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Imaging of paraduodenal pancreatitis: A systematic review

Matteo Bonatti, Nicolò De Pretis, Giulia A Zamboni, Alessandro Brillo, Stefano Francesco Crinò, Riccardo Valletta, Fabio Lombardo, Giancarlo Mansueto, Luca Frulloni

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Abstract

BACKGROUND

Paraduodenal pancreatitis (PP) represents a diagnostic challenge, especially in non-referral centers, given its potential imaging overlap with pancreatic cancer. There are two main histological variants of PP, the cystic and the solid, with slightly different imaging appearances. Moreover, imaging findings in PP may change over time because of disease progression and/or as an effect of its risk factors exposition, namely alcohol intake and smoking.

AIM

To describe multimodality imaging findings in patients affected by PP to help clinicians in the differential diagnosis with pancreatic cancer.

METHODS

The systematic review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-analyses 2009 guidelines. A Literature search was performed on PubMed, Embase and Cochrane Library using (groove pancreatitis [Title/Abstract]) OR (PP [Title/Abstract]) as key words. A total of 593 articles were considered for inclusion. After eliminating duplicates, and title and abstract screening, 53 full-text articles were assessed for eligibility. Eligibility criteria were: Original studies including 8 or more patients, fully written in English, describing imaging findings in PP, with pathological confirmation or

clinical-radiological follow-up as the gold standard. Finally, 14 studies were included in our systematic review.

RESULTS

Computed tomography (CT) findings were described in 292 patients, magnetic resonance imaging (MRI) findings in 231 and endoscopic ultrasound (EUS) findings in 115. Duodenal wall thickening was observed in 88.8% of the cases: Detection rate was 96.5% at EUS, 91.0% at MRI and 84.1% at CT. Second duodenal portion increased enhancement was recognizable in 76.3% of the cases: Detection rate was 84.4% at MRI and 72.1% at CT. Cysts within the duodenal wall were detected in 82.6% of the cases: Detection rate was 94.4% at EUS, 81.9% at MRI and 75.7% at CT. A solid mass in the groove region was described in 40.9% of the cases; in 78.3% of the cases, it showed patchy enhancement in the portal venous phase, and in 100% appeared iso/hyperintense during delayed phase imaging. Only 3.6% of the lesions showed restricted diffusion. The prevalence of radiological signs of chronic obstructive pancreatitis, namely main pancreatic duct dilatation, pancreatic calcifications, and pancreatic cysts, was extremely variable in the different articles.

CONCLUSION

PP has peculiar imaging findings. MRI is the best radiological imaging modality for diagnosing PP, but EUS is more accurate than MRI in depicting duodenal wall alterations.

Key Words: Pancreatitis; Paraduodenal pancreatitis; Diagnostic imaging; Computed tomography; Magnetic resonance imaging; Endoscopic ultrasound

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Core Tip: Paraduodenal pancreatitis (PP) represents a diagnostic challenge, especially in non-referral centers, given its potential imaging overlap with neoplastic processes, namely pancreatic and duodenal carcinoma. Numerous articles show imaging features of PP, but most of them are represented by case reports or reviews with poor scientific background. This systematic review describes the multimodality imaging features (computed tomography, magnetic resonance imaging and endoscopic ultrasound) of PP according to original research articles with pathologic samples and or clinical-radiological follow-up as the gold standard.

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INTRODUCTION

Paraduodenal pancreatitis (PP), also known as groove pancreatitis, is a peculiar form of chronic pancreatitis characterized by an inflammatory mass-forming involvement of the duodenal wall in the so-called groove area, located between the head of the pancreas, the duodenum, and the common bile duct[1]. The inflammatory process may lead to a solid thickening of the duodenal wall and/or to the development of cystic changes centered in the groove area. PP has been subdivided into cystic or solid type, based on the presence or absence of cysts in the groove area at imaging or pathology. According to a large Italian study, two thirds of patients present the cystic type of PP and one third the solid one[2]; similar data were reported on a more limited series from India[3]. The inflammatory process, arising from the groove area, might also extend to the whole pancreas secondary to the compression and obstruction of the main pancreatic duct by the inflamed and thickened groove area, leading to obstructive chronic pancreatitis. No definitive epidemiological data have been published, but PP is a rare disease considering that in an observational study including 893 patients with chronic pancreatitis, PP prevalence was 6%[4]. On the other hand, a German study published in 2014 reported 3.5% of PP on 373 consecutive pancreatic resections in a single center[5].

Adsay *et al*[1] described the typical histological features of PP, namely dilated ducts in the duodenal wall with pseudocystic changes and granulation tissue, Brunner's gland hyperplasia, dense myoid stromal proliferation and fibrosis of the pancreas and of the surrounding soft tissue of the groove area [1].

As reported by many previously published papers, patients suffering from PP are typically middle-aged men, heavy smokers, and drinkers[2-4,6-14]. Acute pancreatitis and abdominal pain have been described as the most frequent presenting symptoms, followed by symptoms related to duodenal obstruction (vomiting and weight loss) and to common bile duct obstruction (jaundice)[2,9-11]. Symptoms related to pancreatic insufficiency (diabetes and steatorrhea) are less frequent and generally reported in patients with advanced disease.

PP diagnosis may be challenging since patients often present with symptoms mimicking pancreatic cancer, such as abdominal pain, vomiting, weight loss or jaundice, and, especially in the solid type, also at imaging the differential diagnosis with pancreatic cancer can be extremely difficult. Therefore, a significant proportion of patients (reported between 5% and 21%, even in referral centers) undergo demolitive pancreatic surgery because of misdiagnosis or malignancy suspicion[2,6,15,16].

Many different therapeutic strategies have been proposed for symptoms' management in PP and, nowadays, no definitive data have been published about the best choice between medical treatment and endoscopic or surgical interventions. A step-up approach should probably be considered, starting with medical treatment based on pain control, alcohol consumption cessation, and smoke cessation. Endoscopic treatment might be considered in the case of bile duct stenosis and surgery should be reserved for patients with intractable pain, duodenal obstruction, or recurrent bile duct obstruction and cholangitis.

Despite the rarity of the disease, a precise radiological and clinical diagnosis is crucial for patients' management and a multidisciplinary approach is needed to reduce the risk of misdiagnosis and of inappropriate surgical resections. Therefore, the aim of our study was to conduct a systematic literature review to show the multimodality imaging appearance of PP and to assess imaging performance in the differential diagnosis between PP and pancreatic cancer.

MATERIALS AND METHODS

Studies selection

The study was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines. We performed a database search on PubMed, Embase and Cochrane Library, looking for articles published from January 1990 to July 2022. The following string was used: (Groove pancreatitis [Title/Abstract]) OR (PP [Title/Abstract]). A total of 593 papers were identified and considered for inclusion. After eliminating duplicates, and title and abstract screening, 53 full-text articles were assessed for eligibility by two radiologists independently. Discrepancies were solved by consensus, which was necessary in 2 cases. Eligibility criteria were original studies including 8 or more patients, written in English, describing imaging findings in PP, with pathological confirmation or clinical-radiological follow-up as the gold standard (Figure 1). Finally, 14 studies were included in our systematic review[2,3,7,9,11,12,15-22].

Data extraction

Study characteristics, including publication date, journal type, inclusion period, aim of the study, study design, characteristics of the patients considered for inclusion, number of patients with PP included, and study limitations were extracted from the included studies (Table 1). The presence of potential bias was evaluated by two Authors in consensus using the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies (https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) (Table 2). The maximum number of points given to each item was 4, 2 and 3, with a total maximum number of 9 points.

The following data were extracted from the included studies: Number of patients examined with the different imaging modalities [computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US), and endoscopic ultrasound (EUS)], PP variant (cystic/solid), lesions' size (mean maximum and minimum diameter), presence of duodenal wall thickening (yes/no), duodenal wall thickening distribution (eccentric/circumferential), presence of second duodenal portion increased wall enhancement (yes/no), presence (yes/no) number (single/multiple) and size (mm) of duodenal wall cysts, presence of a discrete pancreatic mass (yes/no), lesion's signal intensity on T2-weighted images, on T1-weighted images, on high b value diffusion-weighted images and on apparent diffusion coefficient (ADC) map (hypo-/iso-/hyper-intense in comparison to "normal" pancreas), enhancement on arterial, portal venous and delayed phase images (hypo-/iso-/hyper-intense/dense in comparison to "normal" pancreas), enhancement pattern in portal venous phase (hypo/patchy/rim), presence of pancreatic cysts (yes/no), presence of main pancreatic duct dilatation (yes/no), presence of pancreatic calcifications (yes/no), presence of biliary duct dilatation (yes/no), presence of portal vein stenosis (yes/no), presence of gastroduodenal artery displacement (yes/no), presence of peripancreatic fat stranding (yes/no), presence of peripancreatic enlarged lymph nodes (yes/no). The above-mentioned variables were not considered in every study (Tables 3 and 4). The absolute number of patients for which the variable was evaluated is reported in the text as ($n = \#$).

Table 1 Characteristics of the included studies

Ref.	Year	Journal type	Aim	Inclusion period	Study design	Patients considered for inclusion	Paraduodenal pancreatitis patients included	Limitations
Ishigami <i>et al</i> [17]	2010	Radiological	Differential diagnosis cancer <i>vs</i> paraduodenal pancreatitis	2001-2008	Retrospective, single center	Institutional database search using “groove pancreatitis or groove pancreatic carcinoma” (<i>n</i> = 22)	15	Small population, no clear distinction between computed tomography and magnetic resonance imaging findings
Kalb <i>et al</i> [18]	2013	Radiological	Differential diagnosis cancer <i>vs</i> paraduodenal pancreatitis	2007-2010	Retrospective, single center	Institutional database search using “Whipple and/or pancreatectomy” and diagnosis of cancer or paraduodenal pancreatitis (<i>n</i> = 47)	17	Surgically resected patients only, small population
Zaheer <i>et al</i> [19]	2014	Radiological	Findings description	2002-2013	Retrospective, single center	Patients undergoing pancreaticoduodenectomy and histological paraduodenal pancreatitis diagnosis (<i>n</i> = 12)	12	Surgically resected patients only, small population
Arvanitakis <i>et al</i> [11]	2014	Gastroenterological	Endoscopic and medical management	1995-2010	Retrospective, single center	Institutional database search using “paraduodenal pancreatitis” (<i>n</i> = 51)	51	Poor imaging findings description based on radiological reports
Wagner <i>et al</i> [20]	2015	Radiological	Findings description	"14 yr"	Retrospective, single center	Patients with cystic dystrophy in heterotopic pancreas diagnosis at endoscopic ultrasound (<i>n</i> = 138)	76	Only cystic variant of paraduodenal pancreatitis included
Arora <i>et al</i> [3]	2015	Radiological	Findings description	2010-2014	Retrospective, single center	Patients treated for paraduodenal pancreatitis at gastroenterology or surgical units (<i>n</i> = 33)	33	Poor imaging findings description based on radiological reports, no clear distinction between computed tomography and magnetic resonance imaging findings
Shin <i>et al</i> [21]	2016	Radiological	Differential diagnosis cancer <i>vs</i> paraduodenal pancreatitis	2005-2011	Retrospective, 2 centers	Multidetector computed tomography for pancreas protocols (<i>n</i> = 2561) with groove mass	8	Surgically resected patients only, small population
Boninsegna <i>et al</i> [22]	2017	Radiological	Differential diagnosis cancer <i>vs</i> paraduodenal pancreatitis	2012-2015	Retrospective, single center	Abdominal Magnetic Resonance Imaging with groove mass	28	None
de Pretis <i>et al</i> [2]	2017	Multidisciplinary	Clinical and morphological features	1994-2012	Retrospective, single center	Patients with diagnosis of paraduodenal pancreatitis (<i>n</i> = 120)	120	Poor imaging findings description based on radiological reports, no clear distinction between computed tomography and magnetic resonance imaging findings
Muraki <i>et al</i> [9]	2017	Surgical	Imaging and pathologic correlation	2004-2015	Retrospective, single center	All pancreatic resections	47	Surgically resected patients only, poor imaging findings description, no clear distinction between computed tomography and magnetic resonance imaging findings
Tarvainen <i>et al</i> [16]	2021	Multidisciplinary	Diagnosis, natural course and treatment	2005-2015	Retrospective, multicentric	Institutional database search using “groove and/or paraduodenal” (<i>n</i> = 192)	33	Poor imaging findings description, no clear distinction between computed tomography and magnetic resonance imaging findings
Ooka <i>et al</i> [7]	2021	Gastroenterological	Clinical management	2000-2014	Retrospective,	Institutional database search using “groove pancre-	48	No clear distinction between computed

					single center	atitis and/or paraduodenal pancreatitis" (<i>n</i> = 211)		tomography and magnetic resonance imaging findings
Değer <i>et al</i> [15]	2022	Surgical	Clinical features and outcome	2013-2019	Retrospective, single center	Institutional database search using "groove and/or paraduodenal" (<i>n</i> = 28)	25	Poor imaging findings description based on radiological reports, no clear distinction between computed tomography and magnetic resonance imaging findings
Kulkarni <i>et al</i> [12]	2022	Radiological	Findings description	2007-2020	Retrospective, single center	Patients with pancreatitis (<i>n</i> = 2120)	30	None

Diagnostic performance of imaging studies in the differential diagnosis between PP and pancreatic cancer was also assessed.

Statistical analysis

Absolute numbers and percentages were used to describe quantitative variables. For continuous data, mean values were calculated. Sensitivity, specificity, negative predictive value and positive predictive value in differentiating between PP and pancreatic cancer were reported, when available. P values <0.05 were considered statistically significant.

RESULTS

Included studies characteristics

All the included studies had a retrospective design and encompassed a total of 543 patients, 489 (90%) males and 54 (10%) females, with a mean age of 48 years. History of chronic alcohol abuse was reported in 87% of the cases (*n* = 524) and 78% of the patients were heavy smokers (*n* = 334). The included studies were published on radiological journals in 8/14 cases (*n* = 219), on multidisciplinary journals in 2/14 (*n* = 153), on gastroenterological journals in 2/14 (*n* = 99), and on surgical journals in 2/14 (*n* = 72).

Pathology was the gold standard in 9/14 studies (*n* = 261), pathology or clinical-radiological follow up in 3/14 (*n* = 183), follow-up alone in 2/14 (*n* = 99). Cross-sectional images were reviewed by one or two Radiologists in 10/14 studies (*n* = 314), whereas in 4/14 studies (*n* = 229) the described CT and MRI imaging findings were based on the original radiological reports.

Nine out of the 14 evaluated studies included imaging findings obtained from 2 or more imaging modalities, whereas 4 studies were based on CT images only and 3 on MRI only. In 7 of the included studies, it was not always possible to clearly understand if the described findings were derived from CT or MRI images. Therefore, CT findings were described for 292 patients, MRI findings for 231 and EUS findings for 115; US findings were not described in any of the included studies.

Duodenal findings

Duodenal wall thickening was described in 88.8% of the cases (*n* = 420); at EUS, duodenal thickening was recognizable in 96.5% of the cases (*n* = 115), at MRI in 91.0% (*n* = 78) and at CT in 84.1% (*n* = 227). The cutoff value for the duodenal wall thickening definition was reported in three studies[18,21,22] (*n* =

Table 2 Risk of bias assessment

Ref.	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start of study	Comparability of cohorts	Assessment of outcome	Follow-up long enough	Adequacy of follow up	Total
Ishigami <i>et al</i> [17]	±	-	-	-	-	-	NA	NA	6
Kalb <i>et al</i> [18]	±	-	-	-	-	-	NA	NA	6
Zaheer <i>et al</i> [19]	±	NA	-	+	NA	-	NA	NA	2
Arvanitakis <i>et al</i> [11]	±	NA	±	+	NA	-	-	-	3
Wagner <i>et al</i> [20]	+	NA	±	-	NA	+	NA	NA	1
Arora <i>et al</i> [3]	±	NA	±	+	NA	-	-	-	3
Shin <i>et al</i> [21]	±	-	-	-	±	-	NA	NA	4
Boninsegna <i>et al</i> [22]	-	±	-	-	±	-	NA	NA	4
de Pretis <i>et al</i> [2]	-	NA	-	-	NA	-	-	-	6
Muraki <i>et al</i> [9]	-	-	-	-	-	-	NA	NA	7
Tarvainen <i>et al</i> [16]	±	±	-	-	-	-	-	-	6
Ooka <i>et al</i> [7]	-	-	-	-	-	-	-	-	9
Değer <i>et al</i> [15]	-	NA	-	-	NA	-	-	-	6
Kulkarni <i>et al</i> [12]	-	NA	-	-	NA	-	NA	NA	4

-: Low risk of bias; ±: Unknown risk of bias; +: High risk of bias; NA: Not applicable.

53) and was 3 mm in all of them. Mean maximum duodenal wall thickness was assessed in two studies [19,20] and was 19 mm ($n = 88$). Wall thickening distribution was evaluated in one study only[19] and was eccentric, involving the second duodenal portion medial wall, in 81.8% of the cases and concentric in 18.2% ($n = 11$). The second duodenal portion showed an increased enhancement in comparison to the adjacent intestinal walls in 76.3% of the cases ($n = 93$); second duodenal portion increased enhancement was recognizable in 84.4% of the cases at MRI ($n = 32$) and in 72.1% at CT ($n = 61$).

Cysts within the duodenal wall were detected in 82.6% of the cases ($n = 419$); duodenal wall cysts were recognizable in 94.4% of the cases at EUS ($n = 108$), in 81.9% of the cases at MRI ($n = 138$) and in 75.7% of the cases at CT ($n = 173$). Duodenal wall cysts were single in 65.8% of the cases and multiple in 34.2% ($n = 149$). Cyst size was evaluated in three studies[9,18,20]. Muraki *et al*[9] and Wagner *et al*[20] reported a mean maximum size of the cystic component of 13 mm ($n = 123$), whereas Kalb *et al*[18] reported cystic components diameters ranging from 6 to 27 mm ($n = 17$).

The cystic variant of PP was depicted in 72.0% of the cases and the solid variant in 28.0% ($n = 543$).

Groove region findings

A solid mass in the groove region was described in 40.9% of the cases ($n = 88$). Mean maximum diameter of the lesion was 38 mm ($n = 75$), whereas mean minimum diameter was 16 mm ($n = 27$). Lesions' signal intensity on T2-weighted images was evaluated in two articles[17,22] ($n = 43$): The solid lesion was iso-intense to "normal" pancreatic parenchyma in 48.8% of the cases, hyperintense in 30.2% and hypointense in 21.0%. Lesions' signal intensity on other imaging sequences was assessed only by Boninsegna *et al*[22] ($n = 28$): On T1-weighted images the lesion was hypointense in 64.3% of the cases

Table 3 Variables evaluated in the included studies

Ref.	Duodenal wall thickening	Thickening distribution	Duodenal wall enhancement	Duodenal wall cysts	Cysts number	Cysts size	Pancreatic mass	Signal intensity on T2-weighted images	Signal intensity on T1-weighted images, diffusion-weighted images, apparent diffusion coefficient map	Arterial phase enhancement	Portal venous phase enhancement
Ishigami <i>et al</i> [17]				+				+			
Kalb <i>et al</i> [18]	+		+	+		1					
Zaheer <i>et al</i> [19]	1, 2	1		1			1, 2			1	1
Arvanitakis <i>et al</i> [11]	2			+ 2	+ 2						
Wagner <i>et al</i> [20]	1, 2			+ 1, 2	1	1					
Arora <i>et al</i> [3]	+ 1		+ 1	+ 1							
Shin <i>et al</i> [21]	1										1
Boninsegna <i>et al</i> [22]	+							+	+	+	+
de Pretis <i>et al</i> [2]											
Muraki <i>et al</i> [9]						+					
Tarvainen <i>et al</i> [16]											
Ooka <i>et al</i> [7]	1						1				
Değer <i>et al</i> [15]	+ 1			+ 1			1				
Kulkarni <i>et al</i> [12]	1		1	1							

+: Described at MRI; 1: Described at CT; 2: Described at EUS; MRI: Magnetic resonance imaging; EUS: Endoscopic ultrasound; CT: Computed tomography.

and isointense in 35.7%, on high b-value diffusion-weighted images it was isointense in 71.4% of the cases and hypointense in 28.6%, whereas on ADC maps it was isointense in 71.4% of the cases, hyperintense in 25.0% and hypointense in 3.6%. During the arterial phase of the dynamic study, the lesion appeared hypovascular in 82.4% of the cases and isovascular in 17.6% (n = 34). During the portal

Table 4 Variables evaluated in the included studies

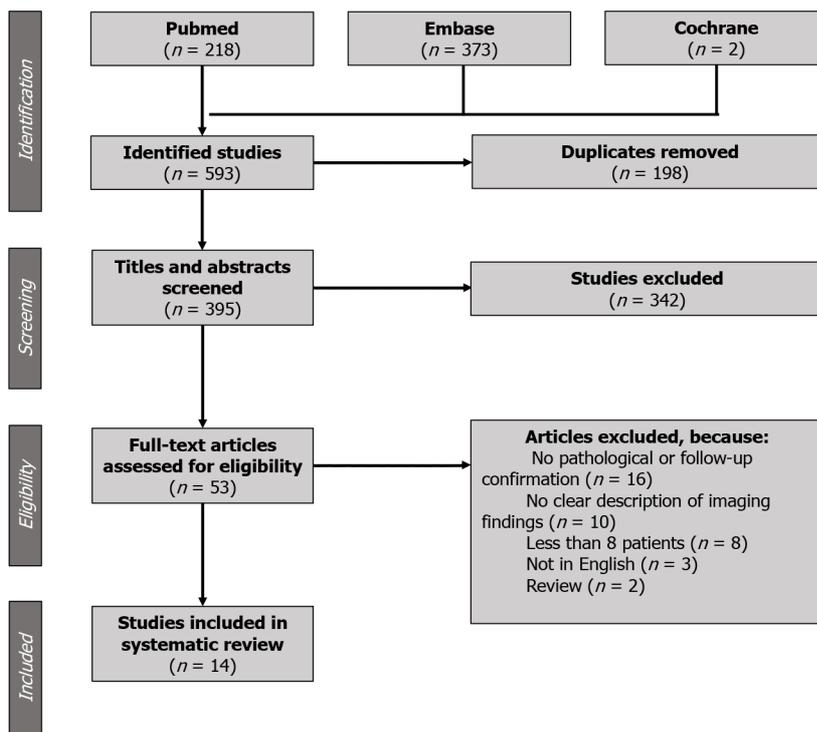
Ref.	Delayed enhancement	Enhancement pattern	Pancreatic cysts	Main pancreatic duct dilatation	Pancreatic calcifications	Biliary duct dilatation	Portal vein stenosis	Gastroduodenal artery displacement	Peripancreatic fat stranding	Peripancreatic lymph nodes
Ishigami <i>et al</i> [17]		+		+	1	+				
Kalb <i>et al</i> [18]			+	+		+	+			
Zaheer <i>et al</i> [19]			2	1	1	1			1	1
Arvanitakis <i>et al</i> [11]				+,1	1	+,1				
Wagner <i>et al</i> [20]				+,1	1	+,1			1	
Arora <i>et al</i> [3]			+,1	+,1	1	+,1		+,1		
Shin <i>et al</i> [21]		1	1	1	1	1		1		1
Boninsegna <i>et al</i> [22]	+		+	+		+				
de Pretis <i>et al</i> [2]					1					
Muraki <i>et al</i> [9]			+	+		+,1				
Tarvainen <i>et al</i> [16]			+,1	+,1	1	+,1				
Ooka <i>et al</i> [7]			1	1	1				1	
Değer <i>et al</i> [15]				+,1						
Kulkarni <i>et al</i> [12]			1	1	1	1		1		

+: Described at MRI; 1: Described at CT; 2: Described at EUS; MRI: Magnetic resonance imaging; EUS: Endoscopic ultrasound; CT: Computed tomography.

venous phase, the lesion appeared isovascular in 47.6% of the cases, hypovascular in 42.9% and hypervascular in 9.5% ($n = 42$). Enhancement pattern during the portal venous phase was described as “patchy” in 78.3% of the cases, whereas no cases of ring enhancement were detected ($n = 23$). During the delayed phase, the lesion appeared hyperintense in 53.6% of the cases and isointense in 46.4% ($n = 28$).

Pancreatic findings

Main pancreatic duct dilatation was present in 56.5% of the cases ($n = 499$); in the single included studies, prevalence of main pancreatic duct dilatation ranged from 28.9%[16] to 95.5%[20]. Pancreatic



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Figure 1 PRISMA flowchart showing studies inclusion and exclusion criteria.

cysts were detected in 64.5% of the cases ($n = 269$); pancreatic cysts detection rate was 80.3% at MRI ($n = 122$), 52.4% at CT ($n = 147$) and 42.9% ($n = 7$) at EUS. Pancreatic calcifications were present in 48.3% of the cases ($n = 383$); in the single included studies, prevalence of pancreatic calcifications ranged from 20% [7] to 100% [11]. Calcifications in the region of the minor papilla were recognizable in 43.4% of the cases ($n = 76$).

Alterations in the adjacent structures

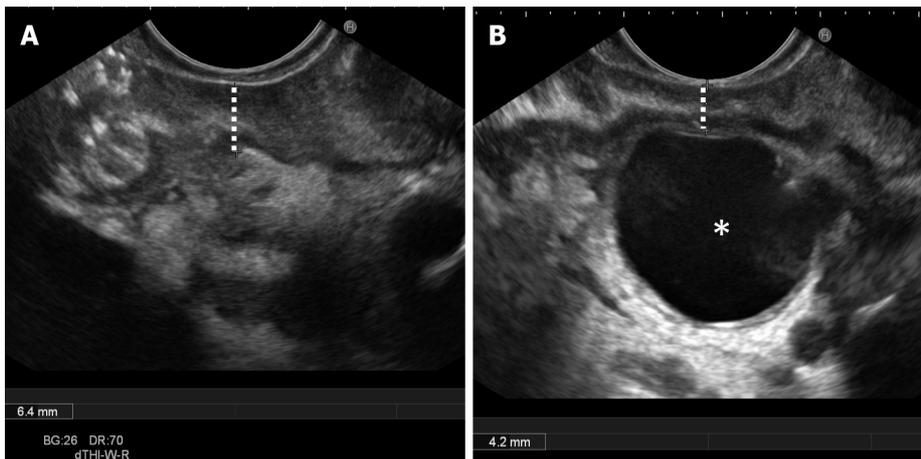
Biliary duct dilatation was observed in 41.2% of the cases ($n = 417$), portal vein stenosis in 47.1% ($n = 17$) and gastroduodenal artery displacement in 64.3% ($n = 84$). Peripancreatic fat stranding was described in 88.1% of the cases ($n = 134$) and enlarged peripancreatic lymph nodes were appreciable in 65.0% ($n = 20$).

Differential diagnosis PP vs cancer

Four articles [17,18,21,22] explored imaging accuracy in the differential diagnosis between PP and pancreatic cancer, including a total of 68 patients with PP and 73 with pancreatic adenocarcinoma. Shin *et al* [21] showed that, at CT, absence of the malignant appearance of biliary duct stenosis (*i.e.* abrupt duct cutoff or shouldering), presence of duodenal wall thickening and presence of cysts in the groove region are significantly associated with PP ($P = 0.002$, 0.026 and 0.001, respectively). Ishigami *et al* [17] found that a patchy enhancement pattern in the portal venous phase at CT and/or MRI is significantly associated with PP ($P < 0.0001$). Kalb *et al* [18] showed that poorly experienced radiologists can correctly diagnose PP at MRI with an accuracy of 87.2% (88.2% sensitivity, 86.7% specificity, 78.9% PPV, 92.9% NPV) by looking for the presence of 3 key imaging findings: Focal thickening (> 3 mm) of the second portion of the duodenum, increased enhancement of the second portion of the duodenum and cysts in the groove region. Boninsegna *et al* [22] observed that, at MRI, iso-/hypo-intensity on high b-value diffusion weighted imaging (DWI), iso-/hyper-intensity on ADC maps and delayed phase iso-/hyper-intensity are significantly associated with PP ($P = 0.004$, 0.005 and 0.003, respectively), as well as focal thickening of the second portion of the duodenum, presence of cysts in the groove area and absence of main pancreatic duct dilatation ($P = 0.001$, 0.001 and 0.005, respectively). Moreover, mean maximum diameter was significantly larger in PP than in adenocarcinoma ($P = 0.0003$).

DISCUSSION

Our systematic review included 14 original articles showing multimodality imaging findings in PP.



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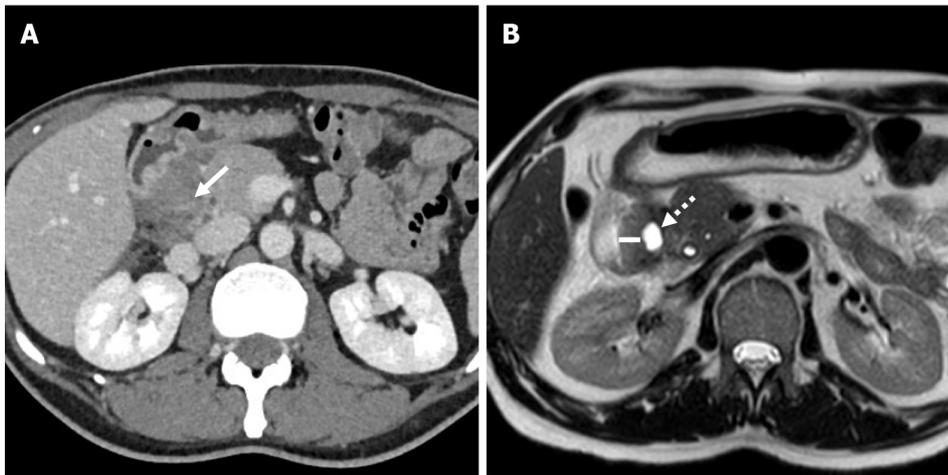
Figure 2 Endoscopic ultrasound. A: Endoscopic ultrasound (EUS) clearly shows second duodenal portion wall thickening in a patient with chronic alcohol abuse history and abdominal pain, findings suggestive of solid subtype of paraduodenal pancreatitis; B EUS shows mild second duodenal portion wall thickening and a large duodenal wall cyst (star), findings pathognomonic for paraduodenal pancreatitis.

Imaging was the main topic in eight of the included articles, whereas it was ancillary in six of them; in these latter articles, imaging findings were not always extensively and accurately described. A total of 22 different imaging features were considered by the Authors in the included articles, with a mean of 4,4 imaging features *per* article. Surprisingly, the most frequently described imaging features were not directly correlated with PP appearance and were in the presence of main pancreatic duct dilatation (reported in 13 studies), presence of biliary duct dilatation (11 studies) and presence of pancreatic calcifications (10 studies). Presence of duodenal wall thickening and of duodenal wall cysts were also frequently assessed in the included studies (10 and 8 studies, respectively).

Typical imaging findings in PP are second duodenal portion wall thickening (88.8% of the cases), which is usually eccentric (81.8%), associated with the presence of duodenal wall cysts (82.6%) and second duodenal portion increased wall enhancement (76.3%). Duodenal wall cysts were more frequently single (65.8%) and showed a mean maximum diameter of 13 mm. The above-described imaging findings detection rates varied largely according to the adopted imaging modality. For example, duodenal wall thickening prevalence was 96.5% at EUS (Figure 2A), 91.0% at MRI and 84.1% at CT, and, similarly, duodenal wall cysts prevalence was 94.4% at EUS, 81.9% at MRI and 75.7% at CT. These differences are probably the consequence of the increased tissue contrast resolution of EUS over MRI and of MRI over CT (Figures 2B and 3). Consequently, the prevalence of cystic and solid subtypes of PP can be extremely variable and depends on the patients' population characteristics (solid subtype prevalence increases in the surgical series, given to the difficulty in differential diagnosis with pancreatic cancer, and decreases in the gastroenterological series) and from the adopted imaging modality (cystic subtype prevalence is higher in MRI and EUS series in comparison to CT series).

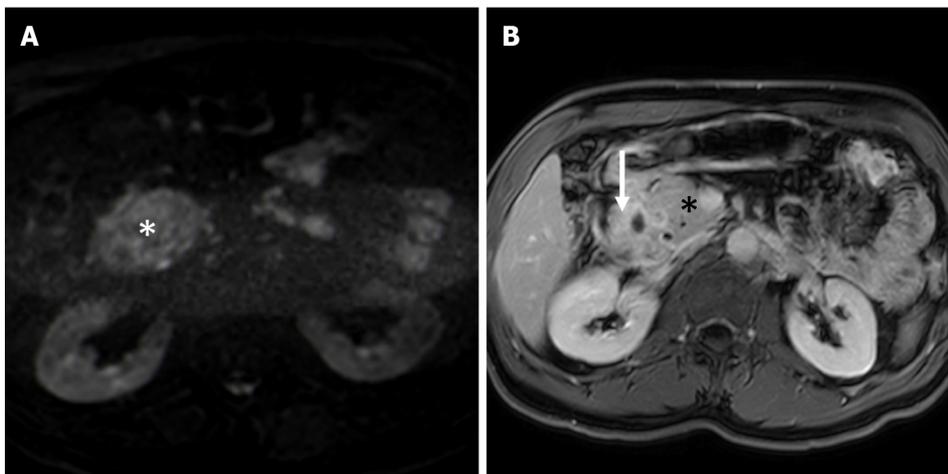
A solid mass in the groove region was described in less than a half (40.9%) of patients with PP. At MRI, lesion signal intensity was quite variable on T1- and T2-weighted images. On the other hand, the included lesions were hypo- to iso-intense in comparison to a normal pancreas on high b-value DWI in 100% of the cases (Figure 4A) and were iso- to hyper-intense on the ADC map in 96.4%. Therefore, the presence of increased diffusivity restriction (*i.e.* hyperintensity on high b-value DWI and hypointensity on the ADC map) has high negative predictive value for the diagnosis of PP. The solid components typically (82.4%) appeared hypovascular in the arterial phase of the dynamic study and showed a progressive enhancement during the portal venous (57.1% iso- to hyper-intense/attenuating) and the delayed (100% iso- to hyper-intense/attenuating) phases (Figure 4B). The enhancement pattern during the portal venous phase was mainly described as "patchy" (78.3% of the cases). Both patchy enhancement during portal venous phase, which is the consequence of the presence of normal pancreatic tissue between the areas of inflammatory changes[9], and delayed phase enhancement, which is the direct consequence of the presence of fibro-inflammatory tissue, are useful in the differential diagnosis between PP and pancreatic cancer.

Presence of radiological signs of obstructive chronic pancreatitis were reported with extremely variable prevalence in the included studies. For example, prevalence of main pancreatic duct dilatation ranged from 28.9% to 95.5%, prevalence of pancreatic calcifications from 20.0% to 100%, and prevalence of pancreatic cysts from 35.1% to 94.1%. The rationale of these wide differences is clearly explained in the work of de Pretis *et al*[2], which demonstrated that the prevalence of both pancreatic calcifications and main pancreatic duct dilatation significantly increases during the course of the disease. Therefore, despite the results reported by Boninsegna *et al*[22], signs of obstructive chronic pancreatitis should not be used for a differential diagnosis between PP and pancreatic cancer.



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Figure 3 A 49-year-old male patient with weight loss and abdominal pain. A: Axial 3 mm thick multiplanar reconstruction of portal venous phase computed tomography acquisition shows a hypodense mass in the groove region with patchy enhancement (arrow); B: Axial T2-weighted magnetic resonance imaging image acquired 2 mo later clearly shows eccentric second duodenal portion wall thickening (line) with cystic component (dotted arrow).



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Figure 4 Magnetic resonance imaging. A: Axial high b value ($b = 800 \text{ s/mm}^2$) diffusion weighted imaging image shows absence of increased diffusivity restriction in the thickened groove area (star) in comparison to adjacent “normal” pancreas, finding associated with paraduodenal pancreatitis and uncommon in pancreatic cancer; B: Axial delayed phase T1-weighted magnetic resonance imaging acquisition shows increased enhancement of the duodenal walls and of the groove region (arrow) in comparison to “normal” pancreas (star), finding often associated with paraduodenal pancreatitis.

Given its expansile inflammatory nature, PP determines reactive alterations in the adjacent structures. The most frequently encountered finding was peripancreatic fat stranding, which was appreciable in 88.1% of the cases, often associated with enlarged reactive peripancreatic lymph nodes (65%). Gastroduodenal artery displacement, without infiltration or occlusion, must also be considered a common finding in PP (64.3%).

Given the central role of duodenal wall changes depiction in the differential diagnosis between PP and pancreatic cancer[21,22], MRI is mandatory if CT is inconclusive, and EUS must be performed if doubts remain even after MRI[23]. Moreover, EUS-guided fine needle aspiration/biopsy should be performed in inconclusive cases, warranting diagnostic sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in differentiating PP from pancreatic cancer of 90%, 100%, 100%, 93%, and 96%, respectively[13].

The main strength of our study is that it is the first systematic literature review of imaging findings in PP. By systematically reviewing 14 different original articles dealing with imaging findings in PP, we have been able to bring together a total of 543 patients affected by PP. The article has also some weaknesses, mainly due to selection bias in the included articles and to the extreme variability of the evaluated and described imaging findings. Moreover, the differential diagnosis between PP and pancreatic cancer, which represents the main criticality, was only addressed in 4 Papers.

CONCLUSION

PP has peculiar imaging findings that enable differential diagnosis with pancreatic cancer, namely second duodenal portion eccentric wall thickening, increased enhancement, and cystic changes. Absence of increased diffusivity restriction in the groove area, patchy enhancement during the portal venous phase and delayed phase enhancement are also imaging features strongly correlated with PP. Signs of obstructive chronic pancreatitis and biliary obstruction are often present in advanced disease and must not be considered worrisome features.

CT can be considered the first line imaging modality in pancreatic pathologies and enables clinicians to perform a differential diagnosis between PP and pancreatic cancer in most of the cases. Given its higher tissue contrast resolution, MRI represents the second level imaging modality of choice in the case of inconclusive CT findings. EUS has higher accuracy than CT and MRI in depicting duodenal wall changes, offers the possibility of obtaining cyto-histologic samples, but is more invasive and less tolerated; therefore, EUS must be considered a problem-solving technique in difficult cases.

ARTICLE HIGHLIGHTS

Research background

Paraduodenal pancreatitis (PP) is a relatively rare benign inflammatory pathology that can create differential diagnosis dilemmas with pancreatic cancer. Many articles deal with imaging findings in PP, but most of them are represented by case reports, short series, or reviews.

Research motivation

The aim of our work was to perform a systematic literature review of imaging findings in PP considering only original research articles with pathology and/or clinical-radiological follow-up as the reference standard.

Research objectives

To critically describe multimodality imaging findings in PP to help clinicians in the differential diagnosis with pancreatic cancer.

Research methods

Systematic review of original articles describing imaging findings in 8 or more patients affected by PP with pathological confirmation or clinical-radiological follow-up as the gold standard.

Research results

14 articles including 543 patients were included. Computed tomography, magnetic resonance imaging (MRI) and Endoscopic ultrasound (EUS) findings were described.

Research conclusions

PP has typical findings at imaging. MRI is the most accurate radiological imaging modality, but EUS has higher sensitivity in depicting duodenal wall alterations.

Research perspectives

Radiomics features extraction may be an option in order to further increase imaging accuracy in the differential diagnosis between PP and pancreatic cancer.

FOOTNOTES

Author contributions: Bonatti M, De Pretis N and Valletta R designed the research; Bonatti M, De Pretis N, Crinò SF and Brillo A performed the research; Bonatti M, De Pretis N and Lombardo F analyzed the data; Bonatti M, Zamboni GA, Lombardo F, Mansueto G and Frulloni L wrote the paper; All authors approved the final version of the article.

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