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RESEARCH

One hundred consecutive pancreatic resections using a novel pancreatico-jejunostomy technique

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Abstract

Background No single technique of remnant pancreas reconstruction after pancreaticoduodenectomy (PD) has been demonstrated to be superior to the others in the prevention of post-operative pancreatic fistula (POPF), and the accumulation of surgical experience is closely related to the quality of this anastomosis. The aim of the current study was to evaluate the feasibility and patient outcomes of a simplified technique involving a single-layer continuous pancreaticojejunostomy (PJA) with Falciform ligament reinforcement that can be used with all types of pancreases.

Methods A single-centre and single-surgeon study was performed. One hundred consecutive patients undergoing pancreatic resection with subsequent PJA using a novel technique performed by a single surgeon were included in the study. Patient demographics, pre-operative treatments, risk factors for POPF, and post-operative morbidity and mortality and long-term patient outcome were prospectively recorded and reported.

Results From March 2018 to March 2022, 59 male and 41 female patients were included. 91 patients underwent PD for malignancy with 32 receiving neoadjuvant treatment. 59 patients were classified as intermediate/high risk for POPF according to validated fistula prediction models. There were 12 POPF Type B and 2 POPF Type C. The overall morbidity rate was 16% with no 90-day mortality. 3 patients underwent reoperation. The median length of hospitalisation was 12.6 days and 82% of eligible patients commenced and completed adjuvant chemotherapy.

Conclusion Single-layer continuous dunking PJA with Falciform ligament reinforcement is a simplified and feasible method for PJA with a low associated complication rate.

Keywords Pancreatic cancer · Pancreaticojejunostomy · Post-operative pancreatic fistula

Introduction

Pancreaticoduodenectomy (PD) is the standard of care for a number of malignant and benign pathologies within the pancreatic head. PD can be performed via a classical Whipple's or pylorus-preserving pancreaticoduodenectomy (PPPD) and in the current era within high volume centres patient mortality is < 5% with a peri-operative morbidity of 40–60% [1–7]. Following PD the remnant pancreatic stump can be anastomosed to the jejunum or stomach but pancreaticojejunostomy (PJA) is the most common method utilised globally [8]. Restoring pancreatico-jejunal continuity preserves both exocrine and endocrine pancreatic function. There remains no universally accepted PJA technique as evidenced by the extensive number of publications on different PJA techniques [9–11]. The essential requirements for a PJA are low associated complication rates and a simple reproducible surgical technique. PJA can broadly be performed using 2 separate techniques; invaginating/dunking (referred to hereafter as dunking) and 'duct-to-mucosa'. Development of post-operative pancreatic fistula (POPF) is the most serious complication after PD. The POPF rates for the 2 PJA techniques have recently been reviewed [10] and numerous PJA techniques and pharmacological interventions have been described to reduce the incidence of POPF [12–17]. However, no PJA technique has proven superior to others concerning the incidence of POPF [18].

Patient-centric factors associated with POPF include soft pancreatic texture, main pancreatic duct (MPD)

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diameter < 3mm, high body mass index (BMI) and poor blood supply [19–21] and intra-operative factors include increased blood loss and pathology other than cancer or chronic pancreatitis [22, 23]. In addition, duct-to-mucosa PJA requires the identification of the remnant MPD which is not always visible or evident at the time of PD. Dunking PJA does potentially mitigate against the latter. Regardless of the PJA technique, POPF Grade C is the most severe type of POPF with 26% patient mortality being associated with its development [24–30]. In addition, development of POPF Type B can increase in-patient stay, peri-operative morbidity and mortality and can impact upon the delivery of adjuvant oncological treatment in eligible patients resulting in inferior survival after PD.

Various prediction models for POPF have been devised based on the above patient and intra-operative factors [22, 23, 31]. However, other important factors that are closely related to the development of POPF after PD are the quality of the pancreatic anastomosis and the surgeon's experience [32, 33]. In this reported study the authors present a novel PJA technique utilising a single-layer continuous PJA using non-absorbable sutures and Falciform ligament reinforcement with selective pancreatic stenting. The primary outcome of this study is the incidence of POPF for this PJA, secondary outcomes were rate of commencement of adjuvant chemotherapy in eligible post-operative patients and overall survival (OS) following PD.

Methods

Patient cohort

This single-centre, single surgeon study that evaluated the short- and long-term outcomes of a single-layer continuous-suture dunking PJA for one hundred consecutive pancreatic resections with the PJAs being performed by a single surgeon (RHB) as described below. The study period was April 2018 to March 2022 inclusive. Patient demographics (age, gender, BMI, co-morbidities), pre-operative treatments (biliary drainage by either percutaneous transhepatic cholangiography (PTCD) or endoscopic retrograde cholangiography (ERCP) and/or neoadjuvant therapy), intra-operative variables (operation time, estimated blood loss, texture of pancreas, MPD and concomitant resection), histologic diagnosis, and post-operative outcomes (intensive care unit [ICU] stay, drain removal time, complications and their severity, length of hospitalization [LoH]) were collected prospectively and analysed retrospectively. All patient data was collected after approval by the institutional review board of The Royal Marsden NHS Foundation Trust (22/YH/0103).

The risk of POPF was evaluated with two validated tools, the fistula risk score (FRS) and the alternative fistula risk score (a-FRS) [22, 23]. Texture of the pancreas was determined by the surgeon as soft or firm, while MPD diameters were measured on pre-operative CT scan at the planned transection line and verified intra-operatively by the surgeon. The study assessed the incidence of POPF, peri-operative complications, 30- and 90-day mortality, disease-free (DFS) and overall patient survival (OS).

Pre-operative patient management

The treatment strategy for every patient was discussed and validated based upon clinico-pathological data and cross-sectional imaging by a dedicated pancreatic multi-disciplinary team (MDT). In cases of pancreatic tumours or malignancy most patients had cytologically or histologically proven diagnoses either by endoscopic ultrasound (EUS) guided fine needle aspiration or biopsy or endoscopic retrograde cholangiopancreatography (ERCP). For those eligible patients, pancreatic resection was offered on the 'fast track' pancreatic cancer pathway. In patients with pancreatic cysts, index EUS was performed and patients were either surveyed or assessed for surgery depending on the MDT decision as to the risk of underlying malignancy.

In patients requiring pre-operative biliary drainage this was achieved by placement of a biliary stent. In patients deemed appropriate and suitable for neoadjuvant treatment (either chemotherapy or chemotherapy-chemoradiation) a covered metal biliary stent was used. If patients were deemed suitable for fast-track pancreatic resection by the MDT then this was offered in preference to biliary stenting. In patients with malignant pancreatic tumours the pancreatic MDT classified these based upon dual phase computed tomography (CT)-scan images into resectable, borderline resectable and locally advanced based upon 2019 National Comprehensive Cancer Network (NCCN) guidelines as previously described by our group [32]. In patients receiving neoadjuvant oncological treatment the length of treatment was dictated by radiological and metabolic response on serial dual phase CT and CT-Positron Emission Tomography (PET) imaging during neo-adjuvant treatment. In addition, selected patients had MRI Liver and CT-PET imaging at initial staging to exclude metastatic disease. Post-chemoradiotherapy staging was assessed by CT-scan and a liver MRI was performed only in the case of suspicion or indeterminate liver lesions to exclude metastasis. The decision of neoadjuvant strategies was based upon individual patient history, cross-sectional imaging and performance status. All patients went through a comprehensive pre-operative assessment including cardiopulmonary exercise testing (CPEX) and additional cardiorespiratory testing was arranged, as required. This was our standard departmental pathway but was stopped during the COVID-19 pandemic which covers part of the study period.

Surgical procedure

All patients provided informed consent prior to surgery. Patients were quoted a POPF rate of 15% (Type B and C) and peri-operative mortality of 3–5%. In general, patients received epidural anaesthesia supplemented with additional analgesic methods. Patients received intravenous antibiotics as per local guidelines. All PDs were carried out using an open surgical approach. The decision for midline or upper transverse incision was made based upon individual patient characteristics. Pancreatic resections were carried out either in the form of classical Whipple's or PPPD depending upon intra-operative findings but in general if the pylorus was macroscopically free of disease/tumour and pyloric resection was not mandated oncologically then the pylorus was preserved. After initial exclusion of peritoneal and/or liver metastasis the duodenum was fully Kocherised followed by skeletonization of the Inferior Vena Cava and left renal vein. In cases were the artery first technique was adopted the superior mesenteric artery (SMA) was dissected free and controlled at the superior border of the left renal vein. Periarterial dissection techniques, including the Heidelberg operation and subadventitial dissection, were utilized when indicated [33, 34]. The superior mesenteric vein (SMV) was in general dissected free and identified and traced to the inferior pancreatic border. Specifically, in the case of standard PD a Nylon tape was passed underneath the pancreatic neck to aid the division of the pancreas (Fig. 1a). In the case of extended PD the Nylon tape was passed at a suitable point away from the tumour to aid pancreatic transection. In cases of central pancreatectomy, the pancreatic neck was stapled, and the distal pancreas mobilised to aid the performance a subsequent PJA. The jejunum and distal stomach/duodenum were divided with appropriate surgical stapling devices. Prior to division of the pancreas with electrocautery, 3/0 prolene stay sutures were placed 1cm away from the intended line of transection at the superior and inferior pancreatic borders respectively (Fig. 1b). In all cases the pancreas was transected with electrocautery. When vascular abutment or involvement of the SMV and/or portal vein (PV) was found, a wedge or segmental resection was included in the procedure to achieve oncological clearance. For segmental resection shorter than 4cm, end to end venous anastomosis without graft was performed. The following lymph node stations were routinely dissected in radical resection: No. 5, 6, 7 (partial), 8a/p, 9 (partial), 12a/b/c/p, 13, 14d, 17, and 11p in cases of pancreatic neck cancer [35]. Digestive tract reconstruction was accomplished in the

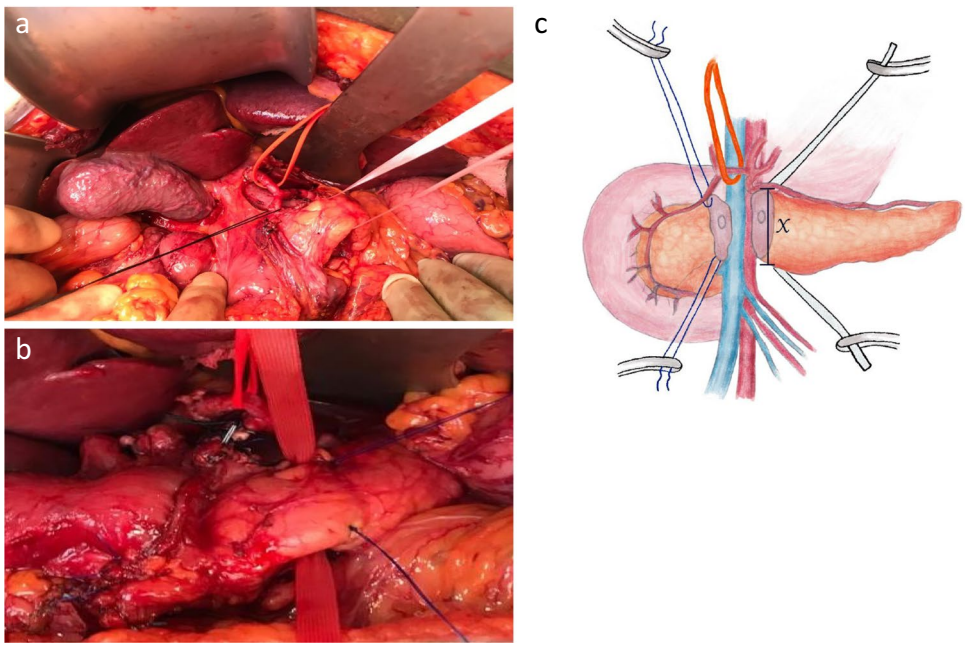

Fig. 1 Following dissection of the pancreatic neck, a Nylon tape is passed the aid transection of the pancreas. The proper hepatic artery (red sloop) and GDA (black tie) have been isolated prior to pancreatic transection. (1b) Following division of the duodenum, jejunum and GDA and prior to pancreatic parenchymal transection double armed 3/0 prolene stay sutures were placed 1cm away from the intended line of transection. These sutures will later be used for the dunking PJA. (1c) The preparation for the PJA. After pancreatic parenchymal division the width of the remnant pancreas is measured (designated x). The superior portion of the previously stapled jejunum is excised in an oblique fashion using electrocautery such that the length excised is half the length of x (designated ½x in Fig. 2b). The remaining staples are left in-situ.

following sequence according to Child's procedure: PJA, hepatojejunostomy, and gastrojejunostomy [36]. The technical details of the single-layer dunking PJA are detailed below. Hepatojejunostomy was performed approximately 10 cm away from the PJA on the jejunal efferent limb in a continuous or interrupted manner depending on the characteristics of the bile duct. Ante-colic gastrojejunal anastomosis was accomplished in a 2-layer fashion using absorbable sutures at staple line of the gastric stump 50 cm from the hepatojejunostomy. Prior to closure of the gastrojejunostomy a fine-bore NJ tube was placed for post-operative feeding and an NG left in the stomach for gastric decompression. Intra-abdominal drainage achieved with two 30Fr Robinson drains with each being placed posterior to the hepaticojejunostomy and PJA respectively. Drain fluid amylase (DFA) was measured on post-operative day (POD) 1 in all patients and POD 3 in selected patients. Prophylactically octreotide (0.1 mg, hypodermic, q8h) was given to all patients for after surgery until drain removal. Removal of the intraabdominal drainage tubes was considered when DFAs were satisfactory. Surgical morbidity was defined as significant surgical post-operative complications of Grade III, IV or V, as classified by Dindo et al. [15].

PJA

Haemostasis at the pancreatic stump was secured prior to PJA. The pancreatic stump was mobilized for 2 cm depending on the gland consistency and peri-pancreatic inflammation. To prepare the jejunum for the PJA the superior corner of the previously stapled jejunum was excised such that the width of the enterotomy was half the width of the pancreas stump and the remaining staples on the jejunum were left in-situ (Fig. 2d). The PJA is then commenced with a continuous double armed 3/0 prolene suture. The previously placed 3/0 prolene stay sutures are manoeuvred to the left of the surgical field such that the posterior aspect of the pancreas was exposed (Fig. 2b). The 3/0 prolene suture was then passed through the full thickness of the superior border of the pancreas 2cm lateral to the superior 3/0 prolene stay suture such that one suture was on the anterior aspect of the pancreas and one suture was on the posterior aspect of the pancreas. The suture on the anterior pancreatic surface is placed in a rubbered haemostat (Fig. 2a and 2b) with the suture present on the posterior aspect of the pancreas being used for the posterior wall of the PJA (Fig. 2b—red suture). The first suture placed in the jejunum is placed at the vertex of the enterotomy 2mm from the enterotomy in a

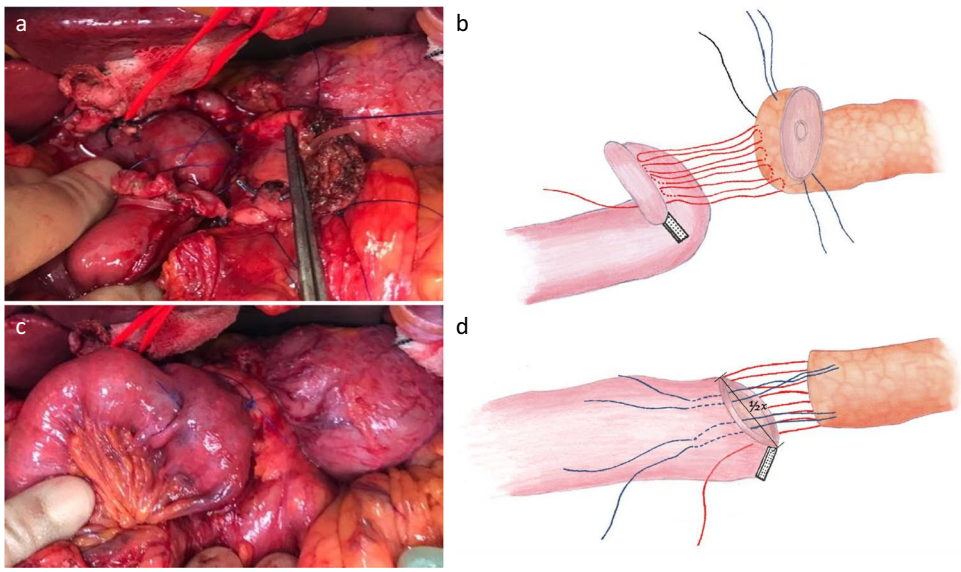

Fig. 2 **(a) & (b)** After oblique division of the jejunum (½x), the previously placed 3/0 prolene stay sutures (shown in blue in [2b]) are manoeuvred to the left side of the surgical field such that the posterior surface of the pancreas is exposed. A 3/0 double armed 3/0 prolene suture is used to begin the PJA. The suture is passed through the superior border of the pancreas and the suture on the anterior surface (black in [2b]) is placed in a rubber shod. The other end was used to complete the posterior wall of the PJA (shown in red in [2b]). Pancreatic sutures are placed 3cm away from the cut surface and the jejunal sutures are placed adjacent to cut surface of the bowel. This is continued until the suture (red) reaches the inferior aspect of the pancreas and is passed from posterior to anterior on the jejunum completing the posterior wall of the PJA. At this point a stent is placed in the pancreatic duct if visible (2a). **(c) & (d)** Once the posterior wall of the PJA is completed the previously placed 3/0 prolene stay sutures are delivered through the jejunum allowing the remnant pancreas to be invaginated into the jejunum (2c). The stay sutures are then tied and cut. The anterior wall of the PJA is then completed in the same manner as described above until the 3/0 prolene sutures meet each other (2d). These are then tied (red and blue). The PJA is then completed by wrapping the Falcifrom ligament around the anastomosis and fixed into position with 3/0 vicryl

seromuscular manner. The suture is then passed through the pancreatic capsule 3cm away from the cut surface avoiding the MPD. The 'back wall' of the PJA is completed in this manner using a parachute technique and ensuring that the same distance between the sutures and pancreatic cut surface and enterotomy is maintained by placing vertical running sutures 3-4mm apart until the lower border of the pancreas is reached (Fig. 2a). At this point the suture is passed through the full thickness of the jejunum superior to the staple line onto the anterior wall of the jejunum. A silicon tube of an appropriate caliber is used as an internal MPD stent and was omitted in patents were the MPD could not be identified [ref]. Following completion of the posterior wall of the PJA the sutures were moisten with saline and gradually tightened to oppose the jejunum to the posterior pancreas. Now, the previously placed 3/0 prolene stay sutures were delivered through the jejunum 3cm beyond the enterotomy in a parallel manner such that they maintain the same width as the remnant pancreas, and this allows the pancreatic remnant to be invaginated or dunked into the jejunum. Care is taken to ensure the sutures are kept parallel with the pancreas with occasional assistance needed with atraumatic forceps to ensure the correct dunking of the pancreas occurs. The 3/0 prolene stay sutures were then tied, in the process ensuring that the pancreatic remnant remained dunked in the jejunum. With 'back wall' completed and stay sutures tied, the anterior wall of the PJA is completed by running the suture in the same manner as described above to the original superior 3/0 prolene suture (black suture in Fig. 2b). The suture is then tied and divided. The Falciform ligament is wrapped around the PJA by passing it posterior to PJA onto the anterior surface and fixing it into position using 3/0 absorbable sutures as previously described [37]. The critical points for this anastomotic technique include ensuring the correct and appropriate dunking of the whole pancreatic stump into the jejunal wall and ensuring complete inversion of the jejunal serosa.

POPF assessment

The definition of POPF is defined by the International Study Group of Pancreatic Fistula (ISGPS) [25]. In the latest version from 2016, POPF Type A is now classified a biochemical leak. The definition of POPF grades B and C has also been modified. The diagnosis and grading of POPF, delayed gastric emptying (DGE), post-pancreatectomy haemorrhage (PPH), and chyle fistula were performed according to the ISGPS criteria, while bile fistula was defined as > 3 times the bilirubin level in drainage fluid compared with that in serum. Clinically relevant POPF was defined as grade B or C. Grade B required a change in the post-operative management; drains were either left in place for more than 3 weeks or replaced by endoscopic or percutaneous procedures. Grade C required reoperation or led to single or multiple organ failure and/or mortality attributable to POPF. The status of the pancreatic parenchyma (soft or firm pancreas) was determined by subjective palpation by the surgeon. The size of the MPD was measured at the presumed surgical transection line on pre-operative contrast-enhanced computed tomography and confirmed intra-operatively.

Histological assessment

A macroscopic pathological examination of the resected specimen followed a standardized protocol by serial slicing of the pancreatic head in a single axial plane, perpendicular to the longitudinal axis of the duodenum, to obtain slices covering the lesion/tumour and its ranges up to the inked margins. R0 resection was defined as margin strictly superior to 1mm. R1 resection were defined as tumour cells on the inked margin.

Follow-up

Patients had follow-up visits with laboratory evaluation every 3 months and CT scans every 6 months for the first 2 years, visits with laboratory evaluation every 3 months and an annual CT scan for year 3, and visits with laboratory evaluation every 6 months and an annual CT scan for years 4 and 5. Additional evaluations prompted by symptoms, results of laboratory tests, or the treating clinician's discretion were also used to score events.

Statistical analysis

Cumulative sum (CUSUM) plots were utilized to analyze the learning curve of PJA [38]. Left and right abdominal drain output was used as a reflection of surgeon's experience. The change point where the cumulative drain output plateaus to the lowest levels in the CUSUM plot, indicated completion of one learning curve and attainment of mastery for this procedure [39]. For analysis PJA learning curve analysis the lower CUSUM trend line was used as the minimum range value, when compared to the population mean. [39]. This is based on the assumption that decreasing drain output is associated with decreased incidence of POPF and thus surgical proficiency. The CUSUM analysis was performed with QI Macros, Excel plugin for Excel software, as used by previous studies [39, 40].

Results

Patient demographics

One hundred consecutive patients undergoing pancreatic resection at The Royal Marsden Hospital were included in

the study. The patients' demographics are summarized in Table 1. The patient cohort had a mean age of 66.2 years with 8 octogenarian patients undergoing pancreatic resection. Most patients presented with jaundice and 25 patients had a pre-operative diagnosis of diabetes mellitus. As most patients had undergone pre-operative biliary drainage (n = 67) and pre-operative serum bilirubin levels were normal in almost all patients (n = 95). 32 patients received neoadjuvant oncological treatment prior to pancreatic resection; 19 patients received neoadjuvant chemotherapy and 13 patients received neoadjuvant chemotherapy-chemoradiation (C-CR) for either borderline-resectable tumour or locally advanced tumours. 21 patients had had previous abdominal or pelvic surgery.

As is the practice in our department 81 patients underwent CPEX testing prior to surgery. 19 patients had not undergone CPEX as these resections had been performed during the early phase of the SARS2-COVID-19 pandemic during which these investigations were temporarily suspended. The cohort mean Anaerobic Threshold (AT) was 12.1 ml/kg/min and mean Maximal Oxygen Consumption (VO_2 Max) was 16.6 kg/min respectively. 16 patients within the study cohort had an AT below 9.0 ml/kg/min with the lowest value being 6.3 ml/kg/min.

Table 1 Patient Demographics

Age (years), mean ± SD	66.2 ± 10.6
Sex	
Male	59
Female	41
Body Mass Index (kg/m^2), mean ± SD	25.4 ± 5.4
Presentation	
Incidental	8
Jaundice	67
Abdominal pain	5
Weight loss	11
Other	9
Diabetes Mellitus	25
Co-morbidities	
Cardiac	13
Respiratory	17
CKD	3
Other	34
Previous Abdominal/Pelvic Surgery	21
Pre-operative Biliary Drainage	67
Pre-operative Bilirubin (µmol/L), median (range)	8 (3–115)
Pre-operative Albumin, (g/L) mean ± SD	37.1 ± 6.5
Pre-operative Haemoglobin, (g/L) mean ± SD	116.9 ± 18.5
Neoadjuvant treatment	
Chemotherapy	19
Chemotherapy + Chemoradiation	13
CPEX	
AT (ml/kg/min), mean ± SD (n = 81)	12.1 ± 4.1
VO_2 Max (ml/kg/min), mean ± SD (N = 81)	16.5 ± 5.2

Peri-operative surgical outcomes and complications

Five patients were deemed appropriate for 'fast-track' PD whilst the majority of patients had surgery after biliary stenting. 3 patients developed post-ERCP pancreatitis, 1 patient had acute severe pancreatitis that required ITU admission. 32 patients received neoadjuvant oncological treatment as detailed above. Pre-operative laboratory data, including total bilirubin, albumin are shown in Table 1.

Forty-one patients underwent classical Whipple's surgery, 58 patients underwent PPPD with 1 patient undergoing central pancreatectomy for a complex cyst in the pancreatic body (Table 2). Four patients underwent concomitant visceral resections; 2 patients having synchronous right hemicolectomy because of tumour involvement, 1 patient having extended right hemicolectomy for a synchronous bowel tumour and 1 patient having simultaneous total gastrectomy. One patient underwent Whipple's with simultaneous liver resection for a segment 6 lesion that had demonstrated complete radiological and metabolic response following 12 cycles of neoadjuvant FOLFIRINOX chemotherapy. Twenty-two patients required vein resection; 20 patients required partial or segmental venous resection which were repaired primarily using non-absorbable sutures and 2 patients required full venous reconstruction that were repaired in an end-to-end fashion using non-absorbable sutures. There were no incidence of acute portal vein thrombosis. In both patients with full vein resection patients were commenced on dual anti-platelet treatment and partial venous resection patients were management with standard thromboprophylaxis.

The peri-operative outcomes for the cohort are summarised in Table 2. The median operative time for the cohort was 307 min. 54 patients were noted to have a soft pancreatic texture. Median MPD was 5mm and 18 patients had no visible MPD either on pre-operative imaging or on intra-operative assessment. The mean time for PJA was 6 min (range 5-11min). In 82 patients an internal stent was placed in the MPD as part of PJA as we have previously described [37]. Six patients required blood transfusions. One patient developed post pancreatectomy haemorrhage and there were no biliary leaks. Overall there were 16 patients with CD > 3a complications with the incidence as follows: 6 patients had DGE, 5 patients had chyle leak, 2 pseudoaneurysm that were managed with radiological embolization. Fourteen patients developed POPF Type B and C (discussed below). Three patients underwent reoperation; one patient had right colonic ischaemia 7 days after PD requiring right hemicolectomy and ileostomy

Table 2 Peri-operative Surgical Parameters

Operation	
Whipple's	41
PPPD	53
PD + multi-visceral resection	4
PD + liver resection	1
Central pancreatectomy	1
Vein Resection	
Partial/segmental venous reconstruction	20
Full vein resection	2
Pancreatic texture	
Hard	46
Soft	54
MPD diameter (mm), median (range)	5 (0–10)
Operative time (min), median (range)	307 (256–613)
Blood loss (mL), median (range)	500 (150–4000)
Complications	
CD > 3a (n)	16
Bile leak (n)	0
PPH (n)	1
POPF	
Type B	12
Type C	2
Re-operation	3
In-patient Stay	
CCU stay (days), mean (range)	2.7 (1–8)
Hospital stay (days), mean (range)	12.6 (5–184)
Readmission (n)	3

formation, 1 patient had intraluminal bowel haemorrhage 48 h after PD that required multiple relook laparotomies and 1 patient exploratory laparotomy 5 days after full venous resection for LAPDAC for suspected small bowel ischaemia that was negative. No completion pancrectomies were required. 30- and 90-day mortality rate was zero. The median post-operative length of hospitalization was 12.6 days (range 5–184 days).

DFA & POPF

DFA1 was measured in all 100 patients from the left and right surgical drains and was measured in 58 patients in both drains on POD3. DFA on POD1 and POD3 in the surgical drains in the consecutive 100 patients is shown in Fig. 3 along with the pancreatic texture. Fourteen patients developed POPF as per the ISGPF definition. Twelve were grade B and 2 were grade C (Table 2). In patients with POPF Type B/C the DFA was > 9000 IU/L on POD3 and in 13 of patients the pancreatic texture was noted to be soft. Seventeen patients had a biochemical leak, none of whom required any intervention. POPF was more frequently noted in patient with a soft pancreatic texture who had not received any neoadjuvant oncological treatment. Indeed, following neoadjuvant C-CR no POPF was noted but was observed in 4 patients after neoadjuvant chemotherapy (21%). There was an increased risk of POPF in patients undergoing PD for duodenal adenocarcinoma with 6 of 8 patients developing Type B and C POPF (Fig. 4a). The development of POPF in risk-stratified groups according to FRS is shown in Fig. 4b. According to the FRS, 30 patients were at intermediate risk of developing POPF and 22 in the high-risk group. Whilst the a-FRS demonstrated that 40 patients were at indeterminate risk of developing POPF and 19 were in the high-risk group. Hence despite FRS and a-FRS demonstrating that 52 and 59 patients respectively were at least in the indeterminate risk group for POPF, 14 patients developed clinically relevant POPF.

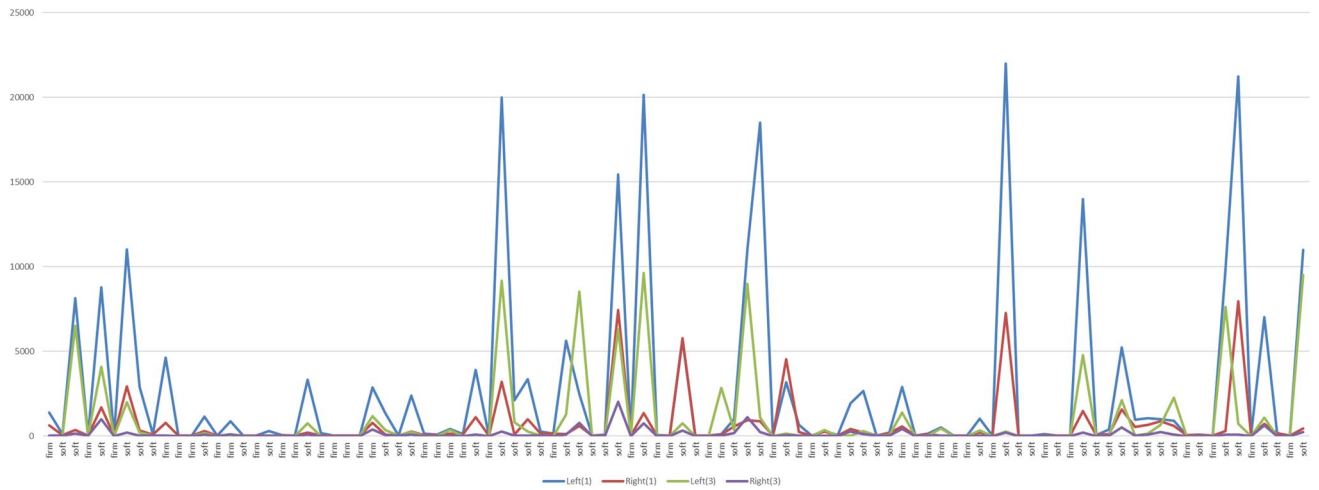

Fig. 3 DFA on POD 1 & POD 3 in 100 Consecutive Patients Undergoing Pancreatic Resection

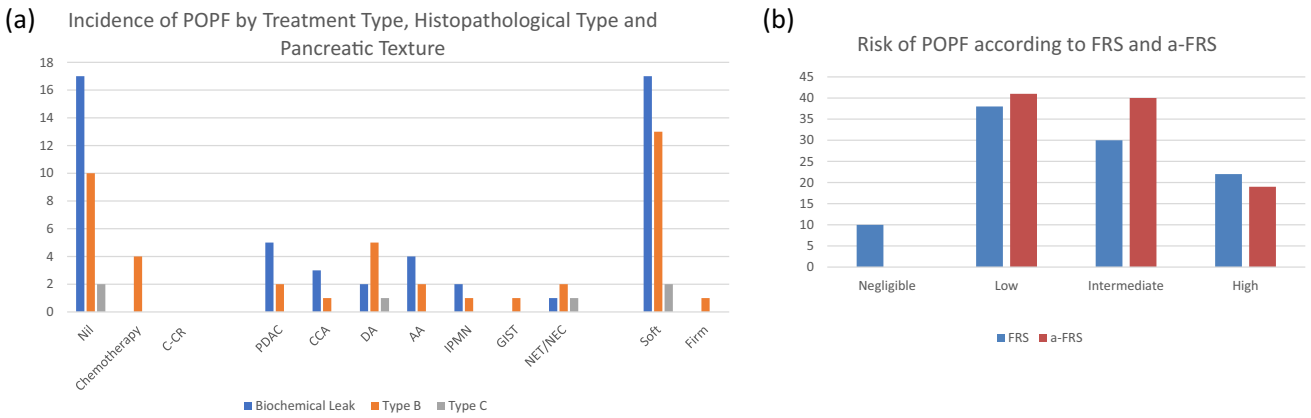

Fig. 4 The Incidence and Risk of POPF in the Patient Cohort

CUSUM analysis

PD patients were divided into two groups according to the incidence of the POPF: low incidence of POPF (Group 1, Cases 1–41) (Fig. 5) and high incidence of POPF (Group 2, Case 42–100). Both groups presented a decreasing trend in the incidence of POPF. In Group 1, both DFA1 and DFA3 showed a decreasing trend of left drain output until 36th case (Fig. 5a and 5b). The right drain on POD 1 and 3 showed a decreasing trend until 36th (Fig. 5c) and 26th case (Fig. 5d), respectively. In Group 2, left drain output on DFA1 and DFA3 decreased until 35th (Fig. 6a) and 41st case (Fig. 6b), respectively. Finally, the right drain output on DFA1 and DFA3 showed a decreasing trend until 35th (Fig. 6c) and 44th case (Fig. 6d), respectively. Mastery of the technique comes following the 26th to 44th case as indicated by the monitor of the DFA1 and DFA3.

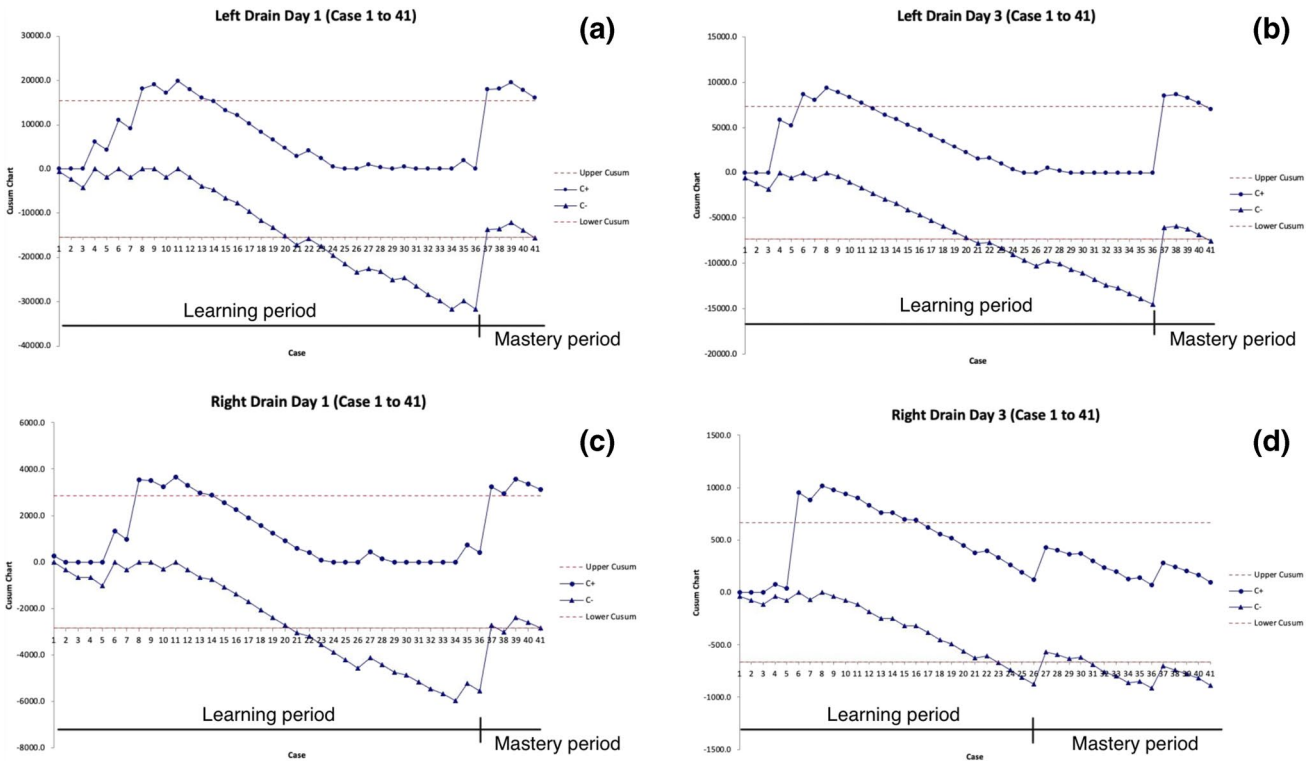

Fig. 5 DFA1 and DFA3 in Left and Right Drains for Patient 1–41

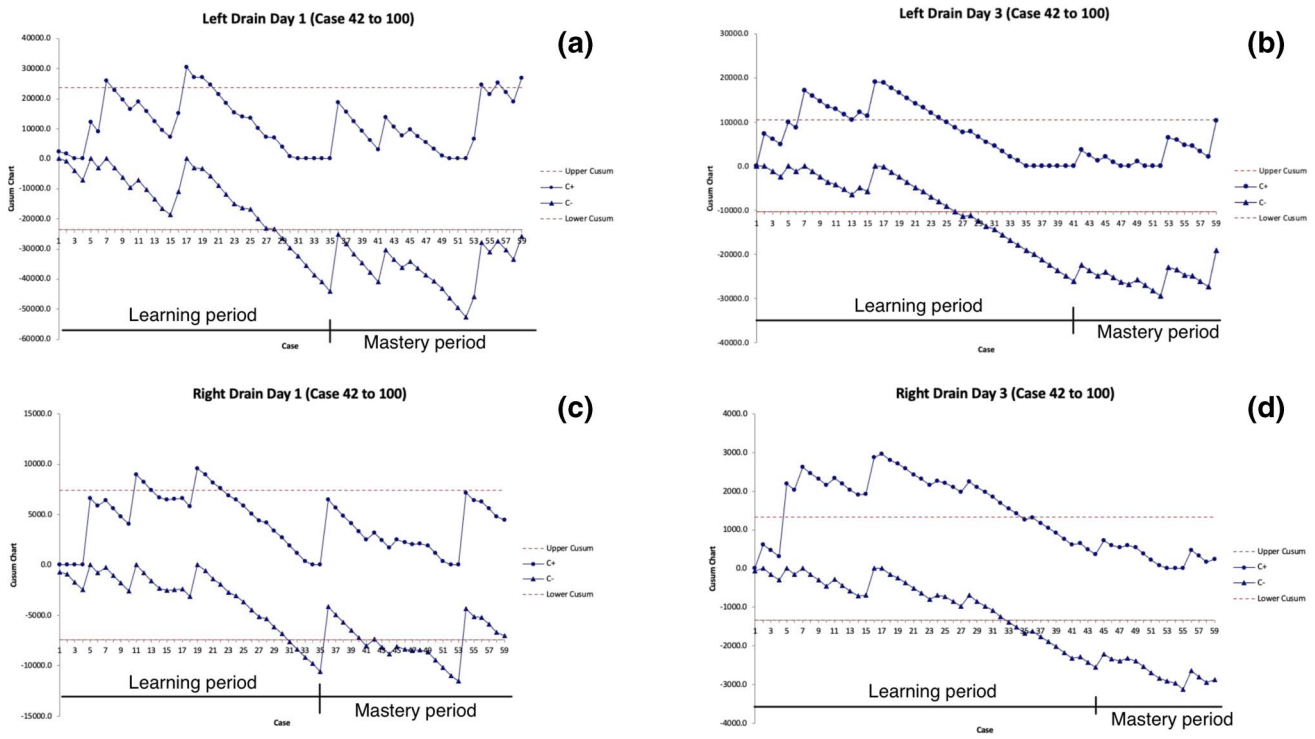

Fig. 6 DFA1 and DFA3 in Left and Right Drains for Patient 42–100

Histological and long-term patient outcome after PD

Table 3 demonstrate the histopathological outcome for the patient cohort. For patients with malignancy the overall R0 resection rate was 90%. The most frequently involved margin after PD was the SMV margin (n = 7) followed by the posterior margin (n = 2). The median lymph node harvest was 24 nodes and lymph node metastases was noted in 51 patients with malignancy. Angiolymphatic invasion and perineural invasion was noted in 55 and 51 patients respectively. Sixty-seven patients were suitable and/or eligible for adjuvant chemotherapy following PD. Fifty-seven of the eligible patients commenced adjuvant chemotherapy (85%). This included 8 patients who had developed POPF Type B patients demonstrating that despite developing POPF patients can still commence adjuvant chemotherapy in a timely manner. The DFS for the whole cohort was 67% at 5 years but was noted to be higher in the NET (1.0) and pancreatic cysts (1.0). DA and CCA demonstrated similar OS at 6 months (63% versus 67% respectively) whilst AA and PDAC had the lowest OS at 44% and 43% respectively (Fig. 7). Five year OS was 66% for the whole cohort with AA (78%) and NET (75%) having the best tumour group survival (Fig. 8). All patients who underwent PD for cystic pancreatic disease were alive whist 5-year survival for PDAC, CCA and DA was 59%, 67% and 63% respectively.

Discussion

There remains no universal accepted method for remnant pancreas reconstruction after PD with over 100 different techniques described within the literature. POPF is the most feared complication after PD and whilst duct-to-mucosa PJA remains the most popular technique there is no randomised data to support its use over other PJA methods [41, 42] especially in terms of preventing POPF [43]. Duct-to-mucosa PJA may not be appropriate in patients with soft glands and small ducts, factors noted in 18 patients in the reported series, primarily because its technically challenging and associated with increased risk of POPF [42]. Hence a PJA technique that can be used in all types of remnant pancreatic stumps would be surgically advantageous. Dunking PJA technique have been recommended for patients with a narrow MPD (< 3 mm) and soft pancreatic tissue [44]. The current technique of continuous single-layer dunking PJA with selective pancreatic stenting and Falciform ligament reinforcement provides a simplified option for PJA in all scenarios especially in cases of soft pancreas with small or no MPD.

Many of the dunking PJA techniques are dependent upon placing interrupted sutures on the posterior side of the pancreas and the jejunal wall that are individually tied making the PJA complex and time consuming and as the current study suggests this may not be needed. Moreover rather than

Table 3 Histopathological and Oncological Outcomes for patients undergoing Pancreatic Resections

	PDAC (56)	CCA (9)	DA (8)	AA (9)	IPMN (9)	GIST (3)	NET/NEC (6)
Histopathological Data							
Lesion/Tumour size (mm) (mean) ± SD	26.2 ± 11.8	23.2 ± 5.2	31.5 ±13.4	24.9 ± 13.3	28.6 ± 7.8	35 ± 13.2	28.1 ± 15.7
T stage							
CR	4	0	1	-	-	-	-
T1	8	3	1	2	-	-	3
T2	29	4	-	4	-	-	-
T3	14	2	3	3	-	-	3
T4	1	0	3	-	-	-	-
N+, n (%)	32 (57%)	6 (67%)	5 (63%)	4 (44%)	-	1 (33%)	2 (33%)
Harvested lymph nodes (mean) ± SD	28.2 ± 10.3	22.2 ± 6.7	22.5 ± 7.1	32.1 ± 15.5	-	13 ± 5.2	27.8 ± 12.1
Positive lymph nodes (mean) ± SD	4.1 ± 3.6	3 ± 3.1	4.2 ± 4.1	5.6 ± 3.3	-	1 (33%)	7 ± 8.4
Perineural invasion, n (%)	40 (71%)	4 (44%)	2 (25%)	2 (22%)	-	0	3 (50%)
Lymphovascular invasion, n (%)	42 (75%)	5 (56%)	3 (38%)	2 (22%)	-	0	3 (50%)
Tumour grading, n							
G1	-	1	2	1	-	-	3
G2	38	4	6	7	-	-	1
G3	14	4	-	1	-	-	2
R0, n (%)	49 (88%)	9 (100%)	8 (100%)	8 (89%)	-	3 (100%)	5 (100%)
Adjuvant chemotherapy							
Number eligible, n	36	9	6	7	-	1	2
Number completed, n	30	8	5	5	-	1	1

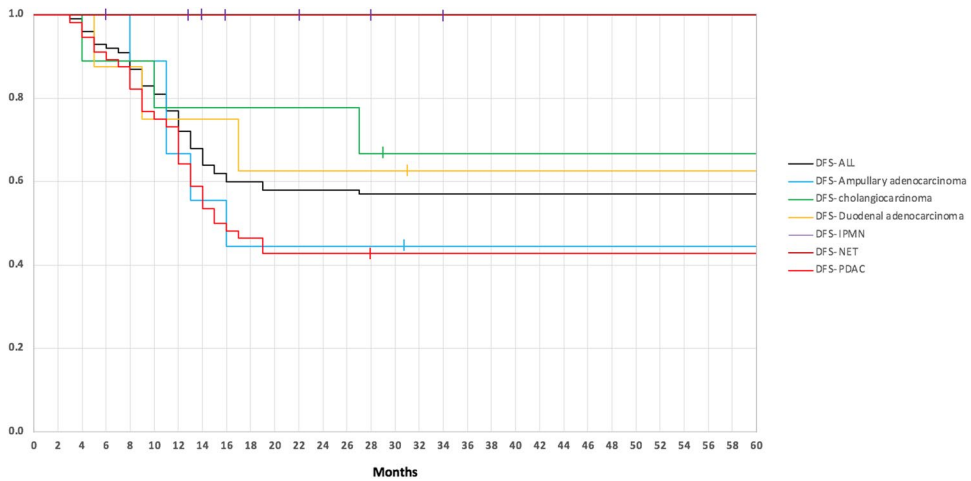

Fig. 7 DFS for Patients Undergoing PD

full-thickness bites of the jejunal wall, the described technique advocates seromuscular jejunal sutures with exclusion of the MPD if not visible or stenting in patients were it can be seen. The current technique utilises features of Kim et al. [45] and Peng 'binding technique' [46] to dunk the remnant pancreas at least 3 cm deep into the jejunum [47]. In addition parts of the Kelemen et al. end-to-side anastomosis are used by dunking the pancreatic stump 2–3 cm into the intestine with minimal stitches [48]. The addition of Falciform ligament reinforcement also add tensile strength to the PJA. Continuous PJA is supported by data demonstrating a lower incidence of the POPF in these anastomoses when compared with interrupted PJA [49]. Furthermore no sutures are placed between the MPD and jejunum which has been

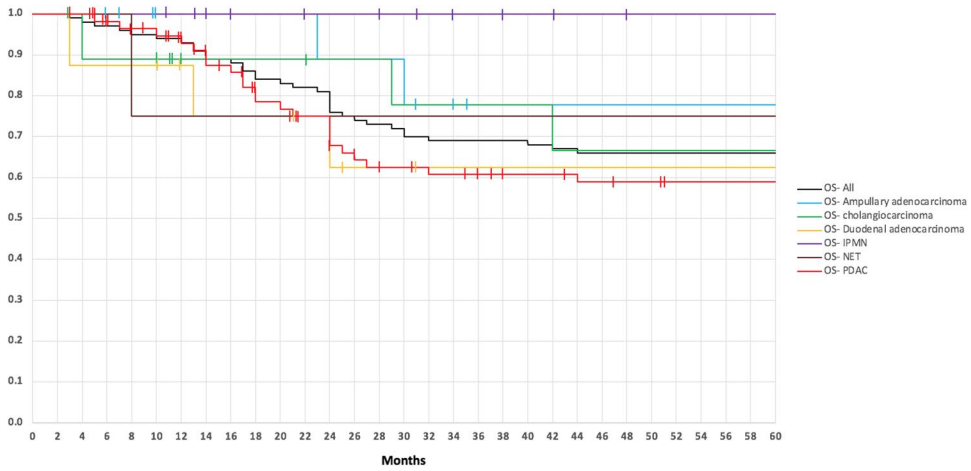

Fig. 8 OS for Patients Undergoing PD

recommended for patients with high risk of POPF (soft pancreas, narrow MPD) [50]. Overall the current PJA technique utilises many of the facets that have been shown to reduce POPF particularly in high risk patients.

The median time for the whole PJA was 6 min including Falciform ligament reinforcement which is similar to other reported series using similar technique. Whilst in the PANDA trial the Falciform ligament wrap was utilised to reduce the incidence of PPH in the reported PJA technique the Falciform ligament to reinforce the PJA around its full circumference adding tensile strength [51]. The study cannot demonstrate the precise effect of the Falciform ligament reinforcement on the incidence of POPF but given that the incidence of Type B (n = 12) and C (n = 2) POPF was 14% this addition to the PJA is likely advantageous without adding complexity to the technique. Furthermore this would still be expected to reduce PPH as demonstrated by the incidence of 1% in this series. Moreover the incidence of 14% of POPF Type B/C is much lower that the predicted approximately 50% based upon the FRS and a-FRS with no 90 day-mortality noted. A comprehensive recent review demonstrated that the incidence of CR-POPF is approximately 21% following PD [24] and the current series compares favourably to this at 14%. The incidence of POPF Type C in a recent meta-analysis was reported as 3.5% similar to the current study although it varied from less than 1% to more than 9% [24] which likely demonstrates that POPF Type C can be limited and minimised but not eliminated [52]. These studies included PJA performed using a variety of methods and as such represent a heterogenous group with respect to this. The mortality of POPF Type C is high, with the described incidence rate of 25%–35% [24, 53] with most patients with POPF Type C needing at least one surgical re-intervention [5] which concurs with the findings from this study. In addition in the 3 patients requiring reoperation a completion pancreatectomy was not required, consistent with a recently published single-centre study that suggested simple drainage as the most suitable method for severe POPF treatment [54]. Taken together these data suggest the reported PJA technique is safe and has an acceptable complication profile with the essential steps being are mobilisation of the remnant pancreas for 2cm, careful measured opening the jejunum, equidistant purse string suture between the pancreas and jejunum using a parachute technique to allow precise placement of sutures and careful placement of the Falciform ligament for reinforcement. In addition the technique allows the minimisation of sutures ensuring a good blood supply to the pancreatic stump critical to the healing of the PJA [55] and ensures that the dunking process keeps the remnant pancreas parallel to the jejunum allowing the MPD to be centred. Furthermore, as suggested by previous authors, single-layer continuous PJA technique can also be used during robotic PD with good POPF rates [56, 57]. The simplicity of the current PJA technique is demonstrated by the fact that is can be mastered after 26 PJAs. Of note all PJAs in this series were performed by one surgeon in a large number of patients in a variety of pancreases reducing one critical factor in the interpretation of the techniques efficacy.

In addition to the anastomotic technique, other aspects in peri-operative management may also have impact on the occurrence of POPF. In particular the "bundle" of MPD stent, prophylactic intra-abdominal drainage with 30F drains and somatostatin analogues will have an effect on the incidence of POPF. Timely healing of the PJA after PD for malignant disease allows patient to commence adjuvant chemotherapy. In total, 61 patients were eligible for adjuvant chemotherapy of which 50 patients (82%) commenced and completed treatment. This is higher than in recently reported series and is a surrogate marker for low complications associated with the PJA [58]. The relatively high frequency of adjuvant chemotherapy is reflected in the good long-term patient survival exemplified in particular in patients with

PDAC with 5-year survival DFS and OS of 43% and 59% respectively despite one quarter of the cohort (25%) having T3 disease.

The current study has limitations. In particular there is no matched duct-to-mucosa comparator group and all PJAs were performed by a single surgeon at a single centre and therefore, the generality and applicability can be questioned. The study is also retrospective and multivariate analysis was not feasible. PD is an operation that demands proficiency of technical skills to achieve the lowest morbidity rate, the single-layer continuous dunking PJA presented in this study is a simplified and feasible method for PJA with equivalence to international outcome standards.

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Author contributions RHB conceived the study, carried out the work and wrote the manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval Provided by the Royal Marsden Hospital Trust (CCR5615).

Conflict of interest Nil to declare.

Competing interests The authors declare no competing interests.

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