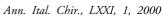
# What Should be the Standard Operation in Chronic Pancreatitis: Whipple



# or Duodenum-Preserving Pancreatic Head Resection?

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#### Introduction

Chronic pancreatitis is a disease primarily found in the civilized world, and is gaining more and more importance in our industrialized society and in the surgical field. It is a disease of the exocrine pancreas, characterized by progressive destruction of the pancreatic parenchyma and remodeling processes leading to the replacement of the exocrine parenchyma by extensive fibrosis [1-3]. Chronic alcohol abuse is the most frequent etiologic factor for chronic pancreatitis in Western countries. Patients are severely impaired by maldigestion and consequent severe loss of weight due to severe exocrine pancreatic insufficiency. In addition, patients with chronic pancreatitis suffer from recurrent attacks of severe upper abdominal pain which frequently does not respond to any analgesics [1, 3].

In most patients with chronic pancreatitis, there is an inflammatory enlargement of the pancreatic head which leads to several local obstructive symptoms, such as jaundice due to compression or stenosis of the common bile duct, impaired gastric emptying and vomiting due to duodenal compression/stenosis, main pancreatic duct obstruction, and compression of the portal vein and/or the superior mesenteric vein with subsequent portal hypertension [4, 5].

Although the therapy of chronic pancreatitis consists primarily of symptom-related treatment – mainly provision of adequate analgesic therapy, pancreatic enzyme replacement, and control of diabetes mellitus - long-term follow-up studies demonstrate that around 50% of patients with chronic pancreatitis will undergo surgical treatment during the course of their disease [5, 6].

Absolute indications for surgical intervention are

#### Abstract

Surgical options in the treatment of chronic pancreatitis have undergone both development and controversial discussion in the past decades. Operations such as the classical and pyloruspreserving Whipple resections are more and more being replaced by operations such as the duodenum-preserving pancreatic head resection, which preserves extrapancreatic organs like the stomach, the duodenum and the extrapancreatic bile duct. The latter operation preserves a normal food passage and glucose metabolism after surgical intervention. In addition, the duodenum-preserving pancreatic head resection provides long-term pain relief and reduction in up to 90% of chronic pancreatitis patients, as well as a general improvement in quality of life.

This article will summarize and compare the surgical options in the treatment of chronic pancreatitis and will provide arguments why the duodenum-preserving pancreatic head resection should replace the classical and the pylorus-preserving Whipple resections as the standard surgical procedure used to treat chronic pancreatitis-related complications.

Key words: Chronic pancreatitis, surgery, Whipple, duodenum-preserving pancreatic head resection.

#### Riassunto

Negli ultimi anni le varie opzioni chirurgiche per il trattamento della pancreatite cronica, hanno fatto registrare sviluppi interessanti ma anche discussioni controverse. Le operazioni classiche come la pylorus-preserving Whipple sono sempre maggiormente rimpiazzate da altre come la resezione della testa pancreatica con conservazione del duodeno, che permette di preservare gli organi extrapancreatici come lo stomaco, il duodeno ed il dotto biliare extrapancreatico. Inoltre mantiene un normale passaggio del cibo e del metabolismo glicidico dopo l'intervento chirurgico. La resezione della testa pancreatica con conservazione del duodeno consente una riduzione o una scomparsa del dolore a lungo termine nel 90% dei pazienti con pancreatite cronica, cui si associa un generale miglioramento della qualità di vita. Questo articolo vuole riassumere e comparare le tecniche chirurgiche per il trattamento della pancreatite cronica e possibilmente fornire argomenti per i quali la resezione della testa pancreatica con conservazione del duodeno dovrebbe essere preferita al classico intervento di Whipple con preservazione del piloro, così come alle altre

tecniche chirurgiche standard usate per trattare le complicanze da pancreatite cronica.

Parole chiave: Pancreatite cronica, chirurgia, Whipple, resezione della testa pancreatica con conservazione del duodeno.

# $Tab.\ I-INDICATIONS\ FOR\ PANCREATIC\ HEAD$ RESECTION IN CHRONIC PANCREATITIS

- severe intractable pain
- obstruction/stenosis of the duodenum
- obstruction/stenosis of the common bile duct
- obstruction/stenosis of the main pancreatic duct
- obstruction/stenosis of major abdominal vessels (portal vein, splenic vein, superior mesenteric vein)
- suspicion of pancreatic cancer

intractable pain which is not responding to analgesic therapy, and the already mentioned local complications, which are summarized in Table I. Additionally, the exclusion of pancreatic cancer as a differential diagnosis for the inflammatory pancreatic head mass may be possible only through surgical intervention if diagnostic procedures do not provide a definitive answer [5].

There is still controversy in the surgical community over which procedure should be the surgical standard in treatment of patients with chronic pancreatitis. On the one hand, the adequate surgical procedure depends on the localization and the pathomorphologic appearance of the chronic pancreatitis lesions. On the other hand, we believe that there is presently enough proof with regard to functional long-term results after pancreatic surgery to confirm the superiority of some surgical procedures over others. In the following review we summarize the data presently available and try to find an answer to what should be the standard surgical treatment of chronic pancreatitis.

### Surgical therapy

Surgical treatment of chronic pancreatitis can be divided into two categories: drainage procedures and pancreatic resection.

## Drainage versus resection: Indications and outcome

The pathophysiology of chronic pancreatitis remains controversial, and different pathophysiological hypotheses have been postulated to explain chronic pancreatitis-related complications. Based on the pathophysiological concept that increased intrapancreatic ductal pressure leads to the destruction of the pancreatic parenchyma and to pain, it would seem logical that drainage of the dilated

pancreatic duct would lead to pain relief [2]. With regard to the preservation of as much exocrine and endocrine pancreatic function as possible, drainage procedures without resection are the preferred option [7]. The longitudinal pancreatico-jejunostomy (Partington-Rochelle) is the most widely used drainage operation in chronic pancreatitis [8, 9]. By constructing a longitudinal pancreatico-jejunostomy anastomosis with a Roux-en-Y jejunal loop, a complete drainage of the Wirsung and the Santorini ducts along the whole pancreas is achieved [8]. This is a safe technique with very low operative mortality and morbidity, and it preserves as much endocrine and exocrine pancreatic parenchyma as possible. This safe operation has a mortality between 0% and 5%, and a postoperative morbidity rate of 20% to 25% [10-12]. Unfortunately, we find in the literature that the main goal of persistent pain relief is not achieved in up to 40% of these patients in the long-term follow-up [13, 14]. One possible reason is that pain generation may be based on an increase in intrapancreatic ductal and/or parenchymal pressure, if the main pancreatic duct is dilated (> 7 mm). [14, 15]. Another possibility is that often concomitant presence of pancreatic head enlargement and an inflammatory mass with multiple neuropathic changes seems to complicate the disease and subsequently lead to the failure of the method [16, 17]. In most patients an inflammatory pancreatic head mass can only be resolved by resection of the pancreatic head. Therefore, for drainage procedures such as the Partington-Rochelle, surgical treatment in chronic pancreatitis must be preceded by application of strict indications, such as a dilated pancreatic duct and the absence of an inflammatory mass in the head of the pancreas.

In order to establish a surgical therapy for malignant processes in the pancreatic head region, the pancreaticoduodenectomy, also termed the Whipple resection, was introduced by Kausch in 1909 and reintroduced by Whipple in 1935. The Whipple resection was for a long time also used as the standard surgical therapy for chronic pancreatitis with pancreatic headrelated complications [18]. Improvements in operative skills in recent years have contributed to a continuous decrease in the initially high postoperative morbidity and mortality of this operation [19, 20]. However, quality control studies following the classical Whipple resection in chronic pancreatitis patients have shown that the longterm results are unsatisfying. Especially concerning quality of life, the data are disappointing due to poor postoperative digestive function, including dumping, diarrhea, peptic ulcer and dyspeptic complaints. In addition, the classical Whipple resection often leads to an insulin-dependent diabetes mellitus which is responsible for the high late-postoperative morbidity and mortality in patients with chronic pancreatitis [15, 21].

Based on these disadvantages of the classical Whipple resection in chronic pancreatitis patients, "organ-preserving" procedures such as the pylorus-preserving

Whipple resection (pylorus-preserving pancreaticoduodenectomy) were introduced [22]. By preserving the stomach, the pylorus and the first part of the duodenum, the pylorus-preserving Whipple resection protects against gastric dumping, marginal ulceration, and bile-reflux gastritis. Furthermore, the first part of the gastrointestinal continuity is restored. Regarding the criteria for quality of life, the pylorus-preserving Whipple resection provides better results than the classical Whipple resection, with weight gain in up to 90% of the patients postoperatively [23-25]. Furthermore, the pylorus-preserving Whipple resection leads to long-lasting pain relief in 85% to 95% of the patients during the first 5 years postoperatively [23-25]. However, the postoperative sequelae of transient delayed gastric emptying (occurring in 30-50% of patients) which is often associated with slower weight gain, the risk for cholangitis, and long-term occurrence of exocrine and endocrine pancreatic insufficiencies (occurring in more than 45%) - represent the drawbacks of the pyloruspreserving Whipple operation in surgical treatment of chronic pancreatitis [26, 27].

### The duodenum-preserving pancreatic head resection

The duodenum-preserving pancreatic head resection was introduced in 1972 by Hans Beger to treat pancreatic head-related complications in patients with chronic pancreatitis [28]. Because surgical therapy in patients with chronic pancreatitis differs from an oncological operation in that it is not necessary to sacrifice pancreatic neighbor organs - such as the stomach, the duodenum, the gallbladder, and the common bile duct - because none of them contribute to the inflammatory process of the pancreatic head, Beger and his coworkers developed a new procedure which takes these aspects into consideration. The duodenum-preserving pancreatic head resection resects the pancreatic head subtotally by preserving the body and tail of the pancreas, the pylorus, the duodenum, and the extrahepatic bile tract [28]. The normal anatomy of the upper gastrointestinal tract and the normal food passage through the stomach and the duodenum are preserved by this operation. This procedure is indicated in patients suffering from chronic pain in combination with an inflammatory mass of the head of the pancreas leading to common bile duct obstruction/stenosis, pancreatic duct obstruction/stenosis and/or obstruction/stenosis of the retropancreatic vessels.

Our large series with 298 patients shows that the duodenum-preserving pancreatic head resection can be performed with low postoperative morbidity, low hospital mortality and low long-term morbidity and mortality [29]: Of 298 patients, one patient died due to a fulminate embolism of the pulmonary artery and two others died due to sepsis after leakage of the anastomosis, corresponding to a hospital mortality rate of 1.01% (3/298). 17 of 298 patients (5.7%) had to undergo reoperation due to early

postoperative complications. These included intestinal bleeding (n = 3), leakage of the anastomosis (n = 5), an intraabdominal abscess (n = 3), postoperative ileus (n = 2), a common bile duct stenosis (n = 1), a duodenum wall ischemia (n = 1), ulcer perforation (n = 1), and sepsis (n = 1) 1). The median postoperative hospitalization time was 13 days (range 7-59 days). Furthermore, we showed excellent postoperative outcome in the long-term follow-up (median follow-up time was 6 years): 258 patients (87%) were available for final evaluation, and 23 patients died in the later postoperative course (late mortality rate 8.9%), resulting in 232 patients with long-term follow-up. 187 of 232 patients (81%) experienced an increase in weight postoperatively. 62% (143/232) of the patients were pain-free and 26% (61/232) reported rare episodes of pain. The professional rehabilitation rate was 63% (147/232). Eleven patients (5%) were unemployed and 74 patients (32%) were retired. Only 6 patients (3%) showed newly developed insulindependent diabetes mellitus postoperatively, indicating a low onset of endocrine pancreatic insufficiency following duodenum-preserving pancreatic head resection [29].

In addition to our study, the results of other groups support the conclusion that the duodenum-preserving pancreatic head resection is a safe procedure (operative mortality nearly zero) which is very effective in long-term pain relief (> 80% after 5 years' follow-up). It has a low late mortality rate (10%) and a very low rate of operation-related endocrine pancreatic insufficiency (2-5%) [4, 28, 29].

Modifications of the duodenum-preserving pancreatic head resection

Longitudinal pancreatico-jejunostomy in combination with a local pancreatic head resection was introduced by Frey and Smith in 1985 [30, 31]. As a modification of the duodenum-preserving pancreatic head resection, it combined two principles in the surgical treatment of chronic pancreatitis: drainage of the main pancreatic duct, and organ-preserving resection of the pancreatic head. It has been stated that the Frey procedure is technically easier to perform than the duodenum-preserving pancreatic head resection, since there is no transsection of the pancreas above the portal vein [15].

This modification of the duodenum-preserving pancreatic head resection seems to be a safe and effective procedure for treating patients with chronic pancreatitis, with favorable results comparable to those of the duodenum-preserving pancreatic head resection [32]. However, the widespread experience and the long-term follow-up data for the Frey procedure are too limited to make a definitive judgment about its clinical value as a surgical treatment option in chronic pancreatitis.

Recently Izbicki and coworkers attempted to modify the Frey procedure to treat also the so-called small duct forms (main pancreatic duct size < 3 mm) of chronic pancreatitis with a combination of duct drainage and local resection

[33]: a longitudinal V-shaped excision of the ventral pancreas with subsequent drainage of the secondary and tertiary ductal branches by a longitudinal pancreatico-jejunostomy. First results in a small patient population with a median follow-up time of 30 months seem to be promising: there was permanent pain relief (pain score decreased by 95%) and significant improvement in quality of life (quality-of-life index increased by 67%). Furthermore, this procedure could be performed with zero mortality and low postoperative morbidity (15.4%) [33].

Which is the better operation in chronic pancreatitis: Pyloruspreserving Whipple resection or duodenum-preserving pancreatic head resection?

Both the classical and the pylorus-preserving Whipple resection were originally invented to treat malignant pancreatic head or periampullary tumors, with their pretension of oncological radicality in malignant disorders. For a benign disorder such as chronic pancreatitis, there is no need – with the exception of the occasional inability to exclude pancreatic cancer definitely – to remove a part of the stomach, the duodenum, the gallbladder and the extrahepatic bile duct, which are only secondarily involved in pancreatic disease. Removing neighboring organs carries with it the risk of more postoperative morbidity and even mortality – an unnecessary radicality.

To definitively answer which procedure is ultimately the best to be performed in chronic pancreatitis with regard to low mortality, low morbidity, long-term pain relief, good functional outcome, and good quality of life, in the last years several prospective randomized studies were performed to compare the various surgical techniques in the treatment of chronic pancreatitis:

- 1) Comparison of the classical Whipple resection and the duodenum-preserving pancreatic head resection [34]: Patients who had duodenum-preserving pancreatic head resection showed a significantly more rapid convalescence (16.5 days vs. 21.7 days postoperative hospital stay). In the long-term follow-up, patients with the duodenum-preserving pancreatic head resection demonstrated significantly better results in pain relief, preservation of the exocrine and endocrine pancreatic function, and postoperative weight gain [34].
- 2) Comparison of the *pylorus-preserving Whipple resection* and the duodenum-preserving pancreatic head resection [4]: There was no difference in the short-term postoperative morbidity (zero in both groups) and mortality. In the sixmonth follow-up, patients with a duodenum-preserving pancreatic head resection showed significantly lower incidence of recurrent pain (6%, compared with 33% in the pylorus-preserving group), which complements the data for hospital readmission (12% after duodenum-preserving pancreatic head resection vs. 27% after pylorus-preserving Whipple resection) and professional rehabilitation (80% after duodenum-preserving pancreatic

head resection vs. 67% after pylorus-preserving Whipple resection), as well as body weight increase (4.4 kg after duodenum-preserving pancreatic head resection vs. 2.1 kg after pylorus-preserving Whipple resection). A deterioration in glucose metabolism appeared 6 months postoperatively in 43% of the patients in the pylorus-preserving Whipple resection group, whereas only 6% of the patients with duodenum-preserving pancreatic head resection showed endocrine insufficiency [4].

3) Comparison of the *Frey procedure and the standard duodenum-preserving pancreatic head resection* [32]: The only difference was the slightly lower postoperative morbidity after the Frey procedure (11%, vs. 21% after the duodenum-preserving pancreatic head resection) [32]. The functional data were comparable.

The first two trials showed a clear advantage of the duodenum-preserving pancreatic head resection over both the classical and the plyorus-preserving Whipple resection [4, 34]. The comparison of the Frey procedure and the standard duodenum-preserving pancreatic head resection showed no significant difference other than a slightly lower early postoperative morbidity rate in the Frey procedure [32]. This fact is not surprising if we take into account the fact that there are no big technical differences between the two procedures – with the exception of the transsection of the pancreas above the portal vein [15].

# Organ-preserving surgery: the standard in the treatment of chronic pancreatitis

The duodenum-preserving pancreatic head resection has a clear advantage over the classical and the plyoruspreserving Whipple procedures with regard to the normal postprandial regulation of the digestive process. By preserving the extrapancreatic organs such as the stomach, the common bile duct and the duodenum, this procedure leads to a normal food passage and to a normal glucose metabolism after surgical intervention. Regarding quality of life and weight gain, the pylorus-preserving Whipple provides clearly better postoperative results in comparison with the classical Whipple. However, many patients who undergo the classical or the pylorus-preserving Whipple operation develop diabetes mellitus postoperatively, which contributes to late morbidity and mortality. A major disadvantage of the classical or the pylorus-preserving Whipple operation, which are still used by many surgeons as the standard procedure to treat chronic pancreatitis, is the resection of the duodenum, which plays a central role in the postprandial regulation of the digestive process and glucose metabolism. This conclusion is underlined by data obtained from prospective randomized clinical trials. Therefore, the duodenum-preserving pancreatic head resection should be considered as the new standard operation in patients with chronic pancreatitis due to its excellent early and late postoperative results.

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