Randomized clinical trial of pylorus-preserving duodenopancreatectomy *versus* classical Whipple resection – long term results

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Background: It is not known whether pylorus-preserving duodenopancreatectomy is as effective as the classical Whipple procedure in the resection of pancreatic and periampullary tumours. A prospective randomized trial was undertaken to compare the results of the two procedures.

Methods: Clinical data, histological findings, short-term results, survival and quality of life of all patients having surgery for suspected pancreatic or periampullary cancer between June 1996 and September 2001 were analysed.

Results: Two hundred and fourteen patients were randomized to undergo either a standard or a pylorus-preserving Whipple resection. After exclusion of 84 patients on the basis of intraoperative findings, 130 patients (66 standard Whipple operation and 64 pylorus-preserving resection) were entered into the trial. Of these, 110 patients with proven adenocarcinoma (57 standard Whipple and 53 pylorus-preserving resection) were analysed for long-term survival and quality of life. There was no difference in perioperative morbidity. Long-term survival, quality of life and weight gain were identical after a median follow-up of 63·1 (range 4–93) months. At 6 months, capacity to work was better after the pylorus-preserving procedure (77 *versus* 56 per cent; $P = 0.019$).

Conclusion: Both procedures were equally effective for the treatment of pancreatic and periampullary cancer. Pylorus-preserving Whipple resection offers some minor advantages in the early postoperative period, but not in the long term.

Introduction

Advances in surgical technique have reduced the operative mortality rate of patients undergoing pancreatic head resection to below 5 per cent in specialist centres[1,2]. Improvements in long-term survival for patients with pancreatic and other periampullary cancers have been less marked. Because of the relative resistance of these tumours to chemotherapy and radiotherapy, any attempt to achieve a cure must include radical resection. Unfortunately, only a minority of patients are candidates for resection as a result

of late presentation and early metastasis. Even after surgery with curative intent, most patients develop early recurrence with rapid physical and psychological deterioration. The 5-year survival rate after resection for pancreatic cancer is between 10 and 15 per cent in recent large series[3,4].

For many years, the surgical procedure of choice was duodenopancreatectomy, the classical operation described by Kausch[5] and Whipple[6]. This operation has a number of side-effects related to the partial gastric resection, notably postoperative weight loss and dumping syndromes. A more conservative procedure, pylorus-preserving Whipple resection, was first performed for the treatment of periampullary cancer by Watson in 1943 and reported

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The Editors have satisfied themselves that all authors have contributed significantly to this publication

the following year[7]. The procedure was later popularized by Traverso and Longmire[8]. Although originally described for the treatment of periampullary tumours, many surgeons have used the pylorus-preserving procedure for cancer of the pancreatic head[9]. There is no evidence from prospective studies to indicate that pylorus-preserving duodenopancreatectomy is oncologically as effective as the classical Whipple resection but with fewer side-effects. Roder et al.[10] reported a reduced survival rate after pylorus-preserving resection in patients with International Union Against Cancer (UICC) stage III pancreatic cancer in a retrospective analysis, although other studies have failed to show a difference in survival for patients with comparable tumour stages[11-13].

As survival is limited for the' majority of patients undergoing pancreatic head resection for cancer, other outcomes that influence quality of life become important. There is no clear evidence that preservation of the pylorus leads to superior postoperative recovery[1,13]. The main advantages of the pylorus-preserving technique appear to be the shorter operating time and reduced blood loss as a result of omission of gastric resection. Furthermore, access to the biliary anastomosis for postoperative endoscopic investigations may be easier than with the standard Whipple resection[14]. On the other hand, postoperative gastric ulceration has been claimed to be a common complication of the pylorus-preserving procedure, although recent data have not confirmed this[15]. Concerns that disturbed postoperative gastric function may result in significantly delayed gastric emptying (DGE) have not been supported by recent studies[10,15,16]. The question of differences in weight gain and quality of life after the two types of resection remains unanswered[1,13].

Only one randomized clinical trial comparing classical and pylorus-preserving Whipple resection, with 15 patients in each group, has been published previously[17]. The present randomized prospective trial was conducted in an unselected and consecutive group of patients referred to the Department of Visceral and Transplantation Surgery at the University of Berne with suspected pancreatic or periampullary cancer.

Patients and methods

This report was prepared in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement[18].

The study protocol was approved by the ethics committee of the University of Berne and consisted of a standard pretreatment evaluation, randomization

to classical or pylorus-preserving Whipple resection, assessment of in-hospital postoperative findings and analysis of outcome at 3-month intervals until 60 months after surgery or death.

All patients suitable for surgery, with suspected pancreatic or periampullary cancer considered resectable on the basis of either computed tomography or magnetic resonance imaging, with no history of previous gastric resection, were included.

Patients with direct tumour invasion of the proximal duodenum, pylorus or stomach were excluded, as were those with peripyloric lymph node metastases confirmed by intraoperative frozen-section examination. Patients with lymph node metastases other than in the peripyloric region were included in the randomization. Patients with distant metastases or tumours that were locally irresectable owing to major retroperitoneal infiltration seen at operation were also excluded. Those requiring an emergency resection were not included. All remaining patients were included in the analysis of efficacy. For long-term evaluation and analysis of survival, patients with lesions other than pancreatic or periampullary adenocarcinoma were excluded.

Before surgery all patients underwent detailed physical examination with haematological and biochemical assessments including measurement of the tumour markers carcinoembryonic antigen (CEA) and CA19-9. Cardiopulmonary function was evaluated by lung spirometry and ergometry. Perioperative risk was classified according to the American Society of Anesthesiologists system[19]. Patients with jaundice underwent preoperative endoscopic retrograde cholangiopancreatography with stent placement in the common bile duct if technically feasible.

Equal numbers of envelopes with detailed protocols for the classical or pylorus-preserving Whipple resection were prepared in a blinded fashion. Envelopes were used sequentially as patients were enrolled in the study and the randomization was carried out the evening before operation to rule out any influence on selection based on intraoperative findings. Envelopes for patients excluded from the study were discarded.

A detailed description of the surgical procedures has been published previously[20]. All patients received a prophylactic antibiotic regimen consisting of 4 g piperacillin (Pipril®; Lederle, Zug, Switzerland) and 1 g ornidazole (Tiberal®; Roche Pharma, Reinach, Switzerland). Octreotide (Sandostatin®; Novartis Pharma, Basle, Switzerland) 100–200 µg subcutaneously was administered three times daily to all patients starting at the time of surgery and continuing for 7 days. Both operations were carried out in combination with a standard lymph node

dissection of the coeliac trunk, hepatoduodenal ligament, superior mesenteric vein, right side of the superior mesenteric artery and the lymphatic tissue behind the pancreatic head. Blood loss and operating time were noted immediately after surgery. All operative specimens underwent intraoperative frozen-section examination, with definitive histological study after surgery. Where intraoperative examination detected positive resection margins, a wider resection was carried out if possible to include a partial portal vein resection or a more distal resection of the pancreas. If total pancreatectomy was performed to achieve clear resection margins, the patient was excluded from the study.

Tumour stage was determined according to the UICC classification and the tumour node metastasis (TNM) system[20]. The postoperative treatment protocol followed general principles of surgical and supportive care, described in detail elsewhere[21,22]. Mortality, and surgical and non-surgical morbidity were recorded prospectively. DGE was defined as a persistent drainage via the nasogastric tube of more than 500 ml/day for at least 5 days after surgery, or recurrent vomiting in combination with oedema of the gastrojejunostomy or duodenojejunostomy and proximal dilatation on contrast radiography. A pancreatic fistula was defined as secretion of 30 ml or more of amylase-rich drainage fluid (more than 5000 units/l) per day for at least 10 days.

Follow-up at 3-month intervals comprised physical examination, laboratory tests including determination of CEA and CA19-9, estimation of tumour recurrence and survival. Quality of life was recorded using a standard questionnaire, the Sickness Impact Profile (SIP), which was developed and validated for estimation of quality of life independent of the underlying disease and has been used extensively in this department[23]. The questionnaire consists of 136 statements; scores are expressed as a percentage of possible disability, with 0 indicating no impairment and 100 representing total incapacity. Patients with a score of 0–10 do well in daily life, those with a score of 11–20 show mild illness-related dysfunction and those with a score greater than 20 are clearly impaired in daily activities.

Patient details, including adverse events, tumour recurrence and any deaths, were documented on the patient record form and were entered into a database (SPSS®; SPSS, Chicago, Illinois, USA). The primary outcome variable was perioperative morbidity (intraoperative and postoperative). Other variables analysed were non-surgical complications, intraoperative blood loss, blood replacement, operating time, survival, tumour recurrence,

postoperative weight, time before return to work or normal daily activities, and quality of life.

Statistical analysis

A power calculation indicated that 58 patients needed to be enrolled for each procedure to detect a 25 per cent difference in morbidity at the two-tailed 5 per cent significance level with a power of 80 per cent. χ^2 or Fisher's exact test (where $n < 5$) was applied for categorical data and the Mann–Whitney U test for numerical data. The Kaplan–Meier method was used to analyse survival and levels of significance were tested with the log rank test. After enrolling more than 110 patients, an interim analysis was performed to compare early clinical (postoperative) results, including operating time, blood loss and blood replacement[20]. The perioperative outcome after reaching the required number of patients is summarized, in addition to long-term findings (tumour recurrence, survival, postoperative weight and quality of life). Survival data are expressed as median values with 95 per cent confidence intervals unless otherwise stated.

Results

Between June 1996 and September 2001, 214 consecutive patients with suspected pancreatic or periampullary tumours were enrolled in the study. Their demographic details are shown in *Table 1* (intention-to-treat analysis). If no radiological evidence of metastatic disease was found, surgical exploration was undertaken. As a result of intraoperative findings, 84 patients (39·3 per cent) were excluded. Forty-four patients had irresectable disease (previously undetected distant metastases or locally irresectable tumour). Twenty-one patients had other types of resection (total pancreatectomy, ten; distal resection, seven; segmental or local resection, four). A pylorus-preserving Whipple resection was not possible in 11 patients because of tumour infiltration of the proximal duodenum or positive peripyloric lymph nodes. Frozen-section examination revealed benign pancreatic lesions in eight patients.

The remaining 130 patients (valid for efficacy analysis) underwent pancreatic resection according to the randomization protocol. Patient characteristics (*Table 2*) and histological findings (*Table 3*) were similar in the two groups. Four patients in whom pancreatic cancer was diagnosed at intraoperative frozen-section examination were shown on histological study to have chronic pancreatitis; these patients were retained in the efficacy analysis. Operating time, blood loss and the volume of blood transfused were all significantly less with the pylorus-preserving

Table 1 Patient demographics (intention-to-treat analysis)

	Total (n = 214)	Standard Whipple (n = 109)	Pylorus-preserving Whipple (n = 105)	P
Men	123 (57·5)	57 (52·3)	66 (62·9)	0·173§
Women	91 (42·5)	52 (47·7)	39 (37·1)	0·173§
Age (years)*	64·9 (26–86)	65·4 (33–86)	65·4 (26–83)	0·450¶
ASA grade				
I–II	149 (69·6)	73 (67·0)	76 (72·4)	0·258§
III–IV	65 (30·4)	36 (33·0)	29 (27·6)	0·258§
Bodyweight (%)*†	93·4 (75–100)	93·4 (75–100)	93·0 (80–100)	0·125¶
Duration of symptoms (weeks)*	8·0 (0–200)	8·0 (1–200)	6·0 (1–180)	0·357¶
Diabetes	37 (17·3)	20 (18·3)	17 (16·2)	0·556§
Cardiac disease	32 (15·0)	19 (17·4)	13 (12·4)	0·761§
COAD	22 (10·3)	8 (7·3)	14 (13·3)	0·184§
Jaundice‡	57 (26·6)	31 (28·4)	26 (24·8)	0·480§
Albumin < 30 g/l	31 (14·5)	18 (16·5)	13 (12·4)	0·331§
Creatinine > 150 mmol/l	11 (5·1)	5 (4·6)	6 (5·7)	0·781§

Values in parentheses are percentages unless otherwise stated; *values are median (range); †bodyweight as a percentage of predisease weight; ‡defined as clinical jaundice in combination with a serum bilirubin level greater than 100 µmol/l. ASA, American Society of Anesthesiologists; COAD, chronic obstructive airway disease. §χ^2 test; ¶Mann–Whitney U test.

Table 2 Characteristics of patients (valid-for-efficacy analysis)

	Total (n = 130)	Standard Whipple (n = 66)	Pylorus-preserving Whipple (n = 64)	P
Men	69 (53·1)	33 (50)	36 (56)	0·287§
Women	61 (46·9)	33 (50)	28 (44)	0·287§
Age (years)*	65·0 (26–86)	65·0 (33–86)	64·8 (26–83)	0·297¶
ASA grade				
I–II	88 (67·7)	41 (62)	47 (73)	0·168§
III–IV	42 (32·3)	25 (38)	17 (27)	0·168§
Bodyweight (%)*†	93·3 (75–100)	93·4 (75–100)	93·1 (80–100)	0·810¶
Duration of symptoms (weeks)*	4·0 (1–180)	4·0 (1–75)	4·0 (1–180)	0·728¶
Diabetes	25 (19·2)	15 (23)	10 (16)	0·325§
Cardiac disease	21 (16·2)	14 (21)	7 (11)	0·813§
COAD	14 (10·8)	6 (9)	8 (13)	0·486§
Jaundice‡	45 (34·6)	26 (39)	19 (30)	0·270§
Albumin < 30 g/l	20 (15·4)	13 (20)	7 (11)	0·191§
Creatinine > 150 mmol/l	10 (7·7)	5 (8)	5 (8)	0·960§

Values in parentheses are percentages unless otherwise stated; *values are median (range); †bodyweight as a percentage of predisease weight; ‡defined as clinical jaundice in combination with a serum bilirubin level greater than 100 µmol/l. ASA, American Society of Anesthesiologists; COAD, chronic obstructive airway disease. §χ^2 test; ¶Mann–Whitney U test.

procedure *(Table 4)*. Perioperative mortality, cumulative overall morbidity (including DGE), as well as specific surgical and medical perioperative complications were similar in the two groups *(Table 5)*. Notably, the incidence of DGE was not significantly influenced by the surgical procedure. All patients with postoperative DGE were successfully treated conservatively. There were two pancreatic fistulas in the pylorus-preserving group and one biliary fistula after the classical procedure; all fistulas were treated without

operation. The two deaths in the classical Whipple group were caused by acute cardiac failure and endocarditis. One patient died from *Candida* sepsis after a pylorus-preserving resection. Three patients (2·3 per cent) required relaparotomy for haemodynamically significant haemorrhage (one patient in each group) and bowel obstruction (one patient who had a pylorus-preserving resection).

Based on the final histological diagnosis, 18 patients with benign lesions and two with mesenchymal tumours

Table 3 Histological findings after duodenopancreatectomy

	Total (n = 130)	Standard Whipple (n = 66)	Pylorus-preserving Whipple (n = 64)	P
Pancreatic tumour	87 (66·9)	48 (73)	39 (61)	0·153†
Benign	7 (8)	5 (10)	2 (5)	0·452‡
Cancer	80 (92)	43 (90)	37 (95)	0·452†
Ampullary tumour	19 (14·6)	7 (11)	12 (19)	0·189†
Benign	7 (37)	2 (29)	5 (42)	0·568‡
Cancer	12 (63)	5 (71)	7 (58)	0·568†
Common bile duct tumour	17 (13·1)	8 (12)	9 (14)	0·743†
Benign	1 (6)	0 (0)	1 (11)	0·999‡
Cancer	16 (94)	8 (100)	8 (89)	0·999†
Duodenal tumour	3 (2·3)	1 (2)	2 (3)	0·541‡
Benign	1 (33)	0 (0)	1 (50)	0·999‡
Cancer	2 (67)	1 (100)	1 (50)	0·999‡
Tumour diameter (cm)*	2·8 (0·8–8·0)	2·9 (0·8–8·0)	2·6 (0·9–6·2)	0·112§
Chronic pancreatitis	4 (3·1)	2 (3)	2 (3)	0·999‡

Values in parentheses are percentages unless otherwise stated; *values are median (range). †χ^2 test; ‡Fisher's exact test; §Mann–Whitney U test.

Table 4 Intraoperative findings and hospital stay

	Total (n = 130)	Standard Whipple (n = 66)	Pylorus-preserving Whipple (n = 64)	P*
Operating time (min)	410 (240–780)	449 (240–780)	382 (240–645)	0·001
Blood loss (ml)	1230 (400–6000)	1500 (400–6000)	1198 (400–4000)	0·041
Blood replacement (units)	1·9 (0–10)	1·9 (0–10)	0·9 (0–6)	0·047
ICU stay (days)	1·8 (1–11)	1·8 (1–11)	1·8 (1–5)	0·878
Hospital stay (days)	20·1 (8–67)	20·8 (8–67)	19·7 (10–61)	0·797

Values are median (range). ICU, intensive care unit. *Mann–Whitney U test.

Table 5 Surgical and medical morbidity, and mortality

	Total (n = 130)	Standard Whipple (n = 66)	Pylorus-preserving Whipple (n = 64)	P
Surgical morbidity				
Delayed gastric emptying*	50 (38·5)	30 (45)	20 (31)	0·096†
Bleeding	6 (4·6)	4 (6)	2 (3)	0·680‡
Fistula	3 (2·3)	1 (2)	2 (3)	0·999‡
Infection (wound or abscess)	8 (6·2)	4 (6)	4 (6)	0·999‡
Medical morbidity				
Pulmonary	17 (13·1)	10 (15)	7 (11)	0·435†
Cardiocirculatory	8 (6·2)	5 (8)	3 (5)	0·465‡
Renal	8 (6·2)	3 (5)	5 (8)	0·489‡
Other	4 (3·1)	1 (2)	3 (5)	0·361‡
Relaparotomy	3 (2·3)	1 (2)	2 (3)	0·616‡
Overall morbidity (%)	80 (61·5)	45 (68·2)	35 (54·7)	0·071†
Mortality	3 (2·3)	2 (3)	1 (2)	0·999‡

Values in parentheses are percentages. *All patients with delayed gastric emptying were unable to tolerate oral food consumption for at least 10 days after surgery and therefore received parenteral or enteral nutrition through a tube jejunostomy until solid oral food intake was tolerated. †χ^2 test; ‡Fisher's exact test.

Table 6 Histological classification and radicality of resection in patients with pancreatic or periampullary cancer

	Total (n = 110)	Standard Whipple (n = 57)	Pylorus-preserving Whipple (n = 53)	P
Pancreatic cancer	80 (72·7)	43 (75)	37 (70)	0·508*
UICC I	5 (6)	1 (2)	4 (11)	0·176†
UICC II	15 (19)	8 (19)	7 (19)	0·971*
UICC III	57 (71)	33 (77)	24 (65)	0·242*
UICC IV	3 (4)	1 (2)	2 (5)	0·593†
R0 resection	63 (79)	31 (72)	32 (86)	0·117*
Ampullary cancer	12 (10·9)	5 (9)	7 (13)	0·547*
UICC I	3 (25)	1 (20)	2 (29)	0·999†
UICC II	4 (33)	2 (40)	2 (29)	0·999†
UICC III	5 (42)	2 (40)	3 (43)	0·999†
R0 resection	12 (100)	5 (100)	7 (100)	0·999*
Distal bile duct cancer	16 (14·5)	8 (14)	8 (15)	0·875*
UICC I	1 (6)	1 (13)	0 (0)	0·999†
UICC II	6 (38)	2 (25)	4 (50)	0·608†
UICC III	8 (50)	4 (50)	4 (50)	0·999†
UICC IV	1 (6)	1 (13)	0 (0)	0·999†
R0 resection	16 (100)	8 (100)	8 (100)	0·999*
Duodenal cancer	2 (1·8)	1 (2)	1 (2)	0·999*
UICC II	2 (100)	1 (100)	1 (100)	0·999†
R0 resection	2 (100)	1 (100)	1 (100)	0·999†

Values in parentheses are percentages. UICC, International Union Against Cancer. *χ² test; †Fisher's exact test.
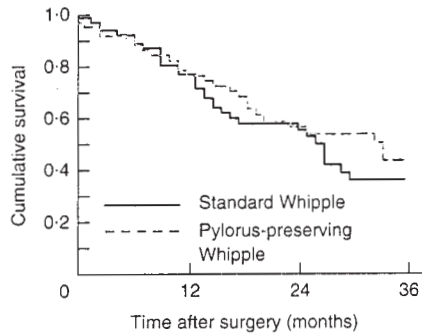
Table 7 Long-term outcome in patients with pancreatic or periampullary adenocarcinoma

	Total (n = 110)	Standard Whipple (n = 57)	Pylorus-preserving Whipple (n = 53)	P
Location				
Pancreatic cancer	80 (72·7)	43 (75)	37 (70)	0·508†
Periampullary cancer	30 (27·3)	14 (25)	16 (30)	0·508†
Lymph node status				
Positive	74 (67·3)	41 (72)	33 (62)	0·280†
Surgical radicality				
R0	93 (84·5)	45 (79)	48 (91)	0·116†
R+	17 (15·5)	12 (21)	5 (9)	0·116†
Tumour recurrence	56 (50·9)	32 (56)	24 (45)	0·255†
Distant metastases	47 (42·7)	27 (47)	20 (38)	0·308†
Survival (months)*	28·0 (21·4–32·6)	27·0 (17·2–36·8)	34·0 (20·8–47·2)	0·259‡
R0	31·3 (21·4–40·6)	28·2 (22·8–33·2)	34·1 (17·3–50·7)	0·959‡
R+	11·2 (6·2–16·1)	9·4 (5·0–13·0)	17·1 (10·6–23·4)	0·151‡
Pancreatic cancer	19·3 (12·4–25·6)	18·2 (8·5–27·5)	19·2 (14·9–23·1)	0·217‡
Periampullary cancer	48·2 (33·9–62·1)	39·4 (21·4–56·6)	49·1 (13·6–84·4)	0·832‡
Postoperative diabetes				
6 months	5 (4·5)	1 (2)	4 (8)	0·194§
12 months	7 (6·4)	2 (4)	5 (9)	0·259§
Capacity to work				
6 months	73 (66·4)	32 (56)	41 (77)	0·019†
12 months	81 (73·6)	39 (68)	42 (79)	0·198†

Values in parentheses are percentages unless otherwise stated; *values are median (range). †χ² test; ‡log rank test; §Fisher's exact test.

were excluded from long-term outcome analysis (nine after standard and 11 after pylorus-preserving Whipple resection). Therefore, 110 patients (57 and 53 patients respectively) were included in the analysis of long-term survival, tumour recurrence and quality of life (*Tables 6 and 7*). Median follow-up for surviving patients was
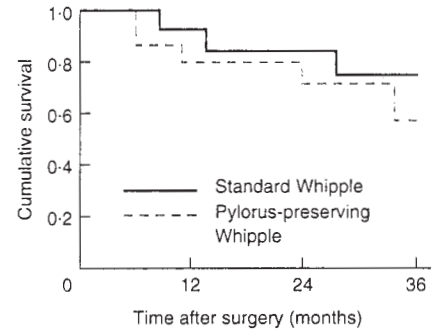
Fig. 1 Actuarial Kaplan–Meier analysis of overall survival in 110 patients with histologically confirmed carcinoma undergoing a standard or pylorus-preserving Whipple resection. $P = 0.259$ (log rank test)
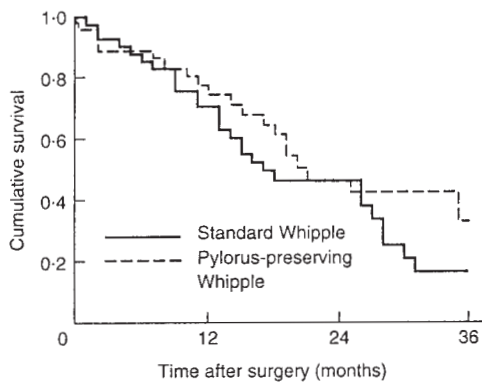
No. at risk

Standard Whipple	43	29	14	3
Pylorus-preserving Whipple	37	25	11	5

Fig. 2 Actuarial Kaplan–Meier analysis of survival in 80 patients with pancreatic adenocarcinoma undergoing a standard or pylorus-preserving Whipple resection. $P = 0.217$ (log rank test)

Fig. 3 Actuarial Kaplan–Meier analysis of survival in 30 patients with periampullary adenocarcinoma undergoing a standard or pylorus-preserving Whipple resection. $P = 0.832$ (log rank test)
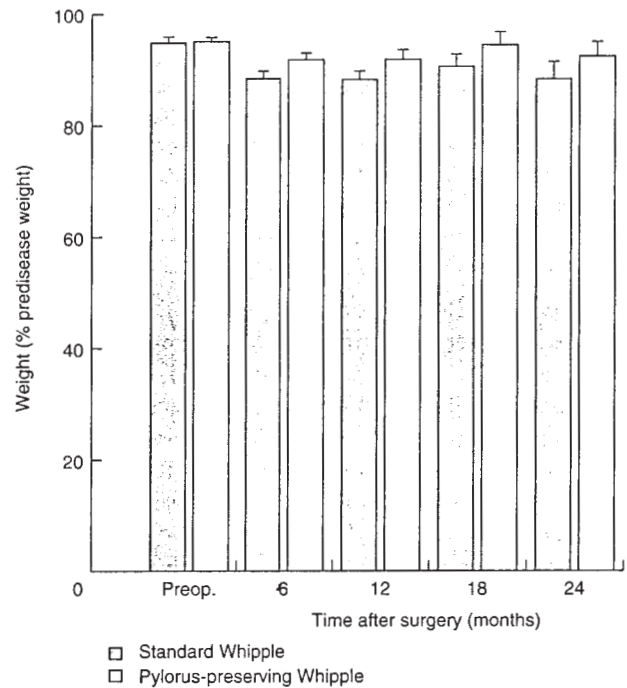

Fig. 4 Postoperative weight gain after duodenopancreatectomy in 110 patients with pancreatic or periampullary cancer treated by standard or pylorus-preserving Whipple resection. Values are mean(s.e.m.). There were no significant differences between the two procedures

63·1 (range 4–93) months. Extent of resection was comparable and lymph node status was well matched between the two groups (*Table* 7). Median tumour diameter was similar (*Table 3*). During follow-up, 56 patients died from tumour recurrence (32 after classical *versus* 24 after pylorus-preserving resection), and seven died from other causes with no clinical or radiological signs of recurrence. There was no difference in overall survival or survival in the subgroups of patients with pancreatic cancer or other periampullary malignancy between the two operations (*Figs 1–3*). For lymph node-negative patients with pancreatic cancer, median survival was 39·0 (14·7

to 63·3) months for patients having a standard Whipple operation and 49·0 (28·7 to 69·3) months for those having pylorus-preserving resection ($P = 0.127$), compared with 18·0 (7·9 to 28·1) and 15·0 (7·8 to 22·2) months respectively for lymph node-positive patients ($P = 0.473$). Survival after
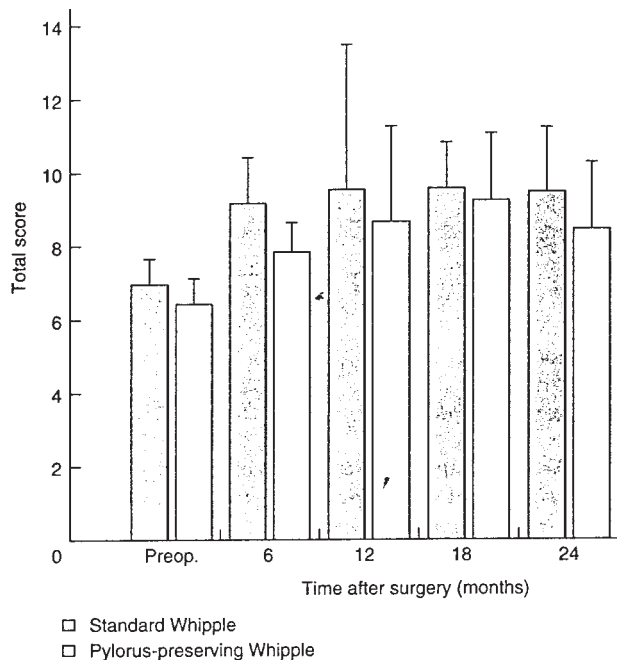
Fig. 5 Quality-of-life assessment in 110 patients with pancreatic or periampullary cancer treated by standard or pylorus-preserving Whipple resection. Values are mean(s.e.m.) total Sickness Impact Profile scores. There were no significant differences between the two procedures

both curative (R0) and non-curative (R+) resection for pancreatic cancer was comparable for the two procedures. The median survival was 28·0 (24·5 to 31·5) months after a curative (R0) standard Whipple operation and 26·0 (6·8 to 45·2) months after curative (R0) pylorus-preserving resection ($P = 0.755$). For non-curative (R+) resection, respective values were 9·0 (4·0 to 14·0) and 16·0 (8·6 to 22·4) months ($P = 0.117$).

Three patients required reoperation for stenosis of the biliodigestive anastomosis and two others developed incisional hernias that required further surgery. These five patients showed no signs of tumour recurrence. One patient underwent oesophageal resection for cancer; no recurrence of the pancreatic carcinoma was detected during this procedure.

Ability to work (patient able to follow a normal schedule of professional or household occupation) was better at 6 months after the pylorus-preserving Whipple procedure ($P = 0.019$) (*Table* 7). At 12 months, the ability to work or engage in normal daily activities was comparable between the groups. Neither postoperative weight based on predisease weight (*Fig. 4*), nor quality of life as measured by the SIP (*Fig. 5*), was affected differently by the two operations. Both groups showed

similar values when the main components of SIP (physical and psychological domains) were analysed separately.

Discussion

Most surgeons in the USA and Europe favour the classical Whipple procedure as the standard resection for pancreatic cancer[24]. Although an increasing number of surgeons now use the pylorus-preserving Whipple technique for patients with pancreatic or periampullary cancer[11–13,15,25], preservation of the pylorus in patients undergoing duodenopancreatectomy for cancer remains a controversial issue and prompted the present prospective randomized trial.

Concerns regarding the pylorus-preserving Whipple procedure centre around the incidence of anastomotic ulceration at the duodenojejunostomy, DGE and a compromised extent of resection (R0)[10]. Recently published results do not support these arguments. For example, the incidence of DGE after pylorus-preserving Whipple resection was comparable to, or even lower than, that observed after the classical procedure in recent series[13,15,16], and may relate more to the rate of surgically related complications[16]. In a prospective randomized trial comparing pylorus-preserving Whipple resection with duodenum-preserving pancreatic head resection in the treatment of chronic pancreatitis, none of 20 patients in the Whipple group suffered from DGE[26]. In the present study, the incidence of DGE was independent of the type of resection, and remained a minor and reversible complication.

As in previous reports[13], there was a significant decrease in operating time, intraoperative blood loss and the need for blood replacement in patients having the pylorus-preserving operation, confirming the early postoperative results published previously[21]. In contrast to that initial report, the cumulative morbidity rate was slightly, but not significantly, lower after pylorus-preserving resection in the final evaluation. Overall mortality and relaparotomy rates were both 2·3 per cent and not influenced by the type of procedure. There was no difference in intensive care unit or hospital stay after the classical and pylorus-preserving procedures.

Only one small retrospective study has reported a decrease in survival after preservation of the pylorus in patients with pancreatic and periampullary cancer[10]. Several other series found no difference[11–13] between the pylorus-preserving and classical Whipple operations. Clinical observations and post-mortem studies have shown that the pancreatic resection margin, rather than the pyloric region or adjacent lymph nodes, is more likely to be

infiltrated by tumour[27,28]. Overall, there is increasing evidence that the long-term outcome after pylorus-preserving resection is comparable to that following the standard Whipple procedure. In the present series, surgical radicality (R0 resection) and lymph node positivity were comparable between the groups and occurred at a frequency similar to that in another recent trial[29]. Different rates of R0 resection and nodal positivity in other studies may be explained by the fact that referral centres for pancreatic surgery recruit patients from various geographical regions and thus a positive selection of patients may influence the long-term results[30]. In addition, the Swiss health system does not involve a 'gatekeeper', such as a general practitioner, to assess the need for a specialist opinion. Consequently, patients are free to involve a gastroenterologist or surgeon directly, which may result in earlier diagnostic investigations and an increased proportion of patients with cancer restricted to the pancreas.

Kaplan–Meier analysis of long-term survival revealed no difference in overall survival between the two procedures or in subgroups of patients operated on for pancreatic or periampullary adenocarcinoma. Tumour recurrence was similar after the two procedures, supporting the conclusion that the pylorus-preserving procedure is as curative as the classical Whipple operation.

Although intended to be curative, pancreatic resection turns out to be a palliative treatment for most of these patients. Therefore, quality of life after pancreatic resection is an important consideration. Issues favouring preservation of the pylorus are improved postoperative weight gain and avoidance of postgastrectomy syndromes[10,11,13,15,25]. The results in terms of nutritional status and quality of life are, however, inconsistent; some authors have observed improved weight gain and quality of life after pylorus-preserving resection[31,32], but others have not[33,34]. These divergent views are, however, based on retrospective or non-randomized prospective studies. In the present study, quality of life was determined with the SIP, a validated behaviour-based questionnaire that assesses various physical, psychological and social functions independent of underlying disease[35,36]. Significantly more patients had returned to work by 6 months after the pylorus-preserving procedure than after the classical operation. In contrast, postoperative weight gain and quality of life did not differ between the two procedures.

The classical Whipple resection and the pylorus-preserving technique are equally effective, with comparable and acceptable perioperative risks. Pylorus-preserving resection offers the advantage of a shorter operating time, less blood loss, decreased need for blood replacement and an increased ability to work at 6 months after surgery. Long-term results showed no differences in terms of overall survival, tumour recurrence or quality of life. The procedures are equally effective for the treatment of pancreatic and periampullary malignancies.

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