

Introduction: To study whether the implementation of a clinical pathway including some enhanced recovery after surgery (ERAS) items for pancreaticoduodenectomy (PD) in a low volume centre for pancreatic surgery was safe.

Material and methods: Patients undergoing elective PD within a clinical pathway between 1 October 2013 and 30 September 2019 were considered for the study and the outcome was compared between the first and second period of the study. The primary endpoint was the achievement of postoperative key targets of the protocol. Secondary endpoints were complications, mortality and readmissions within 90 days postoperatively, and postoperative hospital stay.

Results: Forty-five patients could be analysed. The two groups were balanced for demographic, clinical and histological variables. In the second period more patients achieved key targets: nasogastric tube removal at postoperative day (PoD) 2, oral fluids at PoD 3, drain removal at PoD 5 and hospital discharge at PoD 9. The rates of postoperative complications, mortality and readmissions were not significantly different between the two groups and were similar to data reported for high volume centres.

Conclusions: Our results show that the implementation of a clinical pathway following PD and including some ERAS items was feasible and safe in a low volume centre for pancreatic surgery.

Key words: pancreaticoduodenectomy, low volume centre, clinical pathway.

Contemp Oncol (Pozn) 2022; 26: 102–108
DOI: <https://doi.org/10.5114/wo.2022.117359>

Outcome after implementation of a clinical pathway for pancreaticoduodenectomy in a low volume centre

Thomas Zacharias, Dan Sebastien, Ferreira Nelio

Department of Digestive, Hepatobiliary and Endocrine Surgery, Hôpital Emile Muller, Mulhouse, France

Introduction

In recent years enhanced recovery after surgery (ERAS) pathways have been implemented in the perioperative care after pancreaticoduodenectomy (PD) [1]. These pathways apply evidence-based principles of care for optimisation of postoperative analgesia, drain management, early feeding and mobilisation with the aim of reducing the postoperative stress response and thus enhancing recovery and outcome [2–4]. Pancreaticoduodenectomy performed in high volume centres resulted in low mortality of 3–5.3% [5–7] but was still associated with significant morbidity.

However, recent data showed that a large proportion of pancreatic resections including PD were still performed in low and intermediate volume centres in Europe and elsewhere [8, 9]. Although centralisation of pancreatic surgery will continue, it appears unlikely that all pancreatic resections will be performed in high volume centres in the near future [10]. On the other hand, it remains questionable whether the advances in perioperative care after PD, reported by teams of high volume centres, would be possible to achieve in a low volume centre for pancreatic surgery.

Therefore, the aim of the present study was to report the short-term outcome after implementation of a clinical pathway including some ERAS recommendations for PD in a low volume centre for pancreatic surgery. The hypothesis was that pathway implementation would be safe in this setting.

Material and methods

According to French legislation for the regulation of clinical research, requirements for the provision of informed consent concerning the study were waived because of the retrospective monocentric study design and local data analysis without data transmission [11]. However, patients gave informed written consent for surgery and data collection.

The authors' centre is a tertiary hospital with 2 surgeons performing PD. Individual surgeon experience was over 60 PDs at the beginning of the study period. Sixty-two pancreaticoduodenectomies were performed during 6 years between 1 October 2013 and 30 September 2019 in the authors' institution, classifying the centre as low volume (annual PD volume < 16) [7, 10].

Standard preoperative workup included blood analysis, computed tomography scanning and/or magnetic resonance imaging in all patients. Contraindications for PD were: liver cirrhosis, distant metastases and arterial invasion.

A clinical pathway was considered for patients undergoing elective PD with or without portal/superior mesenteric vein resection, but without simultaneous associated procedures. Accordingly, exclusion criteria for the pathway were emergency PD ($n = 2$), PD with simultaneous associated procedures: hepatectomy ($n = 2$), colectomy ($n = 4$) and total PD ($n = 1$).

A further 8 patients had standard perioperative care at the discretion of the responsible surgeon. Therefore, 45 patients were included in the clinical pathway. The data were retrieved from a prospective database and retrospectively analysed. Patients were followed up for at least 3 months. No patient was lost during follow-up.

Clinical pathway

The items of the ERAS recommendations [12] used and not used in the current study are shown in Table 1. Biliary stenting was performed endoscopically if the total bilirubin level was $> 250 \mu\text{mol/l}$ or if this level would be achieved within a few days without drainage [13]. Preoperative immunonutrition (Oral-Impact) was given for 7 days according to French guidelines [14]. Patient controlled epidural analgesia was routinely used [12]. Alternatively in selected cases (technical reason or not accepted by patients) intravenous (morphine) patient controlled analgesia was used. Allogeneic blood transfusion was given when the haemoglobin level dropped below 8 g/dl and according to haemodynamic tolerance. Intraoperative warming and avoidance of fluid overload were used routinely. Antibiotics were given perioperatively according to French guidelines [15] and in patients with a biliary prosthesis five days of postoperative antimicrobial therapy was given [16]. Bile culture was performed routinely. Patients were monitored in an intermediate care unit for at least 3 days postoperatively and glucose level monitoring and treatment of hyperglycaemia with insulin was used routinely. All patients had thromboprophylaxis with low molecular weight heparin [12]. A somatostatin analogue was not given routinely [12]. A proton-pump inhibitor was given routinely.

Key targets for the postoperative course were derived from the protocol of Robertson *et al.* in 2012 [17] with some modifications: target for nasogastric tube (NGT) removal postoperative day (PoD) 2, target for solid food PoD 5 because of the pancreatogastric anastomosis and target for discharge PoD 8 and are shown in Table 1. Oral nutrition was started at PoD 3 with clear liquids, followed by liquid food at PoD 4 and solid food at PoD 5. Early postoperative enteral nutrition via a percutaneous jejunostomy was included in the pathway following the guidelines of the European Society for Parenteral and Enteral Nutrition (ESPEN) [18].

Deviations from ERAS recommendations were: no oral carbohydrate preload, transoesophageal Doppler not used, routine laxatives and chewing gum not used, routine use of NGT and enteral nutrition.

Surgical technique

After a bilateral subcostal incision with upper midline extension, inter-aorto-caval lymph node sampling with frozen section was performed routinely [19] and in case of no metastatic lymph node a PD without pyloric conservation was performed in all patients. Reconstruction was performed with pancreatogastric anastomosis to the posterior gastric wall [20], end-to-side hepaticojejunal anastomosis and end-to-side retrocolic gastrojejunal anastomosis. Portal or superior mesenteric vein resection, if indicated, was per-

formed *en bloc* and a veno-venous anastomosis was performed [21]. No grafts were used. A percutaneous jejunostomy for postoperative enteral nutrition was placed 30 cm downwards from the gastrojejunal anastomosis. Drainage of the hepaticojejunal and pancreatogastric anastomosis was performed with a multitubular silicon drain (Coloplast) [22, 23].

Definitions

Overall complications were defined as any deviation from an uneventful postoperative course within 90 days after surgery. Severity of complications was defined according to the Clavien-Dindo classification [24]. Postoperative pancreatic fistula (POPF) [25], delayed gastric emptying (DGE) [26] and post-pancreatectomy haemorrhage [27] were defined according to the International Study Group of Pancreatic Surgery. Hospital stay was defined as postoperative hospital stay. Undernutrition was defined with the Nutritional Risk Index (NRI) [28]. Comorbidity was defined according to the Charlson Comorbidity index [29].

Endpoints

The primary endpoint was the achievement of postoperative key targets of the pathway. Secondary endpoints were complications and mortality within 90 days postoperatively, readmissions and postoperative hospital stay. The dataset was split in two to compare the outcome between the first 22 patients and the next 23 patients included in the study, in order to analyse changes in protocol compliance and outcome.

Statistical analysis

Continuous variables were reported as median with interquartile range (IQR) and compared with the non-parametric Mann-Whitney *U* test. Dichotomous variables were reported as *n* (%) and compared with the Pearson χ^2 or Fisher's exact test, as appropriate. All statistical tests were two-sided, and $p < 0.050$ was considered significant.

Results

The first 22 patients were operated on between 1 October 2013 and January 2017, the next 23 patients between January 2017 and 30 September 2019.

Baseline characteristics of all 45 patients are shown in Table 2. Undernutrition defined by an NRI < 97.5 was registered in 26 patients (57.7%) and preoperative anaemia (haemoglobin level $< 12.5 \text{ g/dl}$) in 25 patients (55.5%). Preoperative biliary drainage was required in 23 patients (51.1%) with a preoperative bilirubin level over or near $250 \mu\text{mol/l}$. The median total bilirubin level before stenting is given in Table 2. The intraoperative variables were not different between the two groups and are shown in Table 3. Forty patients (88.9%) were operated on for malignancy. Nine patients (20%) had portal or superior mesenteric vein resection. Two patients had a pancreatico-jejunal anastomosis, one because of a previous gastrectomy and the other because of a difficult mobilisation of the pancreatic tail. The variables impacting POPF, as determined

Table 1. Clinical pathway for pancreaticoduodenectomy

ERAS items [12]	Current study
Preoperative counselling	Applied routinely
Perioperative biliary drainage	Drainage if bilirubin > 250 µmol/l [13]
Preoperative smoking and alcohol consumption	Was attempted
Preoperative nutrition	In malnourished patients: oral supplements
Perioperative oral immunonutrition	Routinely used for 7 day preoperatively
Oral bowel preparation	Bowel preparation not used
Preoperative fasting and Preoperative treatment with carbohydrates	Solid food until 12 p.m. the day before the operation, clear fluid up to 2 h before operation Oral carbohydrate loading not used
Pre-anaesthetic medication	No long acting premedication used
Anti-thrombotic prophylaxis	Low molecular weight heparin and compression routinely used for 4 weeks
Antimicrobial prophylaxis	Routinely used [15], in patients with biliary drainage 5 days treatment [16]
Skin preparation	Routinely used
Epidural analgesia	Peridural anaesthesia routinely used, removed PoD 3
Intravenous analgesia	PCA used alternatively, removed PoD 3
Wound catheters and TAP block	Not used
Postoperative nausea and vomiting	Pharmacological intervention routinely used
Incision	Subcostal incision with upper midline extension
Avoiding hypothermia	Intraoperative cutaneous warming routinely used
Postoperative glycaemic control	Monitoring of glucose levels and insulin treatment used routinely
Nasogastric intubation	Nasogastric tubes routinely used for 24–48 h
Fluid balance	Fluid and salt overload was avoided, transoesophageal Doppler not used
Perianastomotic drain	Drain removal at PoD 5 according to drain amylase level
Somatostatin analogues	Not used routinely
Urinary drainage	Transurethral catheterisation removed PoD 3
Delayed gastric emptying	No prevention strategy
Stimulation of bowel movement	Oral laxatives and chewing gum not used routinely
Postoperative artificial nutrition	Routine enteral nutrition starting PoD1, oral nutrition: PoD 3 liquids, PoD 5 solid food
Early and scheduled mobilization	Active mobilization starting PoD 1
Audit	Current study

Deviations from ERAS recommendation are in bold

PoD	Postoperative key targets (underlined) for the clinical pathway
1	NGT removed if volume < 500 ml/24 h, start enteral nutrition: 10 ml/h, sit for 2 × 30 min
2	<u>NGT removed</u> , enteral nutrition 20 ml/h, sit for 2 × 1 h
3	<u>Epidurals and urinary catheter removed</u> , <u>oral liquids</u> , enteral nutrition 30 ml/h, sit for 2 × 1 h, short walk, discharge of intermediate care unit
4	Tolerating liquid oral diet, enteral nutrition 40 ml/h
5	<u>Drainage removed</u> if amylase < 150 U/l, <u>tolerating solid oral diet</u> , walking in ward
6	<u>STOP i.v. fluids</u>
7	STOP enteral nutrition, normal diet
8	Discharge home or to rehabilitation facility
With oral proton-pump inhibitor, oral nutritional complements if indicated (undernutrition), 3 weeks of thromboprophylaxis with low-molecular-weight heparin	

ERAS – enhanced recovery after surgery, NGT – nasogastric tube, PoD – postoperative day, TAP – transversus abdominis plane

Table 2. Baseline characteristics of 45 patients undergoing pancreaticoduodenectomy in a clinical pathway

Number	First period	Second period	<i>p</i>
	<i>n</i> = 22	<i>n</i> = 23	
Female gender	5	6	1
Age in years	64 (56–70)	72 (64–75)	0.040*
Charlson comorbidity index	3 (2–4)	3 (2–4)	0.682*
COLD	2	2	1
Ischemic heart disease	4	4	1
Cerebrovascular disease	2	1	0.608
Diabetes	9	8	0.763
History of other cancer	3	6	0.459
Haemoglobin level < 12.5 g/dl	14	11	0.372
ASA score ≥ 3	12	15	0.549
Weight loss > 10%	12	11	0.768
NRI < 97.5	13	13	1
Biliary drainage	14	9	0.189
Total bilirubin level (before stenting in μmol/l)	274 (222–385)	381 (300–406)	0.332*
Neoadjuvant chemotherapy	0	2	0.489

ASA – American Society of Anesthesiologists, COLD – chronic obstructive lung disease, NRI – nutritional risk index

Continuous variables are reported as median and interquartile range. Dichotomous variables are reported as *N*. Continuous variables were compared using the Mann-Whitney *U* test*. Dichotomous variables were compared using Fisher's exact test.

by the “fistula risk score” [30], were not different between the two groups.

The main results of the histological analysis of the PD specimen are shown in Table 4. The number of resected and analysed lymph nodes, intraoperative blood loss, perioperative transfusion rate and duration of surgery showed accordance with recommendations for quality control in pancreatic surgery [31, 32]. In 13 patients an R1 resection was registered because of an involved arterial margin; of those patients 12 had pancreatic ductal adenocarcinoma.

Complications were registered in 29 patients (64.4%). Post-pancreatectomy haemorrhage was registered in 6 patients (13.3%) and 5 patients (11.1%) needed reoperations: 3 for early haemorrhage (within 24 h) and 2 for late haemorrhage. Three reoperated patients needed further procedures: 2 patients an arterial embolisation and one patient a second re-operation.

Pancreatic fistula was registered in 10 patients (22.2%) and clinically relevant grade B/C fistula in 9 patients (20%). The fistula risk score [30] was predictive for pancreatic fistula: no and low risk group (score 0–2): 4.3% fistula (1 out of 23), moderate and high risk group (score ≥ 3): 40.9% fistula (9 out of 22) (*p* = 0.004).

Post-pancreatectomy haemorrhage was reported in 4 out of 10 patients (40%) with POPF versus 2 out of 35 patients (5.7%) without a pancreatic fistula (*p* = 0.016).

Delayed gastric emptying was registered in 13 patients (28.8%) and grade B/C in 4 patients (8.9%). Major compli-

Table 3. Perioperative data for pancreaticoduodenectomy in 45 patients in a clinical pathway

Number of patients	Group A	Group B	<i>p</i>
	<i>n</i> = 22	<i>n</i> = 23	
Pancreatogastric anastomosis	22	21	0.489
Feeding jejunostomy	22	22	1
“Hard” consistency of pancreas	9	7	0.542
Pancreatic duct size in [mm]	5 (3–5)	4 (3–5)	0.484
Peri-operative transfusion	8	5	0.336
Duration of surgery in [min]	407 (390–438)	395 (372–420)	0.190
SMV or portal vein resection	4	5	1
Estimated blood loss in [ml]	375 (212–500)	300 (250–325)	0.267
Fistula risk score ≥ 3	13	9	0.238

SMV – superior mesenteric vein

Continuous variables are reported as median and interquartile range. Dichotomous variables are reported as *N*.

Continuous variables were compared using the Mann-Whitney *U* test. Dichotomous variables were compared using Fisher's exact test. Fistula risk score [30]: 0–2: no/low risk, ≥ 3 moderate/high risk.

Table 4. Histological data for pancreaticoduodenectomy specimen in 45 patients in a clinical pathway

Number of patients	Group A	Group B	<i>p</i>
	<i>n</i> = 22	<i>n</i> = 23	
Ductal adenocarcinoma	12	14	0.767
Distal bile duct carcinoma	3	0	0.108
Ampullary carcinoma	2	3	1
Other cancer (IPMN, endocrine, duodenal)	4	2	0.414
Benign disease	1	4	0.346
R1 resection (+ arterial margin)	8	5	0.337
Median number of resected lymph nodes	20 (14–25)	23 (15–29)	0.418
TNM stage pN+	10	13	0.556
TNM stage pT ≥ 3	14	9	0.139
Perineural invasion	14	10	0.236
Perivascular invasion	4	8	0.314
Lymphatic invasion	4	6	0.722

IPMN – intraductal papillary mucinous neoplasm, TNM – tumour, node, metastasis classification

Continuous variables are reported as median and interquartile range. Dichotomous variables are reported as *N*.

Continuous variables were compared using the Mann-Whitney *U* test. Dichotomous variables were compared using Fisher's exact test.

cations (Clavien-Dindo ≥ 3) were registered in 7 patients (15.5%).

Two patients (4.4%) died within 90 days. In both patients post-pancreatectomy haemorrhage caused by POPF was the cause. In the remaining 43 patients median follow-up was 23 months (range 4–62).

After hospital discharge 37 patients (82.2%) went home and 8 (17.7%) were transferred to a rehabilitation facility.

Table 5. Postoperative complications and severity of complications according to the Clavien-Dindo classification [24] in 45 patients undergoing pancreaticoduodenectomy in a clinical pathway

Number	First period	Second period	p
	n = 22	n = 23	
Number of patients with complications	12	17	0.221
Pancreatic fistula (all)	6	4	0.491
Grade B/C (clinically relevant)	6	3	0.284
Delayed gastric emptying (all)	8	5	0.337
Grade B/C	3	1	0.346
Bleeding complications grade B/C	3	3	1
Number of patients with complications grade			
Clavien-Dindo 1	2	5	0.414
Clavien-Dindo 2	7	8	1
Clavien-Dindo 3	1	1	1
Clavien-Dindo 4	1	2	1
Clavien-Dindo 5 (90-day mortality)	1	1	1
Readmission	4	3	0.699
Re-operation	2	3	1

Dichotomous variables are reported as N. Dichotomous variables were compared using Fisher's exact test.

Median length of stay was 11 days (IQR: 8–14) and mean length of stay was 12.5 days for all 45 patients. Median length of stay was 9 days in 35 patients without POPF versus 16.5 days in 10 patients with a pancreatic fistula ($p = 0.019$).

Seven patients (15.5%) were readmitted within 31 days to the hospital for a median of 9 days (IQR: 3.5–18 days). No further readmission was registered after 31 days. Causes of readmissions were: bleeding complications in 3 patients requiring reoperation (2 patients) and arterial embolisation of aneurysm (1 patient), anaemia requiring transfusion (1 patient), undernutrition requiring treatment (1 patient) and non-specific abdominal pain (2 patients). No significant differences for complications, mortality and readmissions were observed between the first and the second period of the study (Table 5).

Postoperative key targets

The nasogastric tube was removed by PoD 2 in 28 patients (Table 6), and by PoD 6 in 41 patients. Clear liquids were given at PoD 3 in 38 patients and solid food at PoD 5 in 18. Oral nutrition was impacted by DGE, which manifested with nausea and vomiting at median PoD 4 (range 3–6 days). A total of 13 patients (29%) developed DGE: in 9 patients (20%) an NGT was re-inserted for a median time of 6 days (range 2–16 days) and in 4 patients the NGT placed during the operation was taken out after PoD 9. All patients, except 4 with DGE grade B/C, were able to eat solid food by PoD 14.

Drain amylase level was measured at PoD 1, 2 and 3 and drains were removed by PoD 5 in 28 patients (Table 6). Ten patients had a pancreatic fistula and in those patients the drainage was removed at median PoD 14.

Table 6. Postoperative key targets in 45 patients after pancreaticoduodenectomy in a clinical pathway

	Number of patients achieving key targets		
	First period	Second period	p
	n = 22	n = 23	
NGT removal PoD 2*	12	16	0.365
Oral clear fluids PoD 3*	15	23	0.004
Tolerating solid diet PoD 5*	7	11	0.365
Epidural analgesia removed PoD 3*	14	19	0.189
Urinary catheter removed PoD 3*	12	18	0.120
I.v. fluid stopped PoD 6*	9	10	1
Drainage removed PoD 5*	10	18	0.033
Median number of key targets achieved (out of 7)	3 (2–5)	5 (4–6)	0.012
Discharge PoD 9	7	14	0.075
Length of stay in days	12.5 (8.25–17)	9 (8–13)	0.028

NGT – nasogastric tube, PoD – postoperative day

*seven key targets of the clinical pathway

Continuous variables are reported as median and interquartile range. Dichotomous variables are reported as N.

Continuous variables were compared using the Mann-Whitney U test. Dichotomous variables were compared using Fisher's exact test.

In the second period of the study more patients achieved key targets: NGT removal PoD 2, oral fluids PoD 3 and drainage removed at PoD 5. The median number of key targets achieved (out of 7) was 3 for the first 22 patients versus 5 for the next 23 patients, reflecting better compliance with the protocol. The median postoperative hospital stay was reduced in the second period and more patients were discharged at PoD 9.

Discussion

The aim of the present study was to report the short-term outcome after implementation of a clinical pathway for PD including some ERAS items in a low volume centre for pancreatic surgery. The hypothesis was that pathway implementation would be safe in this setting.

Outcome data of the present study showed accordance with data reported for PD in French academic centres: complications 64.4% versus 54.4% [33], mortality: 4.4% versus 3.8% [33], reoperation 11.1% versus 11.7% [33], respectively. Ninety day mortality of 4.4% in the present study was similar to data reported by high volume centres in the Netherlands: 4.3% [6] and England: 5.3% [7].

Over 80% of patients in the present study were discharged home. The readmission rate was 15.5% and similar to 15.6% [34] reported by Boteon *et al.* for the Birmingham group.

The number of resected lymph nodes, intraoperative blood loss, perioperative transfusion rate and duration of surgery were in accordance with recommendations for quality control in pancreatic surgery [31, 32]. The rather high rate of arterial margin involvement (46%, 12 out of 26) in ductal adenocarcinoma in the current study was

not significantly different ($p = 0.116$) to the rate of 30% reported by Delpero *et al.* in a French multicentre study [35].

Adherence to the clinical pathway was higher in the second study period (since January 2017), probably reflecting a learning curve, and resulting in a reduced median hospital stay, but without affecting the complication and readmission rates.

The main limitation of the present study was the absence of a control group. In the authors' opinion, the number of patients ($n = 8$) undergoing elective "standard" PD outside the clinical pathway was too small to serve as a control group. These 8 patients were managed outside the pathway because one surgeon started the clinical pathway in September 2013 and the other surgeon followed several months later. A comparison with a "historic" control group (before October 2013) was not done as this long time interval would have included further significant bias.

The small number of patients included per year and the resulting long study period are explained by the setting of a low volume centre. However, no significant changes in the perioperative management were observed during the study period for the included patients. Seventeen patients (27%, 17 out of 62) were managed outside the pathway either because of an emergency, associated procedures, total PD or surgeon preferences. Similar findings were reported by Tremblay St-Germain *et al.*, who reported that 39 out of 122 patients (32%) were managed outside the pathway during the implementation period for the reason of compliance issues and additional procedures [3]. However, in the current study a majority (75%) of elective patients with PD (45 out of 60) were managed within the clinical pathway.

The protocol used in the present study should be criticised as not all items of the ERAS recommendation [12] were strictly applied in our institution.

Two aspects of the protocol that may require revision were the routine use of NGT and enteral nutrition via a percutaneous jejunostomy. We used a pancreatogastric anastomosis and an NGT was routinely inserted for 24–48 hours. However, evidence suggests that routine use of an NGT following PD is not necessary [36].

In the authors' institution enteral nutrition after PD has been preferred over total parenteral nutrition since 2011 based on the ESPEN recommendations [18] and the report of reduced DGE after enteral nutrition [37]. Because undernutrition was frequently registered in our patients, enteral nutrition starting at PoD1 was included in the pathway, although this was not recommended in the ERAS guidelines [12].

In 2016 a randomised study reported a mortality rate of 12.7% after PD with enteral nutrition via a naso-jejunal feeding tube [38]. Although in our experience a similar mortality rate was not observed, the benefit of routine enteral nutrition should be questioned. There is evidence that early oral feeding with "on demand" enteral nutrition is better than routine enteral nutrition [39].

Another challenge was the avoidance of routine drainage and early drain removal as suggested in the ERAS recommendations [12]. Because level I evidence showed increased mortality if drainage was not used after PD [23]

we used routine drainage and early drain removal if amylase levels were below a predefined value. In our institution drain amylase levels were recorded at PoD 1, 2 and 3 and further on if increased values ($> 3x$ upper normal serum value at PoD 3) were registered. The fistula risk score [30] was predictive for POPF in the current study and may be useful for selective drain management in the future.

The major reason for a longer hospital stay in the present study was a pancreatic fistula. The median length of stay (a surrogate marker for a successful ERAS pathway) was 9 days in 35 patients without POPF versus 16.5 days in 10 patients with POPF ($p = 0.019$). In two patients a pancreatic fistula was diagnosed during the re-admission at PoD 11 and 16, after an initial uneventful hospital stay of 8 and 12 days respectively, with normal drain amylase levels at PoD 3 and a fistula risk score of 3 (moderate risk). This raises the question whether a target of discharge at PoD 8 was safe in these patients, as both patients had to be re-operated on for bleeding complications. However, we presume that it is rather unlikely that a longer initial hospital stay would have led to different management of complications. With these experiences in mind, particular care should be taken in identifying pancreatic fistula during the initial hospital stay, as it was the main risk factor for mortality, bleeding complications and a longer hospital stay.

Conclusions

Our results show that implementation of a clinical pathway including some ERAS recommendations for elective PD in selected patients was feasible and safe in a low volume centre for pancreatic surgery.

The authors declare no conflict of interest.

References

- Balzano G, Zerbi A, Braga M, Rocchetti S, Beneduce AA, Di Carlo V. Fasttrack recovery programme after pancreaticoduodenectomy reduces delayed gastric emptying. *Br J Surg* 2008; 95: 1387-1393.
- Nikfarjami M, Weinberg L, Low N, et al. A fast track recovery program significantly reduces hospital length of stay following uncomplicated pancreaticoduodenectomy. *JOP* 2013; 14: 63-70.
- Tremblay St-Germain A, Devitt KS, Kagedan DJ, et al. The impact of a clinical pathway on patient postoperative recovery following pancreaticoduodenectomy. *HPB* 2017; 19: 799-807.
- Ji HB, Zhu WT, Wei Q, Wang XX, Wang HB, Chen QP. Impact of Enhanced Recovery After Surgery programs on pancreatic surgery: a meta-analysis. *World J Gastroenterol* 2018; 24: 1666-1678.
- Schmidt CM, Turrini O, Parikh P, et al. Effect of hospital volume, surgeon experience, and surgeon volume on patient outcomes after pancreaticoduodenectomy. A single institution experience. *Arch Surg* 2010; 145: 634-640.
- Van der Geest LG, van Rijssen LB, Molenaar IQ, et al. Dutch Pancreatic Cancer Group. Volume-outcome relationships in pancreatoduodenectomy for cancer. *HPB* 2016; 4: 317-324.
- Liu Z, Peneva IS, Evison F, et al. Ninety day mortality following pancreaticoduodenectomy in England: has the optimum centre volume been identified? *HPB* 2018; 11: 1012-1020.
- Ansari D, Williamsson C, Tingstedt B, Andersson B, Lindell G, Andersson R. Pancreaticoduodenectomy-the transition from a low-to a high-volume center. *Scand J Gastroenterol* 2014; 49: 481-484.

9. Kanhere HA, Trochler MI, Kanhere MH, Lord AN, Maddern GH. Pancreaticoduodenectomy: outcomes in a low-volume, specialised hepato pancreato biliary unit. *World J Surg* 2014; 38: 1484-1490.
10. Farges O, Bendersky N, Truant S, Delpero JR, Pruvot FR, Sauvanet A. The theory and practice of pancreatic surgery in France. *Ann Surg* 2017; 266: 797-804.
11. Claudot F, Alla F, Fresson J, Calvez T, Coudane H, Bonaiti-Pellié C. Ethics and observational studies in medical research: various rules in a common framework. *Int J Epidemiol* 2009; 38: 1104-1108.
12. Lassen K, Coolsen MME, Slim K, et al. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS) Society recommendations. *Clin Nutr* 2012; 31: 817-830.
13. Van der Gaag NA, Rauws EA, van Eijck CH, et al. Preoperative biliary drainage for cancer of the head of the pancreas. *N Engl J Med* 2010; 362: 129-137.
14. Mariette C, Alves A, Benoist S, Bretagnol F, Mabrut JY, Slim K. Perioperative care in digestive surgery. Guidelines for the French Society of Digestive Surgery. *Ann Chir* 2005; 130: 108-124.
15. Société française d'anesthésie et de réanimation. Antibiotrophylaxis in surgery and interventional medicine (adult patients). Actualization 2010. *Ann Fr Anesth Reanim* 2011; 30: 168-190.
16. Sourrouille I, Gaujoux S, Lacave G, et al. Five days of postoperative antimicrobial therapy decreases infectious complications following pancreaticoduodenectomy in patients at risk for bile contamination. *HPB* 2013; 15: 473-480.
17. Robertson N, Gallacher PJ, Peel N, et al. Implementation of an enhanced recovery programme following pancreaticoduodenectomy. *HPB* 2012; 14: 700-708.
18. Weimann A, Braga M, Harsanyi L, et al. ESPEN Guidelines on enteral nutrition: surgery including organ transplantation. *Clin Nutr* 2006; 25: 224-244.
19. Schwarz L, Lupinacci RM, Svrcek M, et al. Para-aortic lymph node sampling in pancreatic head adenocarcinoma. *Br J Surg* 2014; 101: 530-538.
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: 327-335.
21. Jaeck D, Bachellier P, Oussoultzoglou E, Audet M, Rosso E, Wolf P. Analysis of a series of 100 mesenterico-portal vein resection during pancreatic resection. *Bull Acad Natl Med* 2006; 190: 1495-1506.
22. Bassi C, Molinari E, Malleo G, et al. Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. *Ann Surg* 2010; 252: 207-214.
23. Van Buren G, Bloomston M, Hughes SJ, et al. A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. *Ann Surg* 2014; 259: 605-612.
24. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; 240: 205-213.
25. Bassi C, Dervenis C, Butturini G, et al. International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: An International study Group (ISGPS) definition. *Surgery* 2005; 138: 8-13.
26. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International study Group of Pancreatic Surgery (ISGPS). *Surgery* 2007; 142: 761-768.
27. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery* 2007; 142: 20-25.
28. The veterans affair total parenteral nutrition cooperative study group. Perioperative total parenteral nutrition in surgical patients. *N Engl J Med* 1991; 325: 525-532.
29. Charlson ME, Pompei P, Ales KL, Mac Kenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373-383.
30. Callery MP, Pratt WB, Kent TS, Vhaikof EL, Vollmer CM Jr. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. *J Am Coll Surg* 2013; 216: 1-14.
31. Tomlinson JS, Jain S, Bentrem DJ, et al. Accuracy of staging node-negative pancreas cancer. A potential quality measure. *Arch Surg* 2007; 142: 767-774.
32. Ball CG, Pitt HA, Kilbane ME, Dixon E, Sutherland FR, Lillemoie KD. Peri-operative blood transfusion and operative time a quality indicators for pancreaticoduodenectomy. *HPB* 2010; 12: 465-471.
33. Addeo P, Delpero JR, Paye F, et al. French Surgical Association (AFC). Pancreatic fistula after a pancreaticoduodenectomy for ductal adenocarcinoma and its association with morbidity: a multicentre study of the French Surgical Association. *HPB* 2014; 16: 46-55.
34. Boteon APCS, Boteon YL, Hodson J, et al. Multivariate analysis of predictors of unplanned hospital readmission after pancreaticoduodenectomy: development of a validated risk score. *HPB* 2019; 21: 26-33.
35. Delpero JR, Bachellier P, Regenet N, et al. Pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: a French multicentre prospective evaluation of resection margins in 150 evaluable specimens. *HPB* 2014; 16: 20-33.
36. Ammar K, Varghese C, Thejasvin K, et al. Impact of routine nasogastric decompression versus no nasogastric decompression after pancreaticoduodenectomy on perioperative outcomes: meta-analysis. *BJS Open* 2021; 5: zrab111.
37. Rayar M, Sulpice L, Meunier B, Boujema K. Enteral nutrition reduces delayed gastric emptying after standard pancreaticoduodenectomy with child reconstruction. *J Gastrointest Surg* 2012 May; 16: 1004-1011.
38. Perinel J, Mariette C, Dousset B, et al. Early enteral versus total parenteral nutrition in patients undergoing pancreaticoduodenectomy: a randomized multicenter controlled trial (Nutri-DPC). *Ann Surg* 2016; 264: 731-737.
39. Gerritsen A, Wennink RAW, Besselink MGH, et al. Early oral feeding after pancreatoduodenectomy enhances recovery without increasing morbidity. *HPB* 2014; 16: 656-664.

Address for correspondence

Thomas Zacharias, MD

Department of Digestive, Hepatobiliary and Endocrine Surgery
Hôpital Emile Muller
20, rue du Dr Laennec
68070 Mulhouse Cedex
France
Phone: +33 3 89 64 73 59
e-mail: zachariast@ghrmsa.fr

Submitted: 01.12.2021

Accepted: 13.12.2021