Endotherapy for paraduodenal pancreatitis: a large retrospective case series

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Background and study aims: Paraduodenal pancreatitis is histologically well defined but its epidemiology, natural history, and connection with chronic pancreatitis are not completely understood. The aim of this study was to review the endoscopic and medical management of paraduodenal pancreatitis.

Patients and methods: Medical records of all patients with paraduodenal pancreatitis diagnosed by magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasonography (EUS) between 1995 and 2010 were retrospectively reviewed. Clinical features, imaging procedures, and treatments were investigated. The primary end point was the rate of clinical success, and the secondary end points were the radiological or endoscopic improvement, complication rate, and overall survival rate.

Results: A total of 51 patients were included in the study (88.2 % alcohol abuse; median age 49 years [range 37 – 70]; 50 men). The most frequent symptoms at presentation were pain (n = 50; 98.0 %) and weight loss (n = 36; 70.6 %). Chronic pancreatitis was present in 36 patients (70.6 %), and 45 patients (88.2 %) had cysts. Other findings included stricture of the pancreatic duct (n = 37; 72.5 %), common bile duct (n = 29; 56.9 %), and duodenum (n = 24; 47.1 %). A total of 39 patients underwent initial endoscopic treatment: cystenterostomy (n = 20), pancreatic and/or biliary duct drainage (n = 19), and/or duodenal dilation (n = 6). For the patients with available follow-up (n = 41), 24 patients required repeat endoscopy and 9 patients required surgery after the initial endoscopic management. After a median follow-up of 54 months (range 6 – 156 months), complete clinical success was achieved in 70.7 % of patients, and the overall survival rate was 94.1 %.

Conclusions: This is the largest series concerning the management of paraduodenal pancreatitis using endotherapy as the first-line intervention. Although repeat endoscopic procedures were required in half of the patients, no severe complication was observed and surgical treatment was ultimately needed in less than 25 % of the patients.

Introduction

A duodenal stricture can be observed in the clinical course of chronic pancreatitis [1]. Much less common or well known is the occurrence of cysts within the duodenal wall. Duodenal wall cysts may arise in various situations and have been reported under many different names (cystic dystrophy in heterotopic pancreas, cystic dystrophy of the duodenal wall, groove pancreatitis) [2 – 4]. There are no epidemiological data regarding the prevalence and incidence of cysts within the duodenal wall in the general population. A recent Italian survey, which reviewed data on chronic pancreatitis in Italy in mixed medical-surgical cases between 2000 and 2005, reported that the frequency of groove pancreatitis was 6.2 % (55 out of 893 patients) [5]. Groove pancreatitis has many aspects in common with cystic dystrophy of the duodenal wall, and in most reported cases, the clinical presentation (pain, vomiting, and jaundice) and radiological, endosonographical, and pathological features overlap in so many important aspects that they may be considered variants of the same disease. For these reasons, the unifying name paraduodenal pancreatitis has been proposed [6, 7].

Paraduodenal pancreatitis is believed to be infrequent, and a recent systematic review of the literature reported that the main therapeutic option for these patients remains the surgical approach, with a few cases treated medically and/or endoscopically [8]. Rebours et al. reported a medical-surgical series of paraduodenal pancreatitis, the diagnosis of which was based on validated radiological criteria to avoid the need for surgical resec-

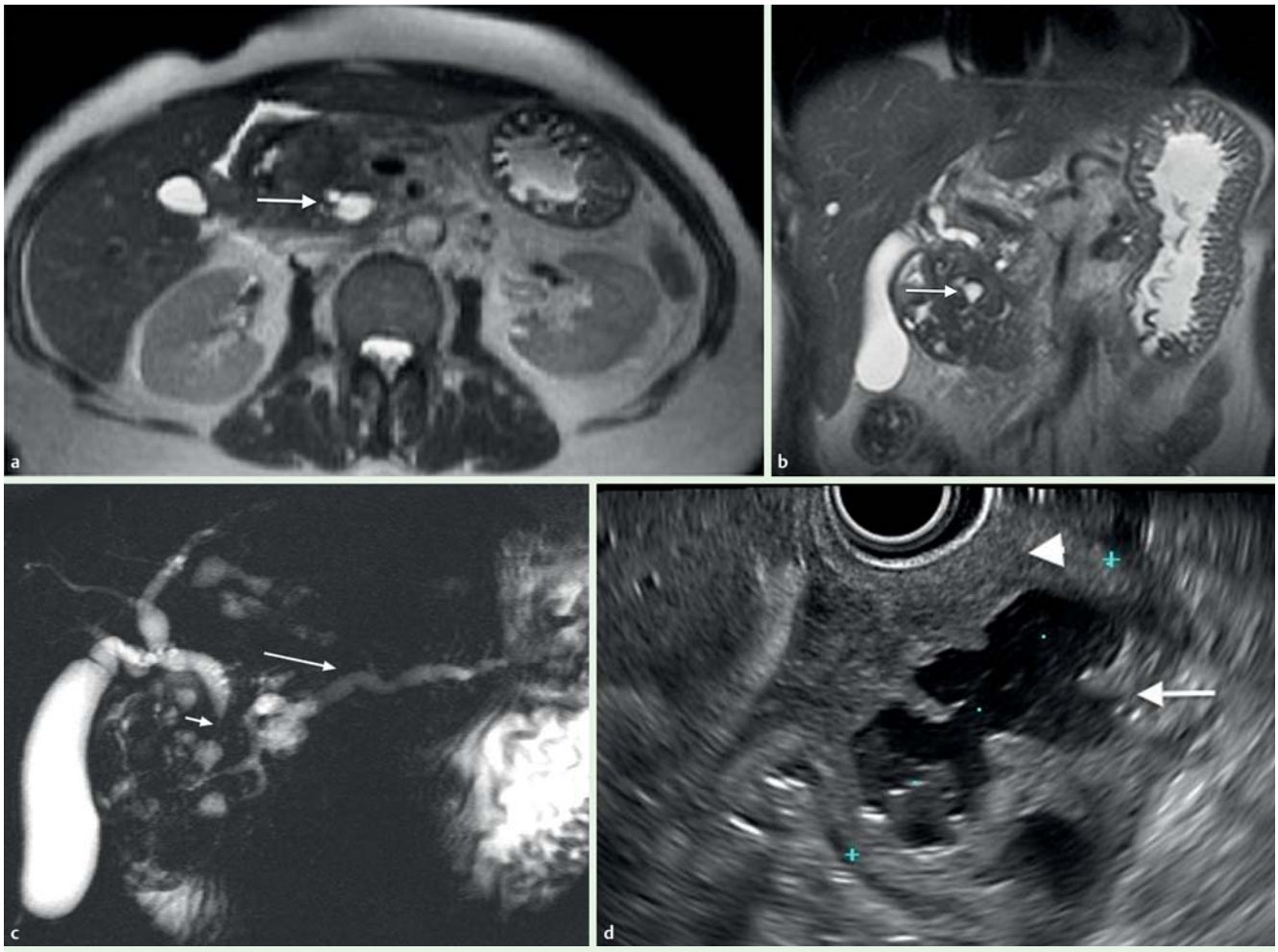

Fig. 1 Periduodenal pancreatitis as shown on magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS). Axial (**a**) and coronal T2-weighted (**b**) images show thickening of the duodenal wall and of the groove with several cysts in the duodenal wall (arrow). **c** Coronal MRCP shows distal stricture of the common bile duct (short arrow) and of the main pancreatic duct associated with an upstream dilation (arrow). **d** EUS shows a hypoechogeneous heterogeneous lesion (arrow) located in the wall of the second portion of the duodenum, inside the muscularis propria, associated with a thickening of the duodenal wall (arrowhead).

tion and pathological specimen examination [8]. Since 1995, magnetic resonance imaging (MRI) findings and endoscopic aspect have been the major criteria for the diagnosis of paraduodenal pancreatitis, and a combined endoscopic and medical approach is always proposed before surgery in the setting of a medical-surgical tertiary care department.

The aim of the current study was to review the outcomes of patients with paraduodenal pancreatitis when this multidisciplinary approach, with endotherapy as the first-line treatment, is followed.

Patients and methods

All consecutive patients attending the medical-surgical digestive unit at Erasme University Hospital between 1995 and 2010, and who fulfilled the radiological criteria of paraduodenal pancreatitis (see below), were included in the study. Inclusion stopped in 2010 in order to include a sufficiently long follow-up period and to coincide with the start of a prospective, randomized, controlled trial of patients with paraduodenal pancreatitis and the role of long-acting somatostatin analogs. All patients underwent MRI or endoscopic ultrasonography (EUS) at the hospital in order to examine the pancreas and wall of the duodenum. Indications for radiological and EUS procedures were abdominal pain, acute pancreatitis, weight loss, vomiting, jaundice, and/or suspicion of pancreatic tumor.

The radiological criteria for paraduodenal pancreatitis were a mass lesion occupying the pancreaticoduodenal groove (hypointense relative to the pancreatic tissue on T1-weighted images, and iso or slightly hyperintense on T2-weighted images); thickening of the duodenal wall; and/or cysts in the groove and/or duodenal wall. The EUS criteria were the presence of one or more hypoechoic lesions located within the duodenal wall inside the muscularis propria (fourth hypoechoic layer), allowing a clear distinction from pancreatic pseudocysts; and duodenal wall thickening. Ultimately, paraduodenal pancreatitis was considered when at least one of the above radiological criteria was present, based on MRI or EUS (mass lesion in the pancreaticoduodenal groove; or duodenal wall thickening; or one or multiple cysts located in the groove and/or duodenal wall) (**Fig. 1**).

All patient files were systematically reviewed by the medical, radiology, and pathology teams at Erasme University Hospital.

Data recorded

The following data were recorded: 1) epidemiological characteristics (age at diagnosis of paraduodenal pancreatitis, sex, alcohol consumption); 2) clinical data (symptoms [vomiting, weight loss, pancreatic pain, jaundice], complications of chronic pancreatitis [diabetes mellitus, steatorrhea], and duration of follow-up); and 3) biochemical features (cholestasis and inflammatory markers).
Radiological and endoscopic features of paraduodenal pancreatitis included: number of cysts within the digestive wall, dilatation of the common bile duct (>10 mm), dilatation of the main pancreatic duct (>5 mm), presence of pancreatic calcifications, duodenal stenosis (complete or incomplete stenosis, impeding or allowing the passage of an endoscope), and presence of duodenal giant folds.
Pathological data included microscopic examination of duodenal biopsies, pancreatic or biliary brushings, and surgical specimens.

Other definitions

The diagnosis of chronic pancreatitis was based on one or more of the following three criteria: pancreatic calcifications demonstrated by plain radiography of the pancreatic area, abdominal computed tomography (CT) scan, or EUS; moderate to marked pancreatic ductal changes on endoscopic retrograde or magnetic resonance cholangiopancreatography (ERCP or MRCP) (Cambridge criteria) [9]; and/or typical histology of an adequate surgical pancreatic specimen. In patients with no morphological abnormalities of the pancreas proper, including ductal imaging, a diagnosis of chronic pancreatitis was considered to have been ruled out as far as possible.
Chronic pancreatitis was considered to be caused by alcohol when alcohol intake exceeded 80 g of alcohol/day for at least 2 years, in the absence of other causes. Other causes of chronic pancreatitis were investigated depending on the clinical context [10]. Chronic pancreatitis was considered to be idiopathic when no cause was identified.
The diagnosis of exocrine pancreatic insufficiency was based on clinical steatorrhea and/or the need for pancreatic enzyme supplements for more than 1 month [11]. Diabetes mellitus was diagnosed by fasting blood glucose of >125 mg/dL (whole venous blood) for at least two determinations. Cholestasis was defined by increased alkaline phosphatase levels above the upper limit of normal values. The inflammatory syndrome was defined by an increased C-reactive protein level above 10 mg/L. The follow-up period was defined as the time between the date of the first sign attributable to paraduodenal pancreatitis and the date of the last visit.

Treatments

No systematic treatment protocol was applied and the choice of therapeutic options was left to the responsible clinical team. Previous treatments (medical, endoscopic, and/or surgical) performed in other hospitals were recorded, as well as initial and further treatments given at Erasme University Hospital.
Specific treatments were as follows: somatostatin analog injections (intramuscular injection of 60 or 90 mg, once per month), endoscopic treatment (ductal drainage and/or cyst fenestration), and surgical treatment (pancreaticoduodenectomy, cyst fenestration, digestive bypass, and biliary bypass). Somatostatin analog injections were administered in cases where initial endoscopic therapy was not possible (nonvisualization of the papilla because of paraduodenal pancreatitis) or not optimal [12,13]. Surgery was proposed if symptoms persisted despite endoscopic therapy. Response to treatment was evaluated clinically (modification of symptoms), radiologically (change in the number and size of cysts within the digestive wall, and change in the common bile duct and the main pancreatic duct dilatation), and endoscopically (change in the duodenal stenosis).
Failure was defined as no improvement in symptoms, or the need for surgery. Temporary success was defined as the complete disappearance of the symptoms after initial treatment and recurrence of the symptoms before the last visit. Complete success was defined as complete disappearance of the symptoms from the treatment period to the last visit or during the last 12 months before the last visit (i.e. sustained pain relief).
The primary end point was the rate of clinical success. Secondary end points were the radiological and endoscopic improvement, the rate of complications, and the overall survival rate.

Statistical analysis

General characteristics are expressed as median and range. The differences between patients with or without chronic pancreatitis and with or without complete success were statistically analyzed using the Mann–Whitney test for continuous data and the chi-squared test or the Fisher's exact test, as necessary, for categorical data. The data were analyzed with the SPSS 20 statistical software for Windows (IBM Corp., Armonk, New York, USA). All statistical tests were two sided. *P* values of <0.05 were considered to be statistically significant.

Results

Patients and symptoms

From 1995 to 2010, 51 consecutive symptomatic patients (median age 49 years, range 37–70 years; 50 men) with a radiological diagnosis of paraduodenal pancreatitis were included in the study. Chronic alcohol consumption was present in 45 patients (88.2%), and 50 were smokers (98.0%). Epidemiological, clinical, and biochemical data are summarized in **Table 1**. The most frequent clinical symptoms were abdominal pain, severe weight loss, and vomiting. The median follow-up after paraduodenal pancreatitis diagnosis was 54 months (range 6–156 months). A total of 10 patients were lost to follow-up (3 deaths and 7 patients who did not return to the hospital after initial treatment).

Imaging features

The most frequently used imaging procedure at the time of paraduodenal pancreatitis diagnosis was MRI, which was performed in all patients. The other imaging procedures were much less frequently performed: CT scan in 13 patients (25.5%), ultrasound in 5 patients (9.8%), and positron emission tomography scan in 2 patients (3.9%). Cysts were present in 45 patients (88.2%), and were multiple in 24 patients (53.3%). Duodenal wall thickening without cysts (solid form) was observed in the remaining six patients (11.8%). Pancreatic calcifications were observed in 13 patients (25.5%). A stenosis of the main pancreatic duct was present in 37 patients (72.5%), and parenchymal atrophy was present in 18 (35.3%). Common bile duct stenosis was present in 29 patients (56.9%).

Upper digestive endoscopy

A total of 48 patients (94.1%) underwent upper digestive endoscopy at diagnosis. EUS was performed in 32/51 (62.7%) patients and confirmed the presence of one (n=17) or multiple (n=9)

Characteristics	All patients (n = 51)	Patients with chronic pancreatitis (n = 36)	Patients without chronic pancreatitis (n = 15)	P
Age at diagnosis, median (range), years[1]	49	48 (39 – 67)	48 (37 – 70)	n.s.
Men, n (%)	50 (98.0)	35 (97.2)	15 (100)	n.s.
Chronic alcoholic consumption, n (%)	45 (88.2)	33 (91.7)	12 (80.0)	n.s.
Symptoms, n (%)				
Abdominal pain	50 (98.0)	36 (100)	14 (93.3)	n.s.
Severe weight loss[1]	36 (70.6)	27 (75.0)	9 (60.0)	n.s.
Vomiting	26 (51.0)	18 (50.0)	8 (53.3)	n.s.
Diabetes	13 (25.5)	12 (33.3)	1 (6.7)	0.049
Steatorrhea	20 (39.2)	19 (52.8)	1 (6.7)	0.02
Inflammatory syndrome	19 (37.3)	16 (44.4)	3 (20.0)	n.s.
Cholestasis	18 (35.3)	16 (44.4)	2 (13.3)	0.028
BMI, median (range), kg/m^2	23 (17 – 35)	22 (17 – 27)	24 (18 – 35)	n.s.

BMI, body mass index.
[1] Weight loss > 10 % of total weight.

Table 1 Epidemiological and clinical characteristics of patients with periduodenal pancreatitis.

cysts in the duodenal wall. Thickening of the duodenal wall without cysts was observed in the other six patients, three of whom presented with a mass in the groove. Endoscopy was normal in 6 patients and showed irregular duodenal mucosa with giant folds in 16 patients. A partial or complete stenosis of the digestive lumen was noted in 24 patients. Inflammatory features of the mucosa were observed in 20 patients.

Pathological findings

Pathology was available for 27 patients. Of these patients, 13 underwent duodenal, pancreatic, and/or biliary biopsies, which showed inflammation and/or necrosis. A total of 11 patients underwent pancreatic and/or biliary brushing, which showed inflammatory cells. The pathological findings of six pancreaticoduodenectomy specimens confirmed the presence of heterotopic pancreas in three patients, severe chronic pancreatitis in two patients, and the final results were unavailable for one patient. Heterotopic pancreatic tissue was observed in the muscularis propria of the duodenum, associated with multifocal hyperplasia of Brunner's glands and fibrosis. The pancreas proper presented features of chronic pancreatitis in all of these six patients.

Association with chronic pancreatitis of the pancreas proper

Paraduodenal pancreatitis was associated with chronic pancreatitis of the pancreas proper in 36/51 patients (70.6 %). Chronic pancreatitis was alcohol related in 33 patients (91.7 %); no other cause was found in the other three patients despite extensive screening. In the 15 patients without evidence of chronic pancreatitis, alcohol consumption was noticed in 12 (80.0 %). Finally, three patients had no sign of chronic pancreatitis and no alcoholism (5.9 % of the total cohort). Diabetes mellitus, steatorrhea, and cholestasis were significantly more frequently observed in patients with chronic pancreatitis (**Table 1**).

Treatment and follow-up

Previous treatment

Prior to their management at the study institution, 30 patients had undergone previous intervention, with a median interval of 6 months (range 1 – 168 months). Interventions included pancreatic or biliary drainage (n = 15), cystoduodenostomy (n = 3), surgical jejunostomy (n = 1), surgical cystogastrostomy (n = 1), and surgical hepaticojejunostomy (n = 1); 12 patients had combined treatments.

Initial treatment

The treatment initially applied at the study institution was medical for 19 patients (37.3 %), and/or endoscopic for 39 patients (76.5 %), and/or surgical for 3 patients (5.9 %). A total of 11 patients received combined (medical and endoscopic) initial treatment.

For patients receiving a medical treatment, in addition to nonspecific analgesic medication, 13 patients were treated with somatostatin analog and 6 patients received nutritional support. For the patients treated with somatostatin analog, the median duration of treatment was 12.5 months (range 1 – 24 months).

Details of the endoscopic treatments (**Fig. 2**) are given in **Table 2**. The median duration of pancreatic and biliary stenting was 26 months (range 1 – 84 months) and 32 months (3 – 84 months), respectively.

Initial surgical treatment included pancreaticoduodenectomy for two patients and gastroenterostomy for one patient.

Further treatment

Recurrence of symptoms after the initial treatment was observed in 30 of the 41 patients for whom follow-up was available. The median interval between initial treatment and treatment for recurrence was 3.5 months (range 1 – 84 months).

A total of 10 patients were treated with somatostatin analog (new treatment for all), for a median duration of 6.5 months (range 1 – 12 months), 24 patients received endoscopic treatment for recurrent symptoms (additional treatment for 21 patients and new treatment for 3 patients), and 9 patients underwent surgery (4 pancreaticoduodenectomies, 3 gastroenterostomies, and 2 hepaticojejunostomies).

Clinical results

A total of 29 of the 41 patients (70.7 %) for whom adequate follow-up data were available experienced complete relief of their symptoms 54 months (range 6 – 156 months) after initial treatment. Temporary success was achieved in three patients (7.3 %), and nine patients (22.0 %) showed no improvement following endoscopic treatment and/or had to undergo surgery. Results of specific treatments (somatostatin analog injections and endoscopic treatment) for patients with available follow-up are shown in **Table 3**. The group of patients with both medical and endoscopic treatments (n = 19) had greater clinical success and less surgery than the group that underwent only endoscopic treatment (n = 19; 15/19 [78.9 %] vs. 11/19 [57.9 %], and 3/19

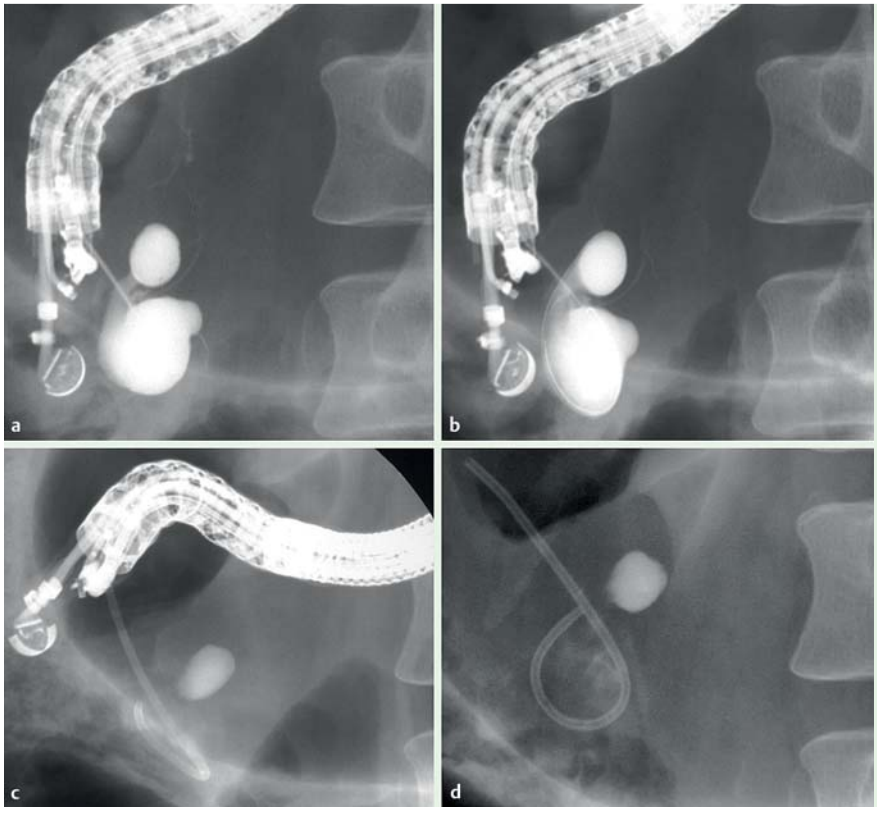

Fig. 2 A 50-year-old man presented with chronic epigastric pain associated with acute attacks. He was a heavy drinker (60 – 100 g/day over 20 years) and a smoker. He was diagnosed with peripancreatic pancreatitis. Cystoduodenostomy was performed to drain a cyst in the duodenum. **a** Puncture of the cyst under endoscopic ultrasound guidance. **b** Guidewire insertion and creation of the cystoduodenostomy with the cystotome. **c,d** A tailor-made 6-Fr single-pigtail stent is placed at the end of the procedure.

Table 2 Details of endoscopic treatment.

Treatment	n
Initial endoscopic treatment	**39**
Pancreatic sphincterotomy	18
Pancreatic stent	15 (15 plastic)
Biliary sphincterotomy	9
Biliary stent	9 (9 plastic)
Pancreatic + biliary sphincterotomy	8
Cyst drainage	20
Cystogastrostomy	3 (3 stents)
Cystoduodenostomy	17 (12 stents)
Duodenal dilation	6
Dilation alone	5
Dilation + duodenal stent	1
Further endoscopic treatment	**24**
Pancreatic stent	16 (16 plastic)
Biliary stent	14 (5 metallic)
Cyst drainage	8
Cystogastrostomy	4 (4 stents)
Cystoduodenostomy	4 (3 stents)
Duodenal dilation (no stent)	5

Table 3 Results of specific treatments for patients with adequate follow-up (n = 41).

	Exclusive somatostatin analog treatment (n = 3)	Exclusive endoscopic treatment (n = 19)	Combined treatment (n = 19)[1]
Complete success	3	11	15
Temporary success	0	2	1
Surgery	0	6	3

[1] Somatostatin analog and endoscopic treatment.

[15.8%] vs. 6/19 [31.6%], respectively), although the differences were not statistically significant, probably due to the small number of patients in each group.

There was no significant difference between patients with complete success and patients with temporary success or failure in terms of clinical and radiological features at presentation or treatment, except for BMI, which was significantly higher for patients with complete success (**Table 4**).

Morphological results

The radiological and endoscopic responses, evaluated in the 41 patients with available follow-up, showed a decrease in the caliber of the main pancreatic duct or the common bile duct in 25 (61.0%) and 26 (63.4%) of the cases, respectively. Decrease in the size or disappearance of the cysts was observed in 30 cases (73.2%) (**Fig. 3**). Duodenal stenosis was reduced or resolved in 26 cases (63.4%).

Adverse events and mortality

Overall, medical treatment was given to 24 patients. Complications occurred in three patients (12.5%), two cases of arterial thrombosis and diabetes in patients receiving somatostatin analog, and one case of sepsis in a patient under parenteral nutrition. For the 42 patients with endoscopic treatment, 6 (14.3%) presented one or more adverse events (3 cases of nonsevere acute pancreatitis, 2 cases of hemorrhage that were medically controlled, and 3 cases of sepsis that resolved with antibiotics). None of the adverse events of endoscopic treatment required admission to the intensive care unit.

Surgery was complicated in two patients (2/12, 16.7%), with one death from sepsis and liver failure and one case of sepsis associated with a fistula.

Table 4 Comparison of patients with and without complete success (n = 41).

	Patients with complete success (n = 29)	Patients with incomplete success or failure (n = 12)	*P*
Age at diagnosis, median (range), years	48.5 (37 – 70)	44 (39 – 60)	n.s.
Men, n (%)	29 (100)	11 (91.7)	n.s.
Chronic alcoholic consumption, n (%)	26 (89.7)	9 (75.0)	n.s.
Symptoms, n (%)			
Abdominal pain	29 (100)	12 (100)	n.s.
Weight loss	23 (79.3)	10 (83.3)	n.s.
Vomiting	17 (58.6)	8 (66.7)	n.s.
Diabetes	9 (31.0)	3 (25.0)	n.s.
Steatorrhea	12 (41.4)	7 (58.3)	n.s.
BMI, median (range), kg/m^2	23 (18 – 35)	22 (17 – 24)	0.01
Inflammatory syndrome, n (%)	13 (44.8)	4 (33.3)	n.s.
Cholestasis, n (%)	10 (34.4)	4 (33.3)	n.s.
Chronic pancreatitis, n (%)	20 (69.0)	10 (83.3)	n.s.
Cysts, n (%)	25 (86.2)	11 (91.7)	n.s.
CBD and/or duodenal stenosis, n (%)	25 (86.2)	10 (83.3)	n.s.
Initial medical treatment, n (%)	12 (41.4)	3 (25.0)	n.s.
Initial endoscopic treatment, n (%)	22 (75.9)	10 (83.3)	n.s.
Medical treatment for recurrence, n (%)	8 (27.6)	2 (16.7)	n.s.
Endotherapy for recurrence, n (%)	17 (58.6)	7 (58.3)	n.s.
Pancreatic stenting duration, median (range), months	29 (3 – 60)	27 (24 – 30)	n.s.
Biliary stenting duration, median (range), months	36.5 (12 – 66)	70 (56 – 84)	n.s.

BMI, body mass index; CBD, common bile duct.

Three patients died, giving an overall survival rate of 94.1 %. The cause of death was surgery in one patient (liver failure from cirrhosis), severe acute pancreatitis in one patient, and the death was indeterminate for the third patient.

Discussion

Knowledge of the clinical and pathological features of paraduodenal pancreatitis is important because it allows a preoperative diagnosis that in most cases correctly differentiates it from pancreatic and periampullary neoplasms and may prevent unnecessary surgical resections [14]. Currently, paraduodenal pancreatitis is a well-defined disease, distinct from chronic pancreatitis of the pancreas proper, and mostly recognized by European and American authors [4, 15 – 20]. Zamboni et al., who proposed the unifying term of paraduodenal pancreatitis, recognized two types of paraduodenal pancreatitis: one characterized by cystic changes and the other characterized by solid lesions [6]. A review of the literature was recently published, including 19 cohort series, 40 case reports, and approximately 400 patients between 1959 and 2010 [7]. The inclusion of 51 patients makes the current study one of the three largest reported to date [8, 20].

The pathophysiology of paraduodenal pancreatitis is unclear. Two theories may explain the disease. First, as initially described by Potet and Duclert in 1970 [3], paraduodenal pancreatitis might be the consequence of an obstruction of small ducts of heterotopic pancreatic exocrine tissue, leading to recurrent acute pancreatitis and to obstructive chronic pancreatitis due to the absence of a functioning ductal system for the secretion of pancreatic juice into the duodenal lumen. This mechanism could explain the occurrence of paraduodenal pancreatitis in nonalcoholic patients without chronic pancreatitis of the pancreas proper (6 % in the present series) [3]. The second mechanism may rely on the toxic effect of alcohol (or any other precipitating factor) on heterotopic pancreas in the same way that it affects the pancreas proper, leading to paraduodenal pancreatitis associated with chronic pancreatitis as described by Leger et al. [21]. This condition was encountered in two-thirds of the current study patients. Other nonalcoholic mechanisms inducing chronic pancreatitis

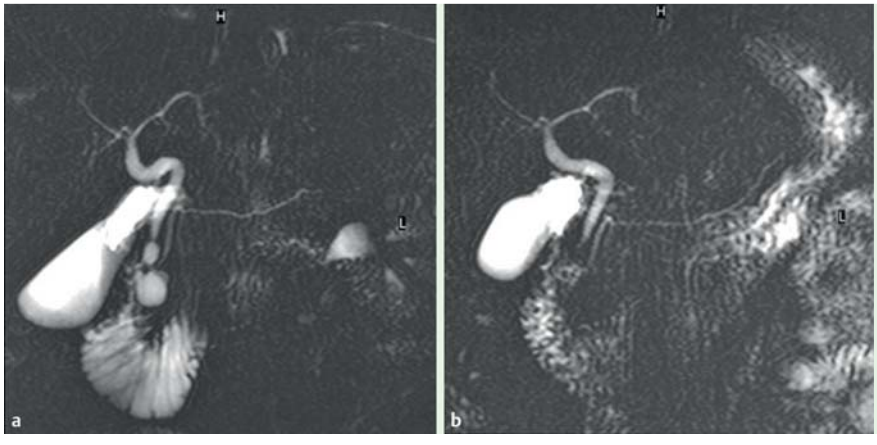

Fig. 3 Secretin-enhanced magnetic resonance cholangiopancreatography performed before (**a**) and after (**b**) endoscopic therapy by cystoduodenostomy and stent insertion, showing complete regression of the duodenal wall cysts.

may involve both heterotopic pancreas and the pancreas proper. This may explain the association of nonalcoholic chronic pancreatitis and paraduodenal pancreatitis in three of the study patients (**Table 1**).

As observed in the current study and in other studies [7,8], paraduodenal pancreatitis occurs mainly in alcoholic men in the fifth decade of life, and interestingly, all but one of them were smokers in the current study. This study further shows that paraduodenal pancreatitis is usually accompanied by major symptoms, such as abdominal pain, severe weight loss, and/or upper digestive obstruction. Indeed, cysts within the duodenal wall are present in almost 90% of the patients, and exist in multiple form in more than half of cases. Moreover, paraduodenal pancreatitis is associated with chronic pancreatitis of the pancreas proper in 71% of the patients. Nevertheless, paraduodenal pancreatitis can also be encountered in patients without any signs of chronic pancreatitis and even in patients with no alcoholic consumption, suggesting that paraduodenal pancreatitis could be an independent disease. The current data underline that paraduodenal pancreatitis can be symptomatic even in patients without chronic pancreatitis of the pancreas proper. It is impossible to clearly distinguish symptoms related to paraduodenal pancreatitis from those of chronic pancreatitis. Indeed, the frequency of symptoms was not different in patients with or without chronic pancreatitis except for those related to pancreatic insufficiency and cholestasis.

One of the major messages to be taken from this cohort study is that a stepwise approach to treatment of paraduodenal pancreatitis is feasible, effective, and associated with an acceptable complication rate. Indeed, in contrast to the literature, where more than 70% of reported patients were surgically managed [7], surgery was required in less than 25% of the current study patients. Different endoscopic modalities, including pancreatic ductal drainage, stricture dilation, and cyst drainage, are the mainstay of the nonsurgical approach and can be tailored according to clinical response. This endoscopic approach, when associated with medical treatment, allowed complete clinical success in nearly 80% of patients (**Table 3**). This is in contrast with the results reported by Rebours et al. [8], where complete success was achieved in only 37.5% (6/16) of their patients who were treated endoscopically. Few adverse events were observed with endoscopic treatment, and none of them were severe. One of the 12 patients who underwent surgery died postoperatively from sepsis and liver failure.

The usefulness of somatostatin analog injections and endoscopic procedures has been suggested by results from a few case reports [8,12,13]. The current results suggest that long-acting somatostatin analog injections, which have been available since 2007, tend to improve the results of the nonsurgical approach. A prospective, randomized, controlled trial would be useful to clearly define their role in the therapeutic management of paraduodenal pancreatitis.

The differential diagnosis of paraduodenal pancreatitis and pancreatic or duodenal malignancy can be challenging, especially in cases of solid form of paraduodenal pancreatitis. In the current series, pathology specimens were available for 27 patients and showed absence of malignancy, and 41 patients had a long follow-up, which permitted the exclusion of pancreatic or duodenal malignancies. Nevertheless, caution should be used when the diagnosis of paraduodenal pancreatitis is made for a solid lesion without cysts, especially in women or in the absence of alcohol consumption. MRI criteria have emerged to allow a noninvasive diagnosis of paraduodenal pancreatitis and a differential diagnosis from malignancy [21–26]. The most characteristic MRI finding is a sheet-like mass between the head of the pancreas and the thickened duodenal wall. The mass shows hypointensity relative to pancreatic parenchyma on T1-weighted images, iso or slightly hyperintensity on T2-weighted images, and delayed contrast enhancement on the late-phase images after injection of contrast medium, reflecting fibrotic changes of this scarring mass. MRCP is also important in the imaging work-up of patients with paraduodenal pancreatitis before endoscopic therapy, as well as in evaluation during follow-up. An important clue to differentiate it from carcinoma is the normal appearance of the peripancreatic vessels in paraduodenal pancreatitis, which may be displaced but show no signs of encasement [2,27,28]. Diffusion weighted MRI, which can contribute in distinguishing malignant tissue, could also be interesting in differentiating paraduodenal pancreatitis from pancreatic or duodenal cancer [29].

There are several limitations of this study. The study design was retrospective, the study group was small because paraduodenal pancreatitis is uncommon, and detailed histopathological correlation could not be performed in all cases because biopsy-proven or radiologically diagnosed cases were included. Moreover, adequate follow-up was only available for 41/51 patients (80%). Therefore, no firm conclusions can be drawn from this experience. Nevertheless, the results of this cohort suggest that further prospective investigations could be conducted in paraduodenal pancreatitis, such as evaluation of the role of long-acting somatostatin analogs in a randomized, controlled trial design and comparison of a stepwise vs. surgical approach.

In conclusion, paraduodenal pancreatitis is mainly encountered in young alcoholic smokers. Chronic pancreatitis of the pancreas proper is associated with paraduodenal pancreatitis in two-thirds of cases. However, paraduodenal pancreatitis may occur in nonalcoholic patients without chronic pancreatitis, suggesting it could be an independent disease and not a complication of chronic pancreatitis. The symptoms are usually severe and similar to those observed with chronic pancreatitis. Most patients can be managed without surgery, with complete long-term clinical success obtained in more than two-thirds of patients with medical and/or endoscopic treatment.

Competing interests: None

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