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12-letnie doświadczenie w resekcji głowy trzustki z oszczędzaniem dwunastnicy i trzustki (modyfikacja Buchler-Farkasa) w chirurgicznym leczeniu przewlekłego zapalenia trzustki u 180 chorych

12-year experience with duodenum and organ-preserving pancreatic head resection (Büchler-Farkas modification) in the surgical treatment of 180 patients with chronic pancreatitis

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Streszczenie**Wstęp.** Przewlekłe zapalenie trzustki jest łagodnym, zapalnym procesem chorobowym odpowiedzialnym za powiększenie głowy trzustki, znaczne dolegliwości bólowe, postępującą utratę wagi ciała i istotne pogorszenie jakości życia (QoL).**Material i metody.** W pracy przedstawiono kliniczne doświadczenie związane z wykonywaniem resekcji głowy trzustki z zachowaniem dwunastnicy i oszczędzaniem mięszu trzustki (duodenum and organ-preserving pancreatic head resection – DOPPHR) u 180 chorych w okresie 12 lat. Oceniano jakość życia (QoL) w okresie pooperacyjnym z wykorzystaniem metody EORTC QoL-C 30.**Wyniki.** Średni czas operacji wynosił 165 minut. Nie obserwowano zgonów w okresie okołoperacyjnym. Z powodu powikłań pooperacyjnych (krwawienie z zespolenia i niedrożność jelit) zaistniała konieczność reoperacji u trzech chorych. Średni czas pobytu w szpitalu wynosił 7-12 dni. Średni czas obserwacji pooperacyjnej wynosił 6,5 lat (0,5-12 lat). 12 chorych zmarło w odległym okresie po operacji, tzw. późna śmiertelność wyniosła 6,7%.

Uzyskano poprawę jakości życia u 89% operowanych. 150 chorych było bezobjawowych, a u 18 chorych objawy chorobowe były miernie nasilone. W okresie pooperacyjnym obserwowano średni przyrost wagi ciała około 13,2 kg (zakres od 4-30 kg). Pooperacyjna czynność endokrynną trzustki była porównywalna do czynności przedoperacyjnej.

Wnioski. 12-letni okres doświadczeń w wykonywaniu operacji DOPPHR wykazał, że technika ta jest bezpieczna i skuteczna w chirurgicznym leczeniu powikłanego przewlekłego zapalenia trzustki.**Słowa kluczowe:** przewlekłe zapalenie trzustki, leczenie chirurgiczne, oszczędzanie dwunastnicy, eracyjna, jakość życia**Summary****Introduction.** Chronic pancreatitis (CP), a benign, inflammatory process, can cause enlargement of the pancreatic head, which is accompanied by severe pain and weight loss, and often leads to a significant reduction in the quality of life (QoL).**Material and methods.** Our clinical experience relates to the results attained with duodenum and organ-preserving pancreatic head resection (DOPPHR) in 180 patients during a 12-year period. The QoL is assessed during the follow-up period by using EORTC QoL-C30.**Results.** The mean operating time was 165 min. Three reoperations were required in consequence of anastomosis bleeding and small bowel obstruction, but no mortality was noted in the postoperative period. Duration of hospitalization ranged between 7 and 12 days. The mean follow-up time was 6.5 years (range 0.5-12.0). The late mortality rate was 6.7% (12 patients). The QoL improved in 89% of the cases. 150 of the patients became complaint-free, while 18 had moderate symptoms, and the weight increased by a median of 13.2 kg (range 4-30). The preoperative and postoperative endocrine functions remained in almost the same stage as preoperatively.**Conclusions.** This 12-year experience clearly demonstrates that this DOPPHR technique is a safe and effective procedure, which should be preferred in the surgical treatment of the complications of CP.**Key words:** chronic pancreatitis, surgery, duodenum and organ preservation, long-term follow up, quality of life**Introduction**

Chronic pancreatitis (CP) is a benign, inflammatory disease of the pancreas, which can

cause enlargement of the pancreatic head with severe pain and weight loss and often reduces the quality of life (QoL) significantly. The enlarged inflamed head of the pancreas can lead 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. The surgical treatment consists in different types of pancreatic head resection (1): pylorus-preserving pancreaticoduodenectomy (PPPD) (2), Beger's duodenum-preserving pancreatic head resection (DPPHR) (3), and Frey's longitudinal pancreaticojejunostomy combined with local pancreatic head excision (LPJ-LPHE) (4). PPPD and Beger's DPPHR involve total and subtotal resection of the pancreatic head, respectively, which can be regarded as too invasive in cases of benign disease and do not adhere to the modern organ-preserving concept. Twelve years ago, therefore, a new duodenum and organ-preserving pancreatic head resection (DOPPHR) method was developed, which is essentially suitable for this purpose (5-8). Preliminary clinical results achieved with this operation, together with follow-up findings, were published recently (9-11). The present article reports on late follow-up (mean, 6.5 years [range 0.5-12.0]) results attained with our DOPPHR on 180 patients, including QoL parameters.

Material and methods

Since 1999, we have performed a DOPPHR to treat inflammatory tumours of the pancreatic head (median diameter 68 mm [range 45-132 mm], as assessed by helical CT scan) in 180 patients (133 men and 47 women; mean age: 48.4 yr. [range 27-68]). The preoperative morbidity involved frequent, sometimes severe abdominal pain, a significant loss in body weight in all patients, jaundice in 10 patients, duodenal obstruction in 16 patients and latent (LDM) and insulin-dependent diabetes mellitus (IDDM) in 33 and 29 patients, respectively. The mean interval between the appearance of the symptoms and the surgical intervention was 7.9 ± 2.6 yr. **The aetiology was connected with chronic alcohol ingestion in 157 patients (87 per cent) and with biliary stone disease in 18 patients (10 per cent), and was unknown in 5 patients.** The diagnosis of CP was confirmed by ERCP, MRCP, sonography and the CT scan. ERCP reveals that the diameter of the main pancreatic duct varied between 2 and 8 mm. In 10 icteric patients and in 21 patients without jaundice, the common bile duct was stenotic, due to inflammatory tumour compression with prestenotic dilatation, combined with high levels of alkaline phosphatase (range 956-1345 U/L). The CT scan demonstrated parenchyma calcification in 95 patients; 27 patients exhibited pseudocystic cavities, and 4 patients portal hypertension (tab. 1).

Table 1. Clinical characteristics of 160 patients undergoing DOPPHR*.

Age (yr, mean, range)	48.4 (27-68)
Sex ratio (male/female)	133/47
Aetiology (per cent)	
Alcohol ingestion	157 (87)
Biliary stone	18 (10)
Unknown	5 (3)
Duodenal obstruction (per cent)	16 (8.9)
Head enlargement (per cent)	180 (100)
Pseudocystic cavity	27 (15)
Parenchymal calcification (per cent)	95 (52.7)
Bile duct obstruction (per cent)	31 (17.2)
Jaundice	10 (5.6)
Portal hypertension (per cent)	4 (2.2)
Pain intensity (per cent)	
Weak	10 (5.6)
Moderate	135 (75)
Severe	35 (19.4)
Preoperative weight (kg, mean, range)	50.2 (42-66)
Diabetes mellitus (per cent)	
None	118 (65.5)

Latent	33 (18.4)
Insulin-dependent	29 (16.1)

*Numbers of patients are shown, percentages given in parentheses.

Pancreatic functions were checked by means of stool elastase determination by a sandwich ELISA method (Pancreatic Elastase1[®], ScheBo Biotech, Giessen, Germany) (12). The glucose tolerance test was applied to check the endocrine function. Blood glucose levels were measured by means of glucose oxidase assay 0, 30, 60, 90 and 120 min following administration of 75 g oral glucose.

Prophylactic antibiotic (ceftriaxone) was administered preoperatively, and in the early postoperative period all of the patients received standard supportive treatment, consisting of total parenteral nutrition for 4 days, a proton pump antagonist (pantoprazole), suppression of TNF synthesis (pentoxifylline) and octreotide medication (13). The oral nutrition was started on postoperative day 5.

Operative procedure

The surgical procedure involved a wide local resection of the inflammatory tumour 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 manoeuvre, 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 icteric patients and in those 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 haemostasis of the operative region, reconstruction, with drainage of the secretion from the remaining pancreas into the intestinal tract, took place through a jejunal Roux-en-Y loop, with the application of one-layer interrupted Vicryl[®] 2/0 sutures (7) (fig. 1.)



Fig. 1. The operation consists in a wide local resection 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. In icteric cases, prepapillary bile duct anastomosis is also performed with the jejunal loop.

Quality of life

The QoL and pain score before and after surgery were assessed by using the European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire (QLQ-C30) (14). The EORTC QLQ-C30 has been re-evaluated and demonstrated to be a valid and reliable with tool which to measure the QoL in patients with benign diseases such as CPI5. It 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 analogue scale, the frequency of pain attacks, the use of analgesic medication, and the duration of the inability to work. The overall pain score was given by the sum of the individual part-scores 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 6.5 years after the operation.

Statistical analysis

The details of the statistical analysis are presented in the manuscript as follows: The results on the parametric data are expressed as means \pm standard deviation, and nonparametric data as medians. Statistical significance was estimated by using Student's t test or the Wilcoxon rank test, as appropriate. The level of significance was set at $P < 0.050$.

Results

In 180 patients, the DOPPHR procedure was performed after the development of an inflammatory tumour of the pancreatic head. The intraoperative parameters and post surgical events are listed in table 2. The mean operation time was 165 min (range 120-230 min) and there was no indication for blood transfusion during the operations. In the postoperative period, three reoperations were required in consequence of anastomosis bleeding (2 patients) and small bowel obstruction (1 patient). Another 3 patients with anastomosis bleeding were treated conservatively, and 1 patient had pneumonia, but

there was no septic complication, anastomosis insufficiency or other problem; the morbidity was therefore 3.9 per cent. There was no mortality in the postoperative period. In the 31 icteric and common bile duct stenotic patients (17.2 per cent), the liver functions normalized following the operation (serum bilirubin < 22 $\mu\text{mol/L}$, and alkaline phosphatase 232 ± 92 U/L; as compared with the preoperative data, the reduction was significant [$P = 0.048$]). The duration of hospitalization ranged between 7 and 12 days, by a mean of 8.5 days. The histological examinations confirmed fibrosis and calcification in 85 and 95 patients, respectively.

Table 2. Intraoperative parameters and early post surgical outcome after DOPPHR in 160 CP patients*.

Operative time (min, mean, range)	165 (120-230)
Intrapancreatic bile duct anastomosis (per cent)	31 (17.2)
Intraoperative blood transfusion	31 (17.2)
Intraoperative blood transfusion	0
Relaparotomy (per cent)	3 (1.7)
Anastomosis bleeding	2
Small bowel obstruction	1
Nonsurgical morbidity (per cent)	4 (2.2)
Bleeding treated conservatively	3
Pneumonia	1
Pancreatic fistula	0
Wound infection	0
Anastomosis leakage	0
Abscesses or fluid collection	0
Overall morbidity (per cent)	7 (3.9)
Mortality (per cent)	0 (0)
Post surgical hospital stay (day, mean, range)	8.5 (7-12)

*Numbers of patients are shown, percentages given in parentheses.

The mean follow-up period was 6.5 years (range 0.5-12.0). Twelve patients were lost to follow-up (6.7 per cent). Complete follow-up data on 168 patients were included in the evaluation; the follow-up rate was therefore 93.3 per cent. 150 patients became complaint-free (83.3 per cent), while 18 patients displayed moderate symptoms; and the body weight increased by a mean of 13.2 kg (range 4-30) ($P = 0.041$). In the long-term period, 9 patients underwent operation again: a bilio-digestive bypass was indicated in consequence of bile duct stenosis that developed in 7 patients, and distal pancreatic resection and splenectomy were performed in another 2 patients. In the follow-up period, a further 13 patients were admitted to the clinic with an acute episode of pancreatitis; all of them were treated conservatively. Readmission was therefore necessary in 22 of the 168 cases (13.1 per cent). The late mortality was 6.7 per cent (12 patients); the reasons were myocardial infarction in 5 patients, a stroke in 2 patients,

gastrointestinal tumour (oesophagus, stomach, and large-bowel) in 4 patients and an accident (1 patient) (tab. 3).

Table 3. Follow-up after DOPPHR (n = 149 patients)*.

Follow-up period (yr, mean, range)	6.5 (0.5-12.0)
Complete follow-up (per cent)	168 (93.3)

Late mortality (pts, per cent)	12 (6.7)
Pain (per cent)	18 (10)
Pain intensity (per cent)	
None	150 (89)
Moderate	18 (10)
Readmission (per cent)	22 (13.1)
Late reoperation (per cent)	9 (5)
Bilio-digestive bypass	7
Distal pancreatic resection	2
Acute pancreatitis (per cent)	13 (7.2)
Late morbidity (per cent)	22 (12.2)
Body weight increase (kg, mean, range)	13.2 (4-30)
Diabetes mellitus (per cent)	
None	97 (57.7)
Latent	22 (13)
Insulin-dependent	49 (29.3)

*Numbers of patients are shown, percentages given in parentheses.

The stool elastase level increased slightly, but not significantly (from 124.3 ± 33 to 132 ± 39 $\mu\text{g/g}$; NS). The preoperative and postoperative endocrine functions were in almost the same stage: 97 patients were normoglycemic, 22 had LDM and 39 had IDDM, in 10 patients LDM becoming IDDM (6.6 per cent).

Both before the operation and during the follow-up, the patients were asked to complete the EORTC QLQ-C30 questionnaire. The completed questionnaires before and after the surgical treatment were evaluated in 134 patients (74 per cent). The other patients were excluded from the evaluation because of incomplete data or a lack of cooperation, or the data on the patients were not available. The questionnaire was compared at two time points: (1) before the operation and (2) at a mean follow-up of 6.5 years (range 0.5-12) after surgery. The median pain score decreased by 90 per cent ($P = 0.001$). No patient subsequently suffered a frequent pain attack and only 10 per cent of the patients mentioned moderate pain occasionally (tab. 4). During the follow-up, the median global QoL improved by 100 per cent. Apart from the cognitive functioning, the physical status, working ability, emotional and social functioning all improved significantly ($P = 0.046$). The results of the symptom scales are presented in table 5.

Table 4. Preoperative and follow-up pain scores (n = 134).

Criterion	Preoperative score (median [range])	Follow-up score (median [range])	P*
Pain visual analogue scale	82 (55-100)	10 (0-15)	
Frequency of pain attack	75 (50-100)	12.5 (0-15)	
Pain medication	22 (20-100)	0 (0-100)	
Inability to work	76 (75-100)	4 (0-100)	
Pain score	65 (50-100)	5.6 (0-37.5)	0.001

*Preoperative values were compared with follow-up values by the Wilcoxon rank sum test ($P < 0.001$).

Table 5. EORTC QLQ-C30 preoperative and follow-up functioning scale scores (n = 134).

Functioning scale	Preoperative score (median [range])	Follow-up score (median [range])	P*
Physical status	60 (20-100)	70 (20-100)	0.049
Working ability	49 (0-100)	71 (0-100)	0.048

Cognitive	50 (40-80)	66 (40-100)	0.190 NS
Emotional	25 (0-75)	66.7 (40-100)	0.045
Social	16 (0-66.7)	65.7 (0-100)	0.040
Overall quality of life	28.5 (14.3-57.1)	57.5 (33.3-100)	0.046

*Preoperative values were compared with follow-up values by the Wilcoxon rank sum test ($P < 0.05$); NS: not significant.

Discussion

Patients with CP who present with inflammatory pancreatic head enlargement commonly require pancreatic head resection because of the development of local complications (eg. stenosis of the common bile duct and/or main pancreatic duct, duodenal obstruction) and persistent, uncontrolled pain. The aims of surgical therapy, therefore, are pain relief, the management of CP-associated complications of adjacent organs, and the possibility for preservation of the endocrine and exocrine functions with reasonably low morbidity rates, and finally, it is important to improve the patients' overall QoL and physical status, and also to provide for their social and occupational rehabilitation (16). For several decades, 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 QoL improvement following these operations were disappointing, with high rates of late morbidity and mortality and with a high incidence (up to 48 per cent) of postoperative DM (17). Although two recently published articles have described better results (18, 19), it is generally accepted that these operations, involving the removal of healthy adjacent organs, do not seem to be warranted in this benign disease unless there is a strong suspicion of cancer (20).

In 1972, Beger performed a more effective organ-preserving procedure, DPPHR, which preserves the entire duodenum and reduces the incidence of postsurgical DM (3). In

1987, Frey et al. described a modification of this procedure, in which resection and drainage were combined into a single procedure (LPJ-LPHE) (4). In both operations, 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 (21-23). Since 1995, some important randomized studies have compared the different types of pancreatic head resection. Büchler demonstrated better pain relief and a better pancreatic function when DPPHR was compared with PPPD (24). Almost the same results were reported by Klempa, who compared DPPHR and PD: the degree of pain relief was the same, but the recovery was quicker and the pancreatic function became better after Beger's operation (25). Möbius et al. reached the same results but in a prospective non-randomized study (26). 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 identical, but the QoL was better following Frey's operation (27, 28). Recently published articles based on the long-term follow-up of randomized trials have concluded that there was no difference between the two operations as regards the mortality, QoL, pain, or exocrine or endocrine insufficiency 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 (29-31). The recent systematic review and meta-analysis by Diener et al. came to the same conclusion: DPPHR and PD seem to be equally effective in terms of the postoperative pain relief, the overall morbidity, and the incidence of postoperative endocrine insufficiency. However, the presented findings suggested the superiority of DPPHR in the treatment of CP with regard to several peri- and postoperative outcome parameters and the QoL (32).

In approximately 30 per cent of patients with CP, the disease is primarily located in the head of the pancreas, which is considered to act as the pacemaker to trigger the inflammatory process; resection of this inflammatory mass must be regarded as pivotal in the surgical intervention (1). Basically, CP is a benign, but sometimes progressive disease, and the duodenum and organ-preserving concept must therefore be accepted. The resection process removes only sufficient of the pancreatic head to guarantee the flow of both ductal systems (the bile and the pancreas) so as to preserve the physiological gastroduodenal and the endocrine functions. In the past six years, a number of publications have proved that the concept for DOPPHR is correct (7-10, 29-30, 33).

The results of two recent prospective randomized control trials which compared DOPPHR with either PPPD or DPPHR demonstrated that DOPPHR is superior to both PPPD and DPPHR not only in the operation data and morbidity, but also in the QoL achieved (34-35).

The present article is concerned with our late follow-up (on average 6.5 years [range 0.5-12.0]) results attained with DOPPHR on 180 patients. These data demonstrated that DOPPHR is a safe operative procedure, as confirmed by the low morbidity (3.9 per cent) and the absence of mortality among the patients in the postoperative period. An additional important feature is the fact that the mean duration of hospitalization was only 8.5 days. In the mean follow-up period of 6.5 years, 150 patients became complaint-free (89 per cent), while 18 displayed only moderate symptoms and the body weight increased significantly by a mean of 13.2 kg (range 4-30). Readmission was required for 22 of the 168 patients (13 per cent) as a consequence of relaparotomy (a bilio-digestive bypass or distal pancreatic resection) or conservatively treated pancreatitis. The late mortality was 6.7 per cent: 12 patients died. The postoperative endocrine function remained in almost the same stage as preoperatively.

The degree of pain relief and the extent of improvement in 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 134 patients (79.7 per cent). The median pain score was found to have decreased by 90 per cent ($P = 0.001$). No patient subsequently suffered from frequent pain attacks and only 10 per cent of them mentioned occasional moderate pain. During the follow-up, the median global QoL improved by 100 per cent. Apart from the cognitive functioning, the physical status, working ability, and emotional and social functioning all improved significantly ($P = 0.046$).

The early and long-term results of DOPPHR operations indicate the advantage of this procedure in a wide scale of indications, involving different pathologic processes, e.g. a subacute or chronic inflammation mass with a pseudocyst, ductal stenosis or obstruction (of the common bile duct or the pancreatic duct) caused by CP.

In conclusion, the results of our clinical study clearly demonstrate that DOPPHR is a safe and effective procedure for resolving the complications following the inflammatory alterations of CP, and suggest that this operation furnishes effective early and late long-term results, mainly with regard to the QoL. However, in the future, a multicentre, randomized controlled trial comparing resection procedures with organ-preserving technique will be expected to provide more data on the best surgical opinion for patients with CP36.

Piśmiennictwo

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