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Delayed gastric emptying after pancreatoduodenectomy: One complication, two different entities

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ABSTRACT

Background: Delayed gastric emptying (DGE) is a common complication after pancreatoduodenectomy associated with a low complication burden but a prolonged hospital stay. The present study aimed to characterize DGE, with a particular focus on its subtypes and related predictors.
Methods: A 2-center retrospective analysis was performed including consecutive pancreatoduodenectomy over 5 years. Primary delayed gastric emptying (pDGE) and secondary delayed gastric emptying (sDGE) were defined according to the presence of concomitant causing factors. Predictors of DGE, pDGE and sDGE were assessed through logistic regression.
Results: Out of 1,170 patients considered, 188 developed delayed gastric emptying (16.1%). Most DGE (71.8%) were secondary. sDGE resolved later ($P = .007$), with hospital stay, duration of total parenteral nutrition, and of enteral nutrition being longer than for pDGE (all $P < .005$). Smoking status, total operative time, indication for surgery other than pancreatic cancer, estimated blood loss, and soft pancreatic texture were independent predictors of DGE. In the subgroup analysis of pDGE, smoking was the only independent predictor, whereas pylorus-preservation was a protective factor. Smoking, indication for surgery, estimated blood loss, soft gland texture, and main pancreatic duct diameter were independent predictors of sDGE.
Conclusion: DGE after pancreatoduodenectomy consists of 2 different subtypes. The primary form resolves earlier, and its occurrence might be reduced by pylorus preservation. For the secondary form, clinicians should focus on preventing and treating other trigger complications. The diagnosis of the DGE subtype has critical therapeutic implications and paves the way for further systematic studies.

Introduction

Despite the significant improvements in both the surgical technique and perioperative care over the past decades, pancreatoduodenectomy (PD) is still burdened by high morbidity and mortality, even at high-volume centers.[1–4] Although postoperative pancreatic fistula (POPF) is by far the most studied and dreadful complication after Whipple procedures, also delayed gastric emptying (DGE) plays a significant role in the postoperative course, given that its incidence ranges between 19% and 57%.[5] Moreover, although DGE is rarely a life-threatening condition and its complication burden is generally limited,[6–8] it is usually associated with prolonged hospital stay and higher costs.

The definition and grading system of DGE by the International Study Group of Pancreatic Surgery (ISGPS) has provided the backbone for its assessment, paving the way for an increased homogeneity among reports and boosting the evidence for a better understanding and characterization of this complication.[5]

Nonetheless, despite the fact that there has been several studies that have focused on the identification of specific predictors of DGE,

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such as the preservation of the pylorus or the route of the gastric reconstruction loop, the results are still controversial.[9–16] Similarly, the existence of a primary and a secondary cause for the development of a DGE has already been proposed,[16–18] although this sharp but potentially crucial distinction has not been universally accepted thus far, limiting the reliability of the obtained results regarding risk factors.

This study aimed to characterize DGE after PD, exploring the existence of 2 separate subtypes, to eventually analyze their specific predictors and impact on the clinical postoperative course.

Methods

Study population, data collection, and study design

This 2-center retrospective study is consistent with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.[19] The study was approved by the Ethics Committee (Comitato Etico delle Province di Verona e Rovigo, approval number 1101CESC).

Consecutive PDs performed at 2 academic institutions—the Unit of General and Pancreatic Surgery, University of Verona Hospital Trust and the Unit of Hepatobiliary Pancreatic Surgery, San Gerardo Monza Hospital—from January 1, 2015 to December 31, 2019 were eligible. Preoperative characteristics, intraoperative findings, and postoperative outcomes were prospectively collected and retrospectively analyzed. Variables that were not systematically collected during the study period and patients whose clinical reports were not available for review were excluded from the analysis.

Patients who developed DGE were separately analyzed and predictors of DGE were explored. DGE patients were subsequently divided into “primary DGE” and “secondary DGE”, and subgroup analyses were performed. Their definition is provided in the outcome measures section.

Operative technique and postoperative management

All PDs were performed according to a standardized technique through an open approach.[1,20] Pylorus-preservation was always preferred, and antrectomy was performed exclusively when deemed necessary (ie, duodenal cancer or suspected tumoral infiltration of the pylorus). Duodenojejunostomy or gastrojejunostomy was routinely performed through antecolic loop reconstruction. When the antrectomy was included, a side-to-side Braun jejunojejunostomy was added to reduce biliary reflux in the stomach. The intraoperative risk of POPF was routinely assessed using the fistula risk score (FRS).[21] Pancreatic anastomosis was carried out through pancreaticojejunostomy (PJ) or pancreaticogastrostomy (PG), depending on the surgeon’s judgment. For high-risk pancreatic anastomosis, a feeding jejunostomy could be added based on the surgeon’s preference.[22]

Postoperative management followed the Enhanced Recovery After Surgery (ERAS) recommendation for PD,[23] and early resumption of oral intake and nutritional support were managed as previously described.[24] Once DGE was diagnosed, total parenteral nutrition (TPN) was started as a standardized practice within 3 days after DGE onset. If DGE did not resolve within 3 to 5 days or if it was associated with either POPF or abdominal collections, a nasojejunal tube was positioned endoscopically and TPN was gradually switched to enteral nutrition (EN). If a feeding jejunostomy had been placed intraoperatively, EN was preferred to TPN in the first place. Additional measures, such as prokinetic drugs, gastric decompression with nasogastric tubes, and drug stimulation of bowel movements, were applied whenever they were deemed to be potentially useful.

Outcome measures

Delayed gastric emptying and other pancreas-specific complications, including POPF, postpancreatectomy hemorrhage (PPH), chyle leak, and postpancreatectomy acute pancreatitis, were defined according to the ISGPS classifications.[25–28] Bile leakage was defined according to the International Study Group of Liver Surgery classification.[29] In particular, DGE was defined as the inability to tolerate solid oral intake by the end of the first postoperative week, and it has been classified into grade A, B, or C according to the ISGPS grading system[5] (Supplementary Table S1). Any DGE of grade B or grade C was considered a clinically relevant DGE (CR-DGE).[6,8] Additionally, DGE was categorized into primary and secondary. “Secondary DGE” (sDGE) was defined as a DGE occurring contemporarily or immediately afterward (<5 days) with the development of another complication including perigastric collection, POPF, PPH, chyle leak, biliary leak, and gastrointestinal leak; DGE was otherwise defined as "primary" (pDGE). Abdominal collections were suspected based on the clinical appearance and regularly confirmed through a computed tomography (CT) scan. For the purpose of this study, perigastric collections were defined as abdominal collections in contact with the gastric walls for at least 5 mm in length.

The time to resolution of a DGE was defined as the time elapsed from the onset of the DGE to its complete clinical resolution, referred to as patient ability to tolerate a solid diet without nausea or vomiting.[5]

The severities of POPF, DGE, and PPH were graded using the Modified Accordion Severity Grading System,[30] and each patient was assigned a severity weight ranging from 0 (no clinical impact) to 1 (death). Major complications were defined as any Clavien-Dindo grade $\geq$ III. The average complication burden (ACB) was finally calculated by summing each patient’s severity weight and dividing the resulting number by the total number of patients who suffered from the given complication.[31]

Statistical analysis

The continuous variables were compared using Student’s *t* test or the Mann-Whitney *U* test, whereas for the categorical variables, the χ^2 analysis or Fisher exact test was used. Pearson’s χ^2 statistic was applied to assess the correlation between dichotomous variables. Predictors of DGE were explored through regression analyses. Variables with *P* values < .2 were selected for multivariable logistic regression to compute odds ratios. The CIs were set at 95%. Multicollinearity was assessed through the analysis of variance inflation factor, and a variance inflation factor value <2 was considered satisfactory. Data were analyzed with SPSS v. 25 (IBM SPSS, Inc, Armonk, NY).

Results

Preoperative and intraoperative features

Out of 1,187 eligible patients, 17 patients (1.4%) were excluded because of missing data in their medical records; thus the analysis was based on complete data derived from 1,170 patients (98.6%). One hundred and eighty-eight patients were diagnosed with DGE (16.1%), and such proportion was comparable between the 2 institutions included. Smoking status ($P < .005$), arterial hypertension ($P = .011$), history of cerebrovascular events ($P = .024$), pylorus-resection ($P = .008$), pancreaticogastrostomy ($P = .014$), and prolonged operative time ($P = .005$) were significantly more frequent

Table I
Demographics and preoperative characteristics

		Total (N = 1170)	No DGE (N = 982) 83.9%	DGE (n = 188) 16.1%	P value
Age (y, median, IQR)		65 (57–72)	65 (56–72)	65 (59–72)	.177
Sex	M	666 (56.9%)	558 (56.8%)	108 (57.4%)	.936
	F	504 (43.1%)	424 (43.2%)	80 (42.6%)	
BMI (median, IQR)		24.2 (22.0–26.7)	24.1 (21.9–26.6)	25.0 (22.5–27.4)	.034
Smoking		358 (30.6%)	276 (28.1%)	82 (43.6%)	< .005
ASA-PS ≥3		279 (23.8%)	228 (23.2%)	51 (27.0%)	.260
Diabetes		226 (19.3%)	193 (19.7%)	33 (17.5%)	.546
Arterial hypertension		451 (38.5%)	361 (36.8%)	90 (47.8%)	.011
COPD		32 (2.7%)	27 (2.7%)	5 (2.7%)	1.000
History of coronary artery disease (or heart disease)		82 (7.0%)	69 (7.0%)	20 (10.6%)	.119
History of cerebrovascular accidents		53 (4.5%)	37 (3.8%)	16 (8.5%)	.024
Chronic renal failure		30 (2.6%)	25 (2.5%)	5 (2.7%)	.783
Jaundice		628 (53.7%)	538 (54.8%)	90 (47.9%)	.093
Indication	PDAC	626 (53.5%)	549 (55.9%)	77 (41.0%)	< .005
	Ampullary cancer	174 (14.9%)	133 (13.5%)	41 (21.8)	
	Cystic tumor	110 (9.4%)	98 (10.0%)	12 (6.4%)	
	Pan-NEN	88 (7.5%)	68 (6.9%)	20 (10.6%)	
	Bile duct cancer	73 (6.2%)	61 (6.2%)	12 (6.4%)	
	Duodenal cancer	39 (3.3%)	25 (2.6%)	14 (7.4%)	
	Pancreatitis	17 (1.5%)	14 (1.4%)	3 (1.6%)	
	Metastasis	12 (1.0%)	8 (0.8%)	4 (2.1%)	
	Benign lesion	5 (0.4%)	5 (0.5%)	0 (0.0%)	
	Others	27 (2.3%)	22 (2.2%)	5 (2.7%)	
Neoadjuvant therapy*		297 (25.4%)	249 (25.4%)	48 (25.5%)	1.000

ASA-PS, American Society of Anesthesiologists performance status; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *DGE*, delayed gastric emptying; *PDAC*, pancreatic ductal adenocarcinoma; *Pan-NEN*, pancreatic neuroendocrine neoplasm.
* Data refers to PDAC patients.

in patients with DGE than in patients without DGE. Similarly, the median FRS was higher among DGE patients (P < .005).

The demographics, preoperative characteristics, and intraoperative findings are detailed in Table I and Table II.

Postoperative outcomes

Among the 188 patients who developed DGE, 53 patients (28.2%) were categorized as pDGE and 135 patients (71.8%) as sDGE. Although mortality was statistically similar between sDGE and pDGE subgroups (5.9% vs 0.0%, P = .108), length of hospital stay, rate of reoperation, and need for readmission in the ICU were significantly higher in the sDGE subgroup (30 vs 18 days, P < .005; 18.5% vs 0.0%, P < .005; 22.2% vs 0.0%, P < .005, respectively). None of the patients underwent reoperation for DGE.

Further details on the postoperative outcomes are listed in Table III.

DGE features and management

The sDGE subtype was more frequently clinically relevant (86.7% vs 69.8%; P = .011). The postoperative day of onset was similar (P = .243), although time to resolution was significantly longer in sDGE (P = .009). Total parenteral nutrition was administered in similar proportions, although its duration was longer in the sDGE subgroup. The sDGE patients were more frequently managed with EN (P < .005), but once administered, the duration of the treatment was longer than in the pDGE subgroup (P < .005).

Table IV shows a detailed comparison between the pDGE and sDGE subgroups.

Predictors of DGE and subtypes

Smoking status (P < .005), indication for surgery (P = .014), soft gland texture (P = .036), estimated blood loss (P = .036), and total operative time (P = .046) were independent predictors of DGE (Table V).

In the subgroup analysis of predictors, smoking was the only independent predictor of pDGE (P = .021), whereas pylorus-preservation was a protective factor (P = .035). For sDGE, smoking status (P = .030), diabetes (P = .034), total operative time (P = .010), indication for surgery (P = .031), estimated blood loss (0.011), soft gland texture (P < .005), and main pancreatic duct diameter (P = .047) were all independent predictors with statistical significance in the multivariable analysis.

Table VI and Table VII display the analyses of the predictors of pDGE and sDGE, respectively.

Discussion

The comprehensive characterization of DGE presented here has substantiates the existence of 2 distinct subtypes with specific clinical characteristics, postoperative paths, and underlying predictors. Overall, DGE was rather frequent after a PD (16.1%), but its complication burden was confirmed to be low (ACB 0.296 ± 0.090). The 2 subtypes of DGE were similar in terms of ACB (P = .256). However, sDGE was more frequent (71.8% vs 28.2%) and was associated with a longer time to resolution, need for nutritional support, and prolonged hospital stay.

The distinction between primary and secondary DGE has already been proposed,[16–18] although a solid agreement on such characterization has not yet been reached. In the present series, the authors defined any DGE as "secondary" if it occurred at the same time or right after the development of other complications (ie, abdominal collections and leaks). The rationale was to include all the possible factors acting as an irritant or mechanical compression on the gastric walls. Of note, the subgroup analysis of predictors showed different risk factors for pDGE and sDGE, supporting their clinical distinction.

Table II
Intraoperative findings

		Total (N = 1170)	No DGE (N = 982) 83.9%	DGE (n = 188) 16.1%	P value
PD type	Pylorus-preserving	899 (76.8%)	769 (78.3%)	130 (69.1%)	.008
	Whipple	271 (23.2%)	213 (21.7%)	58 (30.9%)	
PD type of reconstruction	PJ	1085 (92.7%)	919 (93.6%)	166 (88.3%)	.014
	PG	85 (7.3%)	63 (6.4%)	22 (11.7%)	
Vascular resection		154 (13.2%)	135 (13.7%)	19 (10.1%)	.196
Total operative time (min, median, IQR)		417 (362–475)	415 (360–470)	427 (380–480)	.005
Gland texture	Firm	536 (45.8%)	479 (48.8%)	57 (30.3%)	< .005
	Soft	634 (54.2%)	503 (51.2%)	131 (69.7%)	
Main pancreatic duct diameter (mm, median, IQR)		4 (3–5)	4 (3–5)	3 (2–4)	< .005
Estimated blood loss (mL, median, IQR)		400 (300–600)	400 (300–600)	483 (300–785)	< .005
FRS (median, IQR)[21]		4 (2–6)	3 (2–5)	5 (3–7)	< .005
FRS (risk zone)	Negligible/Low risk (0–2)	392 (33.5%)	355 (36.2%)	37 (19.7%)	< .005
	Intermediate risk (3–6)	630 (53.8%)	531 (54,1%)	99 (52.7%)	
	High risk (7–10)	149 (12.7%)	97 (9.9%)	52 (27.7%)	
Need for intraoperative blood transfusions		123 (10.5%)	89 (9.1%)	34 (18.1%)	< .005
Lymphadenectomy (harvested nodes, median, IQR)		39 (29–48)	39 (29–49)	38 (28–47)	.226
Optimal lymphadenectomy (>28 nodes)[37]		932 (79.7%)	783 (79.7%)	149 (79.3%)	.842

DGE, delayed gastric emptying; *FRS*, fistula risk score; *PD*, pancreatoduodenectomy; *PJ*, pancreatojejunostomy; *PG*, pancreatogastrostomy.

Table III
Outcome measures in patients with either primary or secondary DGE

		Total (N = 188)	Primary DGE (N = 53, 28.2%)	Secondary DGE (N = 135, 71.8%)	P value
Perigastric collection		102 (54.3%)	/	102 (75.6%)	/
POPF[25]		74 (39.4%)	/	74 (54.8%)	/
POPF ISGPS grade	BL	6 (3.2%)	/	6 (4.4%)	/
	Grade B	61 (32.4%)		61 (45.2%)	
	Grade C	7 (3.7%)		7 (5.2%)	
POPF ACB (SD)		0.317 (0.18)	/	0.317 (0.18)	/
PPH[26]		40 (21.3%)	/	40 (29.6%)	/
PPH ISGPS grade	Grade A	4 (2.1%)	/	4 (3.0%)	/
	Grade B	25 (13.3%)		25 (18.5%)	
	Grade C	11 (5.9%)		11 (8.1%)	
PPH ACB (SD)		0.463 (0.28)	/	0.463 (0.28)	/
Chyle leak[27]		10 (5.3%)	/	10 (7.4%)	/
Bile leak[29]		7 (3.7%)	/	7 (5.2%)	/
Gastrointestinal anastomotic leak		12 (6.4%)	/	12 (8.9%)	/
PPAP[28]		42 (22.3%)	4 (7.5%)	38 (28.1%)	< .005
Pneumonia		56 (29.8%)	10 (18.9%)	46 (34.1%)	.051
Sepsis		79 (42.0%)	7 (13.2%)	72 (53.3%)	< .005
Organ failure		26 (13.8%)	1 (1.9%)	25 (18.5%)	< .005
Wound infection		43 (22.9%)	8 (15.1%)	35 (25.9%)	.126
Myocardial infarction		18 (9.6%)	1 (1.9%)	17 (12.6%)	.026
Acute renal failure		17 (9.0%)	0 (0.0%)	17 (12.6%)	.004
Reoperation		25 (13.3%)	0 (0.0%)	25 (18.5%)	< .005
Length of hospital stay (d, median, IQR)		26 (18–39)	18 (14–24)	30 (21–46)	< .005
Need for readmission to the ICU		30 (16.0%)	0 (0.0%)	30 (22.2%)	< .005
In-hospital mortality		8 (4.3%)	0 (0.0%)	8 (5.9%)	.108

ACB, average complication burden; *BL*, biochemical leak; *DGE*, delayed gastric emptying; *ISGPS*, International Study Group of Pancreatic Surgery; *ICU*, intensive care unit; *POPF*, postoperative pancreatic fistula; *PPH*, postpancreatectomy hemorrhage; *PPAP*, postpancreatectomy acute pancreatitis.

As expected, most predictors of sDGE largely overlap those of POPF incorporated into the FRS.[21] Other predictors, such as the median operative time, have already been correlated with the overall development of complications in pancreatic surgery.[32] Consequently, the FRS might become a reliable tool to identify patients at higher risk to develop a sDGE and therefore identify targets for the adoption of intraoperative specific mitigation strategies for DGE (ie, feeding jejunostomy or transanastomotic naso-jejunal tube). Moreover, patients at higher risk for sDGE could benefit from specific pathways for the early postoperative phase, such as those adopted to avoid POPF.

Smoking was found to be the only risk factor for pDGE, which is in line with the hypothesis that its negative effects on vessels might lead to reduced gastric vascularization and consequently impaired gastric motility. Furthermore, against the background of controversial results on the role of pylorus preservation on gastric motility after PD,[9,33] the present analysis corroborates the evidence that pylorus-preserving reconstruction is not associated with a higher rate of DGE.[15,34,35] On the contrary, it herein emerged as a protective factor for the development of pDGE, although only further studies have the potential to validate this finding. That being said, we believe the systematic adoption of antrectomy during a PD should be discouraged if it is performed with the sole purpose of preventing a DGE.

From a technical standpoint, the preservation of the right gastric vessels might play a role in reducing gastric venous congestion/

Table IV
Comparison between primary and secondary DGE

		Total (*N* = 188)	Primary DGE (*N* = 53, 28.2%)	Secondary DGE (*N* = 135, 71.8%)	*P* value
DGE ISGPS grade[5]	Grade A	34 (18.1%)	16 (30.2%)	18 (13.3%)	< .005
	Grade B	92 (48.9%)	30 (56.6%)	62 (45.9%)	
	Grade C	62 (33.0%)	7 (13.2%)	55 (40.8%)	
CR DGE		154 (81.9%)	37 (69.8%)	117 (86.7%)	.011
DGE ACB (SD)		0.296 (0.09)	0.279 (0.10)	0.303 (0.09)	.256
Day of onset (median, IQR)		5 (3–7)	4 (2–8)	5 (3–7)	.243
Day of resolution (median, IQR)		13 (9–21)	11 (9–14)	14 (10–25)	.007
Time to resolution (d, median, IQR)		8 (5–14)	6 (4–10)	9 (5–17)	.009
Use of total parenteral nutrition		150 (79.8%)	42 (79.2%)	108 (80%)	1.000
Duration of parenteral nutritional support (d, median, IQR)		10 (6–20)	6 (4–10)	13 (8–24)	< .005
Use of enteral nutrition		143 (76.1%)	30 (56.6%)	113 (83.7%)	< .005
Duration of enteral nutritional support (d, median, IQR)		11 (6–18)	7 (4–10)	12 (7–20)	.016
CT scan performed		179 (95.2%)	45 (84.9%)	134 (99.3%)	< .005
Upper GI fluoroscopy performed		83 (44.1%)	28 (52.8%)	55 (40.7%)	.145
Upper endoscopy	Not performed	93 (49.5%)	23 (43.4%)	70 (51.8%)	.628
	Negative findings	61 (32.4%)	21 (39.6%)	40 (29.6%)	
	Perianastomotic ulceration	17 (9.0%)	5 (9.4%)	12 (8.9%)	
	Anastomotic stricture	6 (3.2%)	2 (3.8%)	4 (3.0%)	
	Altered outflow angle	5 (2.7%)	0 (0.0%)	5 (3.7%)	
	Esophageal erosion/ulceration	6 (3.2%)	2 (3.8%)	4 (3.0%)	

ACB, average complication burden; *CR*, clinically relevant; *CT*, computed tomography; *DGE*, delayed gastric emptying; *GI*, gastrointestinal; *ISGPS*, International Study Group of Pancreatic Surgery.

Table V
Predictors of DGE

Variable		Univariate analysis			Multivariable analysis		
		OR	CI for OR	*P* value	OR	CI for OR	*P* value
Age		1.010	0.996–1.025	.157	1.018	0.997–1.041	.099
Male sex		1.026	0.748–1.406	.874	/	/	/
BMI		1.046	1.003–1.091	.034	0.998	0.940–1.058	.939
ASA-PS ≥3		0.232	0.871–1.772	.232	/	/	/
Smoking		1.977	1.434–2.726	< .005	1.947	1.279–2.964	< .005
Diabetes		0.873	0.581–1.313	.514	/	/	/
Arterial hypertension		1.575	1.122–2.212	.009	1.499	0.947–2.372	.084
COPD		0.975	0.368–2.582	.960	/	/	/
History of coronary artery disease (or heart disease)		1.562	0.897–2.718	.115	0.844	0.428–1.665	.625
History of cerebrovascular accidents		2.382	1.162–4.883	.018	2.333	0.965–5.640	.060
Chronic renal failure		1.132	0.381–3.362	.823	/	/	/
Jaundice		0.759	0.555–1.039	.085	0.778	0.486–1.245	.295
Indication	PDAC	Reference category		< .005	Reference category		.014
	Ampullary cancer	2.196	1.436–3.359		2.342	1.277–4.293	
	Cystic tumor	0.873	0.457–1.666		0.699	0.273–1.791	
	Pan-NEN	2.094	1.203–3.645		2.477	1.118–5.485	
	Bile duct cancer	1.405	0.723–2.733		1.044	0.422–2.581	
	Others	2.530	1.521–4.209		2.037	0.945–4.389	
Neoadjuvant therapy*		1.010	0.705-1.446	.956	/	/	/
Pylorus preservation		0.621	0.440–0.876	.007	0.896	0.541–1.482	.668
Pancreaticogastrostomy		1.952	1.168–3.262	.011	0.850	0.423–1.709	.648
Vascular resection		0.706	0.425–1.173	.179	1.254	0.600–2.618	.548
Total operative time		1.003	1.001–1.004	.005	1.003	1.000–1.006	.046
Soft gland texture		2.152	1.532–3.021	< .005	1.751	1.037–2.955	.036
Main pancreatic duct diameter		0.863	0.790–0.943	< .005	0.925	0.814–1.051	.230
EBL		1.001	1.000–1.001	< .005	1.001	1.000–1.002	.006
Need for intraoperative transfusion		2.234	1.449–3.445	< .005	1.064	0.541–2.093	.858
Number of harvested lymph nodes		0.993	0.982–1.004	.226	/	/	/

ASA-PS, American Society of Anesthesiologists physical status; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *EBL*, estimated blood loss; *OR*, odds ratio; *PDAC*, pancreatic ductal adenocarcinoma; *Pan-NEN*, pancreatic neuroendocrine neoplasm.
* Data refers to PDAC patients.

ischemia and therefore preserve gastric motility. Venous congestion after left gastric vein ligation is a known cause of gastric ischemia and DGE, leading some authors to recommend its reinsertion.[36] Very little is known about the possible role of right gastric vein preservation together with its arterial counterpart as a strategy for preventing DGE. In this regard, our internal policy is to attempt the preservation of the right gastric pedicle in all cases. The actual preservation of the right gastric vein is still very challenging and has critical implications regarding duodenal-jejunal anastomosis due to the consequent lack of gastric mobility. Future studies should systematically assess the actual importance of such technical aspects to provide definite answers on DGE prevention.

This study also focused on the onset and time to resolution of a DGE. Delayed gastric emptying was diagnosed on postoperative day

Table VI
Predictors of primary DGE

Variable		Univariate analysis			Multivariable analysis		
		OR	CI for OR	*P* value	OR	CI for OR	*P* value
Age		0.999	0.975–1.023	.944	/	/	/
Male sex		0.851	0.489–1.481	.568	/	/	/
BMI		1.026	0.952–1.106	.502	/	/	/
ASA-PS ≥3		0.994	0.512–1.927	.985	/	/	/
Smoking		2.461	1.411–4.295	< .005	2.050	1.116–3.765	.021
Diabetes		1.472	0.783–2.767	.230	/	/	/
Arterial hypertension		1.531	0.860–2.723	.148	1.756	0.951–3.242	.072
COPD		1.425	0.328–6.191	.636	/	/	/
History of coronary artery disease (or heart disease)		1.126	0.390–3.250	.826	/	/	/
History of cerebrovascular accidents		2.824	0.995–8.015	.051	2.456	0.820–7.359	.109
Chronic renal failure		0.000		.999	/	/	/
Jaundice		1.260	0.716–2.217	.423	/	/	/
Indication	PDAC	Reference category		.484	/	/	/
	Ampullary cancer	0.707	0.291–1.717				
	Cystic tumor	0.320	0.076–1.353				
	Pan-NEN	0.921	0.317–2.674				
	Bile duct cancer	0.258	0.035–1.915				
	Others	1.070	0.406–2.821				
Neoadjuvant therapy*		1.515	0.842–2.725	.165	1.435	0.726-2.836	.299
Pylorus-preservation		0.457	0.257–0.813	.008	0.509	0.271-0.955	.035
Pancreaticogastrostomy		1.202	0.420–3.439	.731	/	/	/
Vascular resection		1.116	0.515–2.419	.781	/	/	/
Total operative time		1.001	0.998–1.005	.412	/	/	/
Soft gland texture		0.625	0.355–1.099	.103	0.714	0.386-1.320	.282
Main pancreatic duct diameter		1.057	0.931–1.201	.394	/	/	/
EBL		1.000	1.000–1.001	.261	/	/	/
Need for intraoperative transfusion		1.063	0.412–2.743	.900	/	/	/
No. of harvested lymph nodes		1.006	0.987–1.026	.516	/	/	/

ASA-PS, American Society of Anesthesiologists physical status; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *EBL*, estimated blood loss; *OR*, odds ratio; *PDAC*, pancreatic ductal adenocarcinoma; *Pan-NEN*, pancreatic neuroendocrine neoplasm.
* Data refers to PDAC patients.

Table VII
Predictors of secondary DGE

Variable		Univariate analysis			Multivariable analysis		
		OR	CI for OR	*P* value	OR	CI for OR	*P* value
Age		1.015	0.998–1.032	.084	1.025	0.999–1.052	.059
Male sex		1.105	0.767–1.593	.592	/	/	/
BMI		1.053	1.004–1.104	.032	0.987	0.918–1.061	.714
ASA-PS ≥3		1.346	0.901–2.010	.147	1.768	0.895–3.492	.101
Smoking		1.812	1.251–2.624	< .005	1.751	1.055–2.904	.030
Diabetes		0.672	0.403–1.119	.126	0.459	0.224–0.942	.034
Arterial hypertension		1.593	1.083–2.344	.018	1.429	0.823–2.481	.205
COPD		0.806	0.240–2.707	.727	/	/	/
History of coronary artery disease (or heart disease)		1.714	0.947–3.202	.074	0.716	0.300–1.708	.451
History of cerebrovascular accidents		2.210	0.985–4.956	.054	1.472	0.510–4.246	.474
Chronic renal failure		1.589	0.533-4.736	.406	/	/	/
Jaundice		0.623	0.433–0.896	.011	0.864	0.487–1.532	.616
Indication	PDAC	Reference category		< .005	Reference category		.031
	Ampullary cancer	3.437	2.109–5.599		2.603	1.281–5.291	
	Cystic tumor	1.333	0.647–2.748		0.971	0.334–2.820	
	Pan-NEN	3.071	1.635–5.766		2.929	1.177–7.290	
	Bile duct cancer	2.362	1.154–4.834		1.106	0.405–3.021	
	Others	3.746	2.099–6.687		2.703	1.094–6.679	
Neoadjuvant therapy*		0.842	0.547–1.296	.434	/	/	/
Pylorus-preservation		0.707	0.472–1.060	.093	1.355	0.723–2.539	.343
Pancreaticogastrostomy		2.266	1.295–3.962	< .005	0.599	0.271–1.328	.207
Vascular resection		0.557	0.293–1.059	.074	0.817	0.297–2.246	.695
Total operative time		1.003	1.001–1.005	< .005	1.005	1.001–1.008	.010
Soft gland texture		4.151	2.639–6.530	< .005	3.175	1.613–6.249	< .005
Main pancreatic duct diameter		1.001	1.000–1.001	< .005	0.842	0.710–0.998	.047
EBL		1.726	1.192–2.499	< .005	1.001	1.000–1.002	.011
Need for intraoperative transfusion		2.759	1.729–4.401	< .005	1.290	0.587–2.837	.527
No. of harvested lymph nodes		0.988	0.975–1.001	.065	0.992	0.973–1.011	.378

ASA-PS, American Society of Anesthesiologists physical status; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *EBL*, estimated blood loss; *OR*, odds ratio; *PDAC*, pancreatic ductal adenocarcinoma; *Pan-NEN*, pancreatic neuroendocrine neoplasm.
* Data refers to PDAC patients.

5 on a median, and this was rather constant between the 2 subgroups. Instead, the time to resolution varied significantly between pDGE and sDGE (6 vs 9 days, respectively). Because the occurrence of sDGE is based on the presence of a coexisting complication, its duration reasonably depends on the successful treatment of the primary causes. This makes the course of sDGE more heterogeneous than pDGE, as suggested by the broader range (IQR) of time to resolution among the sDGE patients (5–17 days vs 4–10 days of pDGE). Due to its secondary nature, the suspect of a sDGE should indicate the prompt execution of a CT scan whenever a patient with a high FRS cannot be orally fed or clinical signs of abdominal collections are present (eg, persistent fever, abdominal pain, sinister appearance of drain fluid). Conversely, pDGE pivots on a primary dysfunction of gastric motility, possibly as a result of insufficient vascular supply, gastric denervation, transient mechanical obstruction (ie, anastomotic edema), motilin level reduction, or a combination of these factors. Hence, despite being shorter in this series, the pDGE time to resolution is unlikely predictable.

Based on these findings, the execution of an upper endoscopy has a marginal role, if any role at all, in the characterization of a DGE. It was performed in approximately 50% of patients in the present series, with negative findings in more than half of them. However, it is indeed necessary whenever a nasojejunal tube is required for EN distal to the duodenal-jejunal/gastric-jejunal anastomosis in patients with persistent DGE. Similarly, upper gastrointestinal fluoroscopy was not routinely performed. According to our experience, its clinical impact is negligible and mainly limited to ruling out mechanical obstructions.

Some limitations of the present study, mainly due to its retrospective design, must be mentioned. First, relevant data on comorbidities such as peripheral vascular disease, dyslipidemia, and other cardiovascular risk factors were not consistently collected and therefore were not available for the risk analysis of pDGE. Second, a minor proportion of pDGE patients did not have a CT scan; thus, perigastric collections and leaks were excluded only on a clinical basis. However, these patients accounted for <15% of this subgroup and had a negligible risk of POPF according to the FRS and no abdominal symptoms, thus making the presence of coexisting abdominal complications unlikely. Third, because TPN and EN could be used to treat concurrent complications such as POPF, the duration of nutrition supportive therapy in sDGE patients might have been overestimated and should not be considered as related to the treatment of DGE exclusively. Last, the preservation of the right gastric vessels was not consistently stated in the operative reports of this series, undermining the effort to assess its role in the development of a DGE and calling for further specific perspective studies.

In conclusion, DGE, after a PD, consists of 2 different subtypes as either primary or secondary to other complications. This knowledge calls for further evidence but should already drive clinicians in their clinical practice, to either mitigate or treat such conditions differently. A more comprehensive analysis of risk factors for primary DGE is needed. The prompt identification and treatment of other conditions possibly leading to secondary DGE might reduce its occurrence and clinical impact.

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Conflict of interest/Disclosure

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Supplementary materials

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