# Long-term Follow-up After Organ-Preserving Pancreatic Head Resection in Patients with Chronic Pancreatitis

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**Abstract** In chronic pancreatitis (CP), enlargement of the pancreatic head develops as a result of inflammatory alterations. This report relates to the results attained with an organ-preserving pancreatic head resection (OPPHR) in 135 patients in a 7-year period. The surgical procedure consists of a wide excision of the inflammatory tumor in the region of the pancreatic head, without division and cutting of the pancreas over the portal vein. Reconstruction, with drainage of the secretion from the remaining pancreas into the intestinal tract, takes place through a jejunal Roux-en-Y loop. Only one reoperation was required in consequence to anastomosis bleeding, but no mortality occurred in the postoperative period. The duration of hospitalization ranged between 7 and 12 days. The mean follow-up period was 4.1 years (range, 0.5–7.0). The late mortality rate was 3.7%. The quality of life, measured during the follow-up by using EORTC Quality-of-Life Questionnaire, improved in 89% of the patients. One hundred sixteen patients became complaint-free, while 14 patients had moderate symptoms; the weight increased by a median of 11.3 kg (range, 4–28). The 7-year experience clearly reveals that this OPPHR technique is a safe and effective procedure for definitive control of the complications of CP.

Keywords Chronic pancreatitis  $\cdot$  Organ preservation  $\cdot$  Pancreatic head resection  $\cdot$  Long-term follow-up  $\cdot$  Quality of life

# Introduction

Patients with chronic pancreatitis (CP) characterized by severe pain pose a therapeutic challenge. In nearly one-third of these patients, enlargement of the head of the pancreas develops in consequence to inflammatory alterations, which leads to complications such as obstruction of the pancreatic duct, common bile duct stenosis, and duodenal compression. These are all indications for surgical treatment: resection of the pancreatic head, which is considered to be the pacemaker of the disease in CP.<sup>1,2</sup> The surgical treatment consists of

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different types of pancreatic head resection,<sup>3</sup> i.e., pyloruspreserving pancreaticoduodenectomy (PPPD),<sup>4</sup> Beger's duodenum-preserving pancreatic head resection (DPPHR),<sup>5</sup> the Bern modification of Beger's resection,<sup>6,7</sup> and Frey's longitudinal pancreaticojejunostomy combined with local pancreatic head excision (LPJ-LPHE).<sup>8</sup> In our surgical practice, mainly PPPD has been applied, but since 1999, in accordance with the modern organ-preserving concept, a safe procedure for organ-preserving pancreatic head resection (OPPHR) has been applied. The preliminary clinical results and follow-up achieved with this operation were published recently,<sup>9,10</sup> and in a prospective, randomized, control trial OPPHR was compared with PPPD to define the advantages of each operation with regard to the operation data, the postoperative complications, the induction of diabetes mellitus, the postoperative pain, and the quality of life (OoL) up to 1 year after operation. The prospective trial clearly confirmed that the two procedures are equally safe and effective with regard to pain relief, but OPPHR is superior to PPPD not only in the operative data and morbidity, but also in the QoL 1 year postoperatively.<sup>11</sup> This article reports on the late follow-up [average 4.1 years (range, 0.5-7.0)] results attained with our OPPHR in 135 patients.

### Material and Methods

Since February 1999, an OPPHR procedure has been performed in 135 patients [103 men and 32 women; mean age, 49.5 years (range, 28-63)] after the development of an inflammatory tumor of the pancreatic head [median diameter, 68 mm (range, 46 to 129 mm), as assessed by helical computed tomography (CT) scan. The preoperative morbidity involved frequent, sometimes severe abdominal pain, a significant loss in body weight in all patients, jaundice in ten patients, and latent and insulin-dependent diabetes mellitus (IDDM) in 16 and 21 patients, respectively. The mean interval between the appearance of the symptoms and the surgical intervention was  $7.8\pm2.2$  years. The etiology was connected with chronic alcohol ingestion in 86% (117 patients), the CP was associated with biliary stone disease in 14 patients (10%), and it was unknown in 4 patients. The diagnosis was confirmed by endoscopic retrograde cholangiopancreatograms (ERCP), sonography, and the CT scan. ERCP revealed that the diameter of the main pancreatic duct varied between 3 and 9 mm. In the 10 icteric patients and in 15 patients without jaundice, the common bile duct was stenotic, due to inflammatory tumor compression with prestenotic dilatation, combined with high levels of alkaline phosphatase (1,035±152 U/l). The CT scan demonstrated parenchymal calcification in 72 patients; 21 patients had pseudocystic cavities, and in 4 of them, a pseudocyst caused a subacute inflammation in the pancreatic head. No patient exhibited portal hypertension or superior mesenteric vein thrombosis.

Before the operation, prophylactic antibiotic (ceftriaxone) was used, and in the early postoperative period, all of the patients were treated by standard supportive treatment, consisting of total parenteral nutrition for 4 days, a proton pump antagonist (pantoprazole), suppression of TNF synthesis (pentoxifylline), and octreotide medication.<sup>12</sup> The oral nutrition was started on postoperative day 5.

Pancreatic functions were checked by means of stool elastase determination with a sandwich enzyme-linked immunosorbent assay (ELISA) method (Pancreatic Elastase1<sup>®</sup>, ScheBo Biotech, Giessen, Germany).<sup>13</sup> The glucose tolerance test was applied to check the endocrine function. Blood glucose levels were measured after 0, 30, 60, 90, and 120 min by means of a glucose oxidase assay after the administration of 75 g oral glucose.

#### **Operative Procedure**

The surgical procedure involved a wide local resection of the inflammatory tumor in the region of the pancreatic head and decompression of the organ and the intrapancreatic segment of the common bile duct if the prepapillary duct had become stenotic. The operative procedure started with the Kocher maneuver, partial dissection of the gastrocolic ligament for mobilization, and exploration of the head of the pancreas, without division and cutting of the pancreas over the portal vein. An intraoperative frozen section was performed for all patients; none of them revealed signs of malignancy. The following step of the operative procedure was ligation of the pancreaticoduodenal artery and the veins directed to the duodenum and to the superior mesenteric vein. The enlarged pancreatic head was excised in almost its entirety, leaving behind a bridge of pancreatic tissue about 10 mm wide, while a rim of pancreas (5 to 10 mm) remained beside the duodenum and on the upper margin of the pancreatic head. This wide excision gives a possibility for drainage of the pancreatic juice from the distal pancreas and for opening of the prepapillary obstructed common bile duct in the icteric patients and in patients with a stenotic common bile duct. The prestenotic dilated common bile duct was opened with an incision about 8-10 mm long, and the opened duct wall was sutured to the surrounding pancreatic tissue with interrupted Vicryl® 3/0 sutures. After careful hemostasis of the operative region, the reconstruction, with drainage of the secretion from the remaining pancreas into the intestinal tract, took place through a jejunal Roux-en-Y loop, with application of one-layer interrupted Vicryl<sup>®</sup> 2/0 sutures.<sup>9</sup> There was no indication or necessity for blood transfusion during the operation. The mean operating time was 165 min (range, 120 to 210 min).

#### Quality of Life

The quality of life (QoL) and pain score before and after surgery were assessed by using the European Organization for Research and Treatment of Cancer (EORTC) Qualityof-Life Questionnaire (QLQ-C30).<sup>14</sup> The EORTC QLQ-C30 has been reevaluated and demonstrated to be a valid and reliable tool to measure the QoL in patients with benign disease such as CP.15 The EORTC QLQ-C30 comprises items relating to the physical status, the working ability, the emotional, cognitive, and social functioning, and an overall QoL scale. Pain intensity was estimated by means of a pain scoring system including a visual analog scale, the frequency of pain attacks, the use of analgesic medication, and duration of the inability to work. The overall pain score was given by the sum of the individual values divided by 4. This questionnaire was prospectively assessed at two time points during the study: before the surgical procedure and in the follow-up period (a mean of 4.1 years) after the operation.

### Statistical Analysis

Statistical significance was estimated by using Student's t test or the Wilcoxon rank test, as appropriate. The level of

Criterion	Preoperative Score [median (range)]	Follow-up Score [median (range)]
Pain visual analog scale	82 (55–100)	10 (0–15)
Frequency of pain attack	75 (50–100)	12.5 (0-15)
Pain medication	20 (20–100)	0 (0-100)
Inability to work	75 (75–100)	0 (0-100)
Pain score	63 (50–100)	5.6 (0–37.5) ( <i>P</i> <0.001) <sup>a</sup>

**Table 1** Preoperative and Follow-up Pain Scores (n=105)

<sup>a</sup> Preoperative values were compared with follow-up values by the Wilcoxon rank sum test

significance was set at P < 0.05. The results on the parametric data are expressed as means  $\pm$  SD. Nonparametric data are expressed as medians.

# Results

In 135 patients, the OPPHR procedure was performed after the development of an inflammatory tumor of the pancreatic head. In the postoperative period, only one reoperation was required in consequence of anastomosis bleeding, another case was treated conservatively, and one patient had pneumonia, but no septic complication, anastomosis insufficiency, or other problems; the morbidity was therefore 2.9%. There was no mortality in the postoperative period. In the 25 icteric and common bile duct stenotic patients, the liver functions normalized [serum bilirubin <22 µmol/l and alkaline phosphatase  $332\pm92$  U/l; compared with the preoperative data, the reduction was significant (P < 0.05)] after the operation. The duration of hospitalization ranged between 7 and 12 days, with a median of 8.5 days. The histological examinations confirmed fibrosis and calcification in 63 and 72 patients, respectively.

The mean follow-up period was 4.1 years (range, 0.5 to 7.0). Five patients were lost to follow-up (3.7%). Complete follow-up data on 130 patients were included in the evaluation; the follow-up rate was therefore 96.3%. One hundred sixteen patients became complaint-free (89%), 14 patients had moderate symptoms, and the body weight increased by a mean of 11.3 kg (range, 4–28) (P<0.05).

Within 2 years after operations, five patients were reoperated: a bilio-digestive bypass was performed in consequence of developed bile duct stenosis. In the follow-up period, a further six patients were admitted to the clinic with an acute episode of pancreatitis; all of them were treated conservatively. Readmission was therefore necessary in 11 of the 130 patients (8.4%). The late mortality was 3.7% (five patients); the reason was cardiovascular failure or an accident in four and one patient, respectively.

The stool elastase level increased slightly, but not significantly (from  $124.3\pm33$  to  $132\pm39$  µg/g; NS). The preoperative and postoperative endocrine functions remained in almost the same stage: 95 patients were normoglycemic, 6 had latent DM, and 20 had IDDM, but 9 patients with latent DM became IDDM (6.6%).

Both before the operation and during the follow-up, the patients were asked to complete the QoL questionnaire (EORTC QLQ-C30). A full answer was obtained from 105 patients (78%). The questionnaire was compared at two time points: (1) before the operation and (2) at a mean follow-up of 4.1 years (0.5–7) after the operation. The median pain score decreased by 91% (P<0.001) after surgery. No patient suffered a frequent pain attack, and only 10% of the patients mentioned moderate pain occasionally without any pain killer medication (Table 1). During the follow-up, the median global QoL improved by 100%. Apart from the cognitive functioning, the physical status, working ability, emotional and social functioning all improved significantly (P<0.05). The results of the symptom scales are summarized in Table 2.

 Table 2 Preoperative and Follow-up Functioning Scale Scores (n=105)

Functioning Scale	Preoperative Score [median (range)]	Follow-up Score [median (range)]
Physical status	60 (20–100)	70 (20–100) ( <i>P</i> <0.05) <sup>a</sup>
Working ability	50 (0-100)	70 (0–100) $(P < 0.05)^{a}$
Cognitive	50 (40-80)	66.7 (40–100) NS <sup>a</sup>
Emotional	25 (0-75)	66.7 (40–100) $(P < 0.05)^{a}$
Social	16.7 (0-66.7)	66.7 $(0-100) (P < 0.05)^{a}$
Overall quality of life	28.5 (14.3–57.1)	57.7 (33.3–100) $(P < 0.05)^{a}$

NS Not significant

<sup>a</sup> Preoperative values were compared with follow-up values by the Wilcoxon rank sum test

### Discussion

Enlargement of the pancreatic head due to chronic inflammation causes permanent pain, obstruction of the pancreatic duct alone or together with the common bile duct, and duodenal compression. With these complications, surgical treatment is generally indicated. The aims of surgical therapy, therefore, are not only to eliminate pain, to manage the CP-associated complications of the adjacent organs, and possibly to preserve the endocrine and exocrine functions, but also (more importantly) to improve the patients' overall OoL and physical status, and also to provide for their social and occupational rehabilitation.<sup>16</sup> The objective outcome assessment of surgical treatment was made with the EORTC OLO-C30, which has previously been demonstrated to be a valid and reliable tool with which to measure the QoL in patients suffering from benign diseases such as CP.<sup>15,17</sup>

In the past, classical Whipple's pancreatoduodenectomy (PD) and PPPD were applied as standard surgical procedures for pancreatic head complications in CP, but the long-term results and OoL after these operations were disappointing, with high rates of late morbidity and mortality.<sup>18</sup> Although two recently published articles have described better results,<sup>19,20</sup> it is generally accepted that these operations, involving the removal of healthy adjacent organs, do not seem to be warranted in this benign disease,<sup>21</sup> unless there is a strong suspicion of cancer.<sup>22</sup> In the past 20 years, these operations have generally changed, with the introduction of Beger's DPPHR<sup>5</sup> and Frey's LPJ-LPHE<sup>8</sup> procedure. In both, the resection or excision of the pancreatic head is limited, but achieves reliable pain relief and allows definitive management of the pancreatitis-associated complications of the adjacent organs and an improved QoL.<sup>23-25</sup> In the last 10 years, some important randomized studies have compared the different types of pancreatic head resection. Büchler demonstrated better pain relief and pancreatic function when DPPHR was compared with PPPD.<sup>26</sup> Almost the same results were reported by Klempa, who compared DPPHR vs PD: the degree of pain relief was equal, but the recovery was quicker, and the pancreatic function became better after Beger's operation.<sup>27</sup> Two randomized studies were also performed to analyze the pancreatic function and QoL after Frey's LPJ-LPHE or DPPHR: the level of pain relief was equal, but the QoL was better after Frey's operation.28,29 Recently published articles based on the long-term follow-up of randomized trials have concluded that there was no difference with regard to the mortality, QoL, pain, or exocrine or endocrine insufficiency between the two operations and also indicated that these operations are advantageous for the treatment of CP. The decision as to which procedure to choose should be based on the surgeon's experience.30,31

In approximately 30% of patients with CP, the disease is primarily located in the head of the pancreas, which is known to act as the "pacemaker" to trigger the inflammatory process; resection of this inflammatory mass must be regarded as pivotal in the surgical intervention.<sup>1,2,32</sup> Basically, CP is a benign, but sometimes progressive disease, and the organ-preserving concept must therefore be accepted. The concept for our pancreatic head resection followed this directive, and our preliminary clinical results confirmed it.<sup>9–11</sup> The resection process removes only a sufficient part of the pancreatic head to guarantee the normal flow of both ductal systems (the bile and the pancreas) and to preserve the physiological gastroduodenal function.

This article is concerned with the late follow-up [on average, 4.1 years (range, 0.5-7.0)] results attained with our OPPHR on 135 patients. Our data demonstrated that OPPHR is a safe operative procedure, confirmed by the low morbidity (2.9%) and the absence of mortality among the patients in the postoperative period. An additional important feature is that the median duration of hospitalization was only 8.5 days. In the mean follow-up period of 4.1 years (range, 0.5 to 7.0), 116 patients became complaint-free (89%), while 14 had moderate symptoms, and the body weight increased significantly by a mean of 11.3 kg (range, 4–28). Readmission was required for 11 of the 130 patients (8.4%) as a consequence of relaparotomy (bilio-digestive bypass) or conservatively treated pancreatitis. The late mortality was 3.7% (five patients died). The preoperative and postoperative endocrine function remained in almost the same stage.

Pain relief and improvement of the QoL after surgery for CP in the patients were assessed by using the EORTC QLQ-C30. The completed questionnaires before and after the surgical treatment were evaluated in 105 patients (78%). Other patients were not included in the study because of incomplete data, or the lack of cooperation, or the data on the patients were not available. The median pain score decreased by 91% (P<0.001) after surgery. No patient suffered frequent pain attacks, and only 10% of the patients mentioned moderate pain occasionally. During the follow-up, the median global QoL improved by 100%. Apart from the cognitive functioning, the physical status, working ability, and emotional and social functioning all improved significantly (P<0.05).

On the basis of the early and long-term results of our OPPHR operations, the advantage of this procedure is the wide scale of possible indications, involving different pathologic processes, e.g., a subacute or chronic inflammation mass with a pseudocyst, ductal stenosis, or obstruction (common bile duct, pancreatic duct) caused by CP, small duct CP and some benign endocrine tumors localized in the pancreatic head.<sup>33</sup>

## Conclusions

The results of this study clearly demonstrate that this OPPHR technique is a safe and effective procedure for definitive control of the complications after the inflammatory alterations of CP, and it is suggested that this operation is one of the best options for the management of patients with CP requiring surgery.

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