CIRUGÍA ESPAÑOLA

Original article

Pancreatic and periampullary tumours: morbidity, mortality, functional results, and long-term survival

Luis Sabater,[a],* Julio Calvete,[a] Luis Aparisi,[b] Raúl Cánovas,[a] Elena Muñoz,[a] Ramón Añón,[c] Susana Roselló,[c] Edith Rodríguez,[d] Bruno Camps,[a] Raquel Alfonso,[a] Carlos Sala,[a] Juan Sastre,[e] Andrés Cervantes,[d] and Salvador Lledó[a]

[a]Unidad de Cirugía Hepatobiliopancreática, Servicio de Cirugía General y Aparato Digestivo, Hospital Clínico Universitario de Valencia, Valencia, Spain
[b]Servicio de Hepatología, Unidad de Pruebas Funcionales, Hospital Clínico Universitario de Valencia, Valencia, Spain
[c]Servicio de Gastroenterología, Hospital Clínico Universitario de Valencia, Valencia, Spain
[d]Servicio de Hematología y Oncología Médica, Hospital Clínico Universitario de Valencia, Valencia, Spain
[e]Departamento de Fisiología, Facultad de Medicina, Universidad de Valencia, Valencia, Spain

ARTICLE INFO

ABSTRACT

Aims: To evaluate postoperative morbidity and mortality, pancreatic function and long-term survival in patients with surgically treated pancreatic or periampullar tumours.

Patients and methods: Cohort study including 160 patients consecutively operated on: 80 pancreaticoduodenectomies (PD), 30 distal pancreatectomies (DP), 7 total pancreatectomies, 4 central pancreatic resections, and 3 ampullectomies. The tumour was not resected in 36 patients. Pancreatic function was evaluated by oral glucose tolerance test, faecal fat excretion, and elastase.

Results: Resectability rate was 77.5%. In resected patients (n=124), 38.7% had complications with a pancreatic fistula rate of 6.4% and a mortality rate of 4%. In PD, endocrine function worsened in 41% and 58.6% had steatorrhoea; these figures in DP were 53.6% and 21.7% respectively. In the 36 non-resected patients, postoperative morbidity was 27.7% and mortality 8.3%. Two and 5-year survival rates in resected patients with pancreatic cancer were 42% and 9% respectively; in malignant ampulloma 71% and 53%; in mucinous adenocarcinomas 83% and 33%; in duodenal adenocarcinoma 100% and 75%; and in distal cholangiocarcinoma 50% and 50%.

Conclusions: Morbidity associated with resective pancreatic surgery is still high, but perioperative mortality is low. Endocrine and exocrine disturbances are very common depending on the type of resection. Despite the associated morbidity and functional disorders, surgery provides long-term survival in selected cases.

Corresponding author.
E-mail address: luis_sabater@hotmail.com (L. Sabater).

Neoplasias de páncreas y periampulares: morbimortalidad, resultados funcionales y supervivencia a largo plazo

RESUMEN

Palabras clave:
Neoplasia de páncreas
Neoplasia periampular
Cáncer de páncreas
Función pancreática
Duodenopancreatectomía
Resección pancreática

Objetivos: Evaluar la morbimortalidad postoperatoria, el estado funcional y la supervivencia a largo plazo de pacientes con tumores de páncreas o periampulares a los que se intervino quirúrgicamente.

Pacientes y métodos: Cohorte de 160 pacientes a los que se intervino consecutivamente: 80 duodenopancreatectomías cefálicas (DPC), 30 resecciones corporocaudales (RCC), 7 duodenopancreatectomías totales, 4 resecciones centrales y 3 ampulectomías; en 36 pacientes no se realizó resección. La función pancreática se evaluó mediante test de sobrecarga oral a la glucosa, grasas en heces y elastasa fecal.

Resultados: La tasa de resecabilidad fue del 77,5%. En los pacientes resecados (n = 124) la morbilidad fue del 38,7% (con una tasa de fístulas pancreáticas del 6,4%) y la mortalidad del 4%. En las DPC la función endocrina pancreática ha empeorado en el 41%, con esteatorrea en el 58,6% de los casos; en las RCC estos valores fueron del 53,6 y del 21,7%. En los 36 pacientes no resecados la morbilidad fue del 27,7% y la mortalidad del 8,3%. La supervivencia a 2 a 5 años en los pacientes resecados por adenocarcinoma ductal fue del 42 y del 9%; en los ampulomas del 71 y del 53%; en los adenocarcinomas mucinosos, del 83 y del 33%; en los adenocarcinomas duodenales, del 100 y del 75%, y en el colangiocarcinoma distal, del 50 y del 50%.

Conclusiones: La morbilidad de la cirugía resectiva pancreática continúa siendo alta, aunque la mortalidad perioperatoria es baja. Las alteraciones de la función exocrina y endocrina son muy frecuentes y dependen del tipo de resección. A pesar de estar gravada con frecuentes complicaciones y alteraciones funcionales, la cirugía resectiva ofrece una posibilidad de supervivencia a largo plazo en determinados casos.

Introduction

The treatment of pancreas and periampullary tumours remains a great medical and surgical challenge due to the difficulties it presents in all stages throughout its diagnostic and therapeutic processes: clinically, due to severe jaundice, pain, cachexia, and overall weakness caused by these types of cancer, which require prompt relief; diagnostically, because in many cases an accurate diagnosis is not possible until surgical procedure; therapeutically, as the best treatment continues to be surgical resection, surgery is marked by high morbidity and not except from mortality; and finally, because in some types of tumours, especially pancreatic ductal adenocarcinoma (PDAC) long term survival results continue to be dismal.[1]

An aspect not thoroughly assessed is the alterations in the exocrine and endocrine functions after pancreatic resection surgery.[2] These functions have a significant overall and metabolic impact in these patients and that is why adequate monitoring and treatment turn out to be of great importance.

The progress made in the last decades regarding pre-surgical evaluation, surgical technique, and post-surgical care have resulted in an improvement in perioperative morbidity and mortality, which led to define optimal quality standards.[3]

In Spain there are a few series published with wide ranging experiences in both diagnosis and treatment, as well as results in patients with pancreas and periampullary tumours. The aim of this study is to analyze morbidity and mortality results, function after resection, and long-term survival in patients with pancreatic and periampullary neoplasia who were surgically treated in this centre. A secondary objective is to compare functional results of cephalic resections against resections of body and tail of pancreas.

Patients and methods

Cohort study with 160 patients who were surgically treated for pancreas and periampullary neoplasia consecutively, between February 1998 and February 2008. Data were collected prospectively in a data base specially designed at the onset of the study and analyzed in May 2008.

Both surgical indication and resectability assessment were performed by a multidisciplinary committee on tumours which included surgeons, oncologists, gastroenterologists, radiologists, and pathologists. All patients included in the study were considered pre-surgically resectable with radical intention and were decided intra-surgically against liver metastases or peritoneal implants not suspected pre-surgically. In these cases it was opted for biliary and gastrointestinal bypass, biliary bypass only or biopsy only for histopathology confirmation.

Diagnosis in patients with pancreas tumours was done with computed tomography (CT) with oral and IV contrast,

complemented with magnetic resonance imaging (MRI) or echo-endoscopy when vascular harm was suspected. No diagnostic puncture was carried out on these patients and preoperative biliary drainage was performed in those presenting with jaundice. Diagnosis for ampullary or duodenal neoplasia was performed by cholangio MRI and CT, and was histologically confirmed by biopsies obtained by endoscopic retrograde cholangiopancreatography (ERCP), placing preoperative prosthesis when jaundice was present.

It was evaluated: demographical data, diagnostic methods, resectability, surgical technique, morbidity and mortality, admission time, transfusion requirements, body mass index (BMI) variation, preoperative drainage, post-surgical pancreatic function, adjuvant therapy, and long-term survival.

Surgical technique

Cephalic duodenopancreatectomy

Superior mesenteric vein is approached (SMV) by separating peritoneum covering transverse mesocolon continuing with the greater omentum up to the gastrocolic trunk that is sectioned. Cholecystectomy, dissection of hepatic hilum, section of gastroduodenal artery and lymphadenectomy, from biliary bifurcation to duodenum, and of hepatic artery territory. No Kocher Maneuver is performed at that moment, since the intention is not to manipulate the tumour until removing the surgical sample (*non touch technique*). Gastric resection or pyloric preservation depending on the distance between pylorus and neoplasia (at least 2 to 3 cm of free duodenum) and type of tumour (pyloric preservation was not performed in any duodenal neoplasia). Section of jejunal loop 15 cm from Treitz ligament. Section of neck of pancreas to make intraoperative biopsy of pancreatic edge. Kocher Maneuver and separation of SMV from retroperitoneum which is sectioned. Reconstruction by pancreatogastrostomy (PG) if pyloric preservation had been performed or by pancreatojejunostomy (PJ) if classical Whipple had been performed (in both cases exteriorized duct-to-mucosa with a drain tube), termino-lateral hepaticojejunal anastomosis and, finally, gastrojejunostomy or antecolic duodenojejunostomy with Braun enteroenterostomy and omega loop bypass.

Corporocaudal resection

This is also initiated by vascular-mesenteric approach, but without cutting the gastrocolic trunk. Lymphadenectomy of celiac trunk and splenic artery; sectioning this artery at its origin. Depending on tumour type and distance from spleen, splenic preservation is performed. Separation of pancreas posterior wall from retroperitoneum and section of splenic vein at its joint with SMV. Section of pancreatic parenchyma "fish mouthed," suturing duct of Wirsung and pancreatic parenchyma. The pancreas is occasionally sectioned with mechanical suture methods.

Central resections

Same initial steps as with cephalic duodenopancreatectomy (CDP) and corporocaudal resection (CCR); once SMV is tunnelized the pancreas upper and lower margins are gradually dissected and tumour is isolated until it is framed between 2 *vessel-loops*. Alter resection the pancreas proximal stump is mechanically or manually sutured and the distal stump is anastomosed to the stomach through PG duct-to-mucosa. Both margins are analyzed intraoperatively to rule out tumoural involvement.

Total duodenopancreatectomy

It is performed the same as CDP, but the pancreas is removed in its entirety, continuing with the spleen. Diffuse tumours have been chosen for this series, when the margin of resection is affected in CDPs and after successive enlargements a free margin intraoperatively analyzed is not available and, finally, when it is identified that the pancreatic margin has been affected in the resulting pathological anatomy.

Ampullectomy

The approach is by longitudinal duodenotomy. Peripapillary duodenal mucosa is infiltrated with an adrenaline solution and then the mucosa is incised with an electroscalpel. The papilla is retracted and dissected until the bile duct and the pancreatic duct are identified, sectioned, and sutured to the duodenal posterior wall.

Pancreatic function

Pancreatic function was evaluated when resection of pancreatic parenchyma was performed (CDP, CCR, central resection [CR], and total duodenopancreatectomy [TDP]) 2 months after intervention and once the intrapancreatic drain tube had been removed. Until one week before the functional study all the patients are given supplementary pancreatic enzymes by oral route and glycaemia and insulin needs are monitored depending on admission requirements.

Exocrine function

Exocrine function was evaluated through total fat assessment in stool for 3 days and with faecal test of pancreatic elastase-1 (E1). Fat in stools were determined by the method of van de Kamer et al[4] and steatorrhoea was considered present when fat excretion in stool was >7 g/24 h. Faecal E1 was determined by enzymo immunoanalysis (Schebo-Biotech, Germany) and higher than or equal to 200 µg/g of stool[5,6] and were considered normal values.

Endocrine function

Endocrine function was assessed complying with the criteria of the World Health Organization (WHO)[7] by determining basal plasma glycaemia and by oral glucose stress test. Diabetes mellitus and hydrocarbonate intolerance have been included in the results as endocrine dysfunction.

Morbidity and mortality

Postoperative morbidity and mortality were evaluated, admission time, and perioperative transfusion. Pancreatic fistula was considered to be present when amylase occurred in a concentration 3 times higher than the plasmatic one in the liquid collected by abdominal drainage or any other abdominal collection from day 10 after surgery or when dehiscence was radiologically demonstrated.

Adjuvant treatment

In patients with pancreas cancer adjuvant chemotherapy was performed with gemcitabine and combined therapy by radiotherapy in a total dose of 50.4 Gy and 5-fluorouracil. In patients with duodenum cancer oxaliplatin and capecitabine were administered.

Data presentation and statistical analysis

The results are presented as mean and standard deviation (SD), median and interval, and percentages, and 95% confidence interval (CI). χ^2 test was applied to compare dichotomous variables and Mann-Whitney *U* test for continuous variables; a P<.05 is considered significant. Survival was assessed by the actuarial method and comparisons by the Gehan-Wilcoxon test.

Results

Demografic and preoperative data

The study population included 160 patients, 53.8% male and 46.3% female, with an average age of 61.7 (13) years (range, 14-83) and preoperative BMI of 27 (4). In 28 cases (17.5%) diagnosis and preoperative resectability were evaluated only by CT or MRI, and using both in 87 cases (54.3%); in 43 cases (27%) they were complemented with ERCP and in 2 cases (1.2%) they were complemented with endoscopic ultrasonography. In 75 patients (47%) preoperative biliary drainage was performed, 56% by endoscopy and 44% percutaneously. Preoperative localization of tumour presented the following distribution: head of pancreas (46.9%), papilla Vater (16.3%), body of pancreas (17.5%), tail of pancreas (8.8%), duodenum (5%), diffuse (3.8%), and distal cholangiocarcinoma (1.9%).

Intervention and morbidity and mortality

Of the 160 patients operated resection was achieved in 124 and the resectability rate was of 77.5%. Eighty CDPs were performed (60 with pancreo-gastric bypass and 20 with classic *Whipple*), 30 CCR, 7 TDP, 4 CR, and 3 ampullectomies. Vascular resection was performed in 3 cases. Patient morbidity, admission time and mortality with resection are shown in Table 1. In non-resected cases a double bypass was performed in 22 cases, biliary bypass in 5 cases, and exploratory laparotomy in 9. Morbidity, admission time and mortality for these cases are shown in Table 2.

Ninety-nine patients (62%) were transfused, half of them intra-operatively and the rest post-operatively with an average requirement of 2 for red blood cell concentrates.

Functional study

Twenty-five percent of the patients presented some type of preoperative endocrine dysfunction, including 9.4% with diabetes mellitus with insulin dependence. Results from the function study with exocrine and endocrine alterations after resection, as well as decrease in BMI, are shown in Table 3.

Pathological anatomy, adjuvant therapy, and survival

Distribution of tumour types identified in the anatomopathological study is shown in Table 4.

Of the resected patients 28 with pancreas cancer (32%) and 6 with duodenal cancer (75%) received adjuvant therapy.

Mean follow-up was 21.5 months. In malignant tumours survival rate after resection was 1, 2, and 5 years in 73% (95% CI, 81-65), 55% (95% CI, 64-46), and 32% (95% CI, 40-23) respectively, with a mean survival rate of 35.6 months.

Table 1 – Morbidity and mortality in resection interventions

	CDP (n=80)	CCR (n=30)	TDP (n=7)	CR of pancreas (n=4)	AMP (n=3)	Total (n=124)
Morbidity, n (%)	34 (42.5)	8 (26.7)	2 (28.6)	2 (50)	2 (66.7)	48 (38.7)
Pancreatic fistula, n (%)	5 (6.25)	3 (10)	–	0 (0)	0 (0)	8 (6.4)
With pancreatic-gastric anastomosis, n (%)(n=60)	4 (6.6)					
With pancreaticojejunal anastomosis, n (%)(n=20)	1 (5)					
Biliary fistula, n (%)	5 (6.3)	–	0 (0)	–	0 (0)	5 (5.5)
Gastrojejunal fistula, n (%)	3 (3.8)	–	1 (14.3)	–	–	4 (4.6)
Abscess/collection, n (%)	7 (8.8)	3 (10)	0 (0)	2 (50)	1 (33)	13 (10.5)
RGE, n (%)	7 (8.8)	0 (0)	0 (0)	0 (0)	0 (0)	7 (5.6)
HDH, n (%)	4 (5)	0 (0)	0 (0)	0 (0)	0 (0)	4 (3.2)
Haemoperitoneum, n (%)	4 (5)	0 (0)	0 (0)	0 (0)	0 (0)	4 (3.2)
Wounded infection, n (%)	6 (7.5)	2 (6.7)	0 (0)	0 (0)	1 (33)	9 (7.2)
Reinterventions, n (%)	3 (3.8)	0 (0)	0 (0)	0 (0)	0 (0)	3 (2.4)
Admission days, median (amplitude)	18 (8–81)	12 (7–46)	19 (13–60)	11 (7–21)	18 (16–25)	17 (7–81)
Mortality, n (%)	3 (3.8)	2 (6.7)	0 (0)	0 (0)	0 (0)	5 (4)

AMP indicates ampullectomy; CDP, cephalic duodenopancreatectomy; CR, central resection; CCR, corporocaudal resection; HDH, high digestive haemorrhage; RGE, retarded gastric evacuation; TDP, total duodenopancreatectomy.

Table 2 – Morbidity and mortality in non-resection interventions

	Double bypass (n 22)	Biliary bypass (n=5)	Laparotomy (n=9)	Total (n=36)
Morbidity, n (%)	7 (32)	0 (0)	3 (33)	10 (27.7)
Pancreatic fistula, n (%)	0 (0)	0 (0)	1 (11)	1 (2.8)
Biliary fistula, n (%)	1 (4.5)	0 (0)	0 (0)	1 (2.8)
Gastrojejunal fistula, n (%)	0 (0)	–	–	0 (0)
Abscess/collection, n (%)	2 (9.1)	0 (0)	1 (11)	3 (8.3)
RGE, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
HDH, n (%)	2 (9.1)	0 (0)	0 (0)	2 (5.5)
Hemoperitoneum, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
Wounded infection, n (%)	2 (9.1)	0 (0)	1 (11)	3 (8.3)
Reinterventions, n (%)	1 (4.5)	0 (0)	0 (0)	1 (2.8)
Admission days, median (amplitude)	10 (3–30)	8 (7–18)	13 (5–91)	10 (3–91)
Mortality, n (%)	3 (13.6)	0 (0)	0 (0)	3 (8.3)

HDH indicates high digestive haemorrhage; RGE, retarded gastric evacuation.

Table 3 – Results of exocrine and endocrine function after resection

	CDP (n=77)	CCR (n=23)	TDP (n=7)	CR of pancreas (n=4)	CDP against CCR, P
Steatorrhoea, %	58.6	21.7	100	0	<.05
Fat in stools (g/24 h), median (amplitude)	10 (0.7–59)	5 (0.6–54)	40 (40–50)	3 (0.7–4)	<.05
Elastase, median (amplitude) (VN >200 µg/g)	4.3 (0–227)	172 (0.1–538)	0	271 (200–438)	<.05
Deterioration of endocrine dysfunction, %	41	53.6	85.7	25	NS
DMID, %	38.5	25	100	25	NS
Decrease in BMI (%) (amplitude)	14 (0–35)	9.8 (0–23)	12 (3–20)	4 (1.4–6.4)	<.05

BMI indicates body mass index; CCR, corporocaudal resection; CDP, cephalic duodenopancreatectomy; CR, central resection; DMID, diabetes mellitus insulin dependent; NS, no statistically significant; NV, normal value; TDP, total duodenopancreatectomy.

In tumours that could not be resected survival was 1, 2, and 3 years in 26% (95% CI, 45-13), 14% (95% CI, 26-2), and 0% respectively, with a mean survival rate of 11.3 months (P<.05) (Figure 1). Mean survival and of 2 and 5 years after resection depending on the most frequent and most interesting histologic type was as follows: pancreatic ductal Adenocarcinoma (PDAC) 21 months, 42% (95% CI, 55-29) and 9% (95% CI, 16-1), and ampulloma 60 months, 71% (95% CI, 89-53), and 53% (95% CI, 73-33) (Figure 2).

Discussion

Pancreas and periampullary tumours are increasingly growing diseases, which call for high quality and dedication from medical teams. A multidisciplinary approach by tumour committees or functional units is necessary to optimize therapeutic results. Surgery continues to be the cornerstone for treatment and resection, which must be tried because it is the only therapy that makes long-term

Table 4 – Histologic results

Tumour type	No.	%
Pancreatic ductal adenocarcinoma	89	55.6
Ampulloma	25	15.6
Duodenal adenocarcinoma	8	5
Mucinous adenocarcinoma	6	3.8
Solid cystic tumour	6	3.8
Distal cholangiocarcinoma	6	3.8
Cystadenoma	5	3.1
Carcinoid tumour	5	3.1
Metastases of multiple origins	4	2.5
Infiltration of other tumours	2	1.3
Sarcoma	2	1.3
Neuroendocrine	1	0.6
Adenomyomatous hyperplasia	1	0.6

survival possible. Additionally, the final histology may differ from that suspected preoperatively and thus have a radically different prognosis. Resection, even in unfavourable cases

Survival function
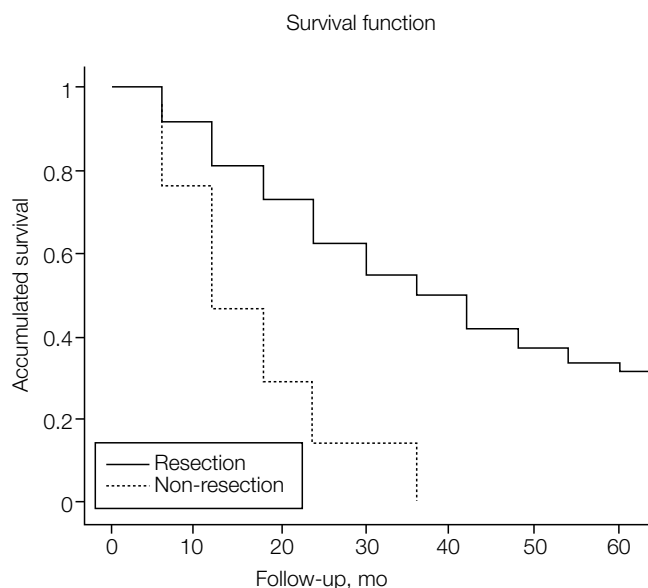
Figure 1 – Malignant tumours: long-term survival depending whether tumour resection was performed or not.

Survival function
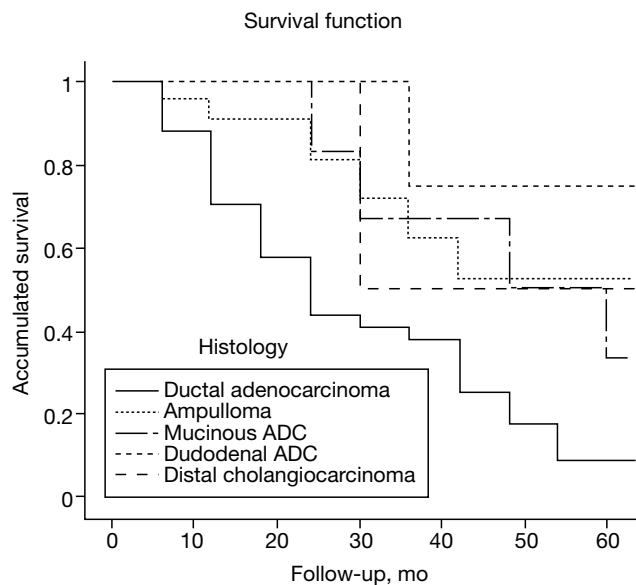
Figure 2 – Survival after resection according to main histological types.

with short life expectancy, may also offer improved quality of life.[8,9]

Most authors agree on that auditing surgical results must be part of quality control procedures in specialized units. In the absence of external audits, the group themselves have to carry out such control, indispensable to know the results themselves and to compare them with other groups in order to achieve improvements in efficacy. CDP quality standards are currently considered at a mortality <10%, morbidity <50%, and 5 year survival >30%.[3] In the present series total mortality is 5% (3.8% corresponding to CPD and 6.7% to CCR). Although mortality has been reduced at experienced centres, morbidity continues to be high. Consequently, in one of its latest revisions John Hopkins group[10] has assumed 38% morbidity, similar to 43% of Indiana University,[11] 46% of Memorial Sloan-Kettering Cancer Center,[12] and 36% of Büchler et al group.[13]

Among the most important complications pancreatic fistula should be noted first because it is usually the most significant. In our series the pancreatic fistula rate we have attained in the CDP is remarkably low (6.25%) and higher in resections of body and tail of pancreas (10%), according to the fistula criterion of Johns Hopkins University,[14] since consent definitions are of recent release.[15] It is striking when analyzing the numerous series that present results with PG that most of them show fistula rates near 5%, whereas when PG and PJ are compared using randomized studies, the difference between each other is not significant, with figures around 10% and 20%.[14,16-24] Although a meta-analysis shows a smaller number of complications with PG,[25] it is our opinion that a meticulous reconstruction technique can be safer than the technique itself. Regarding

pancreatic function, CDP causes exocrine insufficiency in 58.6% of the cases against only 21.7% in the CCR, a statistically significant difference. This high percentage of exocrine alteration in the CDPs matches figures provided by Matsumoto and Traverso[26] and Fang et al,[27] with values between 50% and 52.4%, respectively, but lower to others observed in practically all the patients[28] and that support the need to contribute with enzymatic supplements. In contrast, alterations in hydrocarbonate metabolism worsen similarly when the intervention is either CDP or CCR, with values of 41% and 53.6%, similar to those present in other series for CDP.[29] Endocrine dysfunction figures after CCR in our work appear remarkably high against those values usually present in the medical literature (around 10%),[27,30] but coincide with the series where these alterations are being researched, such as this one, by oral glucose stress test (between 37% and 42%).[31,32]

Finally, we would like to insist, together with other authors,[33] in that therapeutic nihilism against pancreas and periampullary tumours is not acceptable nowadays. Resection is the best therapy and must be offered guaranteeing well-defined morbidity and mortality levels. It is the only possibility for long-term survival, above all when pathological anatomy is not of pancreatic ductal adenocarcinoma (PDAC). But even in these cases, when just a few with a confirmed diagnosis of pancreatic ductal Adenocarcinoma (PDAC) are able to go over the 5-year barrier,[34] resection will clearly increase survival—42% and 29% to 2 and 3 years, respectively, in this series—against those who cannot be resected and, most importantly, as it has already been demonstrated by other researchers,[35] with much improved quality of life.

Acknowledgments

R E F E R E N C E S

1. Garcea G, Dennison AR, Pattenden CJ, Neal ChP, Sutton ChD, Berry DP. Survival following curative resection for pancreatic ductal adenocarcinoma. A systematic review of the literature. JOP J Pancreas (on-line) 2008;9:99–132.
2. Fang W, Su Ch, Shyr Y, Chen T, Lee R, Tai L, et al. Functional and morphological changes in pancreatic remnant after pancreaticoduodenectomy. Pancreas 2007;35:361–5.
3. Figueras J, Valls C, Fabregat J, Serrano T, Jaurrieta E. Equipamiento, experiencia mínima y estándares en la cirugía hepatobiliopancreática (HBP). Cir Esp 2002;71:201–6.
4. van de Kamer J, Huinink B, Woyers H. Rapid method for determination of fat in feces. J Biol Chem 1949;47:347–55.
5. Löser C, Möllgaard A, Fölsch V. Faecal elastase1: A novel, highly sensitive and specific tubeless pancreatic function test. Gut 1996;39:580–6.
6. Aparisi L, Martínez-Costa C, Calvete J, Sabater L. Test fecales ¿aún es necesaria la manipulación de las heces? Elastasa fecal vs quimotripsina fecal. In: Domínguez E, Iglesias J. (editors) Enfermedades del páncreas. Pancreatitis crónica. La Coruña: Congrega; 2001. pp. 95–104.
7. Alberti KGMM, Zimmet PZ, for the WHO Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of Diabetes Mellitus Provisional Report of a Consultation. Diabet Med 1998;15:539–53.
8. Kokoska ER, Stapleton DR, Virgo KS, Johnson FE, Wade TP. Quality of life measurements do not support palliative pancreatic cancer treatments. Int J Oncol 1998;13:1323–9.
9. Huang JJ, Yeo Ch J, Sohn TA, Lillemoe KD, Sauter PK, Coleman J, et al. Quality of life and outcomes after pancreaticoduodenectomy. Ann Surg 2000;231:890–8.
10. Huang Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, et al. 1423 pancreaticoduodenectomies for pancreatic cancer: A single-institution experience. J Gastrointest Surg 2006;10:1199–210.
11. Schmidt CM, Powell ES, Yiannoutsos CT, Howard TJ, Wiebke EA, Wiesenauer ChA, et al. Pancreaticoduodenectomy: A 20-year experience in 516 patients. Arch Surg 2004;139:718–27.
12. Yeh JJ, Gonen M, Tomlinson JS, Idrees K, Brennan MF, Fong Y. Effect of blood transfusion on outcome after pancreaticoduodenectomy for exocrine tumors of the pancreas. Br J Surg 2007;94:466–72.
13. Büchler MW, Wagner M, Schmied BM, Uhl W, Friess H, Z'graggen K. Changes in morbidity after pancreatic resection: Toward the end of completion pancreatectomy. Arch Surg 2003;138:1310–4.
14. Yeo CJ, Cameron JL, Maher MM, Sauter PK, Zahurak ML, Talamini MA, et al. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. Ann Surg 1995;222:580–8.
15. Bassi C, Dervenis Ch, Butturini G, Fingerhut A, Yeo Ch, Izbicki J, et al. Postoperative pancreatic fistula: An international study group (ISGPF) definition. Surgery 2005;138:8–13.
16. Aranha GV, Hodul P, Golts E, Oh D, Pickleman J, Creech S. A comparison of pancreaticogastrostomy and pancreaticojejunostomy following pancreaticoduodenectomy. J Gastrointest Surg 2003;7:672–82.
17. Arnaud JP, Tuech JJ, Cervi C, Bergamaschi R. Pancreaticogastrostomy compared with pancreaticojejunostomy after pancreaticoduodenectomy. Eur J Surg 1999;165:357–62.
18. Kim SW, Youk EG, Park YH. Comparison of pancreatogastrostomy and pancreatojejunostomy after pancreatoduodenectomy performed by one surgeon. World J Surg 1997;21:640–3.
19. Mason GR, Freeark RJ. Current experience with pancreatogastrostomy. Am J Surg 1995;169:217–9.
20. Oussoultzoglou E, Bachellier P, Bigourdan JM, Weber JC, Nakano H, Jaeck D. Pancreaticogastrostomy decreased relaparotomy caused by pancreatic fistula after pancreaticoduodenectomy compared with pancreaticojejunostomy. Arch Surg 2004;139:327–35.
21. Schlitt HJ, Schmidt U, Simunec D, Jäger M, Aselmann H, Neipp M, et al. Morbidity and mortality associated with pancreatogastrostomy and pancreatojejunostomy following partial pancreatoduodenectomy. Br J Surg 2002;89:1245–51.
22. Takano S, Ito Y, Watanabe Y, Yokoyama T, Kubota N, Iwai S. Pancreaticojejunostomy versus pancreaticogastrostomy in reconstruction following pancreaticoduodenectomy. Br J Surg 2000;87:423–7.
23. Bassi C, Falconi M, Molinari E, Salvia R, Butturini G, Sartori N, et al. Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: Results of a comparative study. Ann Surg 2005;242:767–71.
24. Duffas JP, Suc B, Msika S, Fourtanier G, Muscari F, Hay JM, et al. A controlled randomized multicenter trial of pancreatogastrostomy or pancreatojejunostomy after pancreatoduodenectomy. Am J Surg 2005;189:720–9.
25. McKay A, Mackenzie S, Sutherland FR, Bathe OF, Doig C, Dort J, et al. Meta-analysis of pancreaticojejunostomy versus pancreaticogastrostomy reconstruction after pancreaticoduodenectomy. Br J Surg 2006;93:929–36.
26. Matsumoto J, Traverso LW. Exocrine function following the whipple operation as assessed by stool elastase. J Gastrointest Surg 2006;10:1225–9.
27. Fang WL, Su CH, Shyr YM, Chen TH, Lee RC, Tai LC, et al. Functional and morphological changes in pancreatic remnant after pancreaticoduodenectomy. Pancreas 2007;35:361–5.
28. Lemaire E, O'Toole D, Sauvanet A, Hammel P, Belghiti J, Ruszniewski P. Functional and morphological changes in the pancreatic remnant following pancreaticoduodenectomy with pancreaticogastric anastomosis. Br J Surg 2000;87:434–8.
29. Ishikawa O, Ohigashi H, Eguchi H, Yokoyama S, Yamada T, Takachi K, et al. Long-term follow-up of glucose tolerance function after pancreaticoduodenectomy: Comparison between pancreaticogastrostomy and pancreaticojejunostomy. Surgery 2004;136:617–23.
30. King J, Kazanjian K, Matsumoto J, Reber HA, Yeh MW, Hines OJ, et al. Distal pancreatectomy: Incidence of postoperative diabetes. J Gastrointest Surg 2008;12:1548–53.
31. Yamaguchi K, Yokohata K, Ohkido M, Watanabe M, Ogawa Y, Chijiiwa K, et al. Which is less invasive–distal pancreatectomy or segmental resection? Int Surg 2000;85:297–302.

32. Shibata S, Sato T, Andoh H, Yasui O, Yoshioka M, Kurokawa T, et al. Outcomes and indications of segmental pancreatectomy. Comparison with distal pancreatectomy. Dig Surg 2004;21:48–53.

33. Fernández JA, Parrilla P. ¿Cuáles son los principales errores que cometemos los cirujanos en el tratamiento del cáncer de páncreas? Cir Esp 2006;79:215–23.

34. Schnelldorfer T, Ware AL, Sarr MG, Smyrk TC, Zhang L, Qin R, et al. Long-term survival after pancreatoduodenectomy for pancreatic adenocarcinoma: Is cure possible? Ann Surg 2008;247:456–62.

35. Crippa S, Domínguez I, Rodríguez JR, Razo O, Thayer SP, Ryan DP, et al. Quality of life in pancreatic cancer: Analysis by stage and treatment. J Gastrointest Surg 2008;12:783–93.