

Surgical Therapy of Chronic Alcoholic Pancreatitis: A Literature Review of Current Options

Rainer Christoph Miksch Jan G. D'Haese Jens Werner

Department of General, Visceral, and Transplantation Surgery, Ludwig Maximilian University Munich, Munich, Germany

Keywords

Chronic pancreatitis · Surgical treatment · Duodenum-preserving pancreatic head resection · Pancreatic resections · Pancreaticoduodenectomy

Abstract

Chronic pancreatitis (CP) is associated with alcohol abuse in 80% of cases. The primary treatment goals in CP are pain reduction and avoidance of pancreatitis-associated complications. CP should be treated in an interdisciplinary approach. A recent randomized clinical trial showed that early surgery compared with an endoscopy-first approach resulted in reduced pain levels. Surgical resections are, therefore, the most efficient treatment of pancreatitis-associated pain as well as other complications and should be performed early in the course of the disease. Since most of the patients present with chronic inflammation of the pancreatic head, pancreatic head resection is the most common treatment option. Duodenum-preserving pancreatic head resections are the surgical procedure of choice, but pancreaticoduodenectomies (Kausch-Whipple procedures) demonstrate similar outcome with regard to pain control, quality of life, and metabolic parameters. Other surgical procedures, including drainage procedures, pancreatic segmental resections, or left resections, are rarely indicated. © 2020 S. Karger AG, Basel

Introduction

Chronic pancreatitis (CP) is associated with alcohol abuse in 80% of cases. The incidence of CP increases depending on alcohol consumption of the population [1]. Mortality from CP is reported to be between 12 and 20%, and continued alcohol consumption leads to significantly reduced survival. The inflammatory process in the pancreas – mainly the pancreatic head – leads to structural changes with exocrine and endocrine parenchyma being replaced by inflammation and fibrosis in CP. Moderate to severe pain, diabetes mellitus, and signs of exocrine insufficiency are the typical symptoms. Almost 90% of patients with CP suffer from severe recurrent abdominal pain, which is the main reason for significant impairment of hospitalization and quality of life [2–4].

The pathobiology of pain is multifactorial and includes ductal hypertension, neuronal plasticity, as well as pancreatic pseudocysts [5]. Neuronal hypertrophy and pancreatic neuritis lead to neuropathic pain which modulates the central pain memory at the medullary and cortical levels of the central nervous system [6, 7]. Inflammation and fibrosis of the pancreas can trigger further complications, including compression and obstruction of the pancreatic duct, bile duct, duodenum, and the portal vein. Treatment of patients is most effective before such com-

Table 1. Surgical therapy of chronic alcoholic pancreatitis: drainage operation, classical pancreatic head resection as PPPHR or PRPHR according to the oncological resection, and DPPHR

	Indication	Advantages
Drainage operation Cystojejunostomy Laterolateral pancreaticojejunostomy Partington-Rochelle procedure (Puestow procedure)	Rare Pseudocysts Dilated duct, no inflammatory mass Pseudocysts Historic	Low impact on endocrine and exocrine function
Pancreatic resection PPPHR (Traverso-Longmire) PRPHR (Kausch-Whipple) Pancreatic left resection Segmental resection Total pancreatectomy	Rare Suspected malignancy, local complications of CP Suspected malignancy, local complications of CP Isolated inflammation in the tail Isolated inflammation with ductal stenosis in the corpus Pancreatic cancer suspicion in the entire pancreas	Oncological resection Oncological resection Oncological resection Oncological resection
DPPHR Beger Frey Bern modification	Inflammatory mass in the pancreatic head, local complications of CP, not indicated in case of suspected malignancy	Better function and quality of life than duodenum resection, can be performed even in case of portal hypertension No pancreatic dissection of the portal vein necessary Operation time and hospital stay shorter than Beger, no pancreatic dissection of the portal vein necessary, no duct drainage of the pancreatic tail necessary
V-shaped excision	Small duct disease, rare	
Pancreatectomy with islet autotransplantation	Selected patients (children without parenchymal changes), rare	

PPPHR, pylorus-preserving pancreatic head resection; PRPHR, pylorus-resecting pancreatic head resection; DPPHR, duodenum-preserving pancreatic head resection; CP, chronic pancreatitis.

plications develop and before chronification of pain occurs [8–11]. Patients with CP are at an about 20-fold increased risk to develop pancreatic cancer [12], and early pancreatic resection can significantly reduce the risk for malignancy [13].

The aim of this present article is to summarize the current literature on surgical treatment of chronic alcoholic pancreatitis and to outline the advantages and disadvantages of the different surgical techniques.

Surgical Therapy

The dominant localization of CP in most cases is the head of the pancreas. Pain in CP is multifactorial but mainly driven by 2 significant factors: outflow obstruction of the pancreatic and/or the bile duct with consecutive dilatation and subsequent increased intraductal pressure. Secondly, pancreatic inflammation and fibrosis induce neuropathic pain via perineural inflammation and neural plasticity. Drainage procedures, including endoscopic treatment, may not be as efficient since they only treat the dilated pancreatic duct, whereas pancreatic re-

sections additionally extinct the inflamed pancreatic and nerve tissue leading to better pain control [4, 8, 14].

Surgical therapy is indicated in chronic alcoholic pancreatitis in case of opioid-dependent pain, local complications, unsuccessful endoscopic management, and suspicion of malignancy. Nevertheless, indication for surgery should be an interdisciplinary decision. Several treatment modalities and surgical techniques need to be considered depending on the individual situation of the patient, including drainage operations, organ-sparing duodenum-preserving pancreatic resection techniques, or oncological pancreatic resections.

While pancreatic head resections, including the Kausch-Whipple procedure and the pylorus-preserving pancreatic head resection, are the most frequently performed techniques for suspected malignancies, several modifications of the duodenum-preserving pancreatic head resection (DDPHR) are the treatment of choice in specialized centers with great expertise in the surgical therapy of CP. A pancreatic left resection, segmental resection, or even total pancreatectomy are only very rarely performed for CP (Table 1).

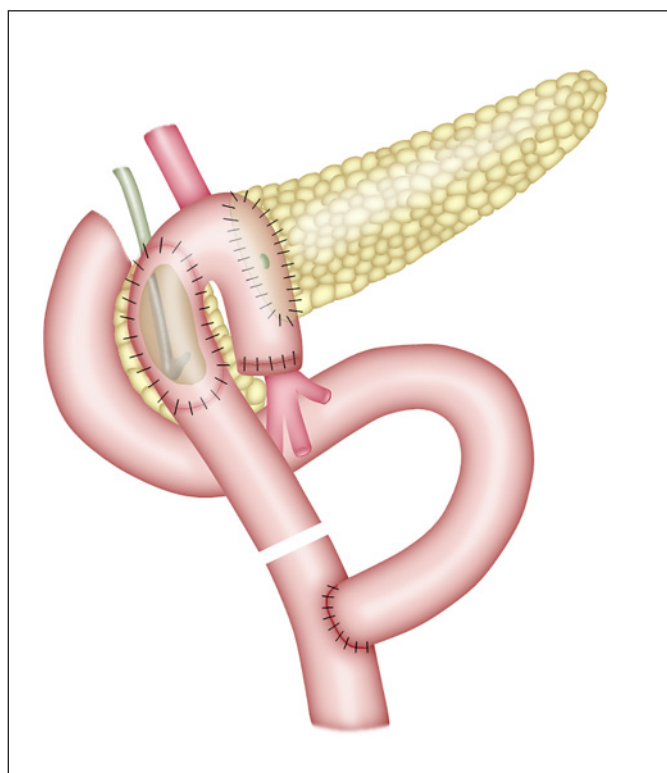


Fig. 1. The duodenum-preserving pancreatic head resection according to Beger comprises a resection of the pancreatic head with preservation of a parenchymal cuff along the duodenum and the preservation of the dorsal pancreatic capsule as well as the transection of the pancreas over the portal vein. It is reconstructed with 2 anastomoses: one to the resection cavity and one to the pancreatic body.

There is currently no role for minimal invasive surgery in CP. In a small series of patients with refractory CP and dilated main duct, Balduzzi et al. [15] described a robotic lateral pancreaticojejunostomy as a feasible but complex operation which is limited to very few patients. Current data are not sufficient to estimate the role of minimal invasive surgery in CP [15–18]. It should be noted, however, that surgery in CP is challenging due to the chronically inflamed surrounding tissue. It is, therefore, questionable whether these patients are good candidates for minimal invasive surgery. Minimal invasive and robotic surgery are currently not established in CP but might be a possible tool in the future.

Drainage Operations

The modification of the Puestow procedure [19–21] according to Partington-Rochelle is suitable for rare cases of CP with a pancreatic duct stenosis without an enlarged pancreatic head but an atrophic pancreas [22]. The longitudinal opening of the pancreatic duct with subsequent

simple pancreaticojejunostomy is performed in those rare cases.

Cahen et al. [22] showed that the surgical drainage of the pancreatic duct achieved better pain control compared to endoscopic treatment in patients with obstruction of the pancreatic duct. In that trial, pain relief was achieved in 32% of patients assigned to endoscopic drainage as compared to 75% of patients assigned to surgical drainage during 24 months of follow-up. A Roux-en-Y jejunal loop might be used to drain a symptomatic pseudocyst in the rare case that endoscopy is not successful [23].

The limited possibility of obtaining histology is a major disadvantage of these procedures compared to resecting procedures because drainage operations cannot exclude malignancy in patients with increased risk of pancreatic cancer [13].

Pancreatic Resections

The pancreatic head resection according to Kausch-Whipple as well as the pylorus-preserving modification as described by Traverso-Longmire are the most frequently used techniques for surgical resection in CP. This is mainly due to the fact that most surgeons are familiar with these resection techniques for pancreatic cancer. However, in contrast to resections performed in cancer patients, an oncological lymph node dissection is not needed in CP, unless in those cases with suspicion for malignancy.

DDPHR was first described by Beger et al. [24] in 1990 (Fig. 1). It comprises a resection of the pancreatic head with preservation of a parenchymal cuff along the duodenum and the preservation of the dorsal pancreatic capsule as well as the transection of the pancreas over the portal vein. It is reconstructed with 2 anastomoses: one to the resection cavity and one to the pancreatic body. The pancreatic body is reconstructed using a duct-to-mucosa pancreaticojejunostomy to the left and the pancreatic head is reconstructed using a side-to-side pancreaticojejunostomy to the same jejunal loop. The final step of the reconstruction is the Roux-en-Y anastomosis (Fig. 1).

The DDPHR according to Frey (Fig. 2) involves a circumscribed exfoliation of the pancreatic head without transection of the pancreas, which is combined with a longitudinal duct resection and pancreatic jejunostomy. It is a combined technique of the Beger and Partington-Rochelle/Puestow procedures. The pancreatic head resection is small and combined with a lateral pancreaticojejunostomy to drain the pancreatic duct.

Finally, the Bern modification (Fig. 3) combines the advantages of both the Beger and the Frey technique. Accordingly, a deep, subtotal resection of the pancreatic

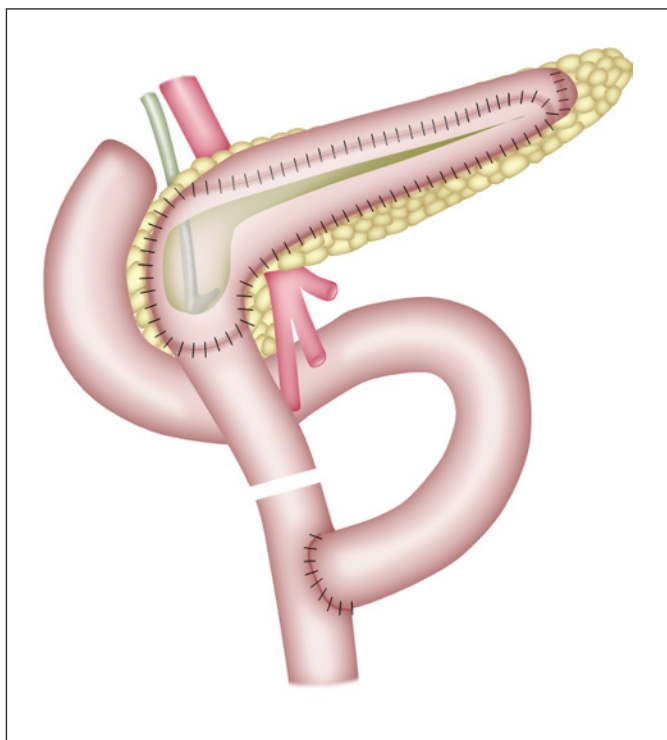


Fig. 2. Frey's duodenum-preserving pancreatic head resection involves a circumscribed exfoliation of the pancreatic head which is combined with a longitudinal pancreatic jejunostomy.

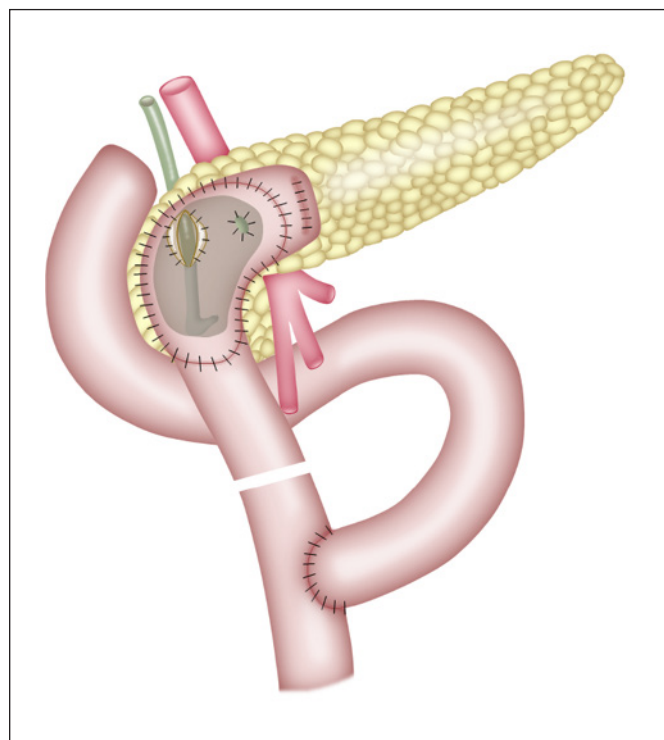


Fig. 3. The Bern modification combines the advantages of the duodenum-preserving pancreatic head resection of Beger and Frey. Accordingly, a deep, subtotal resection of the pancreatic head without transection of the pancreas over the portal vein is performed. This technique does not include the opening of the pancreatic duct of the pancreatic tail and the longitudinal pancreaticojejunostomy.

head is performed similar to the Beger technique. However, it does not require a transection of the pancreas (as performed in the Beger technique) nor the longitudinal pancreaticojejunostomy (as performed by Frey). The single anastomosis is used for reconstruction.

These different duodenum-preserving techniques were compared in several randomized-controlled trials [25, 26]. Results with regard to pain reduction and quality of life were comparable between these 3 variations of the DPPHR. However, DPPHRs have several advantages compared to Whipple procedures with comparable long-term results and should, therefore, be considered as the treatment of choice. Despite this, the Whipple procedure is most commonly performed for malignancy and is, therefore, a routine surgical technique for gastrointestinal surgeons. Long-term outcome of the Kausch-Whipple procedure in CP, in terms of pain relief and quality of life, is comparable to DPPHR; therefore, this procedure may as well be performed for CP in centers not experienced in performing DPPHR. DPPHRs are technically demanding operations that should only be performed in specialized high-volume pancreatic centers. The Bern modification is a technical variation, which is just as ef-

fective but technically less demanding than the Beger procedure. The advantage of the Bern modification is the reconstruction with a single anastomosis, and it is the treatment of choice for patients with portal hypertension.

Total pancreatectomy and islet autotransplantation showed promising first results in patients with early CP [27]. However, this technique is probably not effective in advanced CP and is only very rarely performed [28, 29]. Rare cases of CP might require resection techniques like a V-shaped excision, pancreatic left resection, segmental resection, or even a total pancreatectomy (Table 1) [30, 31].

Surgery or Endoscopy?

As alcohol and nicotine withdrawal play a very important role in the avoidance of progress, invasive therapies should be considered in cases where conservative treatment has been insufficient. Surgical treatment of recurrent pain in chronic alcoholic pancreatitis is superior to endoscopic therapy [32–34]. Randomized trials demonstrated that surgical treatment reduces pain more effec-

tively, preserves pancreatic function better, has a higher success rate of therapy, and is cheaper compared to endoscopy [22, 32, 33]. Pain reduction is especially efficient when surgical resection is performed early in the course of pancreatitis, well before opiates as pain medication are needed and before repetitive endoscopic interventions have been performed [35]. The prospective and randomized ESCAPE trial clearly demonstrates that early surgical resection is superior to a step-up approach, including endoscopic interventions in patients with painful CP, a dilated pancreatic duct, and opioid use for no more than 2–6 months [30, 31, 34].

Retrospective studies have demonstrated that surgery shows the best results when it is performed within 3 years of the onset of symptoms [36]. The German S3 consensus guideline suggests performing surgery if there is persistence of symptoms or cholestasis for >1 year after endoscopic treatment has been initiated [37, 38].

In addition, it is well established and agreed upon that patients with painful CP and parenchymal calcifications in the pancreatic head should undergo surgery even earlier since endoscopic interventions are likely to fail in this condition [37, 39]. Following this approach, further progression of the disease and centralization of pain on the cortical level can be avoided [8].

The multidisciplinary treatment of chronic alcoholic pancreatitis is complex and is, therefore, recommended to take place in specialized pancreatic centers, which will most likely improve treatment outcome [40, 41, 42].

Summary and Discussion

The medical management of chronic alcoholic pancreatitis focuses on avoidance of precipitating factors, such as alcohol and smoking, treatment of pain, and replacement of exocrine and endocrine function [43]. In case of surgery, the indication for surgery is largely independent of etiology. The selection of the intended surgical procedure depends on whether intractable pain, local complications, unsuccessful endoscopic management of dilated bile duct, and/or suspicion of malignancy are present [44].

While drainage operations and endoscopic stenting procedures only counteract the ductal hypertension but do not aim at the inflamed tissue or its local complica-

tions, pancreatic resections lead to better pain control and represent the surgical treatment of choice. Therefore, surgical therapy provides good short and long-term results, including pain relief and improvement of quality of life [14, 45–47]. Since the pancreatic head is the most common site of inflammation, pancreatic head resections are the most frequently performed procedures in CP.

Conclusion

Surgical treatment of chronic alcoholic pancreatitis is indicated for pain, local complications, and when a malignancy cannot be ruled out. Surgery should be considered early in patients who only recently started using prescribed opioid therapy, since early surgery resulted in lower pain scores when compared to a step-up approach including endoscopy. DPPHRs are the treatment of choice for most patients with painful alcoholic pancreatitis, and these pancreatic resections can nowadays be performed with low morbidity and mortality in specialized centers. In conclusion, surgery for chronic alcoholic pancreatitis is safe and effective, but treatment of CP is generally complex and should be carried out in an interdisciplinary team, preferably in specialized pancreatic centers.

Statement of Ethics

Since the paper is only based on aggregated, anonymized data, no ethics committee approval is required.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors have no funding sources relevant to this review.

Author Contributions

Conceptualization and writing of the original draft were performed by R.C.M., J.G.D., and J.W.; final editing of the paper was performed by J.W.

References

- 1 Dufour MC, Adamson MD. The epidemiology of alcohol-induced pancreatitis. *Pancreas*. 2003 Nov;27(4):286–90.
- 2 Olesen SS, Juel J, Nielsen AK, Frøkjær JB, Wilder-Smith OH, Drewes AM. Pain severity reduces life quality in chronic pancreatitis: implications for design of future outcome trials. *Pancreatol*. 2014 Nov-Dec;14(6):497–502.
- 3 Mullady DK, Yadav D, Amann ST, O'Connell MR, Barmada MM, Elta GH, et al.; NAPS2 Consortium. Type of pain, pain-associated complications, quality of life, disability and resource utilisation in chronic pancreatitis: a prospective cohort study. *Gut*. 2011 Jan;60(1):77–84.

- 4 D'Haese JG, Hartel M, Demir IE, Hinz U, Bergmann F, Büchler MW, et al. Pain sensation in pancreatic diseases is not uniform: the different facets of pancreatic pain. *World J Gastroenterol*. 2014 Jul;20(27):9154–61.
- 5 Weniger M, Reinelt L, Neumann J, Holdt L, Ilmer M, Renz B, et al. The Analgesic Effect of the Mitochondria-Targeted Antioxidant SkQ1 in Pancreatic Inflammation. *Oxid Med Cell Longev*. 2016;2016:4650489.
- 6 Demir IE, Wang K, Tieftrunk E, Giese NA, Xing B, Friess H, et al. Neuronal plasticity in chronic pancreatitis is mediated via the neurotrophin/GFRα2 axis. *Am J Physiol Gastrointest Liver Physiol*. 2012 Nov;303(9):G1017–28.
- 7 Demir IE, Tieftrunk E, Maak M, Friess H, Ceyhan GO. Pain mechanisms in chronic pancreatitis: of a master and his fire. *Langenbecks Arch Surg*. 2011 Feb;396(2):151–60.
- 8 D'Haese JG, Hartwig W, Werner J. Chronische Pankreatitis - Update Leitlinie: Eine Frage der richtigen Therapie zum richtigen Zeitpunkt. *Zentralbl Chir*. 2016 Apr;141(2):125–8.
- 9 Mayerle J, Anz D, D'Haese JG, Werner J. [Endoscopic and surgical treatment of chronic pancreatitis]. *Internist (Berl)*. 2019 Mar;60(3):235–46.
- 10 D'Haese JG, Ceyhan GO, Demir IE, Layer P, Uhl W, Löhr M, et al. Pancreatic enzyme replacement therapy in patients with exocrine pancreatic insufficiency due to chronic pancreatitis: a 1-year disease management study on symptom control and quality of life. *Pancreas*. 2014 Aug;43(6):834–41.
- 11 D'Haese JG, Demir IE, Kehl T, Winckler J, Giese NA, Bergmann F, et al. The impact of MFG-E8 in chronic pancreatitis: potential for future immunotherapy? *BMC Gastroenterol*. 2013 Jan;13(1):14.
- 12 Beyer G, D'Haese JG, Ormanns S, Mayerle J. [Chronic Pancreatitis and Pancreatic Cancer - Tumor Risk and Screening]. *Dtsch Med Wochenschr*. 2018 Jun;143(12):895–906.
- 13 Ueda J, Tanaka M, Ohtsuka T, Tokunaga S, Shimosegawa T; Research Committee of Intractable Diseases of the Pancreas. Surgery for chronic pancreatitis decreases the risk for pancreatic cancer: a multicenter retrospective analysis. *Surgery*. 2013 Mar;153(3):357–64.
- 14 D'Haese JG, Ceyhan GO, Demir IE, Tieftrunk E, Friess H. Treatment options in painful chronic pancreatitis: a systematic review. *HPB (Oxford)*. 2014 Jun;16(6):512–21.
- 15 Balduzzi A, Zwart MJ, Kempeneers RM, Boermeester MA, Busch OR, Besselink MG. Robotic Lateral Pancreaticojejunostomy for Chronic Pancreatitis. *J Vis Exp*. 2019 Dec;(154).
- 16 Khan AS, Siddiqui I, Vrochides D, Martinie JB. Robotic pancreas drainage procedure for chronic pancreatitis: robotic lateral pancreaticojejunostomy (Puestow procedure). *J Vis Surg*. 2018 Apr;4:72.
- 17 Moekotte AL, Rawashdeh A, Asbun HJ, Coimbra FJ, Edil BH, Jarufe N, et al. Safe implementation of minimally invasive pancreas resection: a systematic review. *HPB (Oxford)*. 2019 Dec;S1365-182X(19)33198-3.
- 18 Klompmaker S, van Hilst J, Wellner UF, Busch OR, Coratti A, D'Hondt M, et al.; European consortium on Minimally Invasive Pancreatic Surgery (E-MIPS). Outcomes after minimally-invasive versus open pancreatoduodenectomy: A pan-European propensity score matched study. *Ann Surg*. 2020 Feb;271(2):356–63.
- 19 Gillesby WJ, Puestow CB. Surgery for chronic recurrent pancreatitis. *Surg Clin North Am*. 1961 Feb;41(1):83–9.
- 20 Puestow CB, Gillesby WJ. Management of pancreatic cysts and pancreatic lithiasis. *Am Surg*. 1954 Apr;20(4):355–62.
- 21 Puestow CB, Gillesby WJ. Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. *AMA Arch Surg*. 1958 Jun;76(6):898–907.
- 22 Cahen DL, Gouma DJ, Nio Y, Rauws EA, Boermeester MA, Busch OR, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med*. 2007 Feb;356(7):676–84.
- 23 Partington PF, Rochelle RE. Modified Puestow procedure for retrograde drainage of the pancreatic duct. *Ann Surg*. 1960 Dec;152(6):1037–43.
- 24 Beger HG, Büchler M, Bittner R. The duodenum preserving resection of the head of the pancreas (DPRHP) in patients with chronic pancreatitis and an inflammatory mass in the head. An alternative surgical technique to the Whipple operation. *Acta Chir Scand*. 1990 Apr;156(4):309–15.
- 25 Bachmann K, Tomkoetter L, Kutup A, Erbes J, Vashist Y, Mann O, et al. Is the Whipple procedure harmful for long-term outcome in treatment of chronic pancreatitis? 15-years follow-up comparing the outcome after pylorus-preserving pancreatoduodenectomy and Frey procedure in chronic pancreatitis. *Ann Surg*. 2013 Nov;258(5):815–20; discussion 820–1.
- 26 Diener MK, Bruckner T, Contin P, Halloran C, Glanemann M, Schlitt HJ, et al. ChroPactrial: duodenum-preserving pancreatic head resection versus pancreatoduodenectomy for chronic pancreatitis. Trial protocol of a randomised controlled multicentre trial. *Trials*. 2010 Apr;11(1):47.
- 27 Kempeneers MA, Scholten L, Verkade CR, van Hooft JE, van Santvoort HC, Busch OR, et al.; Dutch Pancreatitis Study Group. Efficacy of total pancreatectomy with islet autotransplantation on opioid and insulin requirement in painful chronic pancreatitis: A systematic review and meta-analysis. *Surgery*. 2019 Sep;166(3):263–70.
- 28 Kirchner VA, Dunn TB, Beilman GJ, Chinakotla S, Pruett TL, Wilhelm JJ, et al. Total Pancreatectomy with Islet Autotransplantation for Acute Recurrent and Chronic Pancreatitis. *Curr Treat Options Gastroenterol*. 2017 Dec;15(4):548–61.
- 29 Morgan KA, Lancaster WP, Owczarski SM, Wang H, Borcardt J, Adams DB. Patient Selection for Total Pancreatectomy with Islet Autotransplantation in the Surgical Management of Chronic Pancreatitis. *J Am Coll Surg*. 2018 Apr;226(4):446–51.
- 30 Kempeneers MA, Besselink MG, Issa Y, van Hooft JE, van Goor H, Bruno MJ, et al. [Multidisciplinary treatment of chronic pancreatitis: an overview of current step-up approach and new options]. *Ned Tijdschr Geneesk*. 2017;161:D1454.
- 31 Ahmed Ali U, Issa Y, Bruno MJ, van Goor H, van Santvoort H, Busch OR, et al.; Dutch Pancreatitis Study Group. Early surgery versus optimal current step-up practice for chronic pancreatitis (ESCAPE): design and rationale of a randomized trial. *BMC Gastroenterol*. 2013 Mar;13(1):49.
- 32 Cahen DL, Gouma DJ, Laramée P, Nio Y, Rauws EA, Boermeester MA, et al. Long-term outcomes of endoscopic vs surgical drainage of the pancreatic duct in patients with chronic pancreatitis. *Gastroenterology*. 2011 Nov;141(5):1690–5.
- 33 Díte P, Ruzicka M, Zboril V, Novotný I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy*. 2003 Jul;35(7):553–8.
- 34 Issa Y, Kempeneers MA, Bruno MJ, Fockens P, Poley JW, Ahmed Ali U, et al.; Dutch Pancreatitis Study Group. Effect of Early Surgery vs Endoscopy-First Approach on Pain in Patients with Chronic Pancreatitis: The ESCAPE Randomized Clinical Trial. *JAMA*. 2020 Jan;323(3):237–47.
- 35 Kager LM, Lekkerkerker SJ, Arvanitakis M, Delhaye M, Fockens P, Boermeester MA, et al. Outcomes After Conservative, Endoscopic, and Surgical Treatment of Groove Pancreatitis: A Systematic Review. *J Clin Gastroenterol*. 2017 Sep;51(8):749–54.
- 36 Ahmed Ali U, Nieuwenhuijs VB, van Eijck CH, Gooszen HG, van Dam RM, Busch OR, et al.; Dutch Pancreatitis Study Group. Clinical outcome in relation to timing of surgery in chronic pancreatitis: a nomogram to predict pain relief. *Arch Surg*. 2012 Oct;147(10):925–32.
- 37 Hoffmeister A, Mayerle J, Beglinger C, Büchler MW, Bufler P, Dathe K, et al.; Chronic Pancreatitis German Society of Digestive and Metabolic Diseases (DGVS). [S3-Consensus guidelines on definition, etiology, diagnosis and medical, endoscopic and surgical management of chronic pancreatitis German Society of Digestive and Metabolic Diseases (DGVS)]. *Z Gastroenterol*. 2012 Nov;50(11):1176–224.
- 38 Cahen DL, van Berkel AM, Oskam D, Rauws EA, Weverling GJ, Huibregtse K, et al. Long-term results of endoscopic drainage of common bile duct strictures in chronic pancreatitis. *Eur J Gastroenterol Hepatol*. 2005 Jan;17(1):103–8.
- 39 Kahl S, Zimmermann S, Genz I, Glasbrenner B, Pross M, Schulz HU, et al. Risk factors for failure of endoscopic stenting of biliary strictures in chronic pancreatitis: a prospective follow-up study. *Am J Gastroenterol*. 2003 Nov;98(11):2448–53.
- 40 Polonski A, Izbicki JR, Uzunoglu FG. Centralization of Pancreatic Surgery in Europe. *J Gastrointest Surg*. 2019 Oct;23(10):2081–92.

- 41 Balzano G, Zerbi A, Capretti G, Rocchetti S, Capitanio V, Di Carlo V. Effect of hospital volume on outcome of pancreaticoduodenectomy in Italy. *Br J Surg*. 2008 Mar;95(3):357–62.
- 42 Gódi S, Erőss B, Gyömbér Z, Szentesi A, Farkas N, Párniczky A, et al. Centralized care for acute pancreatitis significantly improves outcomes. *J Gastrointest Liver Dis*. 2018 Jun; 27(2):151–7.
- 43 Pftzter RH, Schneider A. Treatment of alcoholic pancreatitis. *Dig Dis*. 2005;23(3-4):241–6.
- 44 Keith RG, Saibil FG, Sheppard RH. Treatment of chronic alcoholic pancreatitis by pancreatic resection. *Am J Surg*. 1989 Jan;157(1): 156–62.
- 45 Diener MK, Hüttner FJ, Kieser M, Knebel P, Dörr-Harim C, Distler M, et al.; ChroPac Trial Group. Partial pancreatoduodenectomy versus duodenum-preserving pancreatic head resection in chronic pancreatitis: the multicentre, randomised, controlled, double-blind ChroPac trial. *Lancet*. 2017 Sep; 390(10099):1027–37.
- 46 Dominguez-Munoz JE, Drewes AM, Lindkvist B, Ewald N, Czako L, Rosendahl J, et al.; HaPanEU/UEG Working Group. Recommendations from the United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis. *Pancreatol*. 2018 Dec;18(8):847–54.
- 47 Lóhr JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch MM, et al.; HaPanEU/UEG Working Group. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United European Gastroenterol J*. 2017 Mar;5(2):153–99.