or by angiographic coiling of branches of the gastroduodenal or pancreaticoduodenal arteries. Re-laparotomy for bleeding in a setting with experienced interventional radiologists is seldom needed and is (in our institute) not a first choice strategy for bleeding complications after pancreatic surgery.

Our number of drainage procedures is relatively high compared with other published series in which more often resection procedures are performed for CP. We have reported earlier about this discrepancy.57 Patients with CP with an inflammatory mass in the pancreatic head are relatively less referred in our setting, the Netherlands, for surgical treatment compared to other countries such as Germany or the United Kingdom. This might be due to a conservative attitude of referring doctors in the Netherlands, believing that the disease will be self-limiting and burn out.

**Combined Drainage and Resection**

A large proportion of patients referred for surgical treatment of CP have proximal strictures and/or an inflammatory mass besides a dilated pancreatic duct. This has introduced the concept that in CP the head of the pancreas is the ‘pacemaker’ in pain development and its persistence, and should be addressed by intervening surgically. Therefore, symptomatic patients, having a combination of an inflammatory mass in the pancreatic head with a dilated pancreatic duct, might tend to undergo a procedure combining drainage and resection.

The duodenum-preserving pancreatic HR was introduced by Beger et al. for the treatment of CP for patients with an inflammatory mass, predominantly in the pancreatic head.31 HR is associated with less long-term morbidity and a better quality of
life compared to a pylorus-preserving pancreatoduodenectomy (PPPD).\textsuperscript{39} Mortality rates are very low when performed by experienced surgeons and HR offers pain relief in more than 90% of the patients.\textsuperscript{6}

A nowadays widely applied modification to the PJ was introduced in 1985 by Frey.\textsuperscript{30,58} This technique consists of performing a PJ together with a non-anatomical resection of the core of the pancreatic head, leaving some pancreatic tissue adjacent to the portal and mesenteric veins and the duodenum. When compared with HR, the Frey procedure does not necessitate transection of the pancreas, thus bleeding complications and anastomotic leakage are less likely to occur, making the technique more feasible.

For small duct disease, painful CP with a pancreatic duct diameter < 3 mm, a modification by Izbicki et al. has been proposed.\textsuperscript{39} A duodenum-preserving excision of the pancreatic head is combined with a longitudinal V-shaped excision of the ventral aspect of the pancreas, followed by a longitudinal PJ. Another technique was introduced by Gloor et al. in which a pancreatic HR is performed without transection of the gland over the superior mesenteric vein, thus avoiding a significant bleeding risk.\textsuperscript{59} Drainage by a PJ is omitted. This technique is also known as the Berne procedure and whether this procedure offers additional benefit over the Beger procedure is the subject of current research in Germany.\textsuperscript{61}

The best available evidence is of randomized (controlled) trials comparing the different combined drainage and resection procedures for CP (Table 3). While there is some heterogeneity of the studies listed, a cautious interpretation is warranted. Both studies comparing PD and duodenum-preserving procedures clearly demonstrate a benefit of the duodenum-preserving procedure over a PD or PPPD in terms of pain relief and pancreatic function.\textsuperscript{52,63} Strate et al. recently published a study comparing Frey and Beger procedures with a (very long) follow-up time of 104 months.\textsuperscript{64} No difference was observed with respect to pain relief, pancreatic function and quality of life. Choice of procedure should depend on local expertise.

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|l|}
\hline
Ref. & No. patients & Surgical procedures & Follow-up (m) & Results \\
\hline
Klempa et al. \textsuperscript{62} & 43 & HR vs. PD & 36-66 & HR: pain relief 100\% (vs 70\%), better pancreatic function. \\
Büchler et al. \textsuperscript{63} & 40 & HR vs. PPPD & 6 & HR: pain relief 94\% (vs. 67\%), better pancreatic function, morbidity 15\% (vs. 20\%) \\
Izbicki et al. \textsuperscript{29} & 61 & Frey vs. PPPD & 24 & Frey: pain relief 94\% (vs. 95\%), in-hospital complications 19\% (vs. 53\%) \\
Strate et al. \textsuperscript{64} & 74 & Frey vs. Beger & 104 & Equal pain relief and pancreatic function \\
\hline
\end{tabular}
\caption{Prospective randomized studies comparing surgical techniques for CP.}
\end{table}

CP: chronic pancreatitis; HR: (duodenum-preserving pancreatic) head resection PD: pancreatoduodenectomy PPPD: pylorus preserving pancreatoduodenectomy Frey: core resection of the head and pancreaticojejunostomy.
Resection Procedures
Initially introduced as a treatment option for suspicion of periampullary carcinoma, the PD according to Whipple or the pylorus-preserving modification (PPPD) was also the surgical procedure for resection in patients with CP. Although associated with considerable morbidity and mortality, PD nowadays is a relatively safe procedure with hospital mortality prevailing below 1% when performed in a high volume centre. Pain relief is achieved in up to 95% of patients but PPPD is still associated with significant loss of endocrine and exocrine pancreatic function. When compared with other resectional options, quality of life improvement after PPPD for CP is moderate. As stated before, PPPD for the treatment of CP is therefore only indicated in case of strong suspicion of malignancy.

Treatment of the distal pancreas is a procedure in selected cases with complications located in the tail of the pancreas. Left-sided pancreatectomy is a relatively safe procedure and can be performed with or without splenectomy, depending on local residual infection or fibrosis. Results in terms of pain relief differ greatly between studies, but the procedure seems to yield good results (80–90%) if applied to those patients with a single, prominent segmental stricture of the main pancreatic duct (>5 mm), with CP in the obstructed segment (pancreatic body, tail or both), as seen on computed tomography and Endoscopic Retrograde Cholangiopancreatography (ERCP). Notably, almost half of the patients ends up with some kind of pancreatic insufficiency.

The indication for TP might be failure of previous resection or severely disabling pain with complete endocrine and exocrine pancreatic failure. At the cost of significant postoperative morbidity in the form of, often brittle, insulin-dependent diabetes and malabsorption due to exocrine insufficiency, TP is only performed as a last resort. Alexakis et al. performed a duodenum- and spleen-preserving TP in 19 patients. After a median follow-up of 8.5 months 81% experienced complete pain relief.

ENDOSCOPIC THERAPY FOR PAIN CONTROL
The endoscopic management of severe CP has been developed as a less invasive mechanical approach to the treatment of pain and is now widely used as preferred interventional treatment for pain in CP. The aim of therapeutic endoscopy for pain is drainage of pancreatic ducts. Candidates for stenting appear to be those patients with a stricture or stones in the pancreatic head and upstream dilatation of the pancreatic duct. Patients with a ‘chain of lakes’ from head to tail are less likely to benefit from endoscopic therapy. The different procedures for drainage of the main pancreatic duct include: pancreatic sphincterotomy, stone extraction with or without extracorporeal shock wave lithotripsy (ESWL), stricture dilatation followed by pancreatic stenting and endoluminal drainage of the pancreatic duct. In most patients a pancreatic sphincterotomy is performed. Large or impacted stones or stones upstream of a stricture may require ESWL to fragment the stones and make endoscopic removal
possible. Displayed in Table 4 are results of several larger series with variable follow-up demonstrating partial or complete disappearance of pain in 54–91% of the patients (73.8 ± 13.8).

**Table 4** Endoscopic management for pancreatic duct stones/strictures in series ≥30 pts.

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of pts</th>
<th>Complete or partial pain relief (%)</th>
<th>Complete or partial stone removal (%)</th>
<th>ESWL (%)</th>
<th>Mean follow-up (months)</th>
<th>Proceeded to surgery (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delhaye et al. 69*</td>
<td>123</td>
<td>85</td>
<td>59</td>
<td>99</td>
<td>14</td>
<td>8</td>
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<tr>
<td>Binmoeller et al. 70</td>
<td>93</td>
<td>74</td>
<td>n/a</td>
<td>n/a</td>
<td>59</td>
<td>26†</td>
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<tr>
<td>Smits et al. 71</td>
<td>49</td>
<td>82</td>
<td>59‡</td>
<td>n/a</td>
<td>34</td>
<td>10‡</td>
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<tr>
<td>Dumonceau et al. 72</td>
<td>70</td>
<td>54</td>
<td>50†</td>
<td>100</td>
<td>24</td>
<td>6</td>
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<td>Costamagna et al. 71</td>
<td>35</td>
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<tr>
<td>Adamek et al. 73</td>
<td>80</td>
<td>76</td>
<td>n/a</td>
<td>54</td>
<td>40</td>
<td>10‡</td>
</tr>
<tr>
<td>Farnbacher et al. 74</td>
<td>114</td>
<td>48†‡</td>
<td>44</td>
<td>82</td>
<td>29</td>
<td>13</td>
</tr>
<tr>
<td>Rusch et al. 75**</td>
<td>1018</td>
<td>85</td>
<td>67††</td>
<td>64††</td>
<td>59</td>
<td>24</td>
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<tr>
<td>Vitale et al. 76†‡</td>
<td>82</td>
<td>83</td>
<td>n/a</td>
<td>n/a</td>
<td>43</td>
<td>12</td>
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<tr>
<td>Inui et al. 77†‡‡</td>
<td>555</td>
<td>91</td>
<td>73</td>
<td>92</td>
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<td>4</td>
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<tr>
<td>Eleftheriadis et al.78**</td>
<td>100</td>
<td>62‡§§</td>
<td>n/a</td>
<td>n/a</td>
<td>69</td>
<td>4</td>
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<tr>
<td><strong>Mean results (±SD)</strong></td>
<td><strong>2319</strong></td>
<td><strong>73.8±13.8</strong></td>
<td>-</td>
<td>-</td>
<td><strong>40.2±16.9</strong></td>
<td><strong>10.9±7.7</strong></td>
</tr>
</tbody>
</table>

ESWL: extracorporeal shock wave lithotripsy; n/a: not available.
* After a follow-up of 172 m. in 66% of 56 survivors a persistent clinical improvement was observed.† Two pts requiring surgery due to complications of endoscopic therapy.
‡ Complete stone removal.
§ Two pts requiring surgery for biliary stricture and underwent concomitant PJ.
¶ Complete pain relief.
** Multicenter studies.
†† Group with only stones without strictures.
‡‡ Eighty-nine pts in study, 7 underwent surgery prior to stenting.
§§ Pain relief >1y after stent removal during follow-up period.

Careful interpretation of these numbers is warranted as studies differ in methodology: performed procedures (ESWL ± sphincterotomy ± stent placement), different numbers of necessary stent exchanges and whether or not stents are still in situ at the end of follow-up. A substantial number of patients progress to delayed surgery (11 ± 8%).

ENDOSCOPIC VS. SURGICAL DRAINAGE FOR PAIN

Until recently, general opinion in Europe has been that first-line treatment of CP by drainage should be endoscopic therapy as it is a less invasive treatment option than surgery. Moreover, therapeutic endotherapy with stent placement might be safely applied as an initial therapy while it was proved not to be a risk factor for adverse effects on the outcome of subsequent PJ, in case of endoscopic treatment failure.
or disease progression. The real benefit of endoscopy over surgery or vice versa is unclear. Current literature reporting results for drainage as treatment of pain in CP are mostly retrospective, non-randomized and deal with only one treatment modality (endoscopic or surgery) without head-to-head comparison. More important, the main outcome, pain relief, was always measured without the use of general validated instruments for pain measurement. A prospective randomized trial, comparing endoscopic therapy with surgery, was published by Dite et al. Seventy-two patients were randomized to either surgery or endoscopic therapy. After a follow-up of 60 months, complete pain relief was achieved in 34% for the surgical group vs. 15% after endotherapy and partial pain relief was obtained in 52% vs. 46% respectively. The drawback of this study was that different types of surgery (drainage ± resection) were compared with endoscopic therapy without ESWL, consisting of only a single stenting procedure and, again, no validated pain measurement was used. This limits any conclusions. Cahen et al. conducted a prospective randomized trial in the AMC, comparing endoscopic drainage with surgical drainage in patients with dominant obstruction of the pancreatic duct caused by strictures and/or stones, without an inflammatory mass. To evaluate treatment success, patients were longitudinally followed up using a validated pain score. The study was discontinued after a median follow-up of 24 months because an interim analysis revealed a significant benefit of surgery over endoscopic therapy with respect to pain relief. An immediate and consistent pain response after surgery was obtained during a 2-year follow-up period. Endoscopically treated patients underwent more therapeutic interventions compared to surgically treated patients. It was concluded that for patients with advanced CP, surgical drainage was more effective than endoscopic treatment and moreover, resulted in more rapid pain relief requiring significantly less interventions.

CONCLUSION

Chronic pancreatitis is a severe disabling disease requiring intensive medical treatment. Proper and early diagnosis is crucial for patients’ future perspectives while over the last years it has become clear that early intervention might delay and perhaps even halt the disease from progressing. Rehabilitation of diseased pancreatic tissue, to some extent, seems possible. To intervene surgically in the course of disease, careful evaluation of each individual patient is necessary. A more liberal approach to surgical intervention is justified while increasing evidence is showing clear benefits over endoscopic therapy in terms of pain relief, which is the most prominent clinical symptom in patients with CP.
REFERENCE LIST


Buchler MW, Friess H, Muller WR, Weathly AM, Beger HG. Randomized trial of duodenum-preserving pancreatic head resection.


