



The Liverpool duodenum-and spleen-preserving near-total pancreatectomy can provide long-term pain relief in patients with end-stage chronic pancreatitis

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Abstract

Purpose Total pancreatectomy may improve symptoms in patients with severe end-stage chronic pancreatitis. This might be achieved whilst preserving both the duodenum- and spleen-(DPSPTP). Mature clinical outcomes of this approach are presented. **Methods** Single-centre prospective cohort study performed between September 1996 and May 2016. Demographic, clinical details, pain scores and employment status were prospectively recorded during clinic attendance.

Results Fifty-one patients (33 men, 18 women) with a median (interquartile range) age of 40.8 (35.3–49.4) years, a median weight of 69.8 (61.0–81.5) Kg and a median body mass index of 23.8 (21.5–27.8), underwent intended duodenum-and spleen-preserving near-total pancreatectomy for end-stage chronic pancreatitis. Aetiology was excess alcohol in 25, idiopathic (no mutation) in 15, idiopathic (SPINK-1/CFTR mutations) in two, hereditary (PRSS1 mutation) in seven and one each post-necrotising pancreatitis and obstructive pancreatic duct divisum in 1. The main indication for surgery was severe pain. Findings included parenchymal calcification in 79% and ductal calculi in 24%, a dilated main pancreatic duct in 57% and a dilated main bile duct in 17%, major vascular involvement in 27% and pancreato-peritoneal fistula in 2%. Postoperative complications occurred in 20 patients with two deaths. Median pain scores were 8 (7–8) preoperatively and 3 (0.25–5.75) at 5 years ($p = 0.013$). Opiate analgesic use was significantly reduced postoperatively ($p = 0.048$). Following surgery, 22 (63%) of 38 patients of working age re-entered employment compared with 12 (33%) working preoperatively ($p = 0.016$).

Conclusion Duodenum-and spleen-preserving near-total pancreatectomy provided long-term relief in adult patients with intractable chronic pancreatitis pain, with improved employment prospects.

Keywords Chronic pancreatitis · Total pancreatectomy · Duodenum-preserving · Spleen-preserving · Total pancreatectomy · Surgery · Hereditary pancreatitis

Introduction

Chronic pancreatitis (CP) is a chronic fibro-inflammatory disease of the pancreas, resulting in persistent pathological responses to parenchymal injury or stress and pancreatic failure [1]. This has a negative impact on quality of life in addition to life-threatening long-term sequelae reducing life expectancy [2, 3]. Incidence ranges between 5 and 14.4 cases per 10^5 with a prevalence of around 50 per 10^5 , and possibly as high as 120–143 per 10^5 [3]. Aetiological factors include alcohol and tobacco, genetic predisposition, autoimmunity, pancreatic duct obstruction and post-necrotising pancreatitis [2–8]. Continuous pancreatic parenchymal inflammation causes progressive fibrosis of the pancreas leading to loss of exocrine and endocrine parenchyma, calcification and pancreatic duct

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obstruction amongst others [3, 9]. Patients can experience steatorrhoea, weight loss, malnutrition, gastric acid-related symptoms, bloating, vitamin deficiency and osteoporosis due to pancreatic exocrine failure and type 3c diabetes mellitus from endocrine failure [3]. In the long-term, there is a 5–25-fold risk of pancreatic cancer in sporadic CP rising to 70-fold in hereditary pancreatitis [6, 10].

Severe chronic abdominal pain is the most common and distressing symptom [2, 3]. The pathogenesis of pain is multifactorial, and the long-term management is extremely challenging [3, 11, 12]. Patients with end-stage CP who fail to respond to medical measures, may require surgical intervention [3]. The indications for surgery include chronic debilitating pain and complications including biliary and duodenal obstruction, pseudocyst, pancreatic ascites, pancreatic fistula, porto-mesenteric venous compression or occlusion, sinistral portal hypertension with venous collateralisation and pseudo-aneurysm [3, 11, 13–18]. The surgical options depend on disease extent, pancreatic exocrine function and the presence of diabetes. Both drainage and resectional procedures are described; however, symptomatic relief following drainage procedures is short-lived and various resectional procedures are now the current standard of care [3]. Beger's duodenum-preserving pancreatic head resection (DPPHR) is effective for head dominant disease, providing decompression of the duodenum, hepatic portal vein, main pancreatic duct and intra-pancreatic bile duct [13, 14]. Variants of the Beger operation include the Frey and Berne procedures [15, 16]. In situations where a classical Kausch-Whipple partial pancreateoduodenectomy and the duodenum-preserving variants are both possible, the outcomes are similar but the Beger-like procedures can be undertaken in more advanced cases [3, 17, 18]. A subset of patients with debilitating symptoms and disease affecting the entire pancreas will require a total pancreatectomy; this may be performed with duodenum, pylorus or splenic preservation [3, 19–22]. The Liverpool procedure combines these concepts as a duodenum-preserving and spleen-preserving near-total pancreatectomy (DPSPTP) [23]. This paper covers our experience with this operation, modifications to the technique and patient outcomes over the last 20 years.

Material and methods

Study design

This was a single-centre prospective cohort study of 51 symptomatic patients intended to undergo DPSPTP for end-stage CP between September 1996 and May 2016 at the Regional Pancreas Unit, Liverpool, UK. The follow-up censor date was 31 March 2017. The analysis was split into two time periods (1) from September 1996 to December 2002 when all

pancreas tissue was cleared from the duodenum [23], and (2) from January 2003 to May 2006 when a rim of pancreas tissue was left adjacent to the duodenum in line with the principles of the Beger pancreatic head resection [13, 14].

Indications for DPSPTP

This operation is only offered to the subset of patients with debilitating end-stage disease affecting the entire pancreas with chronic severe abdominal pain unresponsive to optimal medical management. Patients having previously undergone partial pancreatectomy with on-going or recurrent symptoms due to progressive disease in the remnant pancreas are also considered. Patients without diabetes mellitus meeting the above criteria are considered after counselling regarding post-operative diabetes management and complications. All patients must demonstrate abstinence from alcohol for more than 6 months. The procedure is contraindicated if malignancy is suspected, but the presence of porto-mesenteric venous thrombosis with varices is only a relative contraindication.

Data collection

A prospective database recorded demographic, clinical, radiological, genetic and histopathological data along with performance status and employment status during initial patient clinical assessment. All patients were asked to complete patient reported pain scores on a visual analogue scale (0–10).

Following discharge, patients were routinely assessed at 6 weeks, 3, 6 and 12 months, then annually with additional review as clinically required. Data collected at follow-up included weight, analgesia requirements, employment status and pain scores. To assist in data analysis, analgesia type was subclassified into parenteral strong opiates (e.g. morphine, oxycodone, buprenorphine, fentanyl), enteral strong opiates (e.g. morphine, oxycodone), enteral weak opiates (e.g. codeine, tramadol), non-opiates (e.g. paracetamol, NSAIDs) and no regular analgesia. Data was censored at the point when patients were discharged, lost to follow-up or died.

Diagnosis of chronic pancreatitis

The diagnosis of CP was based on clinical and radiological criteria and confirmed in all patients following histopathological assessment of operative specimens [3]. The diagnosis of hereditary CP required a germline PRSS1 mutation in phase with family history [6]. CP secondary to alcohol required alcohol consumption of ≥ 62 units per week for ≥ 1 year [4]. For the purposes of this study, idiopathic CP included patients with known CFTR or SPINK-1 mutations and those with no known cause for CP. Diabetes mellitus was diagnosed according to established WHO criteria. The presence of pancreatic exocrine insufficiency was based on clinical assessment and

the response of steatorrhea to pancreatic enzyme replacement therapy.

Operative description

The pancreas and duodenum are exposed as described previously [23]. The common hepatic and splenic arteries are dissected at the coeliac axis trifurcation, and the splenic artery is ligated and divided close to this origin. The gastro-colic trunk of Henle is ligated and divided, followed by the inferior pancreaticoduodenal vein. The pancreas is mobilized along its length dividing the superior and inferior peritoneal reflections. The inferior mesenteric vein and coronary veins are ligated and divided if arising from the splenic vein. The splenic hilum is dissected and transected with a linear stapler leaving the gastrolial ligament intact; splenic vascular supply is maintained on the short gastric vessels. The pancreatic tail is mobilized from the retroperitoneal structures to the confluence of the splenic and hepatic portal veins, and the splenic vein is divided and over sewn 3–4 cm proximal to this confluence.

The pancreatic head is isolated by two rows of circumferential stay sutures, as described by Beger et al. [13, 14].

Near-total pancreatic head resection is performed, preserving a small rim of fibrosed pancreatic tissue on the left lateral aspect of the duodenum, between the intrapancreatic bile duct and the duodenum, inferior to the hepatic portal and superior mesenteric veins and adjacent to the superior mesenteric artery. It is important to preserve either the inferior pancreaticoduodenal artery or the superior posterior pancreaticoduodenal artery to maintain duodenal and distal bile duct vascularization (Fig. 1). The bile duct is marsupialised

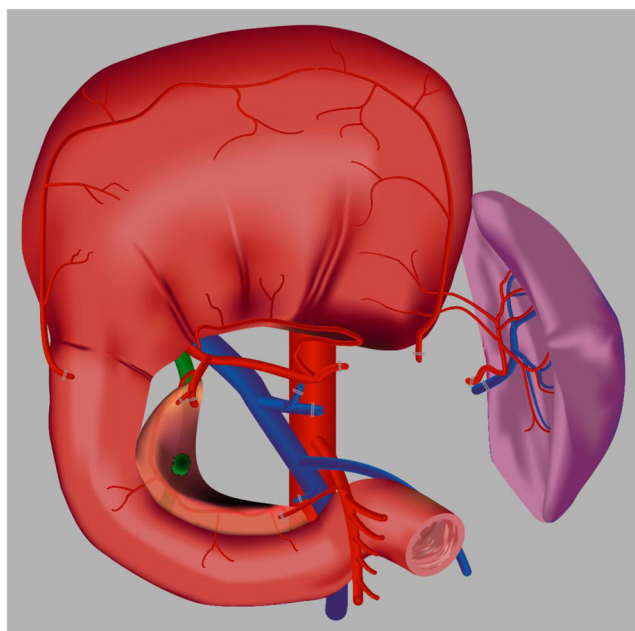


Fig. 1 Operative field following duodenum preserving and spleen preserving near-total pancreatectomy

within the bed of the pancreatic head by opening this longitudinally and then inserting six or more interrupted 4/0 sutures to approximate the edges of the cut bile duct to the adjacent tissues. The bare pancreatic rim is anastomosed to a Roux-en-Y loop. Before 2003, all pancreatic parenchyma was removed to avoid the necessity of constructing a Roux-en-Y loop. In our initial series, two cases of bile duct stricture and one case of duodenal stenosis were reported relating to local ischemia from this more radical technique [23]. Postoperative complications were categorised using the 2009 modification of the Dindo-Clavien classification [24].

Statistical analysis

Continuous variables are presented as median and interquartile range (IQR) and analysed using the Wilcoxon Rank test for paired data based on a 2-tailed alpha. Categorical variables are presented as frequency and percentage and were analysed using χ^2 test with Yates correction, or Fishers exact test. Significance was set at the 5% level ($p < 0.05$). SPSS v22 was used for analyses.

Results

Patients and preoperative details

Since 1996, 1247 patients have been screened with a possible diagnosis of CP. Seven hundred seventy-eight had confirmed CP and gave consent to be recruited to the local database. Of these, 412 (219 male, 193 female) patients have undergone pancreatic surgery. Fifty-one patients underwent intended DPSPTP for end-stage CP (Table 1). Five patients with hereditary pancreatitis (PRSS1 mutation) had a duodenum-and spleen-preserving total pancreatectomy before 2003 and two had a duodenum-and spleen-preserving near-total pancreatectomy from 2003, none of whom developed pancreatic cancer. Two additional patients with a PRSS1 mutation underwent DPSPTP without clinical evidence of CP as part of a pancreatic cancer screening program and are not included in this series, although both had good postoperative long-term outcomes. Eight patients required an intra-operative splenectomy for technical ($n = 6$) or anatomical ($n = 2$) reasons equally split between the two time periods (Fig. 2). In the second period, two patients underwent radical total pancreatectomy following the discovery of an unexpected cancer and a main duct intraductal papillary mucinous neoplasm respectively during the course of the surgery (Fig. 2).

The most common risk factors for CP were alcohol excess and smoking (Table 1). Amongst those consuming excess alcohol, the median intake was 140 (80–200) units/week for 6 (3–15) years. Amongst the ever smokers the median cigarette consumption was 20 (13.3–28.8) pack-years. Other risk

Table 1 Demographics of patients listed for DPSPTP

Intended DPSPTP	Frequency (percentage)/median (IQR)
Total patients	51
Male	33 (65%)
Age, years	40.8 (35.3–49.4)
Weight, Kg	69.8 (61.0–81.5)
Body mass index	23.8 (21.3–27.8)
Symptoms	
Primary symptom severe pain	50 (98%)
Diabetes	33 (65%)
Pancreatic exocrine insufficiency	44 (86%)
Risk factors	
Alcohol (> 62 units per week for > 1 year)	25 (49%)
Current smokers	33 (65%)
Ever smokers	39 (76%)
Idiopathic (no mutation)	15 (29%)
Idiopathic (CFTR/PRSS1)	2 (4%)
Hereditary CP (PRSS1)	7 (14%)
Previous severe acute pancreatitis	1 (2%)
Pancreas divisum	1 (2%)
Previous surgery	
Beger's procedure	8 (16%)
Spleen preserving left pancreatectomy	2 (4%)
Pseudocyst jejunostomy	3 (6%)
Pancreatectomy necrosectomy	1 (2%)
Analgesia*	
Parenteral strong opiates	3 (6%)
Enteral strong opiates	21 (43%)
Enteral weak opiates	20 (41%)
Non-opiates	2 (4%)
No analgesia	3 (6%)
Performance status	
0	5 (10%)
1	11 (22%)
2	9 (18%)
3	22 (43%)
4	1 (2%)
Unknown	3 (6%)
ASA grade	
I	4 (8%)
II	37 (73%)
III	8 (16%)
IV	2 (4%)
Employment status	
Unemployed (medical reasons)	31 (61%)
Employed	15 (29%)
Retired	3 (6%)
Unknown	2 (4%)

*Preoperative analgesic usage was unknown in 2 patients

factors are listed in Table 1. Fourteen patients had undergone previous pancreatic surgery. The predominant symptom was

pain in all except one patient. This patient had symptomatic painful CP associated with hereditary pancreatitis (with a PRSS1 mutation) along with parenchymal calcification and both endocrine and exocrine failure, who requested a DPSPTP in his sixth decade of life mainly as a prophylactic measure against pancreatic cancer.

The median preoperative visual analogue pain score was 8 (7–8) out of a maximum score of 10.90% of patients were taking daily opiate-based analgesia (Table 1). The median daily oral morphine equivalent dose was 50 (24–90) mg/day. Thirty-three patients (65%) were diabetic, 31 (61%) insulin dependent and two (4%) controlled with oral anti-hypoglycaemics. Forty-four (86%) patients had documented pancreatic exocrine insufficiency with a median daily pancreatic lipase dose of 225,000 (150,000–320,000) units. Thirty-one patients were unemployed for medical reasons, 15 were employed, three were beyond retirement age and employment status was unknown in two patients. Performance status and the American Society of Anesthesiologists grade are listed in Table 1.

Preoperative radiological imaging

The most common radiological findings were parenchymal calcification, main pancreatic duct dilatation and pancreatic atrophy (there were missing scans in three patients). Almost a third of patients had vascular involvement including portomesenteric occlusion or thrombosis and varices (Table 2). Examples of radiological features are demonstrated in Fig. 3.

Operative outcomes

All of the patients had CP confirmed histologically. Pancreatic intraepithelial neoplasia (PanIN) was found in five patients but no patient had invasive cancer. The median length of stay was 19.5 (11–39.5) days; pre-2003 ($n = 22$), this was 25.5 (15.0–44.5) days and post-2003 ($n = 16$), this was 13.5 (10.8–25.0) days ($p = 0.076$); data was missing for 3 patients. There early complications in 20 (39.2%) patients including two deaths (Table 3). Before 2003, there were complications in 15 (55.6%) patients including both deaths and since 2003, there were complications in 5 (20.8%) and no deaths (χ^2 test with Yates correction = 5.052, $p = 0.0246$).

Nine (39%) patients were readmitted with late complications pre-2003 of whom eight required a total of twelve surgical procedures: adhesiolysis (4) and ileostomy (1) for small bowel obstruction, hepato-jejunostomies (2) and hepato-duodenostomy (1) for biliary obstruction, Roux-en-Y revision (1), resection of a large uncinate process remnant which had been incompletely removed at the first operation (1), feeding jejunostomy (1) and incisional hernia repair (1). From 2003, only six (33%) patients were readmitted with late complications, with two requiring further surgical procedures ($p =$

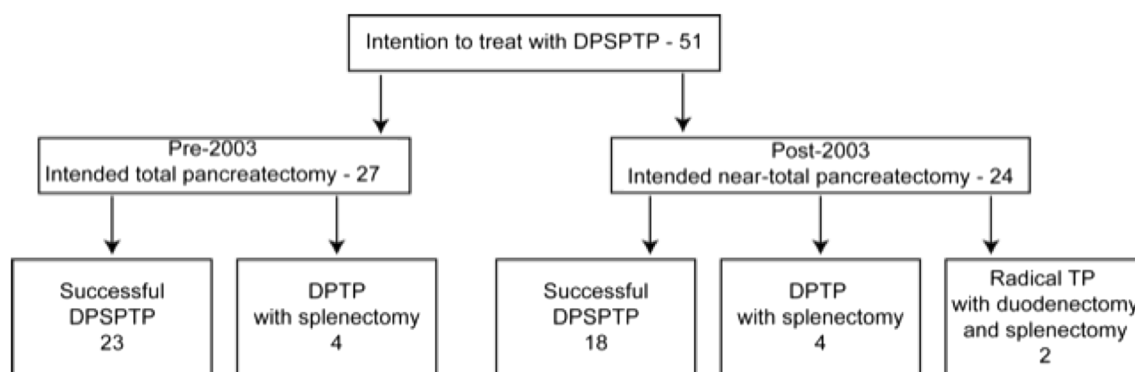


Fig. 2 Flow chart surgery performed. DPSPTP duodenum- and spleen-preserving near total pancreatectomy, DPTP duodenum-preserving total pancreatectomy, TP total pancreatectomy

0.142); an ileo-ileal bypass for small bowel obstruction (1) and a hepato-jejunostomy for a biliary obstruction (1). No patients returned to theatre for splenic complications.

Long-term outcomes

Patients were followed up for a median of 3 years, 5 months (1–6 years, 4 months). During the 20-year study, nine patients died at a median of 5.1 years (range between 13 months and 16.5 years) and seven other patients were lost to follow-up. Median pain scores were 8 (7–8) preoperatively; postoperative median pain scores were significantly reduced at 1, 3 and 6 months and 1, 2, 3 and 5 years; specifically 3 (0.25–5.75) at 5 years ($p = 0.013$). (Fig. 4). Postoperatively, significantly more patients were opiate-free by 3 months ($p < 0.001$) and this remained significant to 5 years ($p = 0.001$) (Fig. 5). The daily oral morphine equivalent dose of analgesia required was significantly reduced at all postoperative time points (Fig. 6). All patients had insulin-dependent diabetes postoperatively. Following surgery, 22 of the 38 patients of working age returned to gainful employment compared to only 12 working preoperatively; 13 patients remained unemployed compared with 24 preoperatively ($p = 0.016$); occupation data was unavailable preoperatively for 2 patients and postoperatively for 3 patients.

Discussion

CP remains a challenging disease to manage and chronic abdominal pain is difficult to treat [3, 11, 12]. The primary aim of surgery in CP is to provide long-term pain relief and control-associated complications, enabling social rehabilitation and the opportunity to increase the prospect of gainful employment. The longer-term oral morphine equivalent intake remained significantly lower after duodenum-preserving total pancreatectomy (with or without spleen preservation), although from year to year there was a variance of opiate intake, reflecting the complex pathophysiological mechanisms of pain in CP [12]. Longitudinal studies have shown that around 40–75% of patients with CP will require surgical intervention at some point during the disease process [25–28]. In our series, 412 (54%) out of 778 patients required surgery. Despite evidence that earlier intervention improves pain outcomes and preserves pancreatic function [28], there remains a cohort of patients who present with end-stage disease, develop associated complications and fail to respond to other treatment modalities. In this case, total pancreatectomy remains the only option. Once a patient has developed both endocrine and exocrine failure the longer-term improvement in symptoms may outweigh the immediacy of postoperative complications, especially in high-volume pancreatic centres. Several series have reported immediate postoperative outcomes of total

Table 2 Frequency and percentage of observed radiological features

Radiological feature	Number assessed	Frequency (percentage)
Parenchymal calcification	48	38 (79%)
Dilated main pancreatic duct	46	26 (57%)
Pancreatic atrophy	48	21 (47%)
Pseudocyst	47	19 (40%)
Vascular involvement	44	12 (27%)
Ductal calculi	45	11 (24%)
Dilated main bile duct	48	8 (17%)
Pancreato-peritoneal fistula	47	1 (2%)



Fig. 3 Clinical examples of radiological features. **a, b** Female with idiopathic (CFTR mutation) chronic pancreatitis. Extensive parenchymal and ductal calcification is seen throughout the pancreas with significant upstream main pancreatic duct dilatation and parenchymal atrophy. **c** Female with PRSS1 N29I mutation (hereditary

pancreatitis). Calcification within the pancreatic head and upstream and main pancreatic duct dilatation. Significant disease progression over 12 months with large volume abdomino-pelvic pancreatic ascites from a pancreato-peritoneal fistula and new gastric and splenic venous collateralisation

pancreatectomy for CP with mortality ranging from 2.9 to 20.6% and complication rates of 15.3 to 51.9% (Table 4) [19, 20, 22, 29–31]. In our series, there were postoperative complications in 20 (39.2%) patients with two (3.9%) deaths. Compliance with long-term follow-up is often a problem with this group of patients and must be regarded as a limitation in this as well as other studies. Nevertheless, there were 22 (57.9%) of the 38 patients of working age who were able to return to gainful work, compared to 28.1% in the one-only previously reported series of total radical pancreatectomy (with duodenectomy and splenectomy) for chronic pancreatitis [28].

Although duodenum-preserving total pancreatectomy has been previously reported [19, 20, 29, 30], and also spleen preserving total pancreatectomy for chronic pancreatitis [21, 29, 30], ours is the only series in which these procedures are combined. The duodenum-and spleen-preserving near-total pancreatectomy conforms to the principle of restricting excisional surgery to the target organ with the intention of optimising preservation of physiological function whilst

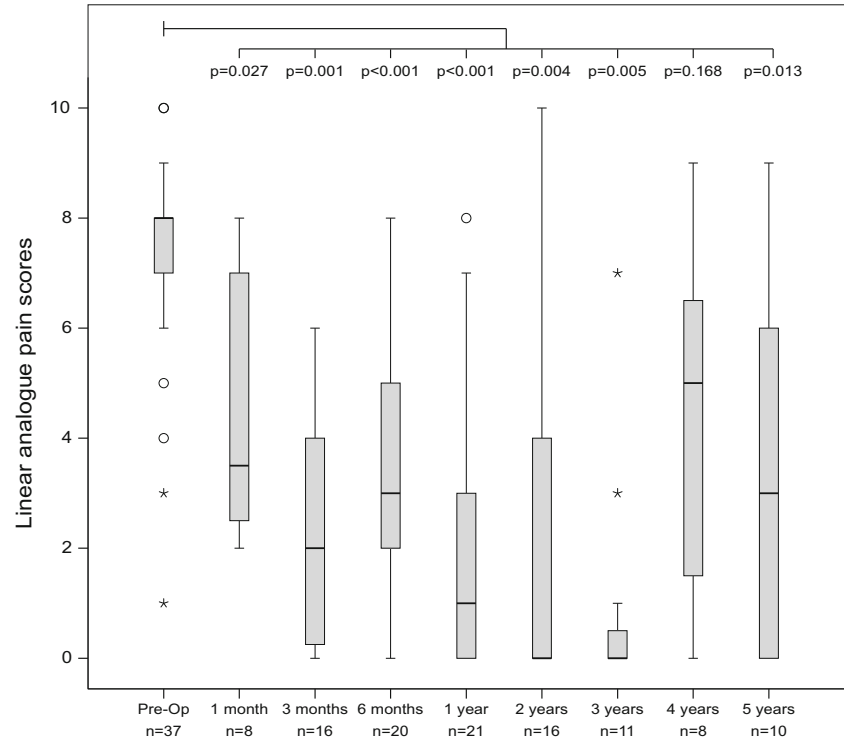
facilitating the procedure itself. Preserving the duodenum helps reduce nutritional compromise, and preserving the spleen lessens the risks of sepsis from encapsulated bacterial organisms [14, 32]. The duodenum-and spleen-preserving near-total pancreatectomy compares favourably with these larger procedures in terms of postoperative results and, unlike almost all these studies, we report sustained long-term benefits.

The key step to this procedure is identification of a readily accessible plane by finger dissection posterior to the splenic hilar vessels between the pancreatic tail and the spleen allowing transection with a linear stapler. This plane is usually easy to dissect in the absence of severe chronic pancreatitis but more challenging to define with end-stage disease affecting the entire distal pancreas. This plane is not previously well described in anatomical or surgical textbooks. In the series by Garcea et al., duodenum preservation was attempted in their first six patients. They abandoned this technique, after two patients required reoperation for duodenal ischemia [31]. Our operative technique was modified post-2003 to preserve a

Table 3 Postoperative complications

1996–2002 Number of patients = 27		2003–2016 Number of patients = 24	
Dindo-Clavien classification grade	Complications	Complications	Number of patients
I	Surgical site infection (<i>n</i> = 1) Delayed gastric emptying (<i>n</i> = 2) Splenic infarction (<i>n</i> = 1)	Surgical site infection (<i>n</i> = 1)	5
II	Abdominal collection (<i>n</i> = 1) Chest infection (<i>n</i> = 1) Subclavian vein thrombosis (<i>n</i> = 1)	Abdominal collection (<i>n</i> = 2)	5
IIIa	Biliary stricture-stented (<i>n</i> = 1) Collection/abscess-interventional drainage (<i>n</i> = 3)	Biliary stricture- stented (<i>n</i> = 1) Collection/abscess–interventional drainage (<i>n</i> = 1)	6
IIIb	Duodenal stenosis–duodeno-duodenostomy (<i>n</i> = 1)	None	1
IVa	Re-laparotomy for bleeding, single organ failure (<i>n</i> = 1)	None	1
V	Multi-organ failure, death (<i>n</i> = 2)	None	2
Total	15 (55.6%)	5 (20.8%)	20 (39.2%)

Fig. 4 Postoperative pain scores at each follow-up time period



rim of pancreatic tissue on the inner aspect of the duodenum, to avoid disruption of the blood supply to the duodenum and distal bile duct. This was based on the principles of

duodenum-preserving pancreatic head resection introduced by Beger in 1980 [13, 14]. There were significantly fewer postoperative complications in the post-modification cohort

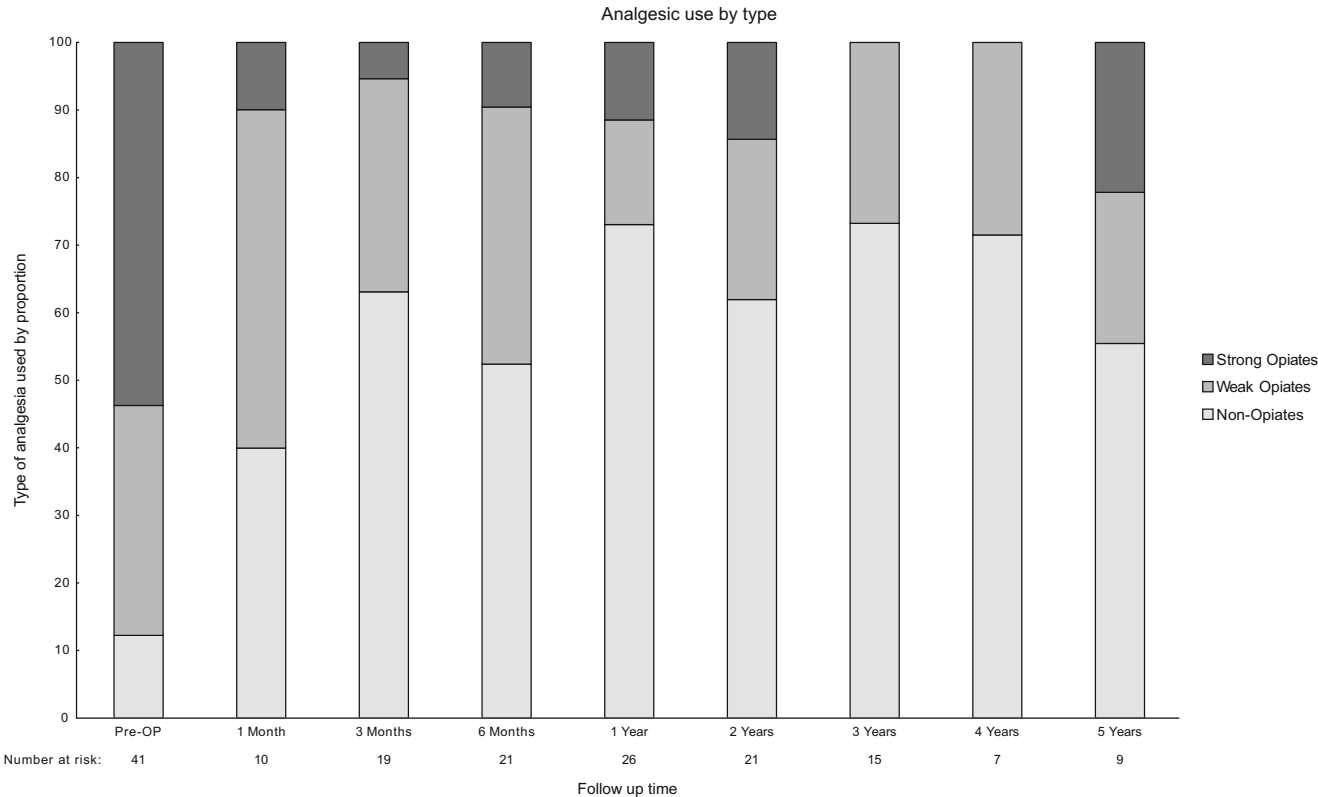
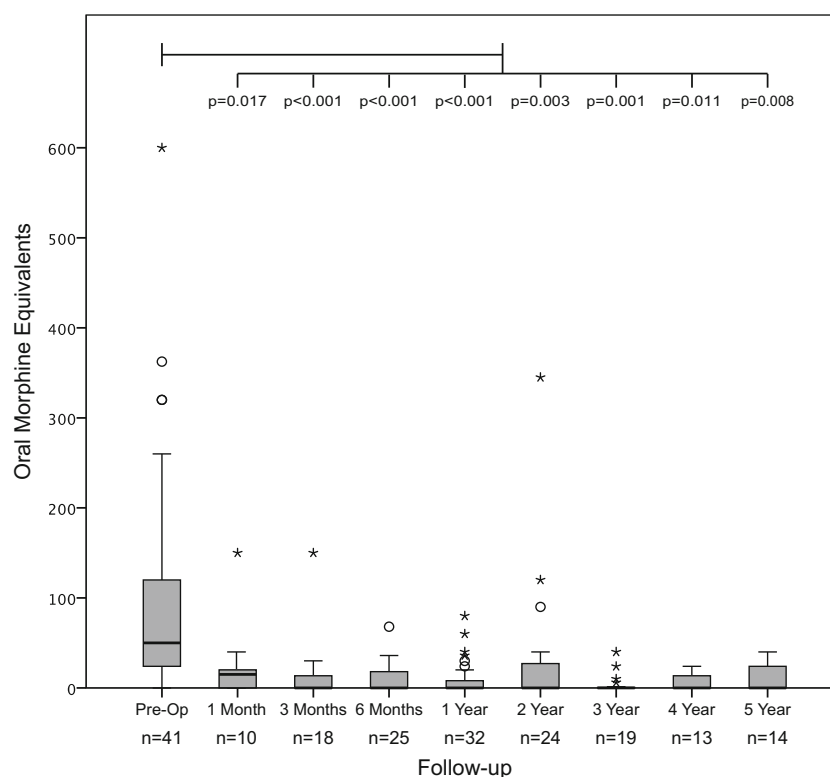


Fig. 5 Proportion of patients classified by strongest analgesic group used at each follow-up time period

Fig. 6 Analgesic use in oral morphine equivalents at each follow-up time period



(55.6% then 20.8% respectively) and no deaths. None of the patients developed malignancy in the rim of pancreatic tissue preserved along the duodenum. Limitations to the current study include a relatively small patient cohort that required this special operation.

The DPSPTP procedure was indicated in only 51 or 6.6% of the 778 patients with confirmed CP in our clinic. We would mainly recommend this procedure in patients with advanced CP when all other medical measures to control symptoms have failed [3, 12]. As a special case, it is also indicated in hereditary pancreatitis with PRSS1 mutations from the fifth decade onwards when the risk of pancreatic cancer rises dramatically [6]. Total pancreatectomy with auto-islet

transplantation is not an option for these kinds of patient because there are little or no functioning islets in the vast majority [3]. The application of total pancreatectomy with auto-islet transplantation (TPIAT) should mainly be restricted to children and young adults with recurrent acute pancreatitis, especially when associated with PRSS1 mutations, although many can be supported well into adult life with medical management [3, 6]. Outside of this indication, the role of total pancreatectomy with auto-islet transplantation is controversial, as it is now recognized that early CP cannot be reliably diagnosed and readily distinguished from chronic abdominal pain syndrome with an otherwise normal pancreas [3, 33–35]. This challenging area is illustrated by the recent study from the

Table 4 Studies since 1980 with 20 or more patients that had a total pancreatectomy for chronic pancreatitis

First author and reference number	Year of publication	Number of patients	Operation*	Postoperative complications	Postoperative mortality	Significantly improved pain relief	Weight gain	Postoperative employment (% of patients)
Gall et al. [28]	1981	68	TP	NR	14 (20.6%)	NR	57.7%	28.1%
Cooper [19]	1987	83	TP, DpTP	NR	4 (4.8%)	83%	NR	NR
Flemming [29]	1995	40	TP, DpTP, SpTP	15 (37.5%)	2 (5%)	79%	NR	NR
Russell [20]	1995	52	Tp, DpTP	27 (51.9%)	2 (3.8%)	39%	NR	NR
White [21]	2000	35	SpTP, TP	10 (28.6%)	1 (2.9%)	82%	NR	NR
Garcea [30]	2009	85	DpTP, SpTP, TP (± AIT)	13 (15.3%)	3 (3.5%)	73%	NR	NR

*Types of operation: TP total pancreatectomy, DpTP duodenum-preserving TP, SpTP spleen-preserving TP, AIT auto islet transplantation. NR = not reported

University of Minnesota Medical School, Minneapolis, Minnesota with the largest series, in which 215 patients were followed up for at least 10 years [36]. In this study, there was no definition of CP or how it was diagnosed; the causes although listed were not defined and given as idiopathic (not defined) in 98 (45.6%) patients, hereditary (not defined) in 31 (14.4%), alcohol (not defined) in 17 (7.9%) and other causes (not defined) in 69 (32.1%) patients [36]. The mean age was 35.7 years with a standard deviation of 13.8 years meaning that the majority were children or young adults [36]. Despite the relative young population, there were 50 deaths with a 1-year survival rate of 95% and a 10-year survival of 72%, mainly from unknown causes (58%) and sepsis and/or pneumonia (20%), with death from enterocutaneous fistula, cerebrovascular accident, cancer, kidney failure, liver failure and diabetic complications each contributing 2% whilst sudden death, suicide and other causes accounting for the remaining 6% [36]. Moreover 159 of the 215 patients were female, that is 74%, which cast serious questions as to patient selection, and the actual underlying diagnosis as gender is not a determinant risk factor for CP [1–4]. In an analysis also from Minnesota Medical School restricted to patients with hereditary pancreatitis and PRSS1 mutations, Bellin et al. concluded that “age greater than 21 years or disease duration longer than 17 years at surgery resulted in insulin dependence after TPIAT, with or without partial islet function. When justified by severe pain symptoms, earlier age at surgery may improve diabetes outcomes after TPIAT” [37].

Conclusion

This study shows that duodenum-and spleen-preserving near-total pancreatectomy can provide positive surgical outcomes in adult patients with end-stage severe chronic pancreatitis including a clinically meaningful reduction in pain and opiate use, and an improvement in employment status in nearly two-thirds of patients.

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Authors' contributions A.R.G. Sheel: study concept and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, critical review of manuscript. R.D. Baron: study concept and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, critical review of manuscript. L.D. Dickerson: acquisition of data, critical review of manuscript. P. Ghaneh: acquisition of data, critical review of manuscript. F. Campbell: acquisition of data, analysis and interpretation of data, critical review of manuscript. M.G.T. Raraty: acquisition of data, critical review of manuscript. C.M. Halloran: acquisition of data, critical review of manuscript. J.P. Neoptolemos: study concept and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, critical review of manuscript.

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Compliance with ethical standards

Conflict of interest JPN has received research grants from NUCANA. ARGS has received research grants from the Royal College of Surgeons of England. RDB, PG and CMH have received research grants from Cancer Research UK. LDD, FC, MGTR and VY declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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