



# Duodeno-jejunal or gastro-enteric leakage after pancreatic resection: a case–control study

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## Abstract

Duodeno-jejunal (DJ) and gastro-jejunal (GJ) anastomosis leakage represents a rare but life-threatening complication after pancreaticoduodenectomy or total pancreatectomy. The aim of this study was to assess its incidence, clinical presentation, and outcomes, and to identify perioperative risk factors for DJ/GJ leak. Prospectively collected perioperative data were reviewed, and a case–control study was performed. Patients who presented with a DJ/GJ leak (cases) were matched in a 1:5 ratio with patients who did not develop it. Match criteria included age, diagnosis, type of surgery, and anastomosis. Perioperative factors and outcomes were compared between groups. From January 2008 to present, 13 cases were observed and compared to 60 controls. Concerning pre-operative variables, cases showed lower pre-operative serum hemoglobin ( $p = 0.021$ ) and increased pre-operative radiotherapy ( $p = 0.037$ ). Cases experienced more severe post-operative complications than Controls, according to the CD classification ( $p < 0.001$ ), with a higher mortality rate (23% vs. 2%;  $p < 0.016$ ). They also experienced a more demanding intra-operative course including an increased estimated blood loss (median 600 vs. 400 mL;  $p = 0.002$ ), a higher rate of blood transfusion ( $n 4 31\%$  vs.  $n 5 8\%$ ;  $p = 0.047$ ) with also a longer operative time (median 360 vs. 318 min;  $p = 0.038$ ). Moreover, the occurrence of a DJ/GJ leak was significantly associated with other post-operative complications: clinically relevant pancreatic fistula ( $p = 0.006$ ), bile leak ( $p = 0.021$ ), and bleeding ( $p = 0.001$ ). In addition, another post-operative finding significantly related to the DJ/GJ occurrence was sepsis ( $p < 0.001$ ). The DJ/GJ fistula required a surgical treatment in the majority of cases (92.3%), while, in only one patient, a conservative management was accomplished. Length of hospital stay and mortality at 90 days were higher in the DJ/GJ leak group ( $p = 0.001$ ). DJ/GJ leakage is a severe complication following pancreatic resection. A higher index of suspicion for DJ/GJ fistula should be maintained in case of concomitant relevant pancreatic fistula and post-operative hemorrhage.

**Keywords** Duodeno-jejunal fistula · Gastro-enteric fistula · Pancreatic resection

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Michele Mazza and Stefano Crippa contributed equally to the present study.

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## Introduction

Pancreaticoduodenectomy (PD) and total pancreatectomy (TP) are complex surgical procedures associated with significant postoperative morbidity. Over the past 13 years, technical advances, the use of interventional radiology and endoscopy, and centralization of pancreatic disease care have led to significant improvements in the management of post-operative complications with a decrease in mortality to less than 3–5% after PD [1, 2]. Most of the observed postoperative morbidity following PD or TP is related to failure of the reconstruction of the gastrointestinal tract, including leakage from the pancreaticojejunostomy (PJ), hepatico-jejunostomy (HJ), duodeno-jejunostomy (DJ) or gastro-jejunostomy (GJ). After PD, pancreatic fistula is a common complication

ranging from 10 to 25% and may lead to other severe complications including sepsis and delayed hemorrhage [3–5]. Biliary leak due to an HJ dehiscence is less common, occurring in approximately 3% of cases [6–8]. The failure of GJ or DJ anastomosis is a very rare event, described in less than 1% of patients after PD. However, its occurrence is a severe complication requiring surgical treatment and is associated with further morbidity and slower recovery. In recent years, only a few publications have focused on this topic and there is a need for well-designed studies to improve our knowledge regarding the risk factors and outcomes of this life-threatening surgical complication [9–11]. Therefore, the aim of the present study is to analyze the incidence, clinical presentation, management and outcomes of the GJ/DJ leak after PD or TP at a high volume center.

## Patients and methods

Demographic data, clinical and pathology characteristics, intra- and postoperative variables including complications were prospectively collected in our institutional electronic database for patients undergoing pancreatic resection. For the purpose of the present study, we retrospectively identified patients with DJ or GJ leakage and performed a case–control study. Patients with a postoperative DJ/GJ leak (cases) were compared to a control group including patients who did not experience it. To dwindle the control group heterogeneity and consequently reducing undesirable confounding factors, each case was individually matched with up to 5 controls according to the following variables: age ( $\pm 5$  years), malignant vs benign disease, pylorus-preserving pancreaticoduodenectomy (PPPD) vs Whipple procedure (Fig. 1). An individual matching approach was used. Each case patient was matched with the 5 chronologically closest control patients' meeting matching variables that a priori could balance both groups and at the same time could not have a primary role in the DJ/GJ development to rationalize

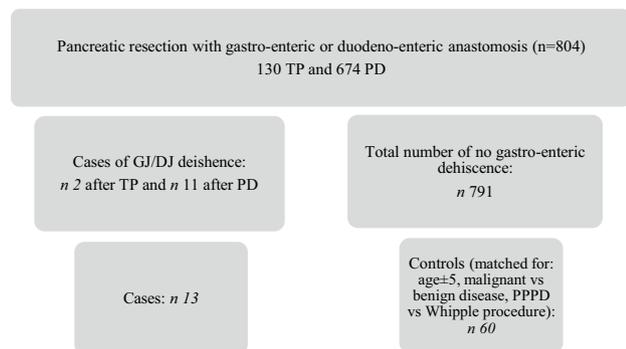


Fig. 1 Study design

the comparison. A 1:5 case–control ratio was also elected to increase the overall sample size, potentially allowing for a stratified analysis [12].

The gastroenteric anastomosis failure was defined as leakage confirmed during relaparotomy or in the radiological presence of peri-anastomotic air, fluid or extravasation of contrast material. Outcomes of interest included 90-day postoperative mortality, morbidity, length of hospital stay and hospital readmissions. The Clavien-Dindo grading system was used to assess the severity of complications following surgery [13]. Pancreatic fistula (PF) and postoperative hemorrhage (PPH) were defined following the latest ISGPF classifications [14, 15]. Diagnosis of bile leak was clinical, based on the appearance of the drainage fluids, confirmed with the measurement of the bilirubin drain concentration three times greater than the direct serum bilirubin. Diagnosis of fascial dehiscence was made on the clinical evidence of a fascial defect. Sepsis was defined as the presence at least of two systemic inflammatory response syndrome criteria associated with a suspected or documented infection (Table S1). Pneumonia diagnosis was considered when a lung infiltrate was present at chest X-rays associated with signs of infection requiring antibiotic therapy. Definition of other complications can be found in supplementary material (Table S1). Perioperative mortality was defined as death within 90 days after the index operation.

## Surgical technique

The standard surgical procedure for PD and TP was a pylorus-preserving technique. Distal gastrectomy was performed only in case of gastric involvement by the tumor or in case of doubtful ischemia of the antrum or pylorus. Pyloric vessels ligation was performed routinely while the left gastric vein preservation was attempted in all cases. Standard lymphadenectomy was achieved in case of cancer. The reconstruction was performed with a retro-colic PJ in case of PD, and an HJ according to Child technique [16]. The DJ was performed in an ante-colic fashion, usually 50–60 cm downstream from the HJ, with an end-to-side technique, in a single-layer interrupted suture using absorbable stitches. In case of Whipple procedure, the GJ was done in an end-to-side fashion with a double layer running absorbable suture. Other technical aspects of PD or TP are described elsewhere [17].

## Postoperative management

At our Institution, an Enhanced Recovery After Surgery (ERAS) pathway was the standard protocol for postoperative care, in keeping with the ERAS Society recommendations [18]. A detailed description of our protocol was previously reported elsewhere [19–21]. Nasogastric tube was routinely

avoided; the patient was usually started on a liquid diet on the first postoperative day (POD 1) and progressed on POD 2 to solid nutrition. Urinary catheter removal was planned on POD 2 and intravenous fluid administration suspended within POD4. Early mobilization, within POD1, was proposed to all patients. In case of PD, somatostatin analog was not routinely used to prevent pancreatic fistula in soft pancreas. Drain management was influenced by daily output, liquid characteristics and by the amylase drain value routinely performed in POD 2 and POD 5, as described by Partelli et al. [17]. Discharge criteria included tolerance of oral diet with no need of intravenous infusion, return to bowel function, autonomous ambulation, and pain controlled with oral medications.

### Statistical analysis

All prospectively collected data were registered in our institutional pancreatic surgery electronic database. Descriptive data are reported as mean (standard deviation), median (25th percentile—75th percentile), or number of patients (percentage). Categorical variables were compared by Fisher's exact test. Continuous variables were compared by the Student's *t* test if normally distributed, or non-parametric Mann–Whitney *U* test. The significance level was set at 0.05. In this case–control study, statistical comparison was made between the two groups, analyzing clinical presentation and outcome of patients with DJ or GJ fistula, compared with matched patients without this complication. Data analysis was performed using Stata® version 13.1 (StataCorp LP, College Station, Texas, USA).

### Results

Between January 2008 and December 2017, 130 TP and 674 PD were performed. Preoperative variables, treatment characteristics and postoperative outcomes are described in Table 1. In this series, 13 patients (cases) with GJ or DJ fistula were identified out of 804 major pancreatic resections (2 patients after TP, 11 patients after PD), with a reported anastomotic failure incidence of 1.6% (3.38% after PPPD and 8% after Whipple procedure). Pathological characteristics and clinical presentation of the cases are described in detail in Table 2. Ten patients of the cases had a pylorus-preserving operation, while in three patients a distal gastrectomy was performed. The most common clinical presentations of DJ or GJ dehiscence were sepsis (*n* 4, 30.8%), septic shock (*n* 4, 30.8%), entero-cutaneous fistula with high volume output suspicious for gastroenteric content (*n* 4, 30.8%) and acute abdomen (*n* 1, 1.76%). Indication for surgical treatment was direct diagnosis of the DJ/GJ leak in ten patients (9 with CT scan, 1 with contrast X-rays) and an undrained pancreatic

fistula in the other remaining 3 cases. DJ/GJ leak was diagnosed after a median of 13 postoperative days from initial surgery. In one case, it had a late presentation after hospital discharge, with an entero-cutaneous fistula and abdominal pain developing on postoperative day 45. Likewise, in the fistula group the pancreatic fistula was diagnosed earlier within the 5 POD.

Out of the 791 patients who did not develop the gastroenteric fistula, 60 patients (controls) were matched with the case group. For two cases, a 1:5 matching ratio was not met because of the restrictive matching criteria. Statistical comparison of preoperative variable, procedural and pathology characteristics of both groups is described in Table 3.

The American Society of Anesthesiologists classification (ASA), body mass index, significant preoperative body weight loss, and concomitant morbidities were similar between the two groups. Preoperative radiotherapy was more frequent among cases (*n* 3, 23% vs. *n* 2, 3%; *p* = 0.037), while there were no differences regarding preoperative chemotherapy (38% vs. 23%; *p* = 0.303). Preoperative hemoglobin level was significantly lower in patients with DJ/GJ leakage (median 11.9 vs. 13.0 g/L; *p* = 0.021). Cases had a more demanding intra-operative course including an increased estimated blood loss (median 600 vs. 400 mL; *p* = 0.002), a higher rate of blood transfusion (*n* 4 31% vs. *n* 5 8%; *p* = 0.047) with also a longer operative time (median 360 vs. 318 min; *p* = 0.038).

Comparison of postoperative outcomes for both groups is described in Table 4. Cases experienced more severe postoperative complications than controls, according to the CD classification (*p* < 0.001), with a higher mortality rate (23% vs. 2%; *p* < 0.016). Specific surgical complications significantly associated with DJ/GJ leakage were clinically relevant pancreatic fistula (*n* 5, 45% vs. *n* 4, 8%; *p* = 0.006), bile leak (*n* 6, 46% vs. *n* 9, 15%; *p* = 0.021) and clinically relevant postoperative hemorrhages (*n* 7, 54% vs. *n* 9, 15%; *p* = 0.001). The cases also had an increased incidence of sepsis (92% vs. 37%; *p* < 0.001). Reoperation rate was higher in the fistula group (92% vs 12%; *p* < 0.001). Postoperative course and type of reoperation are described in detail in Table 5. Successful non-operative management was achieved in only one patient with a small anastomotic leak, who was successfully treated with multiple percutaneous drainages of intra-abdominal fluid collections and with nasogastric decompression. Reoperation included in 8 cases refashioning the gastroenteric anastomosis whereas in 4 patients it consisted in a raffia of the anastomotic leak (Table 5). This latter more conservative approach was preferred in cases of limited dehiscence of the posterior DJ/GJ anastomosis. Three patients surgically treated with the anastomosis refashioned died for postoperative complications. Moreover, in the case group another patients previously treated with a raffia died during a readmission more

**Table 1** Characteristics of the study population

| Characteristics                         | TP ( <i>n</i> = 130) | PD ( <i>n</i> = 674) | Major pancreatic resection ( <i>n</i> = 804) |
|---|----------------------|----------------------|--|
| Patient's variables <i>n</i> (%)        |                      |                      |  |
| Age <sup>†</sup>                        | 67                   | 67                   | 67   |
| Sex                                     | 69 M, 61F            | 342 M, 332 F         | 411 M, 393F                                  |
| ASA I                                   | –                    | 34 (5)               | 34 (4.2)                                     |
| ASA II                                  | 56 (43)              | 399 (59.2)           | 455 (56.9)                                   |
| ASA III                                 | 74 (57)              | 241 (35.7)           | 315 (39.2)                                   |
| Comorbidities <i>n</i> (%)              |                      |                      |  |
| History of diabetes mellitus            | 53 (40.7)            | 134 (19.9)           | 187 (23.2)                                   |
| History of cardiac disease              | 12 (9.2)             | 57 (8.4)             | 69 (8.6)                                     |
| History of hypertension                 | 65 (50)              | 298 (44.2)           | 363 (45.1)                                   |
| History of pulmonary disease            | 2 (2.3)              | 4 (6)                | 6 (0.7)                                      |
| History of kidney disease               | –                    | 6 (0.9)              | 6 (0.7)                                      |
| Treatment characteristics <i>n</i> (%)  |                      |                      |  |
| Whipple procedure                       | 48 (36.9)            | 49 (7.2)             | 97 (12.1)                                    |
| Pylorus preserving                      | 82 (63.1)            | 625 (92.7)           | 707 (87.9)                                   |
| Vascular resection                      | 3 (2.3)              | 8 (1.2)              | 12 (1.5)                                     |
| Additional resection                    | 16 (12.3)            | 25 (3.7)             | 41 (5.1)                                     |
| Pathologic characteristics <i>n</i> (%) |                      |                      |  |
| Malignant disease                       | 88 (67.7)            | 435 (64.5)           | 523 (65)                                     |
| Benign disease                          | 42 (32.3)            | 239 (35.5)           | 281 (35)                                     |
| Pancreatic fistula <i>n</i> (%)         |                      |                      |  |
| Biochemical fistula                     | –                    | 94 (13.9)            | –  |
| Grade B                                 | –                    | 79 (11.7)            | –  |
| Grade C                                 | –                    | 23 (3.5)             | –  |
| Bile leak <i>n</i> (%)                  | 6 (4.6)              | 46 (6.8)             | 52 (6.5)                                     |
| Delayed gastric emptying <i>n</i> (%)   | 16 (12.3)            | 108 (16)             | 124 (15.4)                                   |
| Postoperative outcomes <i>n</i> (%)     |                      |                      |  |
| Minor complications CD I–II             | 40 (31.7)            | 273 (40.5)           | 313 (39)                                     |
| Major complications CD III–IV           | 19 (14.6)            | 134 (19.9)           | 153 (19)                                     |
| Length of hospital stay <sup>†</sup>    | 11                   | 10                   | 10   |
| 90-day mortality <i>n</i> (%)           | 5 (3.8)              | 12 (1.8)             | 17 (2.1)                                     |

(%) Values are number of patients

TP total pancreatectomy, PD pancreaticoduodenectomy, ASA American Anesthesiologist Classification, CD Clavien-Dindo et al. [13]

<sup>†</sup> value expressed as median

than 90 days after the index operation for multiorgan failure related to a severe cholangitis (overall mortality: 31%). The postoperative length of hospital stay was higher in the fistula group compared to controls (median 38 vs. 10 days;  $p < 0.001$ ). The cases also had an increased rate of hospital readmission (46% vs. 10%;  $p = 0.005$ ).

## Discussion

The DJ/GJ leak following major pancreatic resection has been poorly investigated compared to other more frequent complications, especially pancreatic fistula. Historically, DJ

or GJ leak has been considered a rare complication associated with a high mortality and morbidity rate [10, 11]. Nevertheless, it is still poorly characterized with only limited information regarding its etiology, clinical impact and management.

In the present study, the reported incidence of the DJ/GJ leak was 1.6%, in line with previous publications. Tran et al., in a randomized trial of pylorus preserving versus Whipple procedure, reported an overall gastroenteric fistula rate of 1.1% after PD [9]. Eshuis et al. in a series of 1036 PD reported a DJ or GJ leak rate of 1.2%. In this study, the authors showed a correlation with longer operative procedure, additional surgical resections and postoperative

**Table 2** Preoperative, pathological characteristics and clinical presentation of duodeno-jejunal (DJ) or gastro-jejunal (GJ) fistula

| Cases | Age | Sex | Morbidities                 | Type of disease                 | Previous treatment | Index operation        | POD diagnosis | Clinical presentation    | Diagnosis              |
|-------|-----|-----|-----------------------------|---------------------------------|--------------------|------------------------|---------------|--------------------------|------------------------|
| 1     | 52  | M   | Diabetes                    | Chronic pancreatitis            | None               | PD (gastric resection) | 13            | Sepsis                   | Intraoperative finding |
| 2     | 55  | M   | Chronic renal insufficiency | PADC                            | RT-CT              | PD                     | 45            | Entero-cutaneous fistula | Contrast X-rays        |
| 3     | 67  | M   | Diabetes, hypertension      | PADC                            | RT-CT              | PD                     | 11            | Septic shock             | Intraoperative finding |
| 4     | 78  | M   | None                        | Peryampullary adenocarcinoma    | None               | PD                     | 13            | Entero-cutaneous fistula | CT scan                |
| 5     | 76  | M   | Diabetes, hypertension      | Peryampullary adenocarcinoma    | None               | PD                     | 15            | Acute abdomen            | CT scan                |
| 6     | 66  | M   | None                        | PADC                            | RT-CT              | PD                     | 5             | Entero-cutaneous fistula | CT scan                |
| 7     | 82  | M   | None                        | PADC                            | None               | PD                     | 7             | Entero-cutaneous fistula | CT scan                |
| 8     | 73  | F   | Diabetes, hypertension      | Common bile duct adenocarcinoma | None               | PD                     | 25            | Septic shock             | Intraoperative finding |
| 9     | 67  | M   | Diabetes, hypertension      | PADC                            | None               | PD                     | 26            | Sepsis                   | CT scan                |
| 10    | 74  | M   | Hypertension, COPD          | PADC                            | None               | PD                     | 16            | Sepsis                   | CT scan                |
| 11    | 67  | M   | Hypertension                | PADC                            | CT                 | TP                     | 6             | Septic shock             | CT scan                |
| 12    | 79  | M   | None                        | Peryampullary adenocarcinoma    | None               | TP (gastric resection) | 9             | Septic shock             | CT scan                |
| 13    | 68  | M   | None                        | PADC                            | CT                 | PD (gastric resection) | 11            | Sepsis                   | CT scan                |

Values are number of patients

*PADC* Pancreatic ductal adenocarcinoma, *COPD* chronic obstructive pulmonary disease

pancreatic fistula [11]. In a cohort of 3029 major pancreatic resections, Winter et al. reported a gastroenteric leak incidence of 0.4% (10). In this latter study, risk factors for DJ/GJ leak were preoperative BUN-to-creatinine ratio > 20, intraoperative blood loss greater than 1000 mL and total pancreatectomy.

In our investigation, we sought to identify pre-, intra- and postoperative factors associated with this complication. Since the DJ/GJ leak was a rare event even in our cohort (*n* 13), we decided to perform a case–control study rather than a descriptive single cohort series with limited possibility to run a multivariate analysis. Each case was matched to five controls to increase the sample size and favor statistical analysis, using relevant preoperative variable as matching criteria. Preoperative variables significantly associated with gastroenteric dehiscence were preoperative radiotherapy and low serum hemoglobin. These findings have already been reported in colorectal cancer resection series as host-related predictive markers for anastomotic leakage [21, 22]. Cases also showed greater surgical complexity, as underlined by an increased operative time, intra-operative blood loss and

blood transfusions. These aspects, as described previously, have been identified as risk factors for anastomotic fistula, not only for pancreatic surgery but also for other gastrointestinal operative procedures [10–25]. Altogether, these variables are potential surrogates for perioperative hypotension, likely occurring in patients undergoing surgery with a preoperative impaired functional reserve. Evidence on this hypothesis is still lacking, although intestinal microcirculation and tissue oxygen tension are established key factors influencing perioperative outcomes [25, 26]. As a matter of fact, patients with GJ/DJ leak also had a significantly increased incidence of clinically relevant pancreatic and biliary anastomotic fistula associated with more significant PPH. Concomitant leak from another anastomosis (i.e., pancreatic or biliary), intraoperative and postoperative hypovolemia, for example due to relevant bleeding, suggest that perioperative impairment of splanchnic perfusion may play a role in the development of gastroenteric anastomotic leak. Another possible explanation of the DJ/GJ leak etiology may be the significant association with clinically relevant pancreatic fistula. In fact, a high output pancreatic leak could

**Table 3** Preoperative characteristics of patients with gastro-jejunal (GJ) or duodeno-jejunal (DJ) leak versus controls

| Variables   | GJ or DJ leak (n = 13) | Controls (n = 60) | P value |
|---|------------------------|-------------------|---------|
| <b>Patient characteristics</b>                            |                        |                   |         |
| Male gender   | 12 (92.3%)             | 23 (38%)          | 0.049   |
| ASA Score 3+  | 8 (62%)                | 21 (35%)          | 0.117   |
| Body mass index (kg/m <sup>2</sup> )                      | 24.2 [20.2–28.2]       | 24.1 [22.7–26.6]  | 0.894   |
| Obesity   | 3 (23%)                | 5 (8%)            | 0.146   |
| Preoperative body weight loss > 10%                       | 3 (23%)                | 12 (20%)          | 0.723   |
| <b>Concomitant disease:</b>                               |                        |                   |         |
| Diabetes Mellitus   | 5 (38%)                | 18 (30%)          | 0.532   |
| Cardiac disease   | 0                      | 6 (10%)           | 0.583   |
| Hypertension  | 6 (46%)                | 31 (52%)          | 0.768   |
| Chronic respiratory disease                               | 1 (8%)                 | 6 (10%)           | 1.000   |
| Chronic kidney failure                                    | 1 (8%)                 | 0                 | 0.176   |
| Preoperative chemotherapy                                 | 5 (38%)                | 14 (23%)          | 0.303   |
| Preoperative radiotherapy                                 | 3 (23%)                | 2 (3%)            | 0.037   |
| Preoperative hemoglobin (g/dL)                            | 11.9 (1.1)             | 13.0 (1.7)        | 0.021   |
| Preoperative total lymphocytes count (10 <sup>9</sup> /L) | 1.9 (0.5)              | 1.7 (0.5)         | 0.155   |
| Preoperative serum bilirubin (mg/dL)                      | 0.6 [0.2–1.3]          | 0.7 [0.4–1.8]     | 0.403   |
| Preoperative serum albumin level (g/L)                    | 38.8 [37.2–40.1]       | 40.0 [34.9–42.6]  | 0.517   |
| <b>Procedural</b>   |                        |                   |         |
| Whipple procedure   | 3 (23%)                | 10 (17%)          | 0.690   |
| Pylorus-preserving procedure                              | 10 (77%)               | 50 (83%)          |         |
| Vascular resection  | 3 (23%)                | 5 (8%)            | 0.146   |
| Duration of surgery (min)                                 | 360 [315–408]          | 318 [287–350]     | 0.038   |
| Estimated blood loss (mL)                                 | 600 [500–700]          | 400 [250–525]     | 0.002   |
| Intraoperative blood transfusion                          | 4 (31%)                | 5 (8%)            | 0.047   |
| Total intraoperative fluid infusions (ml/kg/hr)           | 9.2 [7.1–10.4]         | 10.7 [7.2–12.3]   | 0.180   |
| <b>Pathology</b>  |                        |                   |         |
| Malignant disease   | 11 (85%)               | 54 (90%)          | 0.626   |
| Node positive disease                                     | 10/11 (91%)            | 37/54 (69%)       | 0.265   |

Values are number of patients (%), or mean (SD) or median [25th–75th percentile]

ASA American Society of Anesthesiologists

reduce the healing of the gastroenteric anastomosis because of an erosive action of activated pancreatic enzymes. However, this last hypothesis does not explain the DJ/GJ leak after total pancreatectomy. Still, the relatively low number of DJ/GJ fistula and the inability to perform a multivariate analysis prevent us from reaching a conclusive determination of underlining causes leading to this rare complication.

In this study, DJ/GJ leaks typically occurred after the first week from the initial operation. Clinically, these patients usually presented with symptoms of sepsis, with increased output from an abdominal drain. Less frequently, they presented with an acute abdomen or an entero-cutaneous fistula through the surgical wound. Since DJ/GJ leak was frequently associated with other more common complications (i.e., pancreatic fistula), it is likely that early clinical symptoms/signs of DJ/GJ leakage were missed, leading to a delayed diagnosis. Therefore, a high index of clinical suspicion in

patients with other severe abdominal complications is necessary to make an early diagnosis of DJ/GJ leak.

Winter et al. reported an operative treatment in 92% of patients with DJ/GJ leak with a surgery-related mortality of 38% [10]. In another series, *Eushis* et al. adopted a conservative treatment with a reparation rate of 58% and postoperative mortality of 8% [11]. In the present study, the DJ/GJ leak required a reoperation in almost all cases (*n* 12/13). At relaparotomy, a distal gastrectomy with gastro-jejunostomy was performed in most of the patients. The aggressive operative management of this type of complication is in contrast with a more conservative approach that most of the time is preferred to manage pancreatic and biliary fistulas or even PPH. Being the gastroenteric leak associated with other anastomotic fistula, it is very important to make a timely diagnosis in order not to delay a necessary surgical treatment.

**Table 4** Postoperative outcomes in patients with gastro-jejunal (GJ) or duodeno-jejunal (DJ) leak versus

| Variables                       | GJ or DJ leak (n = 13) | Controls (n = 60) | P value |
|---------------------------------|------------------------|-------------------|---------|
| <b>Surgical complications</b>   |                        |                   |         |
| Pancreatic fistula              | 5/11 (45%)             | 15/51 (29%)       | 0.311   |
| Clinically relevant (Grade B–C) | 5/11 (45%)             | 4/51 (8%)         | 0.006   |
| Bile leak                       | 6 (46%)                | 9 (15%)           | 0.021   |
| Delayed gastric emptying        | 1 (8%)                 | 8 (13%)           | 1.000   |
| Hemorrhage                      | 7 (54%)                | 9 (15%)           | 0.005   |
| Grade A                         | 0                      | 4 (7%)            | 0.001   |
| Grade B                         | 4 (31%)                | 3 (5%)            |         |
| Grade C                         | 3 (23%)                | 2 (3%)            |         |
| Other surgical                  | 4 (31%)                | 20 (33%)          | 1.000   |
| <b>Medical complications</b>    |                        |                   |         |
| Cardiac                         | 1 (8%)                 | 4 (7%)            | 1.000   |
| Pneumonia                       | 4 (31%)                | 3 (5%)            | 0.016   |
| Thromboembolic                  | 0                      | 2 (3%)            | 1.000   |
| Sepsis                          | 12 (92%)               | 22 (37%)          | < 0.001 |
| <b>Complication severity</b>    |                        |                   |         |
| CD I                            | 0                      | 2 (3%)            | < 0.001 |
| CD II                           | 0                      | 19 (32%)          |         |
| CD III                          | 10 (77%)               | 10 (17%)          |         |
| CD IV                           | 0                      | 3 (5%)            |         |
| CD V—mortality                  | 3 (23%)                | 1 (2%)            |         |
| Reoperation                     | 12 (92.3%)             | 7 (12%)           | < 0.001 |
| Length of hospital stay (days)  | 38 [27–70]             | 10 [7–19]         | < 0.001 |
| Hospital readmission            | 6 (46%)                | 6 (10%)           | 0.005   |

Values are number of patients (%) or median [25th–75th percentile]  
*CD* Clavien-Dindo et al. [13]

The occurrence of a DJ or GJ fistula had a tremendous impact on the patients’ postoperative course. As previously described, according to CD classification all cases were stratified as severe complications (CD ≥ III) and had increased incidence of sepsis (92% vs. 37%; *p* < 0.001). The gastroenteric fistula also profoundly affected the hospital stay and readmission rate. Postoperative length of stay ranged between 22 and 90 days with a median of 38 days. Six patients were readmitted within 30 days after discharge, most of the time because of infectious complications.

This study has some limitations. It is based on a retrospective analysis carrying all the limits associated with this approach. Despite the large series of pancreatic resection presented here, a DJ/GJ leak is a rare complication; thus, our study only included a small number of patients. For this reason, a case–control approach with a univariate analysis, instead of a multivariate model, was preferred to identify relevant risk factors. For the same reason, in the matching process of the two groups, a specific histology was not considered, but only the presence of malignant versus benign disease. However, most of the key variables analyzed in the present study were recorded in prospective fashion. Data regarding nutritional parameters, adjuvant

chemotherapy, quality of life and related outcomes were not assessed and were impossible to retrieve retrospectively. A further limitation of this study was the low number of distal gastrectomies performed. As this procedure was restricted to few patients with tumor involvement of the pyloric region or clinically evident ischemia of the distal portion of the stomach, it is impossible to determine if this approach may have played a role in the occurrence of a DJ/GJ leak.

### Conclusion

DJ/GJ leakage after TP or PD is an uncommon but potentially life-threatening complication, with a relevant impact on the patients’ postoperative course. DJ/GJ fistula etiology remains unclear and further studies are needed. A high index of clinical suspicion is necessary to make an early diagnosis of DJ/GJ leak, a complication that requires surgical reoperation in the vast majority of cases.

**Table 5** Cases postoperative variables

| Cases | PF grade | PPH grade | Other complication                                      | DJ/GJ fistula treatment                                 | CD  | Hospital Dis-charge | Readmission |
|-------|----------|-----------|---|---|-----|---------------------|-------------|
| 1     | –        | –         | Pneumonia   | Fistula raffia  | III | 26                  | No          |
| 2     | –        | –         | None  | Distal gastrectomy, GJ with Roux-en-Y reconstruction    | III | 27                  | Yes         |
| 3     | C        | –         | Bile leak, Bowel ischemia, fascia dehiscence, pneumonia | Fistula raffia  | III | 8                   | Yes         |
| 4     | B        | C         | Bile leak, fascia dehiscence, pneumonia                 | Fistula raffia  | III | 70                  | Yes         |
| 5     | –        | C         | Bile leak, bowel ischemia, pneumonia                    | Distal gastrectomy, GJ with Roux-en-Y reconstruction    | III | 90                  | No          |
| 6     | B        | –         | –   | Distal gastrectomy, GJ with Roux-en-Y reconstruction    | III | 85                  | No          |
| 7     | –        | B         | Bile leak   | Multiple percutaneous drainage                          | III | 31                  | Yes         |
| 8     | B        | B         | Bile leak, fascia dehiscence                            | Distal gastrectomy, GJ with Roux-en-Y reconstruction    | III | 40                  | Yes         |
| 9     | C        | B         | Bile leak, MOF  | Fistula raffia  | V   | 51                  | –           |
| 10    | –        | –         | Cardiac arrhythmia                                      | Distal gastrectomy, GJ with Roux-en-Y reconstruction    | III | 43                  | Yes         |
| 11    | –        | C         | MOF   | Distal gastrectomy, GJ without Roux-en-Y reconstruction | V   | 35                  | –           |
| 12    | –        | –         | MOF   | Distal gastrectomy, GJ without Roux-en-Y reconstruction | V   | 14                  | –           |
| 13    | –        | B         | DGE   | Distal gastrectomy, GJ without Roux-en-Y reconstruction | III | 21                  | No          |

Values are number of patients

PF pancreatic fistula (13), PPH postoperative hemorrhage (14), MOF multiorgan failure, DGE delate gastric emptying, DJ duodeno-jejunal, GJ gastro-jejunal, CD Clavien-Dindo et al. [13]

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Research involving human participants and/or animals** Ethical approval from the Ethical Committee of institution is not required as it is a retrospective investigation. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki declaration of 1975, as revised in 2008.

**Informed consent** Informed consent was obtained from all patients for being included in the study.

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