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Original Article

Clinical features and evolution of paraduodenal (groove) pancreatitis: A multicenter study

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ABSTRACT

Introduction: The pathogenesis and natural history of paraduodenal (groove) pancreatitis (PP) remain unclear, and treatment includes medical therapy, interventional endoscopy, and surgery. This is a multicenter study to explore the burden of the disease, its clinical course, and response to treatment.
Methods: Data were retrospectively collected from both academic and nonacademic Italian centers. All patients diagnosed with PP were included in the study. Data were recorded at the time of diagnosis and follow-up.

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Results: 208 patients (87.5 % male) from 16 centers were recruited. The median age at diagnosis was 50.5 (IQR 13 years), and the mean time from clinical presentation to diagnosis was 18 (±29) months. 90.6 % (n = 107) had a history of alcohol abuse and 90.7 % (n = 185) had smoked. Thirty-six patients (17.9 %) had diabetes at diagnosis, while 80 patients (41.5 %) had chronic pancreatitis. Six (3 %) patients were diagnosed with pancreatic cancer after a mean time of 10.3 (±10.8) months from the PP diagnosis. Forty-nine patients (24.9 %) had pancreatic exocrine insufficiency (PEI) at diagnosis, while 45(24.3 %) developed PEI during follow-up. Conservative treatment was administered in 103 (54.5 %) cases, surgery in 52 (27.5 %), and endoscopic therapy in 34 (18 %). The mean follow-up was 41.1 (±31.92) months.
Conclusions: Alcohol consumption and smoking are major risk factors for PP. Diabetes and PEI commonly develop in these patients. Conservative treatment strategies are often successful.

1. Introduction

Paraduodenal (groove) pancreatitis (PP), also known as groove pancreatitis, is a rare inflammatory disease that affects the groove area, which is defined as the area between the pancreatic head, duodenal walls, and common bile duct [1]. The pathological changes are centered in the duodenal wall near the minor papilla and extended to the groove zone. Microscopically, PP is characterized by chronic inflammation, Brunner gland hyperplasia, proliferation of myoid cells that are more prominent in the submucosa of the minor papilla, neural proliferation, and the presence of acinar elements and cystically dilated ducts that contain mucoproteins that are rarely calcified. The inflammatory process may also involve the adjacent pancreatic tissue and main pancreatic duct, resulting in obstructive chronic pancreatitis that can spread to the body-tail of the gland [2]. However, complicating the field of study even further, due to the shared risk factors with classic chronic pancreatitis, these two entities can also be present in the same patients as a result of common etiology. Though the pathogenesis of PP is still unclear, it has been suggested that alcohol consumption and smoking are causative events through a combination of several different mechanisms: functional obstruction of the minor papilla or duct of Santorini, increasingly viscous pancreatic secretions as a result of alcohol use or smoking, Brunner gland hyperplasia resulting in stasis of pancreatic secretions in the dorsal pancreas, heterotopic pancreas in the duodenum, and peptic ulcer disease have all been suggested as potential contributing factors [3]. The clinical presentation of PP can vary greatly from acute pancreatitis to a more chronic course with nonspecific symptoms, such as abdominal pain, nausea, vomiting, and weight loss, to complications such as gastric outlet obstruction and jaundice [3–5]. Thickening of the duodenal wall in the groove between the pancreatic head and duodenum with cystic changes is a typical feature, which is often confused and masquerades because of mass-like enlargement of the pancreatic head and/or diffuse involvement of the pancreatic gland due to chronic obstructive pancreatitis [6]. To date, no specific diagnostic criteria have been developed or validated [7,8]. Furthermore, no guidelines have been developed to guide the management of these patients; therefore, the management is based on the expertise of pancreatologists at any center. One of the main problems associated with this disease is that it can mimic other pancreatic conditions, such as pancreatic cancer, cystic neoplasms, or autoimmune pancreatitis, making PP a complicated diagnostic challenge [8,9]. Therefore, an accurate diagnosis of PP is crucial to avoid unnecessary major surgery and provide appropriate treatment [2,10], which depends on the symptoms and the presence of complications, such as duodenal obstruction, biliary stenosis, or pancreatic insufficiency [11–13]. Medical therapy and lifestyle changes include cessation of smoking and alcohol consumption, pancreatic enzyme replacement therapy (PERT), and on-demand painkillers [14,15]. Endoscopic interventions [16–18] or surgical resection may be required in severe cases or when malignancy is suspected [16,19,20]. The prognosis of PP is generally favorable, with a low mortality rate and good quality of life (QoL) after treatment [21,22]. However, PP can have long-term consequences, such as exocrine or endocrine pancreatic insufficiency (pancreatic exocrine insufficiency [PEI] and diabetes) or duodenal and biliary strictures in cases of luminal compression [23,24].

Neoplastic evolution is unclear, with no evidence in the literature regarding *de novo* occurrences. The burden and evolution of PP towards PEI and neoplastic evolution are still not well understood, and large-scale studies on this topic are lacking. Therefore, we did a multicenter study to explore the burden of the disease, its clinical course, and response to treatment.

2. Materials and methods

This study was conducted following the “Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)” recommendations [25] (Supplementary Table 1). Data derived from both academic and nonacademic Italian centers were collected from January 2005 to April 2023. Patients were included if they were diagnosed with PP based on specific criteria according to the judgment of the treating physicians. Specifically, the diagnosis of PP was based on surgical specimens in patients undergoing surgery, while it was primarily based on the assessment of morphological characteristics using EUS and the interpretation of radiological images (CT scan or MRI) in patients who had not undergone surgery or who had received derivative surgical treatment. The radiological criteria [9] included any of the following: fat stranding in the pancreatoduodenal groove, hypoenhancing soft tissue, which may lead to delayed enhancement in the groove area, and cystic change in the groove or wall of the second duodenum. In addition, wall thickening of the medial side of the second duodenum and variable involvement of the pancreatic head are accompanying findings considered supportive features [3]. The exclusion criteria were as follows: 1) pediatric patients (<18 years old) and 2) pregnancy. Data at the time of diagnosis and during follow-up were extracted and added anonymously to a dedicated online platform for analysis. The aims of the study were as follows: 1) to evaluate the clinical presentation of the disease at baseline; 2) to evaluate the diagnostic methods used and the most frequent findings in the diagnosis of PP; 3) to evaluate the therapies used in PP; 4) to evaluate the evolution towards exocrine/endocrine pancreatic atrophy/insufficiency; and 5) to determine the risk of developing adenocarcinoma. Diagnosis was made based on clinical, radiological, and pathological findings when surgical specimens were available for patients undergoing resection surgery (Whipple or pylorus-preserving pancreaticoduodenectomy)

[7,10,21]. The collected parameters were based on medical records, including medical history, demographic, histological, radiological, and biochemical data. According to the most widely accepted classification, PPs were categorized as “solid” or “cystic” based on the presence of cyst(s) in the thickened duodenal wall, either at histological examination in the case of surgery or at imaging (EUS and/or CT and/or MR) in non-surgical patients. Furthermore, PPs were classified as “pure” (also defined as “segmental”) or “diffuse”, based on radiological criteria [2,26]. The pure form was grouped with the segmental form because of the lack of consensus in the literature regarding which definition or subgroup best fits this disease. Thus, “pure” and “segmental” were considered together, as both are limited to a specific area, in contrast to the diffuse form, which additionally involves the entire pancreas. Specifically, the “pure” (or “segmental”) form was defined by the presence of thickening of the groove area or medial duodenal wall, increased volume of the head of the pancreas, or presence of cysts in the duodenal wall/groove area on radiological or EUS examination. On the other hand, the additional diagnosis of chronic pancreatitis or hypotrophy of the pancreatic body/tail or other irregularities of the pancreatic duct system at the pancreatic body/tail, as the presence of a dilation of the main pancreatic duct (>4 mm), and/or the presence of pancreatic calcifications in the body-tail of the pancreas were ascribed to the “diffuse” form [26,27]. Data from medical history included endocrine pancreatic insufficiency (fasting serum glucose >126 mg/dL), PEI (clinically detectable steatorrhea or fecal elastase-1 <200 μg/g of stools), history of acute pancreatitis (defined as upper abdominal pain and increase of serum amylase or lipase of greater than 3-fold the upper normal limits ± consistent radiological imaging), and history of other diseases. The outcomes evaluated were the evolution of PEI and the need for medical therapy or surgical or endoscopic intervention. Medical therapy was considered a conservative intervention, including lifestyle adjustments (cessation of drinking and smoking) and PERT in cases of concomitant PEI/CP. Endoscopic treatment included ERCP, enteral stenting, and/or EUS-guided procedures (e.g., EUS-guided gastrojejunostomy in cases of gastric outlet obstruction [GOO] [28]). Surgical data were also collected to identify the type of surgery, whether resective or derivative.

2.1. Statistical analysis

Quantitative variables are expressed as mean (± standard deviation [SD]) or median (interquartile range [IQR]) based on a previous evaluation of the normality of their distribution, assessed both graphically and using the Shapiro-Wilk test. These variables were compared using univariate analyses, including the Mann-Whitney *U* test, Kruskal-Wallis test, or Student's t-test, depending on their respective applicability. Qualitative variables are expressed as numbers and percentages and compared in univariate analyses using the chi-square test or Fisher's exact test, based on the sample sizes and conditions for each test application. A logistic regression model was used to evaluate the association between treatment and outcome. Statistical significance was set at $p < 0.05$. Missing data were not included in the analysis using the pairwise deletion method. The statistics were processed using JAMOVI software (The jamovi project, version 2.3.21) and the SPSS statistical program (SPSS Inc., Chicago, Ill, U.S.A.).

3. Results

3.1. Patient characteristics

We enrolled 208 patients from 16 centers in Italy. The median age at diagnosis of PP was 50.5 (IQR 13) years. One hundred and seven (90.6 %) patients reported a positive history of alcohol abuse (mean 5.94 alcoholic units per day), and 90.7 % (n = 185) had a positive smoking history (mean 21 cigarettes per day). Active smokers comprised 77 % (n = 157), previous smokers 13.7 % (n = 28), and those who had never smoked 9.3 % (n = 19). Among active smokers, 4.5 % (n = 7) were non-drinkers, 42.6 % (n = 66) were previous drinkers, and 52.9 % (n = 82) were active drinkers. Among the active drinkers (n = 98), 84.5 % were smokers (n = 82), 11.3 % were former smokers (n = 11), and 4.1 % had never smoked (n = 4). One hundred twenty-eight patients (63.1 %) had the cystic form of the disease, while the solid form was present in 75 patients (36.9 %). The “diffuse” form was identified in 123 patients (59.1 %), while the “pure” (“segmental”) form was identified in 85 patients (40.9 %) (Table 1).

3.2. Clinical presentation

The clinical onset of PP includes acute pancreatitis, abdominal pain, weight loss, jaundice, and/or vomiting, which were reported in 67.4 %, 89.1 %, 65.0 %, 18.5 %, and 32.6 % of patients, respectively. Abdominal pain (n = 180, 89.1 %), weight loss (n = 115, 65 %), and acute pancreatitis (n = 120, 67.4 %) were the most common symptoms at diagnosis. Transitable duodenal stenosis was found in 17 patients (8.6 %). Patients experienced a mean weight loss between initial clinical presentation and diagnosis of PP of 5.8 (±6.7) kg, which was significantly different between patients undergoing medical therapy and those undergoing surgery or endoscopy (4.81 ± 6.29 vs. 7.44 ± 7.45, respectively, p = 0.003). Diabetes at diagnosis was reported in 17.9 % of patients (n = 36). Initial laboratory tests showed a mean increase in bilirubin of 1.69 (±1.62) times the upper limit of normal (ULN), amylase of 3.236 (±2.39) times the ULN, lipase of 3.64 (±3.10) times the ULN, and γGT of 28.76 (±144.92) times the ULN.

3.3. Diagnosis

Instrumental examinations for diagnosis were computed tomography (CT-scan [93 %]), EUS (82.7 %), EUS-FNA or FNB (42.8 %), MRI (59.4 %), MRCP (57.7 %), and gastroscopy (55.9 %) (Table 2). The frequencies of the examination findings are presented in Fig. 1. PP was diagnosed at a mean time of 18 (±29) months from the initial clinical presentation of the patients. When comparing the solid and cystic forms of the disease, MRCP (28.6 vs. 71.4 %, p = 0.025) was significantly more frequent in the cystic form. No differences in clinical presentation, laboratory tests at baseline, or outcomes were identified between the cystic and solid forms in the univariate analysis (Supplementary Table 2). Moreover, we also found a slight difference in the timing of PP diagnosis from initial clinical presentation to PP diagnosis when comparing cystic and solid variants; specifically, the cystic variant took a mean 21.15 (±31.83) months to be diagnosed, while the solid form took a mean of 12.7 (±23.8) months, even if this difference was only near to achieving statistical significance (p = 0.054). When analyzing differences between the “diffuse” and “pure” forms, we found a higher number of patients with previous alcohol consumption in the diffuse form than in the pure form (75.6 vs. 24.4 %, p < 0.001), with significant differences in the mean number of alcoholic units per day (6.63 ± 5.9 vs. 3.82 ± 3.58, p = 0.043) (Supplementary Table 3). Moreover, significant differences were identified in clinical presentation between the pure and diffuse forms, such as jaundice (25 vs. 75 %, p = 0.048), absence of nausea (69.6 vs. 30.3 %, p = 0.008), history of acute pancreatitis (33.3 vs. 66.7 %, P = 0.019), and PEI at diagnosis (20.4 vs. 79.6 %, p = 0.002).

Table 1
Characteristics of patients (n = 208) at baseline.

Table 1. Characteristics of patients at baseline, n (%) or mean (±SD)[a]	
Age, median (IQR), years	50.5 (IQR 13)
Male (%)	182 (87.5)
History of alcohol intake	107 (90.6)
Positive smoking history	185 (90.7)
Diabetes at diagnosis	36 (17.9)
Chronic pancreatitis	80 (41.5)
Family history of pancreatic diseases	19 (9.4)
Pancreatic carcinoma	8 (42.1)
Chronic pancreatitis	8 (42.1)
Pancreatic cysts	3 (15.8)
Genetic diseases, % (n)	3 (1.6)
Exocrine pancreatic insufficiency (PEI) at diagnosis	49 (24.9)
Weight loss between initial symptoms and diagnosis of PP (Kg), mean (±SD)	5.8 (±6.7)
Oncologic diseases	13 (6.6)
Colorectal cancer	4 (30.8)
Hepatocellular carcinoma	1 (7.7)
Pheochromocytoma	1 (7.7)
Pulmonary cancer	1 (7.7)
Breast cancer	5 (38.5)
Bladder cancer	1 (7.7)
Clinical presentation	
Jaundice	32 (18.5)
Abdominal pain	180 (89.1)
Nausea	82 (47.1)
Vomiting	57 (32.6)
Weight loss	115 (65.0)
Transitable duodenal stenosis	17 (8.6)
History of acute pancreatitis	120 (67.4)
Patterns, n (%)	
Cystic	128 (63.1)
Solid	75 (36.9)
Forms, n (%)	
Diffuse	123 (59.1)
Pure	85 (40.9)

[a] Missing data were excluded from analysis. PP = paraduodenal (groove) pancreatitis; PERT = pancreatic enzyme replacement therapy.

Table 2
Overall view of management of patients with paraduodenal (groove) pancreatitis (n = 208).

Table 2 all variables are reported as n (%) or mean (±SD)	
Treatment, n (%)	
Medical (medical therapy and lifestyle adjustments)	103 (54.5 %)
Surgery	52 (27.5 %)
Endoscopy	34 (18 %)
Type of surgery*	
Derivative	10 (20.4 %)
Resective	39 (79.6 %)
PEI evolution°	
Never	94 (50.8 %)
Resolution during FU	18 (9.7 %)
Onset during FU	45 (24.3 %)
Persistent (PEI since the PP diagnosis)	28 (15.1 %)
Diabetes evolution	
Never	138 (74.2 %)
Resolution during FU	24 (12.9 %)
Onset during FU	16 (8.6 %)
Persistent (diabetes since the PP diagnosis)	8 (4.3 %)
Pancreatic cancer diagnosis during FU, n (%)	6 (3 %)
Resectable	3 (50 %)
Unresectable	3 (50 %)
Time (months) to cancer diagnosis from PP diagnosis, median (IQR)	6 (17.3)

PEI = exocrine pancreatic Insufficiency; SD = standard deviation; FU = follow up; IQR=Interquartile range *Data on the type of surgery was not reported for 3 patients; °data on PEI evolution was reported in 185 patients.

3.4. Evolution and management of the disease

Four groups of patients were identified at the end of follow-up based on the evolution of PEI (Table 2). When exploring this evolution, diabetes at diagnosis was more frequent in those who never had PEI (n = 16, 50 %) than in the other groups (p = 0.044). No further associations based on the evolution of PEI were identified (Supplementary Table 4). On the other hand, four groups of patients were identified at the end of the follow up based on the evolution of diabetes (Table 2). No associations with variables were identified based on the evolution of diabetes (Supplementary Table 5). A history of smoking, alcohol consumption, or both was

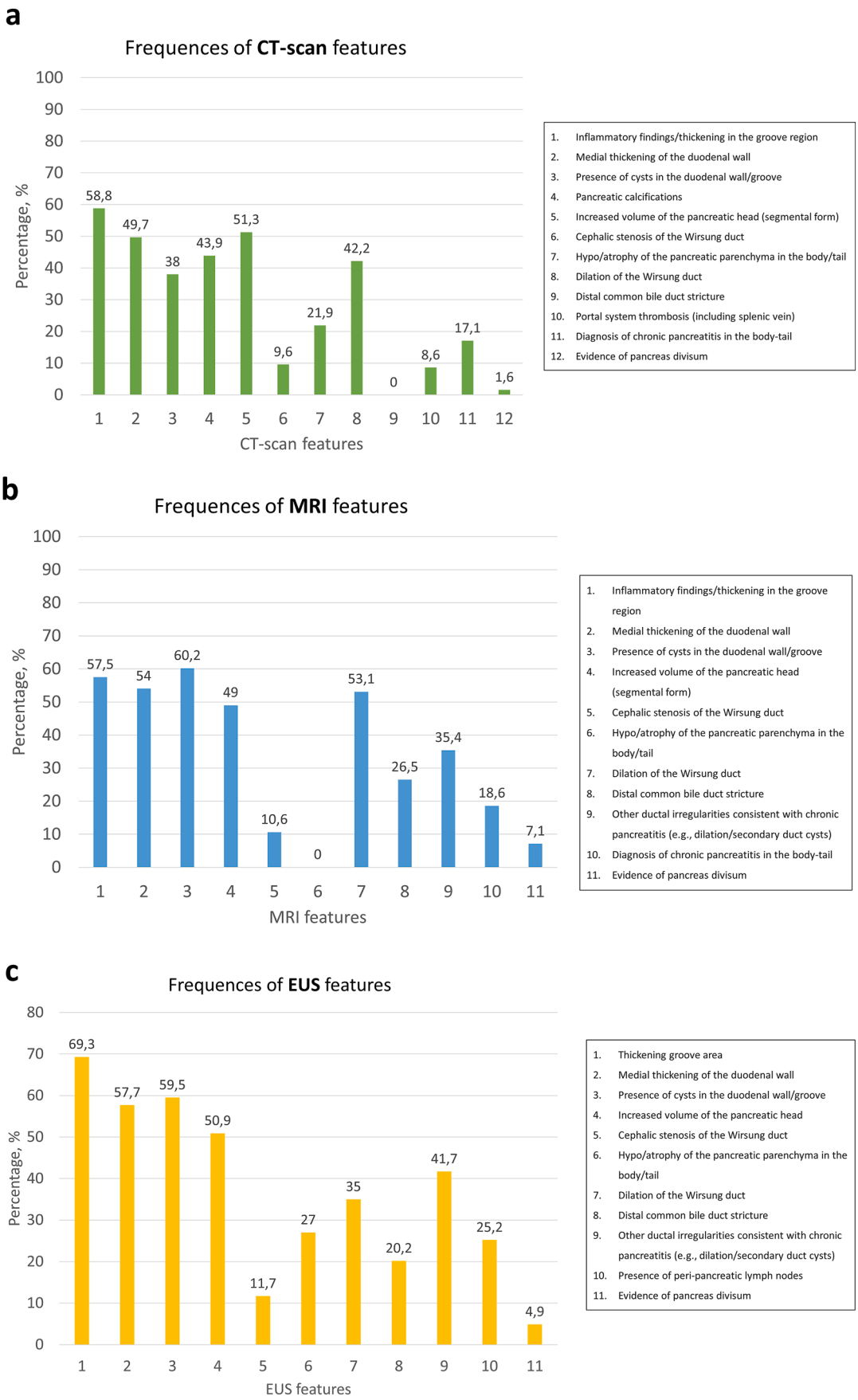

Fig. 1. Frequencies of morphological features identified at different imaging examination: a) Distribution of morphological features at computed tomography (CT) scan; b) Distribution of morphological features at magnetic resonance imaging (MRI); c) Distribution of morphological features at endoscopic ultrasound (EUS).

not associated with a higher rate of PEI or diabetes at diagnosis or during follow-up (Table 3). In 6 patients (3 %), pancreatic cancer was diagnosed after a median of 6 months (IQR = 17.3; two patients after the first month, two patients after 6 months, and two after 24 months), 50 % of whom were at the localized stage.

3.5. Treatment

Conservative treatment (medical therapy and lifestyle adjustments) was administered in 54.5 % of the cases (n = 103), while surgery (n = 52, 27.5 %) was more common than endoscopy (n = 34, 18.0 %) among patients undergoing interventional therapy (n = 86, 45.5 % of total). Medical therapy, including cessation of alcohol consumption and smoking, was prescribed for all patients, and was achieved in 73.3 % (n = 152) and 41.4 % (n = 86) of the cases, respectively. No variables were associated with the different types of treatments (Supplementary Table 6). Nutritional support was provided to 48.7 % of the patients (n = 101). Painkillers were administered to 64.9 % of patients (n = 135). Specifically, medical therapy included proton pump inhibitors (PPI) (64.9 %, n = 122), paracetamol (59.8 %, n = 113), non-steroidal anti-inflammatory agents (NSAIDs) (57.1 %, n = 109), minor opioids (28.1 %, n = 52), and major opioids (8.2 %, n = 15). The most common type of surgery during follow-up was pancreaticoduodenectomy (71.4 %, n = 35), while derivative surgery was performed in 20.4 % (n = 20) of the surgical cases. No differences were observed in clinical presentation, PEI, or diabetes at diagnosis with the various treatments. Among the 17 patients with transitable duodenal stenosis, five developed gastric outlet obstruction (GOO) requiring interventions (four underwent surgery, and 1 endoscopic stenting). Ten deaths were registered among the available data at the last follow-up. The causes of mortality were pancreatic cancer-related in two cases, pulmonary cancer in one case, liver failure in another case, post-surgical adverse events in three cases (one case of bleeding, one case of intestinal ischemia, and the last one not specified), one case of respiratory insufficiency, and two cases not specified. Surgery was associated with a higher likelihood of not requiring pain medication (aOR 10.78, 95 % CI 3.29–35.24), whereas endoscopic treatment showed no significant association (aOR 1.56, 95 % CI 0.54–4.45). Surgery was significantly associated with new-onset PEI (aOR 3.79, 95 % CI 1.59–9.01), but not with stable or resolved PEI. Endoscopic therapy was significantly associated with confirmed PEI (aOR 3.09, 95 % CI 1.08–8.84) (Table 4).

4. Discussion

PP is a rare condition that is usually underestimated because of a lack of knowledge and data in the literature. Considering the scarcity of data, with small cohorts evaluated in the literature, this study included the largest medical-surgical cohort of patients with PP (n = 208) to date. Previous studies on PP included a number of patients between 7 [22] and 120 [21], with the largest number of patients derived from a retrospective single-center study [2] and only two multicenter studies including a few patients (8 and 33) [13,24]. PP symptoms are not specific, and can be shared with other pancreatic conditions, especially cancer [29]; therefore, further variables for differential diagnosis are necessary to suggest the diagnosis of PP, such as a younger age at clinical onset, and high alcohol intake [30]. Similar to the data in the literature, our patients were overwhelmingly middle-aged men (87.5 %) with a history of alcohol abuse (90.6 %) and smoking (90.7 %). Owing to these strong associations with PP, it was hypothesized that alcohol and cigarette smoking directly affected the groove area, causing the development of the disease. It is still unknown whether some factors are related to the pattern (cystic or solid) or form (diffuse or pure). Nonetheless, in a previous large study [2], no differences were observed in the progression of the disease between the cystic and solid patterns or between the diffuse and pure forms. Indeed, our study confirmed no differences in clinical presentation, laboratory tests, or disease evolution between the cystic and solid

Table 3
Analysis of the association between risk factors and (A) PEI evolution and (B) diabetes evolution.

Table 3 A	PEI at diagnosis, %	p-value	PEI at last FU (at least once during the disease), %	p-value	Resolution, %	Stable/Confirmed, %	New onset, %	Never, %	p-value
Smokers	24.3	0.950	38.9	0.701	10.7	13.7	24.4	51.2	0.323
Alcohol consumption	26	0.095	40.6	0.466	10.7	15.5	24.4	49.4	0.430
Both	25.7	0.286	39.2	0.711	11.3	14.4	23.8	50.6	0.330

Table 3 B	Diabetes at diagnosis, %	p-value	Diabetes at last FU, %	p-value	Never, %	De novo, %	Confirmed, %	Resolution, %	p-value
Smokers	18.2	0.952	14	0.987	73.4	8.9	4.7	13	0.499
Alcohol consumption	17.7	0.471	14	0.471	74.1	8.8	4.7	12.4	0.705
Both	17.6	0.820	14.1	0.675	73.9	8.7	5	12.4	0.686

PEI = exocrine pancreatic insufficiency; FU = follow up.

Table 4
Logistic regression analyzing the type of treatments for outcomes.

Outcome		ES	p-value	OR	aOR*	CI 95 %
No need for painkillers	Treatment vs medical therapy					
	Surgery	0.604	**<0.001**	9.77	10.78	3.29–35.24
	Endoscopy	0.535	0.408	1.68	1.56	0.54–4.45
PEI evolution	Treatment vs. medical therapy					
Resolution vs. never	Surgery	0.804	0.177	2.23	2.22	0.69–7.15
	Endoscopy	0.236	0.745	1.27	1.26	0.30–5.25
Stable/Confirmed vs. never	Surgery	0.757	0.174	2.13	2.12	0.71–6.33
	Endoscopy	1.134	**0.034**	3.11	3.09	1.08–8.84
New onset vs. never	Surgery	1.328	**0.003**	3.77	3.79	1.59–9.01
	Endoscopy	0.172	0.770	1.19	1.19	0.37–3.79

ES = estimate; OR = odds ratio; aOR = adjusted OR; CI = confidence interval; PEI = exocrine pancreatic insufficiency; *Adjusted for age.

patterns. Moreover, we found a significantly higher use of MRCP to diagnose the cystic form than the solid form ($p = 0.025$), as expected from the universal management of cystic lesions. Nonetheless, in general, our study also showed a high use of CT scan for diagnosis (93 %), followed by EUS (82.7 %), with 42.8 % of patients who underwent EUS-FNA or FNB and MRI (59.4 %) [21,31]. The wider use of EUS rather than MRI might be explained by the design of our study involving tertiary centers, where EUS is routinely performed for pancreatic diseases. Moreover, the slight difference in the timing of PP diagnosis between cystic and solid variants (21.15 [±31.83] vs. 12.7 [±23.8] months, $p = 0.05$) could be explained by the fear of misdiagnosing cancer in the solid form; therefore, physicians probably perform radiological examinations or tissue acquisition more quickly. In addition, we explored the incidence and evolution of PEI in our cohort, which is another clinically relevant aspect of PP. Half of the patients (50.8 %) had never experienced PEI, while 24.3 % experienced onset during follow-up. Some patients with PEI at PP diagnosis had resolution (9.7 %) during follow-up, while 15.1 % maintained PEI at the last follow-up. Moreover, PEI at diagnosis was significantly more frequent in the diffuse than in the pure form (79.2 vs. 20.8 %, $p = 0.002$), which was also demonstrated by its higher frequency in the subgroups of patients experiencing new-onset PEI (diffuse vs. pure: 64.4 % vs. 35.6 %, $p = 0.006$) or stable PEI at the last follow-up visit (78.6 % vs. 21.4 %, $p = 0.006$). This suggests that the pure form is less likely to be associated with PEI or its new onset than the diffuse form. Moreover, differences in alcohol consumption were identified when comparing pure and diffuse forms, with the latter being more frequently associated with higher alcohol consumption (6.63 ± 5.9 U per day, $p = 0.043$). Diabetes was much rarer, with only 24.8 % of patients experiencing this complication. Regarding potential cancer evolution, our data showed a very low frequency of pancreatic cancer in the cohort (6/208, 3 %), with a median time of 6 months to diagnosis. This finding strongly suggests that an underlying cancer may have initially mimicked PP, perhaps leading to misdiagnosis. Furthermore, our results did not indicate any significant difference in cancer frequency between the cystic and solid variants (3.3 % vs. 2.7 %, $p = 0.813$), though cancers were slightly more frequent among cystic forms than solid ones ($n = 4$ vs. $n = 2$, respectively). Therefore, the solid form may represent a misdiagnosis, whereas the cystic form with cancer could reflect a distinct entity involving concurrent PP and pancreatic cancer, even if the lack of data in the literature does not support either of these hypotheses.

However, overall, and regardless of the form or pattern of the disease, our study showed that the medical approach was the only treatment for more than half of the patients (54.5 %), including the use of PPI, NSAIDs, and paracetamol. On the other hand, the interventional approach, including either endoscopy or surgery, was usually prescribed together or after starting the medical treatment, even if only 72 % of patients interrupted alcohol consumption, 32.5 % interrupted smoking, 46.3 % had nutritional support, and 67.4 % used at least one painkiller. As expected, our findings also showed significantly higher jaundice rates ($p = 0.001$) and γGT levels ($p = 0.041$) in patients undergoing interventional treatments (either surgery or endoscopy) than in those treated with only medical therapy. Moreover, resective pancreatic surgery is considered an option, even as the first treatment, though based more on local internal protocol than evidence in the literature, especially when duodenal obstruction or cancer is suspected. Initial duodenal stenosis was mainly transitable in our cohort, without worsening under medical therapy in most of cases, even if five patients developed benign GOO (bGOO) requiring interventions, which were mainly surgical ($n = 4$ surgical gastrojejunostomy) than endoscopic ($n = 1$ endoscopic stenting). This finding suggests that medical therapy may prevent the progression of initial transitable duodenal stenosis, resulting in the development of GOO in only one-third of the cases. These were mainly treated surgically in our cohort, but less invasive EUS-guided approaches, such as EUS-gastrojejunostomy, could potentially replace traditional surgical bypass in the future, provided that more robust data confirm the favorable clinical outcomes reported thus far for bGOO [17]. However, our findings suggest a wide confirmation of the surgical approach, with 79.6 % of resective surgeries over total surgeries (even if there were no differences between solid and cystic variants [$p = 0.079$] or between diffuse and pure forms [$p = 0.953$]). Additionally, though surgical intervention was associated with improved pain control (aOR 10.78), it also carried a significantly increased risk of new-onset PEI (aOR 3.79), while endoscopic therapy showed no benefit in terms of analgesic requirement, but was linked to confirmed PEI, possibly reflecting underlying disease severity. The strongest limitation of this study is its retrospective design: the presence of missing data leads to a reduced ability to establish cause-and-effect relationships, and the lack of control over outcome assessments reduces the strength of our findings. Moreover, this study did not include a systematic evaluation of all patients presenting with chronic pancreatitis symptoms, so it is possible that some patients with concurrent PP may have been missed. On the other hand, this study has the strength of being the largest published to date to our knowledge, and data were collected in tertiary pancreatic centers where data collection and extraction should be qualitatively high. Furthermore, this study had a long follow-up period (mean 41.1 [±31.92] months).

5. Conclusions

In conclusion, PP is a disease that often resemble other diseases, including pancreatic cancer. The prolonged time required for PP diagnosis highlights the importance of promptly focusing on patients with diagnostic uncertainty between pancreatic cancer and PP, in order to avoid misdiagnosis, which, as our findings suggest, may occur, and subsequent delays in patient care. We offer a reliable real-life picture of the clinical presentation, diagnostic work-up and management of PP. Medical treatment including alcohol and smoking cessation, nutritional support, and painkillers should be considered the first-line treatment, while interventional treatments are a second option for an unmanageable painful disease or when further complications such as duodenal or biliary obstruction develop. Pain control is better achieved with surgery, despite the increased risk of PEI, which arises in half of the patients during the course of the disease, especially in those with overlapping chronic pancreatitis, and must be promptly identified and treated to avoid malnutrition and related complications. In the end, no prospective data exists on this population, so strong efforts from research studies and medical associations are needed in the near future to create more robust evidence for those patients with groove/paraduodenal pancreatitis.

Authors' contributions

G.E.M.R.: writing - original draft, conceptualization, methodology, study design, Resourches, data analysis and software; M.T.: Editing and review – Original draft, Resourches, supervision, validation and comments; S.F.C.: Editing and review – Original draft, Resourches and comments; M.C.C.B.: Editing and review – Original draft, Resourches and comments; N.D.P.: Editing and review – Original draft, resourches and comments; A.A.: Editing and review – Original draft, Resourches and comments; C.B.: Editing and review – Original draft, Resourches and comments; C.C.: Editing and

review – Original draft, Resourches and comments; A.A: Editing and review – Original draft, Resourches and comments; A.F.: Editing and review – Original draft, Resourches and comments; M.B.: Editing and review – Original draft, Resourches and comments; G.D.N.: Editing and review – Original draft, Resourches and comments; G.M.: Editing and review – Original draft, Resourches and comments; A.F.: Editing and review – Original draft, Resourches and comments; E.S.: Editing and review – Original draft, Resourches and comments; P.S.: Editing and review – Original draft, Resourches and comments; L.C.: Editing and review – Original draft, Resourches and comments; M.L.B.: Editing and review – Original draft, Resourches and comments; F.D.M.: Editing and review – Original draft, Resourches and comments; P.G.A.: Editing and review – Original draft, comments; G.B.: Editing and review – Original draft, comments; M.F.: Editing and review – Original draft, comments; F.A.: Editing and review – Original draft, comments; C.F.: Editing and review – Original draft, comments; G.C.: Editing and review – Original draft, supervision, resourches and comments; L.F.: Editing and review – Original draft, supervision, resourches and comments; L.B.: Editing and review – Original draft, Supervision, funding acquisition, methodology, comments and study design. All authors have read and approved thisthe study.

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Conflict of interest/declarations of interest

All authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pan.2025.11.019.

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