## **ORIGINAL ARTICLE**

# Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy: validation of International Study Group of Pancreatic Surgery classification and analysis of risk factors

Giuseppe Malleo, Stefano Crippa, Giovanni Butturini, Roberto Salvia, Stefano Partelli, Roberto Rossini, Matilde Bacchion, Paolo Pederzoli and Claudio Bassi

Department of Surgery, General Surgery B Unit, G. B. Rossi Hospital, University of Verona, Verona, Italy

### Abstract

**Objectives:** This study evaluates the incidence and clinical features and associated risk factors of delayed gastric emptying (DGE) after pancreaticoduodenectomy, employing the International Study Group of Pancreatic Surgery (ISGPS) consensus definition.

**Methods:** Demographic, pathological and surgical details for 260 consecutive patients who underwent pylorus-preserving pancreaticoduodenectomy at a single institution were analysed using univariate and multivariate models.

**Results:** Postoperative complications occurred in 108 (41.5%) and DGE was diagnosed in 36 (13.8%) of 260 patients. Among the 36 DGE patients, 16 had grade A, 18 grade B and two grade C DGE. Resumption of a solid diet (P < 0.001), time to passage of stool (P = 0.002) and hospital discharge (P < 0.001) occurred later in DGE patients. The need for total parenteral nutrition was significantly higher in DGE grade B/C patients (P < 0.001). In the univariate analysis, abdominal collections ( $P \le 0.001$ ), pancreatic fistula (PF) grades B and C (P < 0.001), biliary fistula (P = 0.002), pulmonary complications (P < 0.001) and sepsis (P = 0.002) were associated with DGE. Only abdominal collections (P = 0.009), PF grade B/C (P < 0.001) and sepsis (P = 0.024) were associated with clinically relevant DGE. In the multivariate analysis, PF grade B/C (P = 0.004) and biliary fistula (P = 0.039) were independent risk factors for DGE.

**Conclusions:** The ISGPS classification and grading systems correlate well with the clinical course of DGE and are feasible for patient management. The principal risk factors for DGE seem to be pancreatic and biliary fistulas.

### **Keywords**

pancreatic head resection, surgical morbidity, pancreatic fistula, biliary fistula, duodenojejunostomy

Received 14 April 2010; accepted 3 June 2010

### Correspondence

Claudio Bassi, General Surgery B, G. B. Rossi Hospital, P. Le L. A. Scuro, 10, 37134 Verona, Italy. Tel: + 39 045 812 4552. Fax: + 39 045 812 4622. E-mail: claudio.bassi@univr.it

### Introduction

Generally considered to be one of the most technically demanding of surgical procedures, pancreaticoduodenectomy (PD) has evolved into a safe operation with acceptable perioperative mortality (<5% at high-volume centres), although morbidity remains substantial, at 20–60%.<sup>1</sup> Postoperative delayed gastric emptying

This paper was presented at the International Hepato-Pancreato-Biliary Association, 18–22 April 2010, Buenos Aires.

(DGE) is one of the most common complications after PD and is a potentially serious event that may lead to patient discomfort, prolonged hospitalization and increased hospital costs.<sup>2</sup> DGE is a complex phenomenon with a multifactorial genesis and is believed to be associated with other major intra-abdominal complications, including pancreatic fistula and infected collections.<sup>3</sup> Furthermore, several technical aspects, such as the type of resection (Whipple PD vs. pylorus-preserving PD [PPPD]), the method of reconstruction of gastric drainage (antecolic vs. retrocolic) and mechanical dilatation of the pylorus (in cases of its preservation) have been shown to influence DGE.<sup>4</sup> More importantly, an objective and accurate comparison of past studies is particularly difficult because of the lack of a generally accepted definition of this specific complication. A number of different definitions based on time of nasogastric intubation and ability to tolerate a regular diet have been proposed and opinions about the incidence of DGE and its associated risk factors vary widely among surgical centres.<sup>5</sup> In 2007, the International Study Group of Pancreatic Surgery (ISGPS) proposed a consensus definition based on severity and clinical impact,<sup>3</sup> which has been recently validated in a small number of reports.<sup>6,7</sup> The aim of this study was to evaluate the incidence and clinical presentation of DGE using the ISGPS definition and to analyse the associated risk factors after PPPD, which, at the authors' institution, is the standard procedure for pancreatic head and periampullary diseases.

### **Materials and methods**

### Operative procedure and perioperative management

All PDs carried out at the General Surgery B Unit, G. B. Rossi Hospital, University of Verona between the introduction of the ISGPS definition (November 2007) and October 2009 were retrieved from a prospective electronic database. Only PPPDs were included in the present analysis; Whipple PDs were excluded because of the very small number performed (in patients with tumours involving the first or second duodenal portion or infiltrating the stomach). Resection included the gallbladder, the pancreatic head with distal bile duct, the duodenum (except for the first portion), and the first jejunal loop. In all patients a standard lymphadenectomy was performed, which included dissection of the anterior and posterior pancreaticoduodenal, inferior head, pyloric, common bile duct, superior head, superior mesenteric and superior and inferior pancreatic body nodes.<sup>8</sup>

In the reconstructive phase, anastomoses were constructed on a single jejunal loop repositioned upwards into the supra-mesocolic compartment in a retrocolic fashion. Both end-to-side pancreaticojejunostomy (PJ) and pancreaticogastrostomy (PG) were performed, according to the surgeon's preference. Pancreaticojejunostomy was performed with single-layer, interrupted, nonabsorbable or PDS (polydioxanone) sutures (3/0 or 4/0), whereas PG was performed according to the technique described by our group (via an anterior gastrotomy, with interrupted 4/0 PDS sutures).<sup>9</sup> No pancreatic stent was used. End-to-side hepaticojejunostomy was performed 20 cm distally to the PJ with absorbable or PDS 3/0 or 4/0 interrupted sutures. According to the surgeon's preference, either antecolic or retrocolic duodenojejunostomy (DJ) with mechanical pylorus dilatation was carried out 50 cm downstream with absorbable, single-layer interrupted sutures (3/0). Two flat Penrose drains (12 mm; Redax Srl, Milan, Italy) were positioned, the first beneath the stomach up to the posterior surface of the pancreatic anastomosis, and the second in the vicinity of the biliary anastomosis up to the superior margin of the pancreatic remnant.

### Postoperative management and analysis of DGE

Prophylactic octreotide at a dose of 0.1 mg was given subcutaneously 1 h prior to the operation and continued postoperatively (every 8 h) until the patient was able to tolerate a solid diet, which was normally started on postoperative day (POD) 3. Nasogastric tube removal was scheduled for POD 1. A proton pump inhibitor was administered intravenously following surgery and converted to an oral dosage once an oral diet was tolerable. Intra-abdominal drains were removed on POD 3 in patients at low risk of pancreatic fistula (amylase value in drains <5000 U/l on POD 1) according to our institution's protocol.<sup>10</sup> Definitions of postoperative complications refer to current evidence and are provided in Table 1.11,12 Table 2 shows the ISGPS consensus definition of DGE with a clinical grading system. Demographic and pathological data and surgical details were recorded. The clinical presentation and grading of DGE, as well as postoperative parameters and associated risk factors, were evaluated.

### Statistics

Variables were assessed for normality using the Shapiro–Wilk test. For normally distributed variables, data were expressed as mean  $\pm$  standard deviation (SD); *t*-test was used to compare means. Non-normally distributed variables were expressed as medians (range) and non-parametric tests (Mann–Whitney *U*-test) were employed for statistical comparison. The chi-squared test (with Yates conti-

Table 1 Definitions of complications after pancreatic surgery

Pancreatic fistula: any output rich in amylase content (>3 × ULN of serum amylase, ISGPF definition with clinical grading system [A, B, C])<sup>10</sup>

**Enteric fistula:** enteric secretion that persisted beyond POD 5 with demonstration by fistulography of an instantaneous filling of the jejunal loop anastomosed with the pancreas (without fistulous tract) after injection of contrast media from drain catheters

Biliary fistula: persistence of biliary drainage beyond POD 5, confirmed by fistulography

Abdominal collection: collection of fluid measuring ≥3 cm in diameter demonstrated by transabdominal ultrasound or CT scan

Acute pancreatitis: increase by at least three-fold of normal plasma amylase or lipase values 48 h after the operation, confirmed by CT scan or clinical course

Post-pancreatectomy haemorrhage: defined according to onset, location and severity. The onset is either early (≤24 h after the end of the index operation) or late (>24 h). The location is either intraluminal or extraluminal. The severity of bleeding may be either mild or severe (ISGPS definition with clinical grading system [A, B, C])<sup>11</sup>

ISGPF, International Study Group on Pancreatic Fistula Definition; POD, postoperative day; CT, computed tomography; ISGPS, International Study Group on Pancreatic Surgery

DGE grade	Nasogastric tube required	Unable to tolerate solid oral intake by POD	Vomiting/gastric distension	Use of prokinetics
A	4-7 days or reinsertion > POD 3	7	±	<u>+</u>
В	8–14 days or reinsertion > POD 7	14	+	+
С	>14 days or reinsertion > POD 14	21	+	+

Table 2 International Study Group of Pancreatic Surgery definition of delayed gastric emptying after pancreatic surgery<sup>3</sup>

DGE, delayed gastric emptying; POD, postoperative day

nuity correction in a two-way contingency table) was used for nominal data and Fisher's exact test was used in the case of a small expected frequency. Potential risk factors associated with DGE were analysed by employing logistic analysis (DGE was considered as a dependent dichotomy variable). Variables which were considered significant ( $P \le 0.05$ ) in univariate analysis were entered into a multivariate model using a backward technique by eliminating any variable that did not reach a *P*-value of  $\le 0.05$  according to Wald's test. Odds ratios are presented with respective confidence intervals to 95%. spss Version 17 was used for statistical analysis (SPSS, Inc., Chicago, IL, USA).

### **Results**

The study population consisted of 260 consecutive patients who underwent PPPD at the authors' institution between November 2007 and October 2009. Demographic, pathological and surgical details are shown in Table 3. Perioperative mortality was nil. Total surgical morbidity was 41.5% (108 patients). Pancreatic fistula was found in 60 (23.1%) patients and clinically relevant fistulas (grades B and C) in 52 (20.0%) patients. DGE occurred in 36 (13.8%) of 260 patients and represented the only postoperative complication in 12 patients, but occurred concurrently with other morbidities in the remaining 24 patients. Of the 36 DGE patients, 16 were classified as grade A, 18 as grade B and two as grade C. Data regarding the clinical presentation of DGE are shown in Table 4. Postoperative parameters, including tolerance of a solid diet, time to passage of stool, need for total parenteral nutrition, re-operation rate and postoperative hospital stay were compared between DGE and non-DGE patients (Table 5). The same postoperative parameters were also compared among DGE grades (Table 6). For this analysis, DGE grades B and C (moderate and severe clinical impact) were grouped. Table 7 displays the results of univariate analysis of preoperative, intraoperative and postoperative factors associated with DGE. The same factors were also analysed among DGE grades (grades B and C grouped together); results are shown in Table 8. The multivariate analysis identified two independent risk factors for DGE: clinically relevant pancreatic fistula and biliary fistula (Table 9).

### Discussion

Delayed gastric emptying is one of the most common complications after pancreatic head resection and contributes substantially to overall morbidity and to the impairment of perioperative quality of life.<sup>2</sup> A wide range of mechanisms has been proposed to cause DGE, including the absence of hormonal stimulation caused by the resection of the duodenum, and the denervation/ ischaemia of the antropyloric region resulting from the interruption of vagal branches and the ligation of gastric pedicles.<sup>3</sup> The impact of pylorus preservation on DGE has not been clearly established; some studies have shown a higher incidence of this complication in PPPD,<sup>13,14</sup> whereas others (including a recent metaanalysis) have suggested that classical Whipple PD is associated with a lower rate of DGE.<sup>15–17</sup> It has been proposed that the addition of mechanical pylorus dilatation after PPPD contributes to a decrease in the incidence of this specific complication.<sup>18-20</sup> The introduction into clinical practice of the ISGPS consensus definition should standardize the concept of DGE and provide a common framework with which to express results across different surgical institutions. Prior to the application of an objective and universally applicable classification, the use of various definitions of DGE in homogeneous, single-centre series led to great variety in the reported incidence (20-60%) of the complication, which made it impossible to correctly compare different experiences and the outcome of new operative approaches.<sup>5</sup> This study employed the ISGPS definition to analyse the clinical presentation and grading of DGE in a large series of patients who underwent PPPD at a high-volume centre.

DGE occurred in 36 (13.8%) of 260 patients. It should be noted that the criteria employed in the ISGPS definition are more restrictive than those used in earlier definitions, with the result that the proportion of DGE patients tends to be substantially higher than those described in earlier reports. At our centre, the condition was previously defined by a need for nasogastric tube decompression for >10 days.<sup>18</sup> If we had employed this definition in the present study, the incidence of DGE in the current series would have been 3.8% (10 of 260 patients). A paper from this institution published prior to the introduction of the ISGPS definition reported an overall incidence of DGE after PPPD of 7.9% (12 of 151 patients).<sup>21</sup>

According to the current literature, only two studies have sought to evaluate the feasibility of the ISGPS classification of DGE.<sup>6,7</sup> The first of these reported an incidence of 42% (standard operative manoeuvres included PPPD and subtotal stomachpreserving PD),<sup>6</sup> whereas the latter described an incidence of 33% after PPPD or classical Whipple PD.<sup>7</sup> The current study confirms that DGE significantly affects oral intake tolerance and is associated with the need for total parenteral nutrition, which was

	n	%, SD (range)
Gender		
Male	148	56.9
Female	112	43.1
Mean age, years	62.2	12.0
Mean body mass index, kg/m <sup>2</sup>	24.3	3.18
Disease		
Ductal adenocarcinoma	118	45.4
Ampullary adenocarcinoma	28	10.8
Intraductal papillary mucinous neoplasm	28	10.8
Neuroendocrine tumour	24	9.2
Distal cholangiocarcinoma	14	5.4
Chronic pancreatitis	14	5.4
Serous cystic tumour	12	4.6
Duodenal adenocarcinoma	6	2.3
Mucinous cystic tumour	2	0.7
Other	14	5.4
Median operative time, min	342.5	(180–660)
Intraoperative blood transfusions		
Yes	16	6.1
No	244	93.9
Type of pancreatic anastomosis		
Pancreaticojejunostomy	204	78.5
Pancreaticogastrostomy	56	21.5
Type of duodeno-jejunostomy		
Antecolic	146	56.1
Retrocolic	114	43.9
Postoperative complications		
Total surgical morbidity	108	41.5
Pancreatic fistula	60	23.0
Clinically relevant pancreatic fistula (grades B, C)	52	20.0
Delayed gastric emptying	36	13.8
Abdominal collection	26	10.0
Pulmonary complications	18	6.9
Post-pancreatectomy haemorrhage	14	5.3
Biliary fistula	12	4.6
Sepsis	12	4.6
Enteric fistula	8	3.0
Acute pancreatitis	6	2.3
Postoperative blood transfusions		
Yes	24	9.2
No	236	90.8
Re-operation		
Yes	22	8.4
No	238	91.6
Median hospital stay, days	11	(7–72)

Table 3 Demographic characteristics, pathological and surgical

details in the current study population (n = 260)

SD, standard deviation

# Characteristicn (range)DGE alone12DGE associated with other abdominal complications24ISGPS grading16DGE grade A16DGE grade B18DGE grade C2Emesis34

ing (DGE) (n = 36 patients, 13.8% of study population)

Abdominal distension

Use of prokinetics

Reinsertion of nasogastric tube

Need for total parenteral nutrition

Median day of nasogastric tube reinsertion

required in 17 of 36 patients. Akizuki and colleagues analysed the total amount of dietary intake (defined as the sum of dietary intake during POD 1–21) and demonstrated that, during the entire postoperative course, total food intake was significantly lower in DGE patients and was associated with DGE itself in both the univariate and multivariate analyses.<sup>6</sup> However, the amount of intake differed widely among individuals and, in some instances, non-DGE patients were similarly unable to eat a sufficient amount of food and required longterm parenteral nutrition. As for the grading system, 16 of 36 DGE patients were grade A and mostly devoid of clinical concern, whereas individuals with DGE grade B or C experienced major difficulties in resuming a regular diet and ultimately needed nutritional support.

Emesis was present in 34 of the 36 DGE patients and abdominal distension occurred in 15 patients. An ongoing problem with the ISGPS definition may be its poor ability to differentiate 'true' DGE from postoperative ileus. In our series, all patients classified as DGE underwent an X-ray passage, which showed evidence of a hold-up of the contrast medium in the stomach. However, an associated small bowel or colonic ileus caused by other factors (such as long operative time, and fluid and electrolyte imbalances) may also have contributed to the clinical picture.

Although postoperative hospital stay was significantly longer in DGE patients, no significant differences were observed between patients with grade A DGE and those with clinically relevant DGE (grade B or C). This may be partially explained by evidence that some DGE grade A patients experienced other associated postoperative complications (as discussed later) and by the fact that patients referred to our surgical centre often live a considerable distance from it, which discourages the early discharge of individuals with mild complications.

Similarly, the report by Akizuki *et al.* showed no differences in postoperative hospital stay among DGE grades,<sup>6</sup> whereas Park *et al.* showed a significantly prolonged hospital stay in DGE grade C patients.<sup>7</sup> In a third of DGE patients, no other postoperative

15

10

36

17

8 (3-12)

Table 5 Postoperative parameters in the current study population (n = 260)

Study population: $n = 260$	DGE ( <i>n</i> = 36)	Non-DGE ( <i>n</i> = 224)	<b>P</b> -value <sup>a</sup>
Nasogastric tube removal, POD (range)	10 (3–23)	2 (1–14)	<0.001
Tolerance of solid diet, POD (range)	10.5 (5–24)	4 (2–23)	<0.001
Time to passage of stool, POD (range)	5.5 (3–10)	4 (1–11)	0.002
Median postoperative hospital stay, days (range)	25 (13–72)	9 (7–58)	<0.001
Need for total parenteral nutrition			0.046
Yes	17	65	_
No	19	159	
Re-operation			0.748
Yes	4	18	_
No	32	206	_

<sup>a</sup>*P*-values in bold are significant at  $P \le 0.05$ 

DGE, delayed gastric emptying; POD, postoperative day

Table 6 Postoperative parameters among delayed gastric emptying grades

DGE patients: $n = 36$	DGE A ( <i>n</i> = 16)	DGE B, C ( <i>n</i> = 20)	P-value <sup>a</sup>
DGE alone			0.729
Yes	6	6	-
No	10	14	-
Reinsertion of nasogastric tube			0.132
Yes	2	8	-
No	14	12	-
Nasogastric tube removal, POD (range)	6 (3–7)	13.5 (9–23)	<0.001
Tolerance of a solid diet, POD (range)	7 (5–10)	14.5 (9–25)	<0.001
Time to passage of stool, POD (range)	5 (3–8)	6 (3–10)	0.535
Median postoperative hospital stay, days (range)	24.5 (13–45)	27.5 (17–72)	0.352
Need for total parenteral nutrition			<0.001
Yes	1	16	-
No	15	4	-
Re-operation			0.113
Yes	0	4	_
No	16	16	-

*P*-values in bold are significant at  $P \le 0.05$ 

DGE, delayed gastric emptying; POD, postoperative day

complication was present, whereas the remaining two-thirds of DGE patients exhibited concomitant morbidities. Postoperative complications, such as pancreatic fistula, biliary fistula, intraabdominal collections or abscesses and sepsis were shown to critically influence DGE.<sup>4,22</sup> It seems that DGE rarely occurs in the absence of other complications, and that the majority of patients with severe postoperative morbidity also have DGE, although this issue has not been firmly clarified. In the paper by Akizuki *et al.*, age > 65 years, subtotal stomach-preserving PD and an operative blood loss of >1000 ml were univariately associated with DGE, whereas no independent risk factors emerged in the multivariate model. The percentages of DGE and non-DGE patients with intra-abdominal infections were similar, with no correlation between these two variables.<sup>6</sup> By contrast, in the study by Park *et al.*, the incidence of DGE was significantly greater in patients with clinically relevant pancreatic fistula, which was selected in the multivariate analysis as an independent risk factor (along with a benign histology).<sup>7</sup> In another recent paper by Nikfarjam *et al.*,<sup>23</sup> the presence of postoperative morbidity was not associated with an increase in DGE. Specifically, pancreatic fistula did not seem to play a role in this regard. A trend towards decreased DGE was noted in patients with pancreatic head cancer and in patients who underwent classic Whipple PD (in comparison with PPPD). In multivariate analysis, male gender and an antecolic gastrointestinal anastomosis emerged as independent risk factors.<sup>23</sup> The type of gastrointestinal anastomosis and its route (antecolic vs.

614

Table 7 Univariate analysis of factors associated with delayed gastric emptying	f factors associated with delayed gastric emptying
---	--

Factor	DGE ( <i>n</i> = 36)	Non-DGE ( <i>n</i> = 224)	<b>P</b> -value <sup>a</sup>	Odds ratio (95% Cl)
Gender			0.119	-
Male	24	104		
Female	12	100		
Median age, years (range)	64.5 (50–78)	62.0 (24–82)	0.771	_
Median body mass index (range)	25.1 (19.8–31.2)	24.2 (17.9–35.1)	0.303	_
Median operative time, min (range)	360 (230–490)	340 (180–660)	0.076	_
Intraoperative blood transfusions			1	_
Yes	2	14		
No	34	210		
Type of pancreatic anastomosis			0.446	-
Pancreaticojejunostomy	26	178		
Pancreaticogastrostomy	10	46		
Type of duodeno-jejunostomy			0.055	_
Antecolic	10	104		
Retrocolic	26	120		
Abdominal collections			<0.001	5.0
Yes	10	16		(2.05–12.16)
No	26	208		
Clinically relevant pancreatic fistulas (grades B, C)			<0.001	4.17
Yes	16	36		(1.97–8.82)
No	20	188		
Enteric fistulas			0.604	_
Yes	2	6		
No	34	218		
Biliary fistulas			0.002	7.26
Yes	6	6		(2.20–23.98)
No	30	218		
Acute pancreatitis			0.195	_
Yes	2	4		
No	34	220		
Post-pancreatectomy haemorrhage			1	_
Yes	2	12		
No	34	212		
Sepsis			0.002	7.26
Yes	6	6		(2.20–23.98)
No	30	218		
Pulmonary complications			<0.001	6.11
Yes	8	10		(2.22–16.78)
No	28	214		
Postoperative blood transfusions			0.754	-
Yes	4	20		
No	32	204		
Histology			1	_
Benign	8	48		
Malignant	28	176		

 $^{\rm a}P\text{-}values$  in bold are significant at  $P\leq0.05$  DGE, delayed gastric emptying; 95% Cl, 95% confidence interval

Factor	DGE A ( <i>n</i> = 16)	DGE B and C ( <i>n</i> = 20)	<i>P</i> -value <sup>a</sup>	Odds ratio (95% Cl)
Gender			0.156	-
Male	13	11	-	
Female	3	9	-	
Median age, years (range)	63.5 (50–76)	65.5 (53–78)	0.548	_
Median body mass index (range)	25.2 (19.8–30.0)	25.3 (20.0–31.2)	0.920	_
Median operative time, min (range)	355 (230–450)	360 (290–490)	0.204	-
Type of pancreatic anastomosis			1	_
Pancreaticojejunostomy	12	14	-	
Pancreaticogastrostomy	4	6	-	
Type of duodeno-jejunostomy			1	_
Antecolic	4	6	-	
Retrocolic	12	14	-	
Abdominal collections			0.009	1.28
Yes	4	6	-	(0.29–5.65)
No	12	14	-	
Clinically relevant pancreatic fistulas (grades B, C)			<0.001	45
Yes	1	15	-	(4.68–432.62)
No	15	5	-	
Enteric fistulas			1	_
Yes	1	1	-	
No	15	19	-	
Biliary fistulas			0.196	_
Yes	1	5	-	
No	15	15	-	
Acute pancreatitis			1	-
Yes	1	1	-	
No	15	19	-	
Post-pancreatectomy haemorrhage			0.492	_
Yes	0	2	-	
No	16	18	-	
Sepsis			0.024	NA
Yes	0	6	-	
No	16	14	-	
Pulmonary complications			0.421	_
Yes	5	3	-	
No	11	17	-	
Postoperative blood transfusions			0.619	_
Yes	1	3	-	
No	15	17	-	
Histology			0.421	_
Benign	5	3	-	
Malignant	11	17	-	
-				

Table 8 Analysis of risk factors among delayed gastric emptying grades

 $^aP$ -values in bold are significant at  $P\leq 0.05$  DGE, delayed gastric emptying; 95% Cl, 95% confidence interval; NA, not available

 
 Table 9 Multivariate analysis of risk factors influencing the occurrence of delayed gastric emptying

Risk factor	P-value <sup>a</sup>	Odds ratio	95% CI
Clinically relevant pancreatic fistula (grades B, C)	0.040	3.97	1.31–13.19
Biliary fistula	0.039	17.38	1.11–54.23

<sup>a</sup>*P*-values in bold are significant at  $P \le 0.05$ 

95% CI, 95% confidence interval

retrocolic) have been regarded as additional potential factors influencing DGE. Over the years, numerous studies have focused on these issues, but most of them were conducted prior to the introduction of the ISGPS definition, and the topographic terms used were not consistent.<sup>24-27</sup> Furthermore, reconstruction after PD varies across studies; several Western authors have reported a successful reduction of the incidence of DGE in patients with Billroth II reconstruction,<sup>28</sup> whereas in Japan a significant number of surgeons have firmly favoured the use of Billroth I reconstruction.<sup>29,30</sup> The majority of the reported data, including those from the only prospective randomized trial published in the field, indicate that an antecolic route results in a significant reduction in DGE. Theoretically, an antecolic anastomosis avoids the risk of mechanical outflow obstruction, allows an increased mobility of the stomach, and provides an anatomical barrier from the pancreas, thus minimizing the possible negative effects of an infected collection or a pancreatic fistula. In the current analysis, the route of duodeno-jejunal anastomosis did not significantly influence the incidence of DGE, although the univariate model showed a strong trend in favour of antecolic anastomosis (P = 0.055). Moreover, in patients reconstructed by an antecolic DJ, nasogastric intubation was shorter (P = 0.006) and a solid diet was resumed significantly earlier (P = 0.003) (data not shown). The type of pancreatic anastomosis has also been linked with the occurrence of DGE. In a recent randomized study of PJ vs. PG after PD, we showed that, compared with PJ, PG did not result in any significant differences in the overall postoperative complication rate or incidence of pancreatic fistula, although DGE was significantly reduced in patients treated by PG (in this study DGE was defined as the need for nasogastric tube decompression for >10 days).<sup>20</sup> In the current series, the type of pancreatic anastomosis was not significantly associated with DGE, which is in accordance with a recent meta-analysis of three randomized trials on the topic, which showed an overall comparable rate of DGE for both reconstruction techniques.<sup>31</sup> It should be noted that the data on the effects of the route of DJ and the type of pancreatic anastomosis provided in this study come from a non-randomized series and they should, accordingly, be interpreted with caution. The variables significantly associated with DGE were abdominal fluid collections (P = 0.0001), clinically relevant pancreatic fistulas (P =0.0001), biliary fistulas (P = 0.002), sepsis (P = 0.002) and pulmonary complications (P < 0.0001). The analysis of risk factors among DGE grades showed that moderate and severe DGE

(grades B and C) were associated with the most relevant postoperative complications (clinically relevant pancreatic fistulas [P = 0.0001]), intra-abdominal collections [P = 0.009] and sepsis [P = 0.024]). All of the four DGE patients who needed to be re-operated had grade B or C DGE, showed clinical signs of sepsis and were found to have dehiscence of the pancreatic anastomosis. Finally, the multivariate model indicated pancreatic fistula and biliary fistula as independent risk factors (P = 0.04 and P = 0.039, respectively), demonstrating that the ISGPS classification and the grading system correlate well with the clinical course of the condition and are feasible for patient management.

### Conclusions

The present analysis shows that, using ISGPS definitions, the diagnosis of DGE can be established earlier in the postoperative course, thus enabling the selective care of DGE patients and the implementation of fast-track pathways for subjects who do not develop this complication. Clearly, further investigations focusing on surgical reconstructive methods should be undertaken using randomized controlled trials.

### **Conflicts of interest**

None declared.

### References

- Vin Y, Sima CS, Getrajdman GI, Brown KT, Covey A, Brennan MF *et al.* (2008) Management and outcomes of postpancreatectomy fistula, leak, and abscess: results of 908 patients resected at a single institution between 2000 and 2005. *J Am Coll Surg* 207:490–498.
- Balzano G, Zerbi A, Braga M, Rocchetti S, Beneduce AA, Di Carlo V. (2008) Fast-track recovery programme after pancreaticoduodenectomy reduced delayed gastric emptying. *Br J Surg* 95:1387–1393.
- Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR et al. (2007) Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 142:761–768.
- Lytras D, Paraskevas KI, Avgerinos C, Manes C, Touloumis Z, Paraskeva KD *et al.* (2007) Therapeutic strategies for the management of delayed gastric emptying after pancreatic resection. *Langenbecks Arch Surg* 392:1–12.
- Traverso LW, Hashimoto Y. (2008) Delayed gastric emptying: the state of the highest level of evidence. J Hepatobiliary Pancreat Surg 15:262–269.
- 6. Akizuki E, Kimura Y, Nobuoka T, Imamura M, Nagayama M, Sonoda T et al. (2009) Reconsideration of postoperative oral intake tolerance after pancreaticoduodenectomy: prospective consecutive analysis of delayed gastric emptying according to the ISGPS definition and the amount of dietary intake. Ann Surg 249:986–994.
- Park JS, Hwang HK, Kim JK, Cho SI, Yoon DS, Lee WJ et al. (2009) Clinical validation and risk factors for delayed gastric emptying based on the International Study Group of Pancreatic Surgery (ISGPS) Classification. Surgery 146:882–887.
- Bassi C, Salvia R, Butturini G, Marcucci S, Barugola G, Falconi M. (2005) Value of regional lymphadenectomy in pancreatic cancer. *HPB* 7:87– 92.
- 9. Bassi C, Butturini G, Salvia R, Crippa S, Falconi M, Pederzoli P. (2006)

Open pancreaticogastrostomy after pancreaticoduodenectomy: a pilot study. *J Gastrointest Surg* 10:1072–1080.

- Molinari E, Bassi C, Salvia R, Butturini G, Crippa S, Talamini G *et al.* (2007) Amylase value in drains after pancreatic resection as predictive factor of postoperative pancreatic fistula: results of a prospective study in 137 patients. *Ann Surg* 246:281–287.
- Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J et al. (International Study Group on Pancreatic Fistula Definition). (2005) Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 138:8–13.
- Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ *et al.* (2007) Postpancreatectomy haemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery* 142:20–25.
- 13. van Berge Henegouwen MI, van Gulik TM, DeWit LT, Allema JH, Rauws EA, Obertop H *et al.* (1997) Delayed gastric emptying after standard pancreaticoduodenectomy versus pylorus-preserving pancreaticoduodenectomy: an analysis of 200 consecutive patients. *J Am Coll Surg* 185:373–379.
- Balcom JH, Rattner DW, Warshaw AL, Chang Y, Fernandez-del Castillo C. (2001) Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. *Arch Surg* 136:391–398.
- 15. Tran KT, Smeenk HG, van Eijck CH, Kazemier G, Hop WC, Greve JW et al. (2004) Pylorus-preserving pancreaticoduodenectomy versus standard Whipple procedure: a prospective, randomized, multicentre analysis of 170 patients with pancreatic and periampullary tumours. *Ann Surg* 240:738–745.
- Horstmann O, Markus PM, Ghadimi MB, Becker H. (2004) Pylorus preservation has no impact on delayed gastric emptying after pancreatic head resection. *Pancreas* 28:69–74.
- Diener MK, Heukaufer C, Schwarzer G, Seiler CM, Antes G, Buchler MW et al. Pancreaticoduodenectomy (classic Whipple) versus pyloruspreserving pancreaticoduodenectomy (pp Whipple) for surgical treatment of periampullary and pancreatic carcinoma. *Cochrane Database Syst Rev* (2):CD006053.
- Bassi C, Falconi M, Salvia R, Mascetta G, Molinari E, Pederzoli P. (2001) Management of complications after pancreaticoduodenectomy in a highvolume centre: results on 150 consecutive patients. *Dig Surg* 18:453– 457.
- Fischer CP, Hong JC. (2006) Method of pyloric reconstruction and impact upon delayed gastric emptying and hospital stay after pylorus-preserving pancreaticoduodenectomy. J Gastrointest Surg 10:215–219.
- 20. Kim DK, Hindenburg AA, Sharma SK, Suk CH, Gress FG, Staszewski H et al. (2005) Is pylorospasm a cause of delayed gastric emptying after

pylorus-preserving pancreaticoduodenectomy? Ann Surg Oncol 12:222–227.

- 21. Bassi C, Falconi M, Molinari E, Salvia R, Butturini G, Sartori N *et al.* (2005) Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: results of a comparative study. *Ann Surg* 242:767–771.
- 22. Riediger H, Makowiec F, Schareck WD, Hopt UT, Adam U. (2003) Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy is strongly related to other postoperative complications. J Gastrointest Surg 7:758–765.
- 23. Nikfarjam M, Kimchi ET, Gusani NJ, Shah SM, Sehmbey M, Shereef S et al. (2009) A reduction in delayed gastric emptying by classic pancreaticoduodenectomy with an antecolic gastrojejunal anastomosis and a retrogastric omental patch. J Gastrointest Surg 13:1674–1682.
- 24. Hartel M, Wente MN, Hinz U, Kleeff J, Wagner M, Müller MW et al. (2005) Effect of antecolic reconstruction on delayed gastric emptying after the pylorus-preserving Whipple procedure. Arch Surg 140:1094–1099.
- 25. Tani M, Terasawa H, Kawai M, Ina S, Hirono S, Uchiyama K et al. (2006) Improvement of delayed gastric emptying in pylorus-preserving pancreaticoduodenectomy: results of a prospective, randomized, controlled trial. Ann Surg 243:316–320.
- 26. Manes K, Lytras D, Avgerinos C, Delis S, Dervenis C. (2008) Antecolic gastrointestinal reconstruction with pylorus dilatation. Does it improve delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy? *HPB* 10:472–476.
- 27. Murakami Y, Uemura K, Sudo T, Hayashidani Y, Hashimoto Y, Nakagawa N et al. (2008) An antecolic Roux-en-Y type reconstruction decreased delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. J Gastrointest Surg 12:1081–1086.
- 28. Goei TH, van Berge Henegouwen MI, Slooff MJ, van Gulik TM, Gouma DJ, Eddes EH. (2001) Pylorus-preserving pancreatoduodenectomy: influence of a Billroth I versus a Billroth II type of reconstruction on gastric emptying. *Dig Surg* 18:376–380.
- 29. Takeda T, Yoshida J, Tanaka M, Matsunaga H, Yamaguchi K, Chijiiwa K. (1999) Delayed gastric emptying after Billroth I pylorus-preserving pancreatoduodenectomy: effect of postoperative time and cisapride. *Ann Surg* 229:223–229.
- 30. Ueno T, Takashima M, Iida M, Yoshida S, Suzuki N, Oka M. (2009) Improvement of early delayed gastric emptying in patients with Billroth I type of reconstruction after pylorus-preserving pancreatoduodenectomy. *J Hepatobiliary Pancreat Surg* 16:300–304.
- Wente MN, Shrikhande SV, Müller MW, Diener MK, Seiler CM, Friess H et al. (2007) Pancreaticojejunostomy versus pancreaticogastrostomy: systematic review and meta-analysis. Am J Surg 193:171–183.