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Duodenum-preserving pancreatic head resection: A retrospective analysis of the Hamburg Modification

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ABSTRACT

Background: Chronic pancreatitis remains a challenging inflammatory disease, causing progressive, irreversible fibrosis of the pancreatic parenchyma. Several surgical options for treatment have been established, but duodenum-preserving pancreatic head resections seem to be the most favorable option other than pancreatoduodenectomy. The aim of this retrospective analysis is to evaluate the outcomes of the Hamburg modification of duodenum-preserving pancreatic head resections.

Methods: We retrospectively evaluated—for long-term outcomes concerning pain control, quality of life, and symptom control—500 consecutive patients suffering from painful chronic pancreatitis who had undergone the Hamburg modification of the duodenum-preserving pancreatic head resection. Additionally, the patients were compared with a database of 104 patients who underwent duodenum-preserving pancreatic head resections according to Beger or Frey.

Results: After a mean follow-up of 10 years, overall survival was 90% in those patients having undergone the Hamburg modification. Regarding analgetic medications, the median pain score for frequency of pain attacks, measured by a visual analog scale and inability to work, was 0 (0–100), and the global quality of life revealed a median of 92 (0–100). In addition, we found that a high rate of patients continued consuming alcohol after the operation (37.9%). The rate of redo surgery owing to the recurrence of chronic pancreatitis was 7.6% after this Hamburg modification.

Conclusion: Duodenum-preserving pancreatic head resections provide adequate outcomes in terms of pain control, quality of life, and symptom control. In this retrospective analysis, the Hamburg modification was found to be a good alternative to other forms of duodenum-preserving pancreatic head resections. The choice of a certain modification of the duodenum-preserving pancreatic head resection may depend on the surgeon's expertise and the individual needs of the patient.

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Introduction

Chronic pancreatitis (CP) is an inflammatory disease characterized by calcification and progressive, irreversible fibrosis of the pancreatic parenchyma, causing progressive loss of exocrine and endocrine pancreatic function.[1] The prevalence amounts to 26.4 cases per 100,000 people, with alcohol consumption being the main cause (70%–90% of cases).[2,3] Other causes are nicotindependence genetic predisposition, anatomic variants, and idiopathic CP.[2] Life expectancy in a population with CP is decreased by about 10 to 20 years, with a 3.6-fold increase in mortality compared with a population without chronic pancreatitis.[3,4] Because of the high average annual costs of treatment of approximately $17,000 per patient, the socioeconomic impact of CP is not negligible.[3]

Several treatment options for CP are available, including conservative regimes, interventional endoscopic methods, and a variety of operative techniques, including simple ductal drainage procedures, duodenum-preserving pancreatic head resections (DPPHRs), extensive subtotal, and, even in rare cases, total panceatectomies.[5–8] Subtotal resections of the pancreatic head are more beneficial for patients suffering abdominal pain and head enlargement compared with simple drainage.[6,9–13]

Introduced in 1972, the Beger procedure marked the beginning of a new era, combining the advantages of ductal drainage with a

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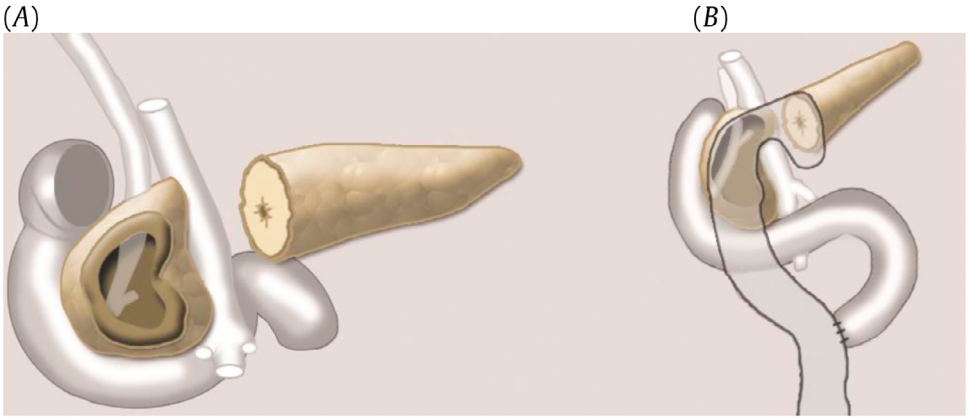

Fig. 1. Duodenum-preserving pancreatic head resection according to Beger. (*A*) Subtotal resection of the pancreatic head followed by (*B*) a reconstruction with a Roux-en-Y limb with an end-to-end pancreticojejunostomy to the remnant body of the gland and a side-to-side pancreticojejunostomy to the resection cavity.[18] Reprinted with permission from Springer Nature.

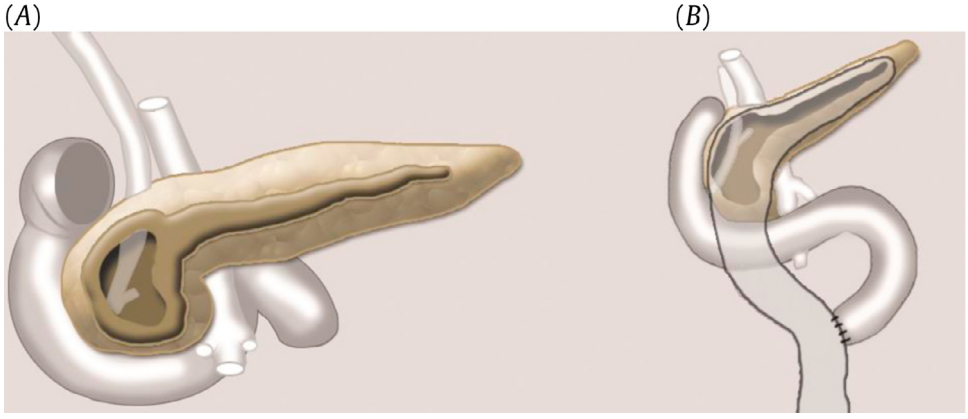

Fig. 2. Duodenum-preserving pancreatic head resection according to Frey. (*A*) Limited nonanatomic "coring out" type resection of the pancreatic head and a longitudinal incision of the pancreatic main duct followed by (*B*) a reconstruction with a longitudinal side-to-side pancreticojejunostomy to the resection cavity, and a pancreticojejunostomy to the body and the tail of the pancreas[18] Reprinted with permission from Springer Nature.

subtotal resection of the pancreatic head (Fig. 1) to eliminate the Longmires's concept of the "pacemaker" of the pain being in the head of the gland. An inflammatory mass in the pancreatic head had been known as a common finding in CP patients and is one of the main causes of the pain that may lead to a high incidence of complications in surrounding organs.[12,14–16]

In 1986, Frey presented a modification of Beger's procedure, combining a limited, nonanatomic excision of the pancreatic head with a longitudinal pancreticojejunostomy to the main pancreatic duct, similar to the Partington-Rochelle procedure, but without the transection of the gland (as in the Beger procedure) along the portomesenteric axis (Fig. 2). To avoid the risk of bleeding complications and to minimize intraoperative trauma, the Berne modification was introduced by Buechler, which involves a deep excision of the pancreatic head without transection of the pancreas along the portomesenteric axis.[17,18]

In 1998, Izbicki introduced the so-called "Hamburg modification," which involved a V-shaped excision of the pancreatic body beyond the deep duodenum-preserving head resection, aiming to reach second-order and third-order pancreatic side branches (Fig. 3).[5,19] The concept behind this V-shaped excision was the idea of eliminating potential stenosis and prevention of stenosis that may appear as the disease, hypothetically resulting in better long-term outcomes. All procedures provide maintenance of the bilioenteric and the gastroduodenal passages.[2,5]

The outcomes of the Beger and the Frey procedures compared in a randomized controlled trial (RCT) indicated that both procedures do not significantly differ from each other regarding short-term and long-term results.[2,20] Another RCT comparing the Beger procedure with the Berne modification revealed certain advantages for Berne modification in short-term follow-up, and pain and quality of life were comparable.[21,22] Several trials and analyses present data on different modifications of DPPHR, but no long-term follow-up studies, including outcomes of the Hamburg modification, have, as of yet, been published. Therefore, this retrospective analysis was conducted to assess the long-term results of the Hamburg modification, relating to pain control, quality of life, and symptom control. In addition, these results were compared with long-term follow-up data of the Beger and Frey procedures from two RCTs that had been done in the same center.

Methods

Participants and data acquisition

We retrospectively assessed 500 consecutive patients from a prospective database who have been treated with the Hamburg modification. Methods concerning the selection of the patients were comparable with two RCTs that have been conducted in the same center and are described elsewhere.[2,23] Patients suffering from painful CP were evaluated for operative treatment by a council of surgeons and gastroenterologists.

After a confirmed indication for the operative treatment, including a persistent need for analgesic medications and intermittent

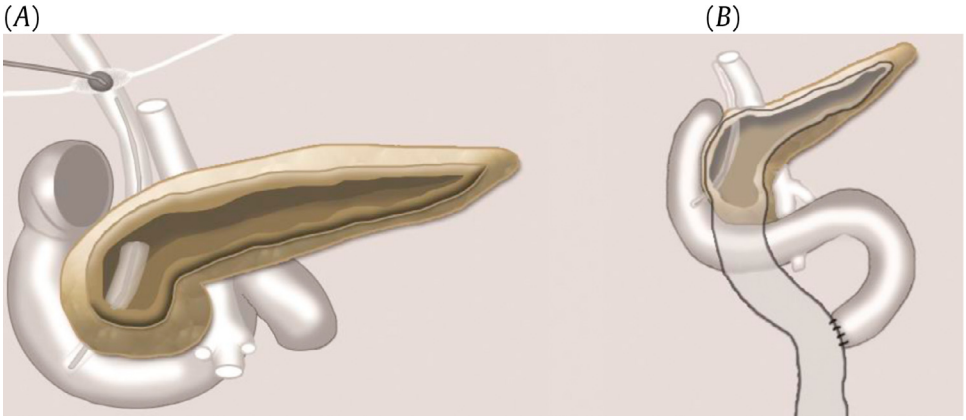

Fig. 3. Duodenum-preserving pancreatic head resection: The Hamburg modification. (*A*) Subtotal nonanatomic "coring out" type resection of the pancreatic head including the uncinate process and a longitudinal V-shaped excision of the ventral aspect of the body and the tail of the pancreas. (*B*) Reconstruction with a Roux-en-Y limb and a side-to-side pancreticojejunostomy with the resection cavity, the corpus, and the tail of the gland.[18] Reprinted with permission from Springer Nature.

need for morphine, the patients underwent DPPHR. In our institute the indication for operative treatment is late-stage chronic pancreatitis, because early stages are primarily treated conservatively or with endoscopic interventions.

Patients who underwent the Hamburg modification under more emergent conditions because of complications of recurrent attacks of acute pancreatitis or patients that refuse informed consent to clinical follow-up in our prospective database were excluded. Since 1998, the Hamburg modification has been the standard procedure in our department in patients without suspicion for malignancy. In the latter patients, pancreatoduodenectomy is performed. Such patients with suspected malignancy underwent pancreatoduodenectomy and were excluded from the analysis.

For the purpose of this retrospective analysis, medical reports and findings from our clinical database were analyzed by a trained investigator. Suitable patients were contacted by letter, including a standardized questionnaire. For those patients not responding to the letters, the general practitioner or the local government administration were contacted to determine whether the patients were still alive. Discrepancies and inconsistencies were resolved by phone calls.

To evaluate the collected data, the outcomes were compared with a 10-year follow-up of 104 patients who had undergone DPPHR according to Beger or Frey in 2 previous RCTs.[2,23]

Surgical procedures

The DPPHR procdures were described elsewhere in detail.[5,24,25] The following main aspects are summarized briefly:

Beger procedure

A deep, anatomic, subtotal resection of the pancreatic head and a transection of the gland along the portomesenteric axis are followed by reconstruction, using the same jejunal Roux-en-Y limb for an end-to-end pancreticojejunostomy to the remnant body of the gland and a side-to-side pancreticojejunostomy to the resection cavity.[26]

Frey procedure

The modification by Frey is considered to be technically easier (and potentially safer) than the Beger procedure.[27] In short, a "coring out" type l excision of the pancreatic head (to a smaller degree in relation to the Beger procedure) is accompanied by a longitudinal incision of the main pancreatic duct. The reconstruction involves a longitudinal, side-to-side pancreticojejunostomy, which includes the resection cavity and the body and the tail of the pancreas, similar to the Partington-Rochelle procedure.[2,5,27]

Hamburg modification

Hypothetically, the DPPHR by Beger and Frey only provide drainage of the main pancreatic duct, possibly resulting in insufficient drainage of the second-order and third-order pancreatic side branches as a late postoperative complication as the underlying disease progresses. Thus, the Hamburg modification focuses on fully opening these side branches and their junction with the main pancreatic duct by performing a subtotal resection of the pancreatic head and a V-shaped excision of the ventral aspect of the body and tail of the gland. This is followed by a reconstruction with a Roux-en-Y limb used for side-to-side pancreatojejunostomy to the resection cavity.[19,25,28]

End points

The primary end point of this retrospective analysis was pain control, with quality of life representing the secondary end point. Therefore, to acquire data concerning quality of life, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire[27,29] was used. We added a validated scoring system for CP,[30] containing 20 specific items, such as a disease-specific symptom scale, a treatment strain scale, and an overall hope and confidence scale.[30] Pain was measured by the validated Izbicki pain score, including frequency of pain attacks, a visual analog scale of pain, analgesic medications used, and inability to work.[20,30] Furthermore, control of complications, arising from adjacent organs, mortality, morbidity, reoperation rates, and occupational rehabilitation were defined as secondary end points.[31]

Statistical analysis

Statistics were calculated with SPSS software version 22.0 (SPSS Inc, Chicago, IL). Descriptive analysis is expressed as median and range or mean with standard deviation. The Student t test was used for continuous data and the Mann-Whitney U test was used for noncontinuous data. The χ^2 test was used for categorical data. Statistical analysis was conducted on an intention-to-treat basis, using a significance level of $P < .05$.[2]

Results

Follow-up and mortality

The mean age of the 500 patients undergoing the Hamburg modification was 49.2 ± 11 years, 74.8% of whom were male. The mean diameter of the pancreatic head was 5.8 cm. In 81%

Table 1
Izbicki pain score system[30]

Izbicki pain score system	Score
Frequency of pain attacks	
Daily	100
Several times a week	75
Several times a month	50
Several times a year	25
None	0
Visual analogue scale (0–100)	
Imaginative maximum of pain	100
No pain	0
Analgetic medication (morphine-related analgesic potency)	
Morphine	100
Buprenorphine	80
Pethidine	20
Tramadol	15
Metamizol	3
Acetylsalicylic acid	1
Time of disease-related inability to work	
Permanent	100
≤ 1 year	75
≤ 1 month	50
≤ 1 week	25
None	0

Pain score = Sum of the values of the 4 aspects divided by 4.

of the patients, the chronic pancreatitis was caused by abuse of alcohol.

The mean follow-up time was 9.9 years. Of the 500 patients, only 48 (9.6%) were classified as lost to follow-up. The survival rate was 90%, and the in-hospital mortality was 2%. Therefore, follow-up of pain relief and quality of life was available in 406/500 patients. The rate of revisional surgery was 7.6%, attributable to the recurrence of chronic pancreatitis, and 4%, attributable to cholestasis with cholangitis.

Pain control

Pain was measured using the validated Izbicki pain score (Table 1).[30] In those patients undergoing the Hamburg modification, the median score was 0 (0–100) regarding analgetic medications, frequency of pain attacks, visual analogue scale and inability to work. The median pain score was 4 (0–100). Results are presented in Table 2.

Quality of life

Evaluating the quality of life in patients undergoing the Hamburg modification, median physical status was found to be 80 (0–100), and median working ability, cognitive, and social functioning was 100 (0–100). In terms of emotional functioning and global quality of life, the assessment revealed a median of 92 (0–100). Results are presented in Table 3.

Symptom control

The symptom scales are presented in Table 4. As shown, median nausea and vomiting was (0–100) in patients who had undergone the Hamburg modification. The patient self-assessments of the treatment strain revealed a median of 33 (0–100), and their median hope and confidence level with respect to therapy was 0 (0–100).

Endocrine and exocrine function

After 10 years, the rate of endocrine insufficiency was 69% after the Hamburg modification. Although only 2% of the patients were treated with oral antidiabetic medication, the vast majority had developed insulin-dependent diabetes mellitus. The rate of exocrine insufficiency was also high—83% of the patients were on enzyme replacement. In 63% of the patients, data concerning stool elastase were available, showing pathologic results in 88.9% (280/315) of the patients. Because the HbA1 is nearly normal in patients with adequately controlled antidiabetic treatment, levels of HbA1 were not evaluated between the groups.

Effects of continuous alcohol consumption

Concerning alcohol consumption, a high rate of patients who had been treated with the Hamburg modification continued drinking after the operation (37.9%). A comparison between continuing alcohol drinkers ($n = 154$) and abstainers ($n = 252$) who had undergone the Hamburg modification revealed important differences between these two populations.

Continuing alcohol consumers suffered from more pain than the abstainers group, as presented in Table 5. Patients who continued to drink alcohol after the operation had a greater pain score, with a median of 19 (0–98) compared with 8 (0–100) in abstainers ($P = .001$). Furthermore, both frequency of pain attacks and inability to work were greater in the alcohol group with medians of 25 (0–100) vs 0 (0–100) in abstinent patients ($P = .001$).

We found worse outcomes for patients who continued consuming alcohol in relation to several other aspects, including overall functioning, pain, symptoms, and quality of life. Cognitive functioning ($P = .025$), emotional functioning ($P = .004$), social functioning ($P = .042$), and global quality of life ($P = .021$) were significantly better in patients who ceased consuming alcohol (Table 6). Relating to symptom control, patients who ceased alcohol consumption after the operation had a better outcome as well.

Comparison with Beger and Frey procedure patients

The long-term follow-up data of the patients undergoing the Hamburg modification were compared with a collective of patients from two RCTs who had been treated with the Beger or Frey procedures.

The baseline parameters were similar. In the Beger or Frey group, the mean age was 43.6 ± 10.5 years. In the Hamburg group, the patients tended to be older (49.2 ± 11.1 years vs. 43.6 ± 10.5 years; $P = .001$). Both groups were similar concerning sex (Hamburg: 74.8% male, DPPHR: 76.9% male; $P = .375$), the mean diameter of the pancreatic head (5.7 cm vs 5.8 cm), and rates of pancreatitis caused by alcohol consumption (79% vs 81%) were comparable.

Although the mean follow-up for the Beger or Frey group was 10.5 years, with only 7 (6.7%) patients lost to follow-up, the survival rate was 81% (vs 90% [Hamburg]; $P = .003$). The in-hospital mortality was 0% in Beger or Frey patients (vs 2% [Hamburg]; $P = .236$).

Concerning pain control, the significant advantages of the Hamburg modification were found regarding analgesic medications ($P = .021$). In addition, the median frequency of pain attacks was greater in the Beger or Frey group: 10 (0–85) compared with 0 (0–100) in the Hamburg group ($P = .03$). The total Izbicki pain score revealed no differences between the two groups ($P = .546$). In terms of emotional functioning ($P = .011$), social functioning ($P < .001$), and global quality of life ($P = .003$), the Hamburg group had better results compared with the Beger or Frey group. The patients' self-assessment of treatment strain ($P < .001$) and their hope and confidence with respect to therapy ($P = .009$) appeared to be better in patients who had undergone the Hamburg modification.

Compared with the data of the Frey or Beger group, no significant differences were found with rates of endocrine and exocrine insufficiency of 67% and 84%, respectively. Although only 14.3% of

Table 2
DPPHR (Hamburg modification) versus DPPHR (Beger/Frey) procedures[2,23]: Follow-up results of the pain score of the surviving patients.

Pain score	Hamburg ($n=406$)		Beger/Frey ($n=79$)		P value
	Median	Range	Median	Range	
Frequency of pain attacks	0	0–100	10	0–85	.03
Visual analogue scale	0	0–100	0	0–100	.319
Analgetic medication	0	0–100	0	0–100	.021
Inability to work	0	0–100	0	0–100	.158
Pain score	**4**	**0–100**	**6**	**0–96**	**.546**

Table 3
DPPHR (Hamburg modification) versus DPPHR (Beger/Frey) procedures[2,23]: Follow-up results of the function scale scores of the surviving patients.

Functional scale*	Hamburg ($n=406$)		Beger/Frey ($n=79$)		P value
	Median	Range	Median	Range	
Physical status	80	0–100	100	0–100	.117
Working ability	100	0–100	100	0–100	.054
Cognitive functioning	100	0–100	100	0–100	.108
Emotional functioning	92	0–100	75	0–100	.011
Social functioning	100	0–100	33	0–100	< .001
Global quality of life	92	0–100	67	0–100	.003

* Items corresponding to questionnaire. Scores range from 0 to 100 (the greater the score, the greater the functioning level).

the Beger or Frey group continued consuming alcohol after the operation, the rate in the Hamburg group was more than 2.5-fold (37.9%, $P=.001$).

The rate of revision surgery attributable to the recurrence of symptomatic chronic pancreatitis in the remnant of the organ was greater after Frey or Beger procedures compared with the Hamburg modification (18.3% vs 7.6%, $P=.001$). In addition, 4% of the patients in the Hamburg group and 3% of the patients in the Beger or Frey group needed reoperation because of cholestasis or recurrent cholangitis.

Discussion

Assuming that the second-order and third-order pancreatic side branches have a relevant impact on the course of CP, Izbicki et al. published a modification of the DPPHR in 1998 drawing particular attention to these side branches, hence also addressing small duct diseases associated with painful chronic pancreatitis.[18,19,32,33] The so-called Hamburg modification combines the advantages of a subtotal, nonanatomic resection of the head of the gland, including the uncinate process and a longitudinal incision of the pancreatic duct with a V-shaped excision of the ventral aspect of the body and the tail of the gland.[2,33] The main element of the Hamburg modification, the V-shaped excision, is performed to eliminate partial or total obstruction of the second-order and third-order pancreatic side branches and to prevent stenosis that may appear as a late postoperative complication. Thus, the Hamburg modification of the DPPHR focuses on sustaining drainage of the pancreatic side branches and their junction with the main duct. For this reason, the Hamburg modification has become the standard operation in our center.

The detailed pathophysiologic mechanism in the development of pain is not fully understood, but it is known that it is multifactorial. The inflammatory mass of the pancreatic head and increased pressure in the main pancreatic duct and pancreatic parenchyma appear to play important roles. A drainage operation is not necessary for most CP patients to achieve a high rate of pain control and improved quality of life, because similar results can also be provided by performing a Whipple procedure.

Our retrospective analysis is the first to present long-term data of the Hamburg modification of the DPPHRs first described by Beger and Frey for the operative treatment of chronic pancreatitis. The results of the current analysis showed adequate outcomes for the Hamburg modification in patients suffering from painful CP. Compared with the Beger or Frey patients from the two RCTs, the Hamburg modification appeared to be superior in several aspects concerning quality of life, including emotional and social functioning and global quality of life. Patients in the Beger or Frey group

Table 4
DPPHR (Hamburg modification) versus DPPHR (Beger/Frey) procedures[2,23]: Follow-up of the symptom scales scores of the surviving patients. Significant values are in bold.

Symptom scale and/or item*	Hamburg ($n=406$)		Beger/Frey ($n=79$)		P value
	Median	Range	Median	Range	
Fatigue	11	0–100	43	0–100	**< .001**
Nausea and vomiting	0	0–100	0	0–100	**< .001**
Pain	11	0–100	0	0–100	.632
Loss of appetite	0	0–100	0	0–100	.746
Dyspnea	0	0–100	6	0–83	**.005**
Sleep disturbance	0	0–100	33	0–100	**< .001**
Constipation	0	0–100	0	0–100	.752
Diarrhoe	0	0–100	0	0–100	.410
Financial strain	0	0–100	0	0–100	.959
Loss of body weight	0	0–100	0	0–100	.812
Fever or shivering	0	0–100	0	0–100	.056
Jaundice	0	0–67	0	0–67	**.040**
Bloating	0	0–100	33	0–100	**< .001**
Thirst	0	0–100	0	0–100	**.034**
Itching	0	0–100	0	0–67	.110
Treatment strain	33	0–100	67	0–100	**< .001**
Hope and confidence	0	0–100	17	0–100	**.009**

* Items corresponding to questionnaire. Scores range from 0 to 100 (the greater the score, the greater the degree of symptoms).

Table 5
Hamburg Modification—Comparison of patients who continued alcohol consumption and abstainers: Follow-up of the pain score of the surviving patients.

Pain score	Alcohol ($n = 154$)		Nonalcohol ($n = 252$)		P value
	Median	Range	Median	Range	
Frequency of pain attacks	25	0–100	0	0–100	< .001
Visual analogue scale	1	0–100	0	0–100	.084
Analgetic medication	1	0–100	0	0–100	.175
Inability to work	25	0–100	0	0–100	< .001
Pain score	**19**	**0–98**	**8**	**0–100**	**< .001**

Table 6
Hamburg modification—Comparison of patients who continued alcohol consumption and abstainers: Follow-up of the function scale scores of the surviving patients.

Functional scale*	Alcohol ($n = 154$)		Nonalcohol ($n = 252$)		P value
	Median	Range	Median	Range	
Physical status	80	0–100	90	0–100	.354
Working ability	100	0–100	100	0–100	.276
Cognitive functioning	100	0–100	100	0–100	.025
Emotional functioning	92	0–100	92	0–100	.004
Social functioning	83	0–100	100	0–100	.042
Global quality of life	92	0–100	92	0–100	.021

* Items corresponding to questionnaire. Scores range from 0 to 100 (the greater the score, the greater the functioning level).

also complained about fatigue, nausea, vomiting, dyspnea, sleep disturbance, and bloating more often than patients who underwent the Hamburg procedure. Obviously, many of these symptoms are not specific to measure procedure-related quality of life after DP-PHR for treatment of CP, but we continued to analyze these to be in line with other reports on the subject that also use the same symptoms as measurements.

Several items included in the pain score, such as frequency of pain attacks and analgesic medications, also appeared to be more favorable in the Hamburg group. The frequency of pain attacks, which was significantly less in the Hamburg group, may lead to the misunderstanding that there was no pain in this group. Considering that the items within the pain score are shown as medians with ranges and not as averages with standard deviations, a median of 0 (0–100) must not be interpreted as no pain. There were patients suffering from pain in the Hamburg group, especially regarding the high rate of continuous alcohol consumers, because continuing to drink alcohol was associated with more pain. An association between pain relief and quality of life is well known, but the exact cause is unknown. Thus, the outcomes concerning several items relating to quality of life, such as the ability to work and cognitive functioning, could be similar in both groups, and pain attacks appeared to be more common in the Beger or Frey group than in the Hamburg patients, because there is no one-to-one correlation between quality of life and pain.

Long-term mortality was found to be 10% in the Hamburg group, which was less than mortality rates reported for the natural course of the disease after 10 years (20%–35%).[34] It was also less than the mortality in the Beger or Frey group (19%). These results must be interpreted cautiously because of the differences between the cohorts. The Hamburg group was older (49.2 ± 11.1 years vs. 43.6 ± 10.5 years) and contained a greater rate of patients who continued consuming alcohol after the operation(37.9% vs 14.3%). Our retrospective analysis revealed an association between continued alcohol abuse and a greater pain score, worse quality of life, and worse symptom control. Thus, it reinforces the available evidence regarding alcohol consumption in chronic pancreatitis, which shows better results for pain control in abstainers from alcohol ingestion.[35,36]

Although cognitive, emotional, and social functioning and global quality of life were significantly worse in patients who continued consuming alcohol, the Hamburg modification was found to be superior compared with Beger or Frey in terms of emotional and social functioning and of global quality of life. Consequently, we assume that the 62% of the Hamburg procedure patients who ceased consuming alcohol had excellent results, thus having a high impact on the outcomes of the total group. Considering the fact that continuing alcohol consumers have worse long-term outcomes after operation compared with abstainers, the results of this study might have been even more different with equal rates of alcohol drinkers in both groups. This means that patients who have been treated with the Hamburg modification and did not continue consuming alcohol seemed to have excellent long-term outcomes. Of interest, continuing alcohol consumption after operation appeared to have no impact on recurrence rates, reoperation rates, and morbidity.

It is generally agreed that initial therapy for CP should be conservative and symptom-related. A variety of interventional therapies has been described, including endoscopic stone extraction, sphincterotomy, and ductal stenting. Operative treatment of CP is indicated in select patients because it is superior to endoscopic treatment in an RCT by Cahen et al.[10] Taking into consideration that an enlargement of the pancreatic head of less than 4 cm was defined as an inclusion criterion and that a Partington–Rochelle procedure instead of a DPPHR was performed, the advantage of operative intervention will be obvious.[2,10,37,38]

Recently, it was shown in a long-term follow-up that symptomatic patients suffering from progressive CP, who had initially been treated with the Partington-Rochelle procedure to eliminate pancreatic duct obstruction, experienced more pain relief than patients who had undergone endoscopic treatment first.[9,39,40]

Another RCT comparing endoscopic therapy with operative therapy with a 5-year follow-up was published by Dite et al.[11] The authors presented better outcomes after operative treatment with complete absence of pain in 37% of patients who had experienced either DPPHR or partial pancreatoduodenectomy as opposed to 14% of patients who had been treated endoscopically by sphincterotomy and stenting combined with stone removal or stone removal only.[11] Moreover, a greater increase in body weight of about 20% to 25% was observed in patients after operative treatment.[11]

When comparing endoscopic to operative intervention, Ahmed Ali et al.[37] found a lesser risk for development of exocrine insufficiency of the pancreas after operative treatment. It must be remembered, however, that the literature shows that, in the long-term, endocrine and exocrine pancreatic function cannot be retained by any DPPHR, despite the organ-sparing character of the procedures, but endocrine function appears to be preserved for a greater time.[20,21] Potentially, exocrine and endocrine pancreatic function may improve if operative intervention is performed earlier during the course of the disease.[41]

A total of 6 RCTs comparing different modifications of the DP-PHR with pylorus-preserving pancreatoduodenectomy (PPPD) have been published to date.[12,13,42–45] The Beger procedure was shown

to be superior to PPPD in terms of recuperation and postoperative hormonal status in a RCT, as reported by Klempa et al.[42] The short-term follow-up of an RCT published by Buchler et al.[12] found several advantages of the Beger procedure related to pain relief, quality of life, and increase in body weight, whereas this superiority was not be confirmed in the 14-year follow-up published by Muller et al.[46] Izbicki et al.[13] found the Frey procedure to be superior to PPPD, but Strate et al.[47] published a 7-year follow-up of the same RCT, reporting no significant differences between the two groups in relation to endocrine and exocrine insufficiency, need for reintervention, and mortality. The 15-year long-term follow-up reported by Bachmann et al.[23] showed survival to be significantly better in the Frey group, and both groups seemed to be comparable in terms of pain control and quality of life. The authors favored the organ-sparing procedure because of its better survival and short-term results.[23] Farkas et al.[43] published an RCT comparing PPPD with the Berne modification of the DPPHR reporting on lesser morbidity, greater increase in body weight, shorter operating time, and lesserh ospital stay in patients undergoing the Berne modification.[48]

These results from the RCTs suggesting DPPHR to be superior to pancreatoduodenectomy, however, were not confirmed by the multicenter, randomized, controlled, double-blind ChroPac trial.[44,49] Indeed, no differences were found between the groups concerning quality of life 24 months after operation.[49]

Keck et al.[45] published a prospective randomized trial comparing short-term and long-term outcomes for the Beger and Frey procedures with PPPD. Except for shorter operating times for DPPHR (360 vs 435 minutes), there were no significant differences concerning the need for intraoperative blood transfusions, duration of hospital stay, postoperative and surgical complications, need for reoperation, and pancreatic leakage in short-term follow-up; moreover, there were no differences in pain control, quality of life, or exocrine and endocrine insufficiency in the long-term follow-up.[45]

A meta-analysis published in 2008 revealed no significant differences between DPPHR and PPPD concerning postoperative pain relief, endocrine insufficiency, and overall morbidity, but Diener et al. preferred DPPHR with respect to better perioperative and postoperative outcomes and quality of life.[50]

Until now, only two RCTs have been published comparing different modifications of DPPHRs with one another.[8,22,27] Izbicki et al.[27] initiated an RCT comparing the Beger and the Frey procedures and presented outcomes up to a mean follow-up time of 1.5 years. Apart from a significantly greater perioperative morbidity rate in the Beger group (15% versus 9%), both groups were comparable in terms of pain control, quality of life, endocrine and exocrine insufficiency, and control of complications affecting surrounding organs.[27] The 8-year follow-up of this trial was published by Strate et al.,[47] where the authors observed a mortality rate of 22%, which is greater than our mortality (10%) with the Hamburg modification. Both procedures were comparable in mortality, pain control, quality of life, and endocrine and exocrine insufficiency.[20] The same applied to the 16-year long-term follow-up published by Bachmann et al.[2]

Another RCT comparing the Beger procedure the and Berne modification was performed by Koninger et al.,[22] revealing no significant differences between the two procedures with respect to complications, need for blood transfusions, and reoperation rates.[8] There were significant differences in relation to operating time, duration of hospital stay, and postoperative quality of life using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Pancreatic Cancer, favoring outcomes with the Berne modification in the short-term.[22] The 10-year follow-up recently published by Klaiber et al.[21] showed no significant differences between both procedures.

Our report is the first analysis presenting long-term outcomes of the Hamburg modification, confirming existing evidence on the advantageous long-term results of DPPHRs in the treatment of chronic pancreatitis. This modification appears to be a good alternative to other techniques of DPPHR, with adequate long-term results with respect to pain control, quality of life, and symptom control.

Our study has several limitations. First, this is a retrospective study, but the follow-up is remarkably complete. Second, other than pain relief and quality of life, the recurrence rate of chronic pancreatitis leading to the need for reoperative intervention is quite low. Although these patients required a technically demanding operation, with relevant morbidity, such as a repeat DPPHR, pancreatoduodenectomy, or total pancreatectomy, the rate was significantly less after use of the Hamburg modification (7.6%) compared with the results of the Beger and Frey procedures in which the rate of reoperation in published data was 5%–35%.

A limitation of this analysis is that we do not have reliable data on the duration between onset of the disease and operation. But the indication for operative treatment of CP in our medical center is late-stage pancreatitis, as the early stage is treated by the gastroenterologist conservatively or with endoscopy, similar to the step-up approach.[41,51] Considering the high rate of patients continuing excessive alcohol consumption after the Hamburg modification (37.9%), the long-term outcome of this modification is excellent.

In conclusion, DPPHR provides adequate outcomes concerning pain control, quality of life, and symptom control. In this retrospective analysis, the Hamburg modification of the Frey procedure was found to be an excellent alternative to the other forms of DPPHR. The choice of a certain modification ultimately depends on the surgeon's expertise and the individual needs of the patient.

Authors contribution

E. Bellon and M. Roswora contributed equally to this work.

References

1. Sarles H, Bernard JP, Gullo L. Pathogenesis of chronic pancreatitis. *Gut*. 1990;31:629–632.
2. Bachmann K, Tomkoetter L, Erbes J, Hofmann B, Reeh M, Perez D, et al. Beger and Frey procedures for treatment of chronic pancreatitis: Comparison of outcomes at 16-year follow-up. *J Am Coll Surg*. 2014;219:208–216.
3. Mayerle J, Lerch MM. Is it necessary to distinguish between alcoholic and non-alcoholic chronic pancreatitis? *J Gastroenterol*. 2007;42(Suppl 17):127–130.
4. Lowenfels AB, Maisonneuve P, Cavallini G, Ammann RW, Lankisch PG, Andersen JR, et al. Prognosis of chronic pancreatitis: An international multicenter study. International Pancreatitis Study Group. *Am J Gastroenterol*. 1994;89:1467–1471.
5. Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. *Pancreas*. 1987;2:701–707.
6. Beger HG, Witte C, Krautzberger W, Bittner R. Experiences with duodenum-sparing pancreas head resection in chronic pancreatitis. [In German.]. *Chirurg*. 1980;51:303–307.
7. Strobel O, Buchler MW, Werner J. Surgical therapy of chronic pancreatitis: Indications, techniques and results. *Int J Surg*. 2009;7:305–312.
8. Koninger J, Seiler CM, Wente MN, Reidel MA, Gazayakan E, Mansmann U, et al. Duodenum preserving pancreatectomy in chronic pancreatitis: Design of a randomized controlled trial comparing two surgical techniques [ISRCTN50638764]. *Trials*. 2006;7:12.
9. Cahen DL, Gouma DJ, Laramee 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;141:1690–1695.
10. 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;356:676–684.
11. Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy*. 2003;35:553–558.
12. Buchler MW, Friess H, Muller MW, Wheatley AM, Beger HG. Randomized trial of duodenum-preserving pancreatic head resection versus pylorus-preserving Whipple in chronic pancreatitis. *Am J Surg*. 1995;169:65–69 discussion 69–70.

13. 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 pancreticojejunostomy combined with local pancreatic head excision with the pylorus-preserving pancreatoduodenectomy. *Ann Surg*. 1998;228:771–779.
14. Izbicki JR, Bloechle C, Knoefel WT, Rogiers X, Kuechler T. Surgical treatment of chronic pancreatitis and quality of life after operation. *Surg Clin North Am*. 1999;79:913–944.
15. Beger HG, Buchler M. Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis with inflammatory mass in the head. *World J Surg*. 1990;14:83–87.
16. Hackert T, Schneider L, Buchler MW. Surgical approach to chronic pancreatitis: draining and resection procedure. [In German.]. *Chirurg*. 2013;84:112–116.
17. Gloor B, Friess H, Uhl W, Buchler MW. A modified technique of the Beger and Frey procedure in patients with chronic pancreatitis. *Dig Surg*. 2001;18:21–25.
18. Bellon E, Izbicki JR, Bockhorn M. Pancreatic anastomosis in operative treatment of chronic pancreatitis. [In German.]. *Chirurg*. 2017;88:18–24.
19. Izbicki JR, Bloechle C, Broering DC, Kuechler T, Broelsch CE. Longitudinal V-shaped excision of the ventral pancreas for small duct disease in severe chronic pancreatitis: Prospective evaluation of a new surgical procedure. *Ann Surg*. 1998;227:213–219.
20. Strate T, Taherpour Z, Bloechle C, Mann O, Bruhn JP, Schneider C, et al. Long-term follow-up of a randomized trial comparing the beger and frey procedures for patients suffering from chronic pancreatitis. *Ann Surg*. 2005;241:591–598.
21. Klaiber U, Alldinger I, Probst P, Bruckner T, Contin P, Koninger J, et al. Duodenum-preserving pancreatic head resection: 10-year follow-up of a randomized controlled trial comparing the Beger procedure with the Berne modification. *Surgery*. 2016;160:127–135.
22. Koninger J, Seiler CM, Sauerland S, Wente MN, Reidel MA, Muller MW, et al. Duodenum-preserving pancreatic head resection—A randomized controlled trial comparing the original Beger procedure with the Berne modification (ISRCTN No. 50638764). *Surgery*. 2008;143:490–498.
23. 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;258:815–820 discussion 820–1.
24. Traverso LW, Longmire Jr WP. Preservation of the pylorus in pancreaticoduodenectomy. *Surg Gynecol Obstet*. 1978;146:959–962.
25. Kutup A, Vashist Y, Kaifi JT, Yekebas EF, Izbicki JR. For which type of chronic pancreatitis is the "Hamburg procedure" indicated? *J Hepatobiliary Pancreat Sci*. 2010;17:758–762.
26. Bachmann K, Mann O, Izbicki JR. Surgery in chronic pancreatitis. *G Chir*. 2012;33:5–9.
27. 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. *Ann Surg*. 1995;221:350–358.
28. Bachmann K, Kutup A, Mann O, Yekebas E, Izbicki JR. Surgical treatment in chronic pancreatitis timing and type of procedure. *Best Pract Res Clin Gastroenterol*. 2010;24:299–310.
29. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85:365–376.
30. Bloechle C, Izbicki JR, Knoefel WT, Kuechler T, Broelsch CE. Quality of life in chronic pancreatitis—Results after duodenum-preserving resection of the head of the pancreas. *Pancreas*. 1995;11:77–85.
31. Frey CF, Pitt HA, Yeo CJ, Prinz RA. A plea for uniform reporting of patient outcome in chronic pancreatitis. *Arch Surg*. 1996;131:233–234.
32. Yekebas EF, Bogoevski D, Honarpisheh H, Cataldegirmen G, Habermann CR, Seewald S, 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. *Ann Surg*. 2006;244:940–946 discussion 946-8.
33. Bachmann K, Mann O, Izbicki JR, Strate T. Chronic pancreatitis—A surgeons' view. *Med Sci Monit*. 2008;14:RA198–RA205.
34. Lankisch PG, Lohr-Happe A, Otto J, Creutzfeldt W. Natural course in chronic pancreatitis. Pain, exocrine and endocrine pancreatic insufficiency and prognosis of the disease. *Digestion*. 1993;54:148–155.
35. Ammann RW, Largiader F, Akovbiantz A. Pain relief by surgery in chronic pancreatitis? Relationship between pain relief, pancreatic dysfunction, and alcohol withdrawal. *Scand J Gastroenterol*. 1979;14:209–215.
36. Leger L, Lenriot JP, Lemaigre G. Five to twenty year followup after surgery for chronic pancreatitis in 148 patients. *Ann Surg*. 1974;180:185–191.
37. Ahmed Ali U, Pahlplatz JM, Nealon WH, van Goor H, Gooszen HG, Boermeester MA. Endoscopic or surgical intervention for painful obstructive chronic pancreatitis. *Cochrane Database Syst Rev*. 2015;19.
38. van der Gaag NA, Gouma DJ, van Gulik TM, Busch OR, Boermeester MA. Review article: Surgical management of chronic pancreatitis. *Aliment Pharmacol Ther*. 2007;26(Suppl 2):221–232.
39. Adler DG, Lichtenstein D, Baron TH, Davila R, Egan JV, Gan SL, et al. The role of endoscopy in patients with chronic pancreatitis. *Gastrointest Endosc*. 2006;63:933–937.
40. Dumonceau JM, Costamagna G, Tringali A, Vahedi K, Delhaye M, Hittelet A, et al. Treatment for painful calcified chronic pancreatitis: Extracorporeal shock wave lithotripsy versus endoscopic treatment: A randomised controlled trial. *Gut*. 2007;56:545–552.
41. Ahmed Ali U, Issa Y, Bruno MJ, van Goor H, van Santvoort H, Busch OR, et al. Early surgery versus optimal current step-up practice for chronic pancreatitis (ESCAPE): Design and rationale of a randomized trial. *BMC Gastroenterol*. 2013;13:49.
42. Klempa I, Spatny M, Menzel J, Baca I, Nustede R, Stockmann F, 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. [In German.]. *Chirurg*. 1995;66:350–359.
43. Farkas G, Leindler L, Daroczi M, Farkas Jr G. Prospective randomised comparison of organ-preserving pancreatic head resection with pylorus-preserving pancreaticoduodenectomy. *Langenbecks Arch Surg*. 2006;391:338–342.
44. Diener MK, Bruckner T, Contin P, Halloran C, Glanemann M, Schlitt HJ, 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.
45. Keck T, Adam U, Makowiec F, Riediger H, Wellner U, Tittelbach-Helmrich D, et al. Short- and long-term results of duodenum preservation versus resection for the management of chronic pancreatitis: A prospective, randomized study. *Surgery*. 2012;152(3 Suppl 1):S95–102.
46. Muller 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. *Br J Surg*. 2008;95:350–356.
47. Strate T, Bachmann K, Busch P, Mann O, Schneider C, Bruhn JP, et al. Resection vs drainage in treatment of chronic pancreatitis: Long-term results of a randomized trial. *Gastroenterology*. 2008;134:1406–1411.
48. Farkas G, Leindler L, Daroczi M, Farkas Jr G. Long-term follow-up after organ-preserving pancreatic head resection in patients with chronic pancreatitis. *J Gastrointest Surg*. 2008;12:308–312.
49. Diener MK, Huttner FJ, Kieser M, Knebel P, Dorr-Harim C, Distler M, et al. Partial pancreatoduodenectomy versus duodenum-preserving pancreatic head resection in chronic pancreatitis: The multicentre, randomised, controlled, double-blind ChroPac trial. *Lancet*. 2017;390:1027–1037.
50. 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. *Ann Surg*. 2008;247:950–961.
51. 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 option. [In Dutch.]. *Ned Tijdschr Geneeskd*. 2017;161:D1454.