CHAPTER 56

Short-term and long-term outcome after interventional and surgical treatment of chronic pancreatitis with inflammatory mass

Volker Assfalg, Norbert Hüser, and Helmut Friess
Klinikum rechts der Isar, Technische Universität München, Munich, Germany

No cause or curative approach has yet been found for chronic pancreatitis and therapy is rather symptom-oriented. Consequent avoidance of injuring factors, which most frequently demands absolute abstinence from nicotine and alcohol , adequate pain management, and treatment of exocrine and endocrine pancreatic insufficiency through application of enzymes and substitution of insulin allow for distinct therapeutic targets. Furthermore, interventional and operative options are available for therapy of obstructive pancreatitic disorders and for treatment or prevention of complications of chronic pancreatitis with stenosis of the pancreatic duct or common bile duct or development of pseudocysts. The latter can be distinguished as resective procedures and draining procedures. However, the choice between an endoscopic or radiologic interventional approach and an operative approach has to be reassessed individually in every case, always bearing in mind the cluster of symptoms, the development of the disease, and the patient's clinical status. The indications for operative drainage have been made more restrictive because of improvements in endoscopy. Nevertheless, chronic pancreatitis demands surgical action whenever pain or organ complications cannot be brought under control by medical or interventional therapy. This chapter gives an overview of short- and long-term outcomes of the distinct therapeutic procedures and thereby evaluates their respective significance within the overall therapeutic concept of chronic pancreatitis.

Pain management in chronic pancreatitis

Chronic pancreatitis (CP) typically appears together with recurring episodes of abdominal pain. For patients with ethyl-toxic pancreatitis the first therapeutic measure is absolute abstinence from alcohol. In this way, the disease's progress can be decelerated and pain management can be easier to handle (1). Antacid drugs fail to affect pain progression favorably, apart from those patients with peptic ulcers who can frequently be seen among patients with ethyl-toxic CP. In a meta-analysis including 10 publications, the effectiveness of oral supplementation with pancreatic enzymes with regard to the development of abdominal pain revealed no differences in quality of life (2). Therefore, analgesic therapy as recommended by the World Health Organization (WHO) pain management guidelines comes to the fore to treat chronic pain. First, peripherally active analgesics are applied that can then be combined with diverse adjuvants (e.g., tricyclic antidepressants or anticonvulsives) or with first-line opioids in the next step. The positive effect of the gabapentoid pregabalin as a complementary medication was demonstrated in patients with CP (3). In cases where this therapy remains insufficient, opioids with higher potency are necessary: not on-demand but according to a fixed time interval, which has to be adapted to both the patient's pain symptoms and the pharmacological profile of

Pancreatic Cancer, Cystic Neoplasms, and Endocrine Tumors: Diagnosis and Management, First Edition. Edited by Hans G. Beger, Akimasa Nakao, John P. Neoptolemos, Shu You Peng, and Michael G. Sarr.

the drug. Interestingly, investigations from the United States describe the phenomenon that patients with continuing pain but independent of the pain's intensity are hospitalized significantly more often and need more pain killers compared with patients with intermittent pain. Additionally, continuous pain was associated with lower quality of life (4).

Interventional procedures for therapy: refractory pain

Endoscopic procedures for pain management, such as celiac plexus block and mainly draining interventions to remove obstructions in the pancreatic duct and the bile duct, aim for a reduction of neurogenic sensations.

The anatomical approach of the plexus block is to disconnect the sensory nerves from the pancreas to the celiac ganglion. Usually a mixture of a steroid and a long-lasting local anesthetic is injected into the plexus. Besides this method, high-proof alcohol or phenol can be applied alternatively for the so-called *celiac plexus neurolysis*. This variant induces a chemical splanchnicectomy to alleviate pain mainly in patients with pancreatic cancer.

Different studies reveal a positive effect of ultrasound-guided plexus block for pain control in CP (5–7) and some investigators even report a tendency toward an advantage compared with radiological, computed tomography (CT)–guided approaches. The reason for this might be the direct access path to the application area (8). Within short-term follow-up, significant improvements in the overall pain score were reported; however, this proportion diminished substantially during the further course. A meta-analysis of ultrasound-guided celiac plexus blockades in CP demonstrated more than 50% overall successful pain reduction (9). In another meta-analysis of 9 studies with a total number of 376 patients who underwent both celiac plexus block and neurolysis for CP, nearly 60% showed short-term pain relief (10). Infiltration of the celiac ganglion with steroids led to an improvement of pain in 38% of the patients, whereas the application of alcohol was successful in 80% (11). Taken as a whole, only few qualitatively convenient studies have been published so far and in addition to that there exist no valid data on long-term follow-up. Undesirable side effects, from transient diarrhea via hypotension to temporarily increased pain, may occur. The relative overbalance of the visceral, parasympathetic activity is likely to be the morphological correlate; however, the access path—either endoscopic or radiologic percutaneous intervention—did not turn out to be the decisive factor. Less-frequent complications of this therapy can be the development of a pneumothorax, retroperitoneal hemorrhage, or renal lesions. The direct access path of the endoscopic procedure is the reason for its outstanding advantages because it circumnavigates the pleura, the diaphragm, and the paraspinal area.

The basis for adequate pain management is the knowledge of the underlying pathologic mechanism and therefore the verification or morphological exclusion, respectively, of a pancreatic duct stenosis or impacted calculi or stones. According to investigations by Rosch et al., ERCP-driven sphincterotomy, dilatation, stenting, or calculi removal was performed successfully and pain was reduced in an average of 65% of patients with CP suffering from constrictions and stones (12). Every inflammatory exacerbation may lead to cicatricial strictures and therefore causes stenosis of the pancreatic duct. The specific impact of these morphological changes on the character of pain is hard to assess. Results from a prospective study reported a decrease of pain after ERCP with dilatation and stenting in nearly 90% of all patients. However, these short-term results were not reproduced in the long-term follow-up. In 30% of the patients further therapy was necessary (13). Whether stent changes should be performed regularly within distinct intervals or on demand—which means in the case of recurrent attacks of pain—remains unclear. Even in larger series the on-demand concept sometimes required five stent changes (14). Repeatedly performed stenting succeeded in 80% freedom from pain and afflictions, respectively, during an observation period of 38 months (15). Prospective studies have to be performed to investigate this therapeutic approach because so far there is no comparison of single and multiple stenting. Recent tests additionally evaluate the effectiveness of completely covered, self-expanding metal-stents. The first results appear to be promising; however, the long-term course has to be analyzed.

Surgical options for pain management

The discussion whether to prefer endoscopic stenting versus operative drainage or resection procedures in patients with symptomatic CP remains controversial. Therefore, the need for a comparative investigation on

medical, interventional, and operative approaches with regard to the long-term development of pain and quality of life has to be emphasized. In a first prospective analysis endoscopy was performed for transpapillary stone removal (without previous extracorporeal shock wave lithotripsy [ESWL]) both with and without stenting. In the surgical group 80% of the patients received a resection and 20% received a draining procedure. The 1-year results of both groups with regard to pain control were comparable and therefore the interventional procedure could be proposed for "first-line" therapy because of the less-invasive approach. However, operative therapy turned out to be superior in chronic obstructive pancreatitis in the 5-year observation. Complete or partial freedom from pain was seen in 85% of patients after surgery compared with 61% after endoscopic intervention (16). Another study investigated the favorite strategy against intractable pain and compared endoscopic stenting (with or without ESWL) versus surgical drainage by means of lateral pancreaticojejunostomy and published the short-term outcome in 2007. Patients who received surgery reported partial or complete freedom from pain in 75%, whereas only 32% of the interventionally treated patients did (17). Cahen et al. published the long-term results in 2011 (18). Out of multiple investigated parameters that were monitored for a total period of 79 months, patients with symptomatic, advanced CP and initially performed surgical drainage turned out to have significantly less pain and less-frequent interventional or surgical therapy during the further course. Almost half of the patients who initially were treated endoscopically later received surgical treatment.

In another study, Ahmed and colleagues developed a nomogram for prediction of postoperative relief of pain (19). The evaluation of 266 patients with a median follow-up period of 62 months revealed a short time interval between diagnosis and operation to be the most significant predictor of effective pain reduction. Surgery within 3 years after making the diagnosis and/or surgery in patients with a maximum of five endoscopic stenting procedures leads to a significantly improved relief of pain. These particularly promising findings in patients with only few preceding endoscopic interventions could be supported by an investigation on 146 patients with surgery for symptomatic CP (20). Therefore—even though not yet confirmed by a controlled randomized trial—an early operative approach must be strongly recommended. Besides the high significance of interventional therapeutic approaches in patients with symptomatic CP, the need for an interdisciplinary change of thinking arises and demands the evaluation for surgical therapy in every single case, despite the low number of studies and the heterogeneity of indications in recent data from the literature. These considerations are particularly important in patients with a tenuous pancreatic duct and the obstructive variant of CP, respectively.

Decompression of pseudocysts

With an incidence of up to 40%, pancreatic pseudocysts represent the most frequent complication of CP. To some extent they disappear spontaneously as a result of a perforation into the pancreatic duct, which is the equivalent of a natural, internal drainage of the cyst. However, when the cyst persists for a prolonged period of several weeks, the probability of spontaneous regression decreases and although pseudocysts per se do not demand intervention they now may become symptomatic due to size, infections, abscess formation, or erosional bleeding and development of pseudoaneurysms. Occasionally, growth leads to displacement or compression of adjacent structures with consecutive development of pressure pain or gastroduodenal passage disturbances. Symptomatic pseudocysts therefore have to be treated. However, interventional therapy for cysts beyond a certain size is no longer considered obligitory.

Interventional therapy for pseudocysts

With regard to therapeutical consequences, the depiction and classification of different peripancreatic fluid accumulations is essential. The first differentiation of acute and chronic pseudocysts was made by the Atlanta classification in 1992 (21). This classification was reviewed and edited in view of today's requirements and defined and depicted according to pathomorphologic findings in the Guidelines of the American Society for Gastrointestinal Endoscopy (ASGE). It is safe to say that for drainage of a pseudocyst in CP the endoscopic approach entails the best results, with a success rate above 90%. However, the application of this procedure in acute pancreatitis or pancreatic necrosis turned out to be less successful (22).

Pseudocysts in CP may derive from either recurring acute exacerbations with local autodigestion or so-called retention pseudocysts resulting from stenoses or calculi in side branches of the pancreatic duct and lose their epithelium secondarily. This is why these pseudocysts are frequently intrapancreatic and their etiology has to be considered in treatment planning. In general, interventional therapy for CP and its complications has gained greater significance. The indication for percutaneous drainage as an established therapeutical procedure for diagnosed pseudocysts has decreased steadily with further development of internal drainage techniques. However, the advantage of this technique is the feasibility to drain even pseudocysts not adjacent to hollow organs. Currently, this procedure, guided by either ultrasonograpy or CT, is mainly deployed for emergency therapy of infected cysts and necroses. The reason for this is the high incidence of recurrence, in up to 70% of cases, and the frequent development of percutaneous fistulas, in more than 20% of the cases. Taken as a whole the numerous investigations on the effectiveness of percutaneous drainage for pancreatic pseudocysts show very heterogeneous results and can only be partially compared. The biggest difficulty is most likely due to the inconsistent handling of nomenclature and therefore one cannot consider the pseudocyst as a direct result of CP with the necessary differentiation. Data from long-term monitoring do not exist.

Pseudocysts that occur together with CP are frequently associated with a stenosis of the main pancreatic duct. These morphologic changes have to be treated either endoscopically or surgically to avoid recurrence. This decision is accompanied by the question whether endoscopic retrograde pancreatography should be performed prior to drainage of a pseudocyst. Without a doubt it is a suitable diagnostic investigative tool for assessing the pancreatic duct (23). In CP, imaging techniques yield additional information on the connection of the pseudocyst to the duct and on the duct's anatomy with pathologic findings such as discontinuation or stenosis, which must be evaluated.

Endoscopic drainage of pancreatic pseudocysts can be performed by either a transgastric and transduodenal (=transmural), a transpapillary, or a combined approach. Whenever a connection of the cyst and the pancreatic duct exists a transpapillary drainage should be favored because this access to the pseudocyst can be assumed to be the least traumatic. Prospective data on both the best point in time to change the stent and the necessary length of time for stent therapy do not exist. In general, stents for drainage of the pancreatic duct are changed every 6 weeks and 2–3 months after complete regression of the pseudocyst. The reasons for this strategy are concerns about the redevelopment of pseudocysts. Studies have revealed an increased recurrence rate as a consequence of premature stent removal.

In the case of a transmural drainage, the distance between the cyst and the organ's wall should be as short as possible to minimize the risk of dislocation of the drainage. By using endoscopic and Doppler sonography the localization of the cyst and the most suitable draining procedure can be evaluated. Decreasing rates of procedure-related complications such as bleeding, perforation, and infections led to an increased use of this method. In the literature mortality is reported to be below 1%. A prospective, randomized study assessed the superiority of the endoscopic ultrasonography (EUS)–guided compared with the non-EUS-guided, conventional transmural drainage. Besides a technical success rate of 94% versus 72%, no differences in complication rates could be found and sufficient treatment of the pseudocysts was comparable in short-term follow-up (24).

In those cases where a pseudocyst more than 5 cm in diameter (e.g., resulting from an obstructed duct or an impacted calculus) is intended to be preferentially drained by a transmural procedure, a combined transmural and transpapillary approach together with stenting is chosen, to reduce the risk of early recurrence.

Different investigations have analyzed the long-term success of interventional cyst management. However, a meticulous interpretation of the results is difficult because frequently the etiology of pseudocysts was not considered and therefore patients with both acute and chronic pancreatitis had been included in the analyses. The successful dissolution of the pseudocysts has been reported to be higher than 90%, more-recent studies prove symptom resolution to be as high as 91%, and the recurrence rate in long-term follow-up is between 16% and 18% (23,25,26).

Operative therapy for pseudocysts

Treatment for pseudocysts has been a surgical domain for a long time. Operative therapy is increasingly moving toward the treatment of complex pseudocysts as they may develop for instance within CP. This concerns huge

pseudocysts, multiple pseudocysts, and the like, with strictures, calculi, or discontinuation of the pancreatic duct, respectively (27). Of course, the aim of the different operative methods is not only to drain and definitively treat the cyst itself, but also has to consider a complex scenario of chronic pain, surrounding inflammation, vascular affliction, and pathologic duct anatomy. Therefore, *resections* as a third operative category can be applied besides *internal* and *external drainage procedures*.

External drainage is considered doubtful because of a low prospect of long-lasting success. Furthermore, it is rarely necessary to perform an operative external drainage on the basis of anatomical conditions. However, for temporary decompression of infected pseudocysts as frequently seen in acute pancreatitis, this method is a good option; this is why numerous studies rather refer to the follow-up of acute pancreatitis.

Internal drainage procedures are performed as pseudocystogastrostomy, pseudocystoduodenostomy, and pseudocystojejunostomy. Hence, the anastomosis connects the nonepithelialized tissue of the cyst with the epithelialized stomach or small bowel, respectively. The crucial point during the operation is to place the anastomosis and therefore the drainage at the lowest part of the cyst; however, only a small number of patients qualify for this procedure because of anatomical and clinical reasons. The operation is accompanied with an average lethality of 2.5% and a morbidity of 16%. The technical success rate is about 90%–100% and recurrence occurs on average in 12% of patients within a long-term follow-up of up to 96 months dependent on the localization of the pseudocyst and the underlying disease, respectively (27). The literature does not feature any operative method without restrictions, and controlled randomized trials are missing. Nonetheless, pseudocystjejunostomy—in most centers performed as Roux-en-Y jejunostomy—seems to be advantageous compared with pseudocystgastrostomy. Besides the drainage of sterile cysts, good results have been reported for infected pseudocysts as well (28).

For resection different generally accepted procedures are defined: left or lateral pancreatic resection, pylorus-preserving pancreatoduodenectomy, Beger's operation, and Frey's procedure. These operations principally can be performed for biliary or pancreatic duct obstructions and advanced CP. See Chapters 54 and 55 for comments on the respective outcome in short- and long-term follow-up.

A direct comparison of operative procedures and interventional therapy of pancreatic pseudocysts only has been performed for percutaneous but not for endoscopically applied drainage (29). There is a lack of randomized studies, particularly in view of the fact that a bias in selection of patients can be assumed in practice. Patients not qualifying for surgery because of marked comorbidities frequently have been treated interventionally.

Further development of conventional surgery uses the *laparoscopic approach* and the modified operation is performed in analogy to the open cyst–enteric drainage techniques. However, there is still discord on both the most convenient laparoscopic technique and the most suitable patient population for the minimally invasive approach. Most frequently the pseudocystjejunostomy, the combined laparoendoscopic intragastric pancreatic pseudocyst gastrostomy (lesser sac), and the pancreatic pseudocyst gastrostomy via an anterior approach are described in the literature. The cystogastrostomy is particularly suited for the drainage of pseudocysts closely adjacent to the gastric wall. Whereas the anterior access appears to be easier, the more-complex posterior access allows for a good exposition and enables a larger anastomosis, which is essential for a sufficient drainage of fluids from the cyst and the removal of necrotic debris. Hitherto there are no prospective, randomized data but the lethality and the technical success rate of the published studies are reported to be 0% and more than 90%, respectively. Therefore the operation seems to be a safe procedure; however, the number of patients included in the studies is low. Combined, the complication rate is stated to be below 10%, the long-term follow-up of some studies reaches more than 6 years (30), and the recurrence rate turns out to be between 0% and 13% (31). Hence, the laparoscopic operation provides comparable results in terms of efficacy and security compared with the open drainage procedures.

Taken as a whole, the patient population and the texture of pseudocysts are very inhomogeneous. Therefore, not only the indications but also the short- and long-term success of endoscopic, percutaneous, and surgical drainage and excision of pseudocysts, respectively, are highly dependent on numerous factors: the localization of the cyst; the maturity of the cyst or cyst wall when the patient presents with symptoms; combined complications; and the respective experience and expertise of the endoscopist or surgeon, of course.

Numerous publications reflect this difficulty of heterogeneity and achieve, if any, level 3 evidence, and meta-analyses and multicenter trials would be significantly flawed. Therefore, to evaluate the adequate therapeutic procedure of pseudocysts and the respective assessment of short- and long-term results, pancreatologists, surgeons, and radiologists first must adhere to strict definitions of pseudocysts and the etiology of pancreatitis as an appropriate starting point to properly classify patients (32).

Therapeutic concepts for ductal stenoses

Stenoses of the pancreatic duct and the intrapancreatic bile duct can develop during a protracted course of chronic inflammation of the pancreas. In calcifying courses of the disease they are especially distinct. However, a strict therapeutic algorithm does not exist because of the variable clinical course. Whereas the interventional therapy can be applied early and effectively for isolated obstructions, surgery has to be chosen in all cases with suspicion of malignant obstruction. Whenever interventional measures do not lead to a sufficient result or even cause organ complications, operative resection or drainage procedures are applied. Results after operations as reported in the literature can hardly be compared with those from endoscopy because in the publications resections and drainage procedures are frequently handled as one. Strictly speaking, only operative procedures for drainage should be considered.

Endoscopic treatment of ductal stenoses and concretions

Endoscopic therapy plays an important role for stenoses of the pancreatic duct or the bile duct. The underlying disorder is due to ductal strictures, concretions, or stenoses in the area of the major and minor papillary sphincter, respectively. The aim of therapy is intraductal hypotension because the current hypothesis of pain development in CP regards both ductal hypertension and inflammation of peripancreatic and celiac nerves to be causative (33). The success-rate of endoscopic treatment depends on a variety of factors such as the number of calculi and strictures, their length and localization, and a potentially dilated ductal segment upstream.

In 2003 Kahl et al. showed the absence of calcification of the pancreatic head to be the only factor of prognostic value for successful endoscopic treatment (34). Whereas only 7.7% of the patients with calcifications could be treated successfully by endoscopy, 59.1% of the patients without calcifications showed a benefit from stenting after a median follow-up of 40 months.

In a report on a total number of 491 patients who underwent stenting because of ductal stenosis, 65%–95% showed early recurrence of symptomatic pain, and persisting pain was present in 52%–90% of the subjects. During a follow-up period of 14–69 months, 4%–26% finally received surgical revision (35). In an overview of 15 studies and nearly 1500 patients, endoscopic treatment turned out to be particularly effective for dominant strictures and a dilated pancreatic duct. During the follow-up of 8–72 months a reduction of pain as a clinical correlate of a positive effect was found in 31%–100% (36). A multicenter study analyzed the long-term success after endoscopic decompression of the pancreatic duct. Follow-up data was ascertained in more than 1000 of 1211 patients who mainly presented with strictures, calculi, or a combination of both strictures and calculi. During the observation period of 2–12 years (mean, 4.9 years) a complete or at least significant pain reduction after endoscopic treatment and drainage was proven in 86% of the cases but only 65% in an intention-to-treat analysis. The results were independent of the localization of the stricture and the calculi's impaction in the pancreatic head or body. In the long-term course, for 60% of the patients therapy was finished after endotherapy but in one out of four patients surgical intervention became necessary. In case of pain and an underlying stricture in the pancreatic duct this therapeutic concept does not present an obstacle for potential subsequent operation (12).

It is well known that the intensity of pain may decrease in long-term course of CP. This phenomenon, called burn-out, makes investigation of the benefit of stenting difficult and potentially causes some bias due to lack of a control group without intervention. A 2009 study considers this problem and besides endotherapy randomization refers patients in a second branch with a so-called sham-procedure. Results from this study are pending (37).

Evidence of larger, impacted pancreatic stones usually requires extracorporeal shock wave lithotripsy (ESWL) prior to endoscopy. Lithotripsy is an effective procedure

with a low complication rate but has to be repeated sometimes. The success rate of the subsequently performed complete removal of the stones with consequent alleviation of pain can be as high as 75% (38). The results from a meta-analysis indicate that ESWL appears to be effective in both relief of main pancreatic duct obstruction and alleviation of pain in chronic calcific pancreatitis, in combination with endoscopy (39). A time interval of approximately 2 days is recommended between the interventions. Unfortunately, the positive results in short-term follow-up are not reflected in long-term surveillance. Recurrent lithiasis and de novo pain attacks occur in many cases.

Dumonceau et al. compared ESWL alone and in combination with endoscopic intervention. Pain relapse in both groups of this randomized controlled trial was comparable (38% vs. 45%) after a 2-year observation period. Additionally, in an intention-to-treat analysis the results from this study showed a median delay of 1.1 years in terms of occurrence of CP and permanent pain relief in patients who either received ESWL alone or in combination with endotherapy, compared with 4 years in the untreated reference group (40).

Strictures and intraductal calculi may cause upstream localized leakages or fistulas of the main pancreatic duct or side branches. The appearance is manifold and besides pseudocysts, representing one variant of internal fistulas, external, cutaneous fistulas may develop. However, currently no comparative studies exist on surgical and endoscopic treatment strategies of pancreatic leakage.

The incidence of biliary strictures of the bile duct on the basis of CP varies from <5% to nearly 50% (41). Endoscopic intervention with plastic or self-expanding metal stents is a possible alternative to surgery. However, to date, sufficient long-term results from randomized trails are missing. The technical feasibility has been demonstrated repeatedly but during the follow-up periods of up to 58 months only 10%–38% lead to disappearance of biliary strictures (35). By using simultaneous stenting with several biliary stents, outcome could be improved and studies report on a successful resolution rate between 44% (observation period of 4 years) (42) and 92% (mean treatment period of 14 months) (43). Noncovered and partially covered, self-expanding metal stents with permanent positioning in the bile duct have proved short-term suitability in CP. According to different studies a patency rate of 100% could be found after 1 year. However, stent occlusion was found in up to 62% during long-term follow-up of up to 50 months in some cases (44,45).

Operative treatment of chronic pancreatitis

The indications for operative therapy of CP become effective when there is suspicion of malignancy, when pain is resistant to treatment, and in cases of intra- or extrapancreatic complications that cannot be treated conservatively. Furthermore, operative therapy has to be performed for vascular obstructions of, for example, the portal vein or the superior mesenteric vein. However, especially surgery for venous vascular affections frequently turns out to be technically challenging. In conformity with pathophysiologic perceptions and underlying morphologic changes, different therapeutic strategies have been established. *Draining operations* and *resections* can be differentiated, with every resection having a draining effect, too. *Organ-preserving resections* have a crucial significance in pancreatic surgery, leaving the duodenum, the bile duct, the stomach, and—in particular—healthy pancreatic tissue to maintain the endocrine function.

The demand for organ- and parenchyma-preserving surgery is realized by the drainage procedures according to the Partington–Rochelle procedure and the V-shaped longitudinal incision of the pancreatic duct and lateral pancreaticojejunostomy. Whereas the Partington–Rochelle method is well suited for patients with large-duct disease, the V-shaped excision together with a limited head resection is superior in all cases of patients with a small-duct disease (approximately 5% of patients) as it also directly drains the secondary and tertiary ducts. The Roux-en-Y jejunal loop allows for drainage of both the duct of Wirsung and the duct of Santorini in their complete dimensions. These interventions entail a low overall morbidity and mortality (46), but a negative aspect of these drainage procedures is that they do not exclude malignancy. Furthermore, complications such as duodenal or biliary stenoses cannot be cured sufficiently by either procedure. In numerous noncontrolled studies low morbidity rates together with good short- and long-term results could be demonstrated. However, there remains the difficulty of assessing a patient cohort that most often is inhomogeneous, with varying extent of changes in organs. Frequently, drainage procedures had to be combined with a limited

Table 56.1 Overview of results of studies on lateral anastomotic techniques after Partington–Rochelle and V-shaped excision of the ventral pancreas[a]

Authors, year	Title (Ref.)	Operation	No. of patients	Freedom from pain
Proctor et al., 1979	Surgery for chronic pancreatitis. Drainage versus resection (49)	PR	22	50%
Warshaw et al., 1980	Long-term patency, pancreatic function, and pain relief after lateral pancreaticojejunostomy for chronic pancreatitis (50)	PR	10	80%
Bradley, 1987	Long-term results of pancreatojejunostomy in patients with chronic pancreatitis (51)	PR	46	28%
Prinz and Greenlee, 1981	Pancreatic duct drainage in 100 patients with chronic pancreatitis (52)	PR	53	21%
Adams et al., 1994	Outcome after lateral pancreaticojejunostomy for chronic pancreatitis (46)	PR	62	42%
Sielezneff et al., 2000	Long term results of lateral pancreaticojejunostomy for chronic alcoholic pancreatitis (53)	PR	57	28%
Schnelldorfer and Adams, 2003	Outcome after lateral pancreaticojejunostomy in patients with chronic pancreatitis associated with pancreas divisum (54)	PR	147	20%
Yekebas et al., 2006	Long-term follow-up in small duct chronic pancreatitis: a plea for extended drainage by "V-shaped excision" of the anterior aspect of the pancreas (47)	VsE	41	89%
Cahen et al., 2007	Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis (17)	PR	20	75%
Cahen et al., 2011	Long-term outcomes of endoscopic vs surgical drainage of the pancreatic duct in patients with chronic pancreatitis (18)	PR	39	80%

[a] Adapted from Schneider et al., 2009 (48). Reproduced with permission from Springer Science + Business Media.
PR, Partington–Rochelle; VsE, V-shaped excision.

pancreatic head resection. In a prospective trial by Cohen et al., a significant difference between surgical and endoscopic drainage of the pancreatic duct was seen after a follow-up period of 2 years. Partial freedom from pain was achieved in 75% of patients after the Partington–Rochelle procedure and in 32% of the endoscopically treated patients (17). In their 5-year long-term follow-up Cahen et al. could demonstrate superior pain relief (80% vs. 38%) after surgery. However, levels of quality of life and pancreatic function were comparable (18) and there are only a few studies reporting unsuccessful treatment of pain after lateral pancreaticojejunostomy. The prospective investigation by Yekebas et al. demonstrated effective pain control with respectively good quality of life (73% of the patients) for the V-shaped excision, too. Facing a low perioperative (30 days) morbidity and 0% mortality, the procedure is as safe as it is effective (47) (Table 56.1).

The extended drainage procedure according to Frey combines a limited pancreatic head resection and the pancreaticojejunostomy (55). The rationale of this approach is the idea of persisting pain due to incomplete decompression of the duct in the pancreatic head in the case of lateral drainage only. The intensity of pain was investigated by a more recent study including 60 out of 134 patients who underwent the Frey procedure (56). In the prospective follow-up with a median observation period of 6.4 years, the Izbicki pain score revealed a median decrease from 46.4 before to 10 points after surgery. Furthermore, partial or complete pain

reduction was found in 75% of the patients during this interval. The Izbicki pain score was developed by the Hamburg study group to assess the intensity of pain in CP and was validated and certified to be reliable, together with the European Organization for Research and Treatment of Cancer (EORTC) quality-of-life questionnaire before it.

The duodenum-preserving pancreatic head resection (DPPHR, Beger procedure) belongs to the resective procedures that represent the concept that subtotal resection of the pancreatic head may help for complications and symptoms of CP without further organ resection and with a reduced risk of operation-associated long-term side effects (57). This operation is suited for patients suffering from therapy-refractory pain and inflammatory changes and consequent space-consuming lesion in the pancreatic head, concomitant biliary and/or pancreatic duct obstruction, and possibly even obstruction of the retropancreatic vessels. The DPPHR turned out to be a safe operative procedure with nearly zero mortality and it gained general acceptance, especially in Europe. In North America, however, this procedure has not become generally prevalent yet. In a survey of pancreatic surgeons at academic medical centers in North America fewer than half of them stated that they perform a DPPHR in case of CP. In the survey the DPPHR was frequently said not to have the respective evidence to support the effectiveness of operations (58). A major retrospective single-center study on more than 500 patients and an observation period of 26 years revealed freedom from pain in more than 90% of patients 2 and 5 years after the operation, respectively (59).

The "Bern modification" is a technical simplification of Beger's DPPHR as the pancreatic transection atop the portal vein and the left-sided pancreatic duct anastomosis of the Frey procedure are abandoned. It can be categorized as the most organ-protective and technically easiest variant (60). Randomized controlled trials showed comparable functional results for the Beger and Frey procedures (61) and for the Beger procedure and Bern modification (60), respectively (Table 56.2). After a long median follow-up of 104 months an evaluation was performed using the EORTC quality-of-life questionnaire and the pain score. In this investigation no significant differences between DPPHR and the Frey procedure were seen, too. In the group of patients who underwent the Frey procedure, 78% developed exocrine insufficiency and 60% developed endocrine insufficiency with a pathologic oral glucose tolerance test (62). However, no studies comparing the Frey versus the Bern operation have been performed so far.

The classical pancreaticoduodenectomy (Whipple procedure) was the standard therapy for CP with inflammatory changes in the head region. In specialized centers this operation can be performed with a lethality below 5%. However, investigations of the quality of life turned out to be dissatisfying in long-term observation. Undesirable effects such as diarrhea, dumping, peptic ulcers, and dyspeptic complaints occurred. Additionally, about 50% of these patients developed diabetes mellitus (74). Initial reservations in terms of morbidity and mortality after pylorus-preserving resection could be weakened by numerous randomized controlled trials. Therefore, this procedure provides a fair alternative. A comparison of both operations—mainly performed for malignant findings—could not demonstrate any improvement in the unfavorable aspects of the classical Whipple procedure. No significant difference was found for operation time, blood loss, morbidity and mortality, hospital stay, and quality of life (75,76).

Distinct prospective studies compared the DPPHR and the pancreatoduodenectomy (PD) and found conformable results (64–67). The DPPHR, in particular, turned out to have a shorter operation time (65,66), a reduced postoperative morbidity (65,66), and a shorter hospital stay (66,68). In a direct comparison, pain control was significantly better in patients who underwent DPPHR (64,67,68) and in several studies an improved gain in body weight was detected in this patient collective, additionally (64,66,68). In the patient interviews and the answers to the EORTC quality-of-life questionnaire, an improved postoperative course was seen in both groups; however, a significant advantage in the DPPHR group was found 24 and 63 months after surgery, respectively (67,68) (Table 56.2). These findings could initially be approved in a meta-analysis on the DPPHR and the classical Whipple procedure. Besides comparable outcome in terms of pain control, morbidity, and endocrine insufficiency, significant advantages of the DPPHR were found for hospital stay, exocrine function, and quality of life (77). However, strictly speaking, in more-recent investigations with a longer follow-up period no differences were obvious with regard to pain control, quality of life, and development of endocrine and exocrine pancreatic insufficiency (69,78). This loss

Table 56.2 Overview of results of studies on pancreatic resection procedures[a]

Author (Ref.)	Year	Design	Patients	Follow-up	Investigated procedures	Main results
Büchler et al. (64)	1995	PRC	40	6 m	DPPHR vs. PPPD	Comparable morbidity and mortality Less pain, greater weight gain, better glucose tolerance, higher insulin secretion capacity after DPPHR
Izbicki et al. (65)	1998	PRC	60	Median, 24 m	LPJ-LPHE vs. PPPD	Comparable effectiveness in pain relief and definitive control of complications Better QOL after LPJ-LPHE
Farkas et al. (66)	2006	PRC	40	1 y	DPPHR vs. PPPD	Comparable safety and effectiveness in pain relief Shorter operation time, less morbidity, shorter hospital stay, greater weight gain, and superior QOL after DPPHR
Möbius et al. (67)	2007	PNR	51	5 y	DPPHR vs. cWh	Comparable frequency of acute episodes and analgesic medication, no difference in endocrine–exocrine function and BMI Better QOL, less pain after DPPHR
Belina et al. (70)	2005	PNR	104	Median, 39 m	LPJ-LPHE vs. PPPD/cWh	No significant differences in morbidity and mortality Improved QOL and pain relief after both procedures
Witzigmann et al. (68)	2003	PNR	70		DPPHR vs. cWh	No significant differences in morbidity, mortality, and endocrine–exocrine function, comparable frequency of acute episodes and analgesic medication Shorter hospital stay, lower postoperative pain intensity, better QOL, and higher increase of BMI after DPPHR
Klempa et al. (71)	1995	PRC	43	Range, 36 m to 5.5 y	DPPHR vs. cWh	Faster convalescence and significant benefit in postoperative hormonal status after DPPHR
Müller et al. (69)	2008	PRC	40	Median, 7 and 14 y	DPPHR vs. PPPD	No differences in pain status and exocrine pancreatic function Loss of appetite significantly better 14 years after DPPHR Early advantages of DPPHR no longer present after 14 years
Varghese and Bell (58)	2007	National survey Plus results from an in-house series	21		DPPHR	Significant improvement in pancreatic-related pain and digestive function compared with a general population of patients with CP, significantly less pain after operation

Table 56.2 (*Continued*)

Author (Ref.)	Year	Design	Patients	Follow-up	Investigated procedures	Main results
Aspelund et al. (72)	2005	PNR cohort study	86	Mean, 3 y	DPPHR vs. LPJ-LPHE vs. PPPD/cWh vs. DPR	Lower morbidity and mortality, and less incidence of new diabetes after DPPHR and LPJ-LPHE Significantly shorter operation time for DPPHR
McClaine et al. (73)	2009	R	81	Sept 1999–Aug 2006	DPPHR, LPJ-LPHE, Bern vs. PPPD/cWh	Comparable morbidity, mortality, postoperative pain relief, and QOL Significantly shorter operation time, shorter hospital stay, and less blood loss for DPPHR
Strate et al. (62)	2005	R	74	Median, 104 m	DPPHR vs. LPJ-LPHE	Comparable late mortality, QOL, pain score, and exocrine–endocrine function
Köninger et al. (60)	2008	PRC	65	24 m	DPPHR vs. Bern	Comparable QOL, shorter operation time and shorter hospital stay for Bern

[a] Adapted from Strobel et al., (63) with permission from Springer Science + Business Media.
PRC, prospective randomized controlled trial; PNR, prospective nonrandomized trail; R, retrospective database analysis; m, months; y, years; DPPHR, duodenum-preserving pancreatic head resection (Beger); LPJ-LPHE, longtitudinal pancreaticojejunostomy and local pancreatic head excision (Frey); Bern, Bern modification; PPPD, pylorus-preserving pancreatic head resection; cWh, classical Whipple procedure; DPR, distal pancreatectomy; QOL, quality of life; BMI, body mass index.

of significance can most likely be ascribed to the loss of patients during long-term follow-up and consequent failure due to the lower number of cases to achieve significant findings.

Therefore the ChroPac trial was initiated with the intention to further evaluate the question of adequate surgical therapy. In this randomized multicenter trail duodenum-preserving pancreatic head resection was compared with the classical or pylorus-preserving duodenopancreatectomy in patients with chronic pancreatitis. The study protocol has already been published in trials (79) and the primary end point is the mean quality of life 2 years after the operation. The study currently includes the intended number of 100 patients per group to achieve a power of approximately 90%.

References

1 Witt H, Apte MV, Keim V, Wilson JS. Chronic pancreatitis: challenges and advances in pathogenesis, genetics,

diagnosis, and therapy. Gastroenterology. 2007;132(4): 1557–1573.
2 Shafiq N, Rana S, Bhasin D, et al. Pancreatic enzymes for chronic pancreatitis. Cochrane Database of Systematic Reviews. 2009;(4):CD006302.
3 Olesen SS, Bouwense SA, Wilder-Smith OH, van Goor H, Drewes AM. Pregabalin reduces pain in patients with chronic pancreatitis in a randomized, controlled trial. Gastroenterology. 2011;141(2):536–543.
4 Mullady DK, Yadav D, Amann ST, et al. Type of pain, pain-associated complications, quality of life, disability and resource utilisation in chronic pancreatitis: a prospective cohort study. Gut. 2011;60(1):77–84.
5 Gress F, Schmitt C, Sherman S, Ikenberry S, Lehman G. A prospective randomized comparison of endoscopic ultrasound- and computed tomography-guided celiac plexus block for managing chronic pancreatitis pain. The American Journal of Gastroenterology. 1999;94(4):900–905.
6 Gress F, Schmitt C, Sherman S, Ciaccia D, Ikenberry S, Lehman G. Endoscopic ultrasound-guided celiac plexus block for managing abdominal pain associated with chronic pancreatitis: a prospective single center experience. The American Journal of Gastroenterology. 2001;96(2): 409–416.
7 Faigel DO, Veloso KM, Long WB, Kochman ML. Endosonography-guided celiac plexus injection for abdominal pain due to chronic pancreatitis. The American Journal of Gastroenterology. 1996;91(8):1675.
8 Levy MJ, Wiersema MJ. EUS-guided celiac plexus neurolysis and celiac plexus block. Gastrointestinal Endoscopy. 2003;57(7):923–930.
9 Kaufman M, Singh G, Das S, et al. Efficacy of endoscopic ultrasound-guided celiac plexus block and celiac plexus neurolysis for managing abdominal pain associated with chronic pancreatitis and pancreatic cancer. Journal of Clinical Gastroenterology. 2010;44(2):127–134.
10 Puli SR, Reddy JB, Bechtold ML, Antillon MR, Brugge WR. EUS-guided celiac plexus neurolysis for pain due to chronic pancreatitis or pancreatic cancer pain: a meta-analysis and systematic review. Digestive Diseases and Sciences. 2009; 54(11):2330–2337.
11 Levy MJ, Topazian MD, Wiersema MJ, et al. Initial evaluation of the efficacy and safety of endoscopic ultrasound-guided direct ganglia neurolysis and block. The American Journal of Gastroenterology. 2008;103(1): 98–103.
12 Rosch T, Daniel S, Scholz M, et al. Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow-up. Endoscopy. 2002;34(10): 765–771.
13 Weber A, Schneider J, Neu B, et al. Endoscopic stent therapy for patients with chronic pancreatitis: results from a prospective follow-up study. Pancreas. 2007;34(3): 287–294.
14 Binmoeller KF, Jue P, Seifert H, Nam WC, Izbicki J, Soehendra N. Endoscopic pancreatic stent drainage in chronic pancreatitis and a dominant stricture: long-term results. Endoscopy. 1995;27(9):638–644.
15 Costamagna G, Bulajic M, Tringali A, et al. Multiple stenting of refractory pancreatic duct strictures in severe chronic pancreatitis: long-term results. Endoscopy. 2006;38(3): 254–259.
16 Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. Endoscopy. 2003;35(7):553–558.
17 Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. The New England Journal of Medicine. 2007;356(7): 676–684.
18 Cahen DL, Gouma DJ, Laramee P, et al. Long-term outcomes of endoscopic vs surgical drainage of the pancreatic duct in patients with chronic pancreatitis. Gastroenterology. 2011;141(5):1690–1695.
19 Ahmed Ali U, Nieuwenhuijs VB, van Eijck CH, et al. Clinical outcome in relation to timing of surgery in chronic pancreatitis: a nomogram to predict pain relief. Archives of Surgery. 2012;147(10):925–932.
20 van der Gaag NA, van Gulik TM, Busch OR, et al. Functional and medical outcomes after tailored surgery for pain due to chronic pancreatitis. Annals of Surgery. 2012; 255(4):763–770.
21 Bradley EL 3rd. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, GA, September 11 through 13, 1992. Archives of Surgery. 1993;128(5): 586–590.
22 Baron TH, Harewood GC, Morgan DE, Yates MR. Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. Gastrointestinal Endoscopy. 2002; 56(1):7–17.
23 Arvanitakis M, Delhaye M, Bali MA, et al. Pancreatic-fluid collections: a randomized controlled trial regarding stent removal after endoscopic transmural drainage. Gastrointestinal Endoscopy. 2007;65(4):609–619.
24 Park DH, Lee SS, Moon SH, et al. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: a prospective randomized trial. Endoscopy. 2009;41(10):842–848.
25 Kahaleh M, Shami VM, Conaway MR, et al. Endoscopic ultrasound drainage of pancreatic pseudocyst: a prospective comparison with conventional endoscopic drainage. Endoscopy. 2006;38(4):355–359.
26 Cahen D, Rauws E, Fockens P, Weverling G, Huibregtse K, Bruno M. Endoscopic drainage of pancreatic pseudocysts: long-term outcome and procedural factors associated with safe and successful treatment. Endoscopy. 2005;37(10): 977–983.

27 Rosso E, Alexakis N, Ghaneh P, et al. Pancreatic pseudocyst in chronic pancreatitis: endoscopic and surgical treatment. Digestive Surgery. 2003;20(5):397–406.
28 Boerma D, van Gulik TM, Obertop H, Gouma DJ. Internal drainage of infected pancreatic pseudocysts: safe or sorry? Digestive Surgery. 1999;16(6):501–505.
29 Morton JM, Brown A, Galanko JA, Norton JA, Grimm IS, Behrns KE. A national comparison of surgical versus percutaneous drainage of pancreatic pseudocysts: 1997–2001. Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract. 2005;9(1):15–20; discussion-1.
30 Oida T, Mimatsu K, Kano H, et al. Laparoscopic cystogastrostomy via the posterior approach for pancreatic pseudocyst drainage. Hepato-Gastroenterology. 2011;58(110–111):1771–1775.
31 Hindmarsh A, Lewis MP, Rhodes M. Stapled laparoscopic cystgastrostomy: a series with 15 cases. Surgical Endoscopy. 2005;19(1):143–147.
32 Behrns KE, Ben-David K. Surgical therapy of pancreatic pseudocysts. Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract. 2008;12(12):2231–2239.
33 Ceyhan GO, Bergmann F, Kadihasanoglu M, et al. Pancreatic neuropathy and neuropathic pain—a comprehensive pathomorphological study of 546 cases. Gastroenterology. 2009;136(1):177–86 e1.
34 Kahl S, Zimmermann S, Genz I, et al. Risk factors for failure of endoscopic stenting of biliary strictures in chronic pancreatitis: a prospective follow-up study. The American Journal of Gastroenterology. 2003;98(11):2448–2453.
35 Nguyen-Tang T, Dumonceau JM. Endoscopic treatment in chronic pancreatitis, timing, duration and type of intervention. Best Practice & Research Clinical Gastroenterology. 2010;24(3):281–298.
36 Wilcox CM. Endoscopic therapy for pain in chronic pancreatitis: is it time for the naysayers to throw in the towel? Gastrointestinal Endoscopy. 2005;61(4):582–586.
37 Wilcox CM, Lopes TL. A randomized trial comparing endoscopic stenting to a sham procedure for chronic pancreatitis. Clinical Trials. 2009;6(5):455–463.
38 Costamagna G, Gabbrielli A, Mutignani M, et al. Extracorporeal shock wave lithotripsy of pancreatic stones in chronic pancreatitis: immediate and medium-term results. Gastrointestinal Endoscopy. 1997;46(3):231–236.
39 Guda NM, Partington S, Freeman ML. Extracorporeal shock wave lithotripsy in the management of chronic calcific pancreatitis: a meta-analysis. JOP: Journal of the Pancreas. 2005;6(1):6–12.
40 Dumonceau JM, Costamagna G, Tringali A, et al. Treatment for painful calcified chronic pancreatitis: extracorporeal shock wave lithotripsy versus endoscopic treatment: a randomised controlled trial. Gut. 2007;56(4):545–552.
41 Abdallah AA, Krige JE, Bornman PC. Biliary tract obstruction in chronic pancreatitis. HPB: The Official Journal of the International Hepato Pancreato Biliary Association. 2007;9(6):421–428.
42 Draganov P, Hoffman B, Marsh W, Cotton P, Cunningham J. Long-term outcome in patients with benign biliary strictures treated endoscopically with multiple stents. Gastrointestinal Endoscopy. 2002;55(6):680–686.
43 Catalano MF, Linder JD, George S, Alcocer E, Geenen JE. Treatment of symptomatic distal common bile duct stenosis secondary to chronic pancreatitis: comparison of single vs. multiple simultaneous stents. Gastrointestinal Endoscopy. 2004;60(6):945–952.
44 Cantu P, Hookey LC, Morales A, Le Moine O, Deviere J. The treatment of patients with symptomatic common bile duct stenosis secondary to chronic pancreatitis using partially covered metal stents: a pilot study. Endoscopy. 2005;37(8):735–739.
45 van Berkel AM, Cahen DL, van Westerloo DJ, Rauws EA, Huibregtse K, Bruno MJ. Self-expanding metal stents in benign biliary strictures due to chronic pancreatitis. Endoscopy. 2004;36(5):381–384.
46 Adams DB, Ford MC, Anderson MC. Outcome after lateral pancreaticojejunostomy for chronic pancreatitis. Annals of Surgery. 1994;219(5):481–487; discussion 7–9.
47 Yekebas EF, Bogoevski D, Honarpisheh H, et al. Long-term follow-up in small duct chronic pancreatitis: a plea for extended drainage by "V-shaped excision" of the anterior aspect of the pancreas. Annals of Surgery. 2006;244(6):940–946; discussion 6–8.
48 Schneider CG, Cataldegirmen G, Mann O, Yekebas EF, Izbicki JR. Lateral anastomosis techniques: Partington–Rochelle and V-shaped excision]. Der Chirurg; Zeitschrift für alle Gebiete der operativen Medizen. 2009;80(1):28–33. Laterale Anastomosentechniken: Partington–Rochelle und "V-Shape-Exzision".
49 Proctor HJ, Mendes OC, Thomas CG Jr, Herbst CA. Surgery for chronic pancreatitis. Drainage versus resection. Annals of Surgery. 1979;189(5):664–671.
50 Warshaw AL, Popp JW Jr, Schapiro RH. Long-term patency, pancreatic function, and pain relief after lateral pancreaticojejunostomy for chronic pancreatitis. Gastroenterology. 1980;79(2):289–293.
51 Bradley EL 3rd. Long-term results of pancreatojejunostomy in patients with chronic pancreatitis. American Journal of Surgery. 1987;153(2):207–213.
52 Prinz RA, Greenlee HB. Pancreatic duct drainage in 100 patients with chronic pancreatitis. Annals of Surgery. 1981;194(3):313–320.
53 Sielezneff I, Malouf A, Salle E, Brunet C, Thirion X, Sastre B. Long term results of lateral pancreaticojejunostomy for chronic alcoholic pancreatitis. The European Journal of Surgery = Acta Chirurgica. 2000;166(1):58–64.

54 Schnelldorfer T, Adams DB. Outcome after lateral pancreaticojejunostomy in patients with chronic pancreatitis associated with pancreas divisum. The American Surgeon. 2003; 69(12):1041–1044; discussion 5–6.
55 Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. Pancreas. 1987;2(6): 701–707.
56 Negi S, Singh A, Chaudhary A. Pain relief after Frey's procedure for chronic pancreatitis. The British Journal of Surgery. 2010;97(7):1087–1095.
57 Beger HG, Krautzberger W, Bittner R, Buchler M, Limmer J. Duodenum-preserving resection of the head of the pancreas in patients with severe chronic pancreatitis. Surgery. 1985;97(4):467–473.
58 Varghese TK, Bell RH Jr. Duodenum-preserving head resection for chronic pancreatitis: an institutional experience and national survey of usage. Surgery. 2007;142(4):588–593; discussion 93 e1–3.
59 Beger HG, Schlosser W, Friess HM, Buchler MW. Duodenum-preserving head resection in chronic pancreatitis changes the natural course of the disease: a single-center 26-year experience. Annals of Surgery. 1999;230(4):512–519; discussion 9–23.
60 Köninger J, Seiler CM, Sauerland S, et al. Duodenum-preserving pancreatic head resection—a randomized controlled trial comparing the original Beger procedure with the Bern modification (ISRCTN No. 50638764). Surgery. 2008;143(4):490–498.
61 Izbicki JR, Bloechle C, Knoefel WT, Kuechler T, Binmoeller KF, Broelsch CE. Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis. A prospective, randomized trial. Annals of Surgery. 1995;221(4): 350–358.
62 Strate T, Taherpour Z, Bloechle C, et al. Long-term follow-up of a randomized trial comparing the beger and frey procedures for patients suffering from chronic pancreatitis. Annals of Surgery. 2005;241(4):591–598.
63 Strobel O, Büchler MW, Werner J. Duodenum-preserving pancreatic head resection: technique according to Beger, technique according to Frey and Bern modifications. Der Chirurg; Zeitschrift für alle Gebiete der operativen Medizen. 2009;80(1):22–27.
64 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. American Journal of Surgery. 1995; 169(1):65–69; discussion 9–70.
65 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. Annals of Surgery. 1998;228(6):771–779.
66 Farkas G, Leindler L, Daroczi M, Farkas G Jr. Prospective randomised comparison of organ-preserving pancreatic head resection with pylorus-preserving pancreaticoduodenectomy. Langenbeck's Archives of Surgery/Deutsche Gesellschaft für Chirurgie. 2006;391(4):338–342.
67 Möbius C, Max D, Uhlmann D, et al. Five-year follow-up of a prospective non-randomised study comparing duodenum-preserving pancreatic head resection with classic Whipple procedure in the treatment of chronic pancreatitis. Langenbeck's Archives of Surgery/Deutsche Gesellschaft für Chirurgie. 2007;392(3):359–364.
68 Witzigmann H, Max D, Uhlmann D, et al. Outcome after duodenum-preserving pancreatic head resection is improved compared with classic Whipple procedure in the treatment of chronic pancreatitis. Surgery. 2003;134(1): 53–62.
69 Müller MW, Friess H, Martin DJ, Hinz U, Dahmen R, Buchler MW. Long-term follow-up of a randomized clinical trial comparing Beger with pylorus-preserving Whipple procedure for chronic pancreatitis. The British Journal of Surgery. 2008;95(3):350–356.
70 Belina F, Fronek J, Ryska M. Duodenopancreatectomy versus duodenum-preserving pancreatic head excision for chronic pancreatitis. Pancreatology: official journal of the International Association of Pancreatology. 2005;5(6): 547–552.
71 Klempa I, Spatny M, Menzel J, et al. 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]. Der Chirurg; Zeitschrift für alle Gebiete der operativen Medizen. 1995;66(4):350–359. Pankreasfunktion und Lebensqualität nach Pankreaskopfresektion bei der chronischen Pankreatitis. Eine prospektive, randomisierte Vergleichsstudie nach duodenumerhaltender Pankreaskopfresektion versus Whipple'scher Operation.
72 Aspelund G, Topazian MD, Lee JH, Andersen DK. Improved outcomes for benign disease with limited pancreatic head resection. Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract. 2005;9(3):400–409.
73 McClaine RJ, Lowy AM, Matthews JB, et al. A comparison of pancreaticoduodenectomy and duodenum-preserving head resection for the treatment of chronic pancreatitis. HPB: The Official Journal of the International Hepato Pancreato Biliary Association. 2009;11(8):677–683.
74 Sakorafas GH, Farnell MB, Nagorney DM, Sarr MG, Rowland CM. Pancreatoduodenectomy for chronic pancreatitis: long-term results in 105 patients. Archives of Surgery. 2000;135(5):517–523; discussion 23–24.
75 Lin PW, Shan YS, Lin YJ, Hung CJ. Pancreaticoduodenectomy for pancreatic head cancer: PPPD versus Whipple procedure. Hepato-Gastroenterology. 2005;52(65):1601–1604.

76 Seiler CA, Wagner M, Bachmann T, et al. Randomized clinical trial of pylorus-preserving duodenopancreatectomy versus classical Whipple resection—long term results. The British Journal of Surgery. 2005;92(5):547–556.

77 Diener MK, Rahbari NN, Fischer L, Antes G, Buchler MW, Seiler CM. Duodenum-preserving pancreatic head resection versus pancreatoduodenectomy for surgical treatment of chronic pancreatitis: a systematic review and meta-analysis. Annals of Surgery. 2008;247(6):950–961.

78 Strate T, Bachmann K, Busch P, et al. Resection vs drainage in treatment of chronic pancreatitis: long-term results of a randomized trial. Gastroenterology. 2008;134(5):1406–1411.

79 Diener MK, Bruckner T, Contin P, et al. ChroPac-trial: duodenum-preserving pancreatic head resection versus pancreatoduodenectomy for chronic pancreatitis. Trial protocol of a randomised controlled multicentre trial. Trials. 2010;11:47.