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Differentiating benign from malignant pancreatic cysts on computed tomography

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ABSTRACT

Purpose: It is important to identify features on computed tomography (CT) that can distinguish between benign and premalignant or malignant pancreatic cysts to avoid unnecessary surgeries. This study investigated the preoperative diagnostic evaluation of cystic pancreatic lesions to determine how advanced imaging and clinical factors should guide management.

Methods: In total, 53 patients with 27 benign and 26 premalignant or malignant cysts were enrolled. CT features of the cysts were compared using univariate and multivariate analyses.

Results: On univariate analysis, a solid component ($p < 0.01$), septation ($p < 0.01$), location ($p < 0.01$), border ($p < 0.01$), wall enhancement ($p = 0.01$), lesion margins ($p < 0.01$), pancreatic atrophy ($p = 0.04$), and a cystic wall ($p < 0.01$) were all significantly different between benign and premalignant or malignant cysts. On multivariate analysis, only a solid component ($p < 0.01$) and septation ($p < 0.01$) were significant.

Conclusion: A thin cystic wall, uniform homogeneity, a clear border, the presence of septation, pancreatic atrophy, and the absence of both wall enhancements and solid components were more frequently seen in benign cysts. A thick wall, lack of homogeneity, the presence of wall enhancements and solid components, absence of septation, only a small degree of pancreatic atrophy, and unclear borders were more frequent among premalignant or malignant cysts. The only CT features to differentiate benign from premalignant or malignant cysts were a solid component and septation.

1. Introduction

Pancreatic cystic lesions are frequently detected as incidental findings in cross-sectional imaging [1,2], likely because of recent improvements in high-resolution imaging technologies, including MDCT. Incidental pancreatic cystic lesions were detected on 8.7 % of MDCT images in an outpatient population imaged for diseases unrelated to the pancreas [2].

CPNs, which may be congenital, inflammatory, or neoplastic, are diagnostically challenging, accounting for 10 %–15 % of pancreatic cystic lesions and 5 % of primary pancreatic neoplasms [18,19], with most studies reporting an increasing prevalence. They are commonly found incidentally in CT scans [20] and present a growing indication for pancreatic surgery at referral centers [18,21]. The diagnosis relies primarily on CT and MRI. Efforts to differentiate these tumors using advanced imaging have yielded mixed results [22,10]. Although certain features are considered characteristic of specific kinds of CPN, their diagnostic abilities have not been subjected to rigorous analysis. Endoscopic ultrasound is currently used to investigate cystic pancreatic lesions, particularly as a means of cyst aspiration [24]. Whether analyzing

Abbreviations: US, Ultrasonography; CEA, Carcinoembryonic antigen; CPR, Curved planar reformation; CTA, CT angiography; DWI, Diffusion-weighted imaging; ERCP, Endoscopic retrograde cholangiopancreatography; FDG PET, Fluorodeoxyglucose PET; FNA, Fine-needle aspiration; HASTE, Half-Fourier acquisition single-shot turbo spin-echo; IPMN, Intraductal papillary mucinous neoplasia; MCA, Mucinous cystadenoma; MCB, Mucinous cystic borderline tumor; MCC, Mucinous cystadenocarcinoma; MCN, Mucinous cystic neoplasm; MPD, Main pancreatic duct; MPR, Multi-planar reformation; MRA, MR angiography; MRCP, MR cholangiopancreatography; MRI, Magnetic resonance imaging; MSCT, Multi-slice helical computed tomography; PACS, Picture archiving and communicating system; PCN, Cystic neoplasms of the pancreas; PDAC, Pancreatic ductal adenocarcinoma; PET, Positron emission computed tomography; ROI, Region of interest; SCA, Serous cystadenoma; SMA, Serous microcystic adenoma.

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cystic fluid will improve the diagnostic algorithm remains unconfirmed [25].

Congenital cysts, SCA, the macrocytic variant MCN, IPMN of the branch duct type, and tumors with cystic change—including solid pseudopapillary and neuroendocrine tumors—and PDAC may have macrocytic morphologic features that overlap on imaging despite having different malignant potential [3–17]. Benign cysts, including congenital cysts and macrocytic SCA, can be clinically managed unless the lesions are symptomatic. Conversely, MCN and IPMN of the branch duct type and tumors with cystic change are premalignant or malignant and typically require surgical resection [3–13].

CT is the most common imaging modality for the initial detection and characterization of these pancreatic lesions. It is crucial to differentiate benign from premalignant and malignant cysts to avoid unnecessary surgery.

1.1. CT imaging techniques

High-resolution, dual-phase (arterial and portal), contrast-enhanced CT is essential for evaluating suspected pancreatic masses. Negative oral contrast is routinely administered before image acquisition. Arterial phase imaging generally performed 30–40 s after contrast injection, allows superior visualization of pancreatic masses and peripancreatic arteries. Maximal contrast between hypovascular or cystic masses and the background pancreas provides optimal tumor visualization in this phase [70]. Arterial phase images are routinely displayed at 3 mm intervals. Portal phase imaging is usually performed 60–70 s after injection, providing optimal visualization of the peripancreatic venous system. The portal venous phase provides optimal imaging of liver metastases. Portal venous images are routinely displayed at 5 mm intervals.

1.2. MR imaging techniques

An optimal pancreatic MRI imaging protocol comprises rapid image acquisition of both T1-weighted and T2-weighted sequences. The acquisition of unenhanced and enhanced T1-weighted images is essential for the optimal assessment of cystic pancreatic lesions. Axial 3D T1-weighted gradient-recalled echo in opposed-phase images of the entire abdomen can be obtained during a single breath-hold. Unenhanced T1-weighted images are essential to detect hemorrhage or identify protein deposits within cystic lesions. Enhanced T1-weighted images provide optimal visualization of enhanced soft tissue components within cystic lesions. Enhanced axial T1-weighted images are obtained through the pancreas at serial intervals for up to 5 min following IV gadolinium administration. T2-weighted imaging is also essential for analyzing cyst contents and optimally visualizing the pancreatic ductal system. Multiplanar, T2-weighted, single-shot, fast spin-echo sequences are routinely obtained. Axial T2-weighted imaging with fat saturation is also regularly performed to highlight pancreatic or peripancreatic inflammatory changes.

MRCP uses heavily T2-weighted sequences obtained in the wreath plane to provide an optimal depiction of the pancreatic ductal and biliary system. DWI was initially applied to neuroimaging for detecting acute ischemia but has been increasingly used in abdominal imaging applications over the past decade. DWI measures the movement of water molecules within a cellular matrix as representative apparent diffusion coefficient (ADC) values [71]. Several variables account for the movement or diffusion of water molecules within the extravascular space, including tissue cellularity and organization, extracellular area tortuosity, and the integrity of cellular membranes [72]. The physics of DWI is beyond the scope of this article. However, simple cysts demonstrate increased signal intensity on DWI with a comparatively low b value ($b = 50\ s/mm^2$), reduced signal intensity on high-b-value imaging ($b = 800\ s/mm^2$), and high signal intensity on ADC maps owing to T2 shine-through. The high ADC values associated with cystic lesions are attributable to the freedom of motion of water molecules in a fluid environment [23].

1.3. Overview of lesions

Frequently encountered primary cysts include pseudocysts, SCA, various mucinous cystic lesions, mucinous cystadenomas, and IPMT. Lymphoepithelial cysts occur less commonly. Solid pancreatic tumors with cystic degeneration also account for a minority of cystic pancreatic lesions. Cyst-like degeneration does not occur often in pancreatic ductal adenocarcinomas, solid pseudopapillary tumors, and pancreatic endocrine (islet cell) tumors. Cystic pancreatic metastases are extremely rare.

1.4. Pseudocysts

Pseudocysts, the most encountered pancreatic cystic lesions, occur due to fat necrosis in pancreatitis. They are called pseudocysts because they lack a true epithelial lining. Pseudocysts result from the encapsulation of fluid, tissue, debris, pancreatic enzymes, and blood by granulation tissues with a fibrous capsule [73]. They evolve over months from poorly marginated, heterogeneous fluid collections with irregular homogeneity to progressively well-circumscribed, discrete cystic lesions. Pseudocysts on unenhanced CT generally present as homogeneous, hypodense lesions with attenuation values similar to water.

However, hemorrhage or infected pseudocysts may have regions with variably increased attenuation. Contrast-enhanced CT may demonstrate capsular enhancement but not an enhancement of the internal contents. The presence of gas within a pseudocyst is suggestive of either infection by a gas-forming organism or communication with the adjacent gut. CT is useful for evaluating the complications of pseudocyst formation, including secondary pseudo-aneurysm formation. Unilocular cysts have no solid components, central scarring, wall calcification, or collection of pancreatic enzymes, blood, or necrotic tissue. Debris within a cystic lesion is a specific MR finding [74]. Following a history of pancreatitis or abdominal trauma, cysts develop within 4–6 weeks and decrease in size over time. However, they may grow or become infected and can be found anywhere in the pancreas or abdomen and even in the chest.

1.5. Serous cystadenomas

SCAs account for 30 % of pancreatic cystic neoplasms. They can arise from any part of the pancreas but are typically found in the body and tail. SCAs are more common in women in their sixth decade [75,76] and may cause non-specific symptoms, including epigastric abdominal pain and weight loss. They are classified into microcystic (multilocular) and oligocystic (unilocular). SCAs are usually <5 cm in diameter with a median size of 25–30 mm. They have a well-defined, lobulated contour and, on cytology, have a clear or eosinophil-rich cytoplasm.

These tumors can be associated with VHL disease [77,78], a syndrome including hemangioblastomas of the retina and central nervous system and pheochromocytomas. The VHL gene may also be seen in sporadic cases of SCA. SCAs are usually benign. A meta-analysis of 673 lesions found the risk of malignancy to be <3 %, which may be an overestimation as not all incidentally found SCAs have been reported in the literature [37,79–81].

1.6. Mucinous cystic lesions

Mucinous cystic lesions include MCA and IPMNs. MCA is the most common cystic pancreatic neoplasm, accounting for approximately 10 % of all pancreatic cystic neoplasms. These lesions are thick-walled, low-grade, malignant tumors that comprise large, mucin-containing cysts. Mucinous cystadenomas are typically unilocular or contain a few cystic elements >2 cm. They typically arise from the body or tail of the pancreas [83]. Unlike IPMNs, these lesions do not communicate with the pancreatic duct [82]. Most MCAs occur in females (mean age, 50 years).

MCCs arise from the malignant transformation of MCAs. Patients with cystadenocarcinomas are generally significantly older than those with newly diagnosed benign mucinous cystadenomas, suggesting a progression from benign to malignant MCC [84]. On CT, MCA typically presents as a hypodense, unilocular or multilocular cyst, often with a thick, enhancing wall. Multilocular lesions may also demonstrate enhancement of thin internal septa. Focal mural or septal calcifications are occasionally seen.

1.7. Lymphoepithelial cysts

Lymphoepithelial or true congenital cysts of the pancreas are rare, representing <1 % of all pancreatic cysts [37]. These lesions mostly occur in males (mean age, 55 years). The lesions are usually <2 cm, round or oval, and contain no internal solid elements. They have no malignant potential and are often indistinguishable from pseudocysts. A prior clinical history of pancreatitis will often aid in differentiating between the two. Multiple, simple cysts within the pancreas are rarely encountered but can be seen in association with VHL disease or autosomal dominant PKD. On CT, a lymphoepithelial cyst is a simple, unilocular cyst with the attenuation value of simple fluids. Cyst walls should be thin or imperceptible. On MR, these lesions are uniformly T2 hyperintense, T1 hypointense, and do not communicate with the pancreatic duct. They demonstrate no mural or internal enhancement.

1.8. Intraductal papillary mucinous neoplasms

These tumors are more commonly seen in males [85,87], typically in the 7–9th decade of life, with epigastric abdominal pain frequently exacerbated by food [86]. They may resemble pancreatitis, with symptoms caused by blockage of the pancreatic ducts by mucin. Other signs and symptoms include weight loss, fever, and jaundice [88]

1.9. Solid pancreatic tumors with cystic degeneration

1.9.1. Ductal adenocarcinoma

PDAC is the most common and most lethal of all pancreatic tumors, accounting for 90 % of pancreatic neoplasms [46]. Its prognosis is dismal, with a 5-year survival rate <3 %. Although these tumors are predominantly solid, cyst-like features from cystic degeneration, retention cysts, or pseudocysts may be seen on histology in up to 8 % cases [40]. Early, distant metastatic disease to the liver, peritoneum, and regional lymph nodes is common.

On CT, ductal adenocarcinoma typically presents as a heterogeneous, poorly marginated, ill-defined, hypodense mass with early pancreatic ductal and/or common bile duct obstruction. These lesions are most seen in the pancreatic head, followed by the body and tail. Direct local invasion of adjacent structures and vascular invasion is frequently seen at an early stage. Cystic degeneration, mimicking a more benign primary cystic pancreatic mass, can infrequently occur.

1.9.2. Solid pseudopapillary tumors

Solid pseudopapillary tumors, previously known as solid and papillary epithelial neoplasms, are uncommon lesions that predominantly occur in women with a mean age of 28 years. They have a low incidence of malignant degeneration and tend to be large, well-defined, and heterogeneous. Their appearance varies from completely solid to mostly cystic, depending on the degree of internal degeneration. On CT, these lesions typically present as a large, encapsulated, solid mass with a variable degree of cystic or hemorrhagic foci.

1.9.3. Pancreatic endocrine tumors

Pancreatic endocrine tumors (PET), also known as islet cell or neuroendocrine tumors, arise from pancreatic endocrine cells or the islets of Langerhans. These relatively rare tumors show no sex predilection and occur in middle-aged adults with a mean age of 53 years. The most common subtype is insulinoma, followed by gastrinoma and other nonfunctional subtypes. These lesions tend to be small but may be as large as 10 cm and are generally solid and well vascularized. Cystic PETs are relatively rare, occurring in approximately 17 % of 170 surgically resected specimens in a recent study [48]. The cystic elements found in PETs may be caused by tumor degeneration [90]. The presence of a cystic PET may be highly relevant because these patients are much more likely to have an underlying multiple endocrine neoplasia syndrome than a patient with a uniformly solid PET [48]. A non-functioning endocrine neoplasm, also known as an islet cell tumor, is hypervascular with ring-enhancement. This is unlike serous cystic neoplasms which have center-enhancement and are more solid.

1.9.4. Cystic pancreatic metastases

Cystic metastases to the pancreas are very uncommon. Hypovascular metastases have been described in primary malignancies of the lung, breast, colon, melanoma, and sarcoma. Such lesions may be sufficiently hypodense and appear cystic on both CT and MR, depending on the size and chronicity of these lesions.

This study aimed to investigate the preoperative diagnostic evaluation of cystic pancreatic lesions to determine how imaging and clinical factors can guide management.

2. Materials and methods

2.1. Study

This was a retrospective study, accessing all abdominal CT scan images from Sun Yat-Sen Memorial Hospital (August 10, 2010 to July 2, 2013) and Sun Yat-Sen University Cancer Center (April 18, 2007 to March 5, 2012) via a PACS workstation (GE, Centricity 2.0).

The inclusion criteria included images scanned with a three-phase contrast-enhanced MDCT through 64 layers; enhanced imaging with isotropic multi-planar reconstructions (MPR) with no greater than a 2 mm thin layer; either a cystic mass or a lesion that was at least 50 % cystic; surgical tumor resection in the Sun Yat-Sen Memorial Hospital or Sun Yat-Sen University Cancer Center; and a complete medical record and histopathological findings available.

Exclusion criteria included biopsy or surgery without imaging; uncertain pathological diagnosis; and no history of other malignancies.

2.2. Clinical data

Clinical data included sex, age at onset, clinical presentation, laboratory examination, and pathological results. The tumor marker tests included CA19-9, CEA, and CA125-5 with normal values of <37IU/ml, 0–5 ng /L, and <35U/ml, respectively.

2.3. Imaging methods

All imaging data was assessed by two radiologists, each with >5 years' experience in abdominal imaging, who were unaware of the patients' clinical data. The information noted included lesion site (divided into pancreatic head, body, tail, and all or most of the pancreas), lesion shape (round or oval and lobulated), maximum diameter of the cyst (repeated measurement on axial and MPR images of multiple slices), wall thickness (≤2 mm or>2 mm thick wall and a lumen diameter at least 25 % of the wall thickness), a cystic wall with or without enhancement (portal phase scan density >20 hu), septation (multiple or single cysts), calcification and location (when specified, unenhanced density exceeded 80 HU), solid components other than separation caused by a wall nodule (capsule contents on enhanced CT imaging with at least a 20 Hu higher density than unenhanced components), pancreatic atrophy (pancreatic diameter <10 mm, with the diameter of the front and rear areas <8 mm), main pancreatic duct dilatation >3 mm with dilatation >2 mm in the body and tail, border, and homogeneity

(asymmetric or uniform).

2.4. Research equipment

- Siemens 64-slice CT scanner (Somatom Sensation 64) and Wizard workstation (software version VB30).
- General Electric 64-slice CT scanner (Light Speed VCT) and Centricity 2.0 workstation.
- Giant Shark 2 M medical monitor.

2.5. CT scanning method

Each patient underwent enhanced abdominal scanning. Approximately 30–45 min before scanning, patients consumed 600–800 ml of water to expand the stomach and duodenum, and an additional 300–500 ml of water was given orally immediately before scanning. An injection of 80–120 ml of non-ionic iodine contrast agent (Omnipaque, Amersham, Shanghai China or Ultravist, Schering Guangzhou) was administered with a high-pressure syringe (Medrad, Pittsburgh, USA) through an 18 G catheter in the antecubital vein, with an injection flow rate of 2.5–3.0 ml/s. The patients were in the supine position and scanned with their breath held on inspiration.

Following the contrast injection, dynamic enhanced scans were obtained at the following intervals: arterial phase (25 s), portal phase (60 s), and equilibrium phase (90 s). The scan parameters were tube voltage (130 kV), tube current (260 mA), pitch (1.25), collimation (16 × 1.5 mm), and thickness (0.75–1 mm).

2.6. After-image processing

All patients had thin layer MPR with a thickness of 0.75–1 mm to carefully observe the lesion and its relationship with the surrounding organs, vessels, and biliary and pancreatic ducts.

2.7. Statistical analysis

Normally distributed quantitative variables were presented as the means, plus or minus the standard deviation (SD). Non-normally distributed variables were presented as the median and inter-quartile ranges. The mean maximum dimensions of the two groups were compared using independent-samples t-test, and the Kruskal–Wallis test was used for three groups. For univariate analysis, statistical differences in the CT features of two groups were analyzed using Chi-squared test and Fisher's exact test. A multivariate stepwise logistic regression model was used to determine the most significant CT features differentiating the two groups. Significant differences were defined as a p-value <0.05. All statistical analyses were performed with SPSS software package version 17.0 (SPSS, Chicago IL).

2.8. Pathological classification

The diagnosis of pancreatic cystic lesions is based on histopathological examination according to the World Health Organization (WHO), which published a classification system for cystic neoplasms in 1996 and revised it in 2000. This classification system categorized pancreatic cystic neoplasms as malignant (in situ or invasive), borderline (uncertain malignant potential), and benign (adenomas) [26,27]. Microcystic, glycogen-rich, serous tumors are almost universally benign, and macrocystic, mucinous tumors may be either malignant or premalignant. Malignant tumors include serous cystadenocarcinomas, mucinous cystadenocarcinomas, intraductal papillary mucinous carcinomas, invasive papillary mucinous carcinomas, and acinar cell cystadenocarcinomas. Borderline tumors comprise mucinous cystic tumors with moderate dysplasia, IPMN with moderate dysplasia, and solid pseudopapillary tumors. Benign or adenomatous tumors are serous cystadenomas, mucinous cystadenomas, and certain IPMNs.

2.9. Pathological classification of 53 cases

Fifty-three patients with pathologically proven diagnoses were studied. The results are presented below:

Benign: serous cystadenoma, 17; mucinous cystadenoma, 7; intraductal papillary mucinous adenoma, 1; pseudocyst, 5

Premalignant: solid pseudopapillary tumor, 12

Malignant: pancreatic ductal adenocarcinoma, 11; mucinous cystadenocarcinoma, 3

3. Results

3.1. Univariate analysis

3.1.1. General information

Of the 53 cystic lesions, 47 were symptomatic, whereas 6 were asymptomatic. Among the 47 symptomatic patients, 23 lesions were benign, whereas 24 were either premalignant or malignant. Seven patients had abdominal discomfort and pain, and 15 cases had other physical findings before their preoperative examination, including gallstones and abdominal masses. There was no statistically significant difference among patients with symptoms to differentiate between benign or malignant lesions ($p = 0.67$).

The age of patients with benign lesions ranged from 19 to 76 years, with a mean age of 52 years. Of these, 44 % were male and 56 % female. In those with premalignant or malignant lesions, the average age was 46 years with a range of 13–71 years. There was a predominance of women (77 %), but no statistically significant difference in terms of sex distribution ($p = 0.10$).

Age differences between patients with benign lesions and those with premalignant or malignant lesions were not statistically significant ($t = 1.30$, $p = 0.20$) (Table 3).

3.1.2. CT features

The maximum dimension of the 53 benign cysts ranged from 3.7–26 cm (IQR, 5.0–8.7 cm).This was similar to premalignant and malignant cysts (range, 2.8–11.9 cm; IQR, 5.4–8.9 cm).There was no significant difference between the two groups with respect to size ($p = 0.73$).The maximum diameter of the cavity of the benign cysts was >5 cm in 19 cases and ≤ 5 cm in eight cases. Among premalignant and malignant cysts, the largest lesion was >5 cm in 20 cases and ≤ 5 cm in six cases. There was no difference between the frequency of benign or premalignant and malignant cysts having maximum diameters either >5 cm or≤ 5 cm.

There was no statistically significant difference in lesion size ($t = -0.34$, $p = 0.73$) (Table 4).

Of the thirteen premalignant and malignant cysts were in the head of the pancreas, 11 in the body, and two in the tail (Figs. 1,2, 5, and 7). Of the benign cysts, eight were located in the head, six in the body, eight in the tail, and five throughout the pancreas (Figs. 4,8,9,13).The location of lesions significantly differed between the groups ($p < 0.01$).

Among the benign cysts (Figs. 9,13), nine were oval or round, whereas 18 were lobulated. This was like premalignant or malignant cysts (Fig. 3) with nine oval or round and 17 lobulated cysts. There was no significant difference between the groups with respect to shape ($p = 0.92$).

Thick cystic walls (>2 mm), (Figs. 1,12) were found in 10 benign and 21 premalignant or malignant cysts. Thin cystic walls (Figs. 4,9) were significantly more common in benign cysts ($p < 0.01$) Fig. 6.

Wall enhancement was visibly present in 20 benign and 26 premalignant or malignant cysts (Figs. 10,11), which was statistically significant ($p = 0.01$).

Septation was noted in 20 benign and 7 premalignant or malignant lesions (Figs. 4,9), which was statistically significant ($p < 0.01$).

Asymmetric homogeneity was present in 55.6 % of benign (Figs 3,8) and 92.3 % of premalignant or malignant cysts (Fig. 1), which was

statistically significant ($p < 0.01$).

Calcification was found in six benign (Fig. 14) and three premalignant or malignant cysts, which was not significantly different ($p = 0.47$).

A solid component was seen significantly less often ($p < 0.01$) in benign (Fig. 4) than in premalignant or malignant cysts (Fig. 1).

Atrophy of the pancreas was seen significantly more often in benign than in premalignant or malignant cysts ($p = 0.04$).

Cystic dilatation of the pancreatic duct was present in only 25.9 % of benign and 30.8 % of premalignant or malignant cases, which was not statistically significant ($p = 0.7$).

Overall, 92.6 %of the benign cysts had clear borders, whereas only 53.8 % of premalignant or malignant cysts had no clear borders, which was quite significant ($p < 0.01$, Fig. 2). Although a clear border alone cannot confirm a benign lesion, an unclear border (Fig. 6), without septation, along with the presence of a solid component could virtually confirm malignancy, which is quite useful for differentiating benign from malignant lesions.

*Wilcoxon test**Fisher's exact test

* Solid component ($p < 0.01$, 95 % confidence interval [2.13,44.22]); and septation ($p < 0.01$, 95 % confidence interval [0,0.30]) were statistically significant.

3.2. Multivariate analysis

There were eight significant CT features found on univariate analysis. Multivariate analysis with stepwise logistic regression found that septation ($p < 0.01$, 95 % CI [2.13, 44.22]) and a solid component ($p < 0.01$, 95 % CI [0, 0.30]) were statistically significant CT features for differentiating benign from premalignant or malignant cysts (Table 17).

4. Discussion

4.1. Clinical manifestations

The most common clinical problem with pancreatic lesions is not their detection but their characterization and the choice of a therapeutic plan. However, neither imaging studies nor cystic aspirations can determine whether each pancreatic lesion is benign, premalignant, or malignant [6]. Therefore, it is clinically valuable to identify the CT features predominantly associated with benign and premalignant/malignant lesions, which would enable close follow-ups of likely benign lesions unless they are clinically symptomatic and the surgical resection of lesions that are likely malignant.

The most common pancreatic cystic lesions are pseudocysts [10]. Although cystic neoplasms and pseudocysts can mimic each other on imaging [28], a clinical history of pancreatitis with laboratory findings (elevated amylase or lipase) and/or imaging evidence of pancreatic and peripancreatic inflammation, atrophy, or ductal calcification may allow the diagnosis of a cystic lesion as a pseudocyst [5,10,11,14,32].

Serous cystic tumors will cause symptoms owing to enlargement and impingement on other structures [60–62]. Cysts that are <4 cm are likely to cause symptoms, including abdominal discomfort, a palpable mass, and common bile duct and/or viscous outlet obstruction [64], and be found on physical examination [63]. MCNs can present with abdominal pain, continuous pancreatitis, internal organ outlet obstruction, and/or a palpable mass [64]. Jaundice and/or weight loss are more common with malignant lesions. IPMNs are asymptomatic. However,

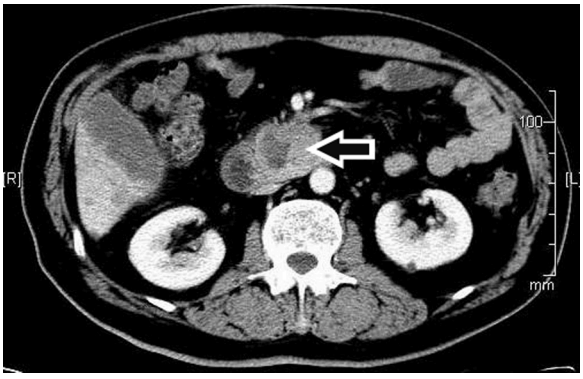

Fig. 1. PADC in the head of the pancreas with a solid component within a cystic lesion (arrow), lobulated shape, thick cystic walls, and asymmetric homogeneity in the head of the pancreas.

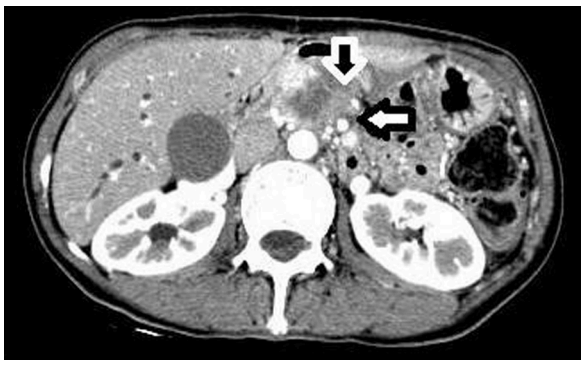

Fig. 2. PADC in the head and neck of the pancreas with an unclear border (White arrow) and a solid component (Black arrow) in the head and neck of the pancreas.

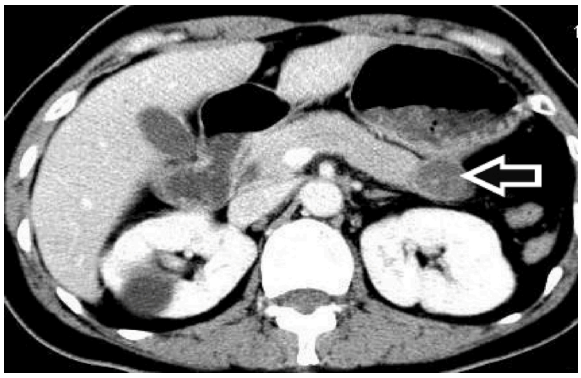

Fig. 3. Solid pseudopapillary tumor with a lobulated cystic lesion (Arrow) containing septation and asymmetrical homogeneity in the body of the pancreas.

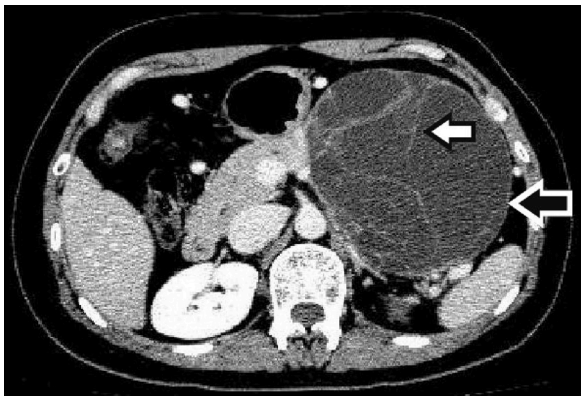

Fig. 4. Pancreatic MCA with the absence of a solid component, presence of septation (White arrow), an oval or round shape, clear borders (Black arrow), and a thin cystic wall in the tail of the pancreas.

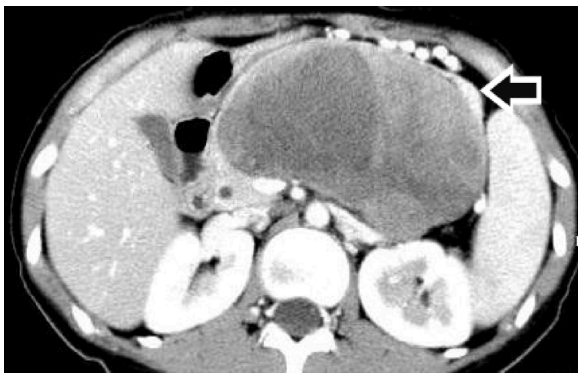

Fig. 5. PADC with atrophy of the pancreas (Arrow), wall enhancement, and septation with a solid component and clear border in the head of the pancreas.

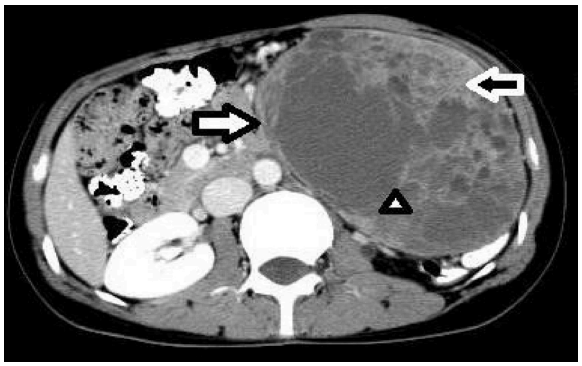

Fig. 6. Pancreatic solid pseudopapillary tumor with a clear border and a cystic lesion (black arrow) with oval or round shape and septation (asterisk). There is a solid component (white arrow) within the tail of the pancreas.

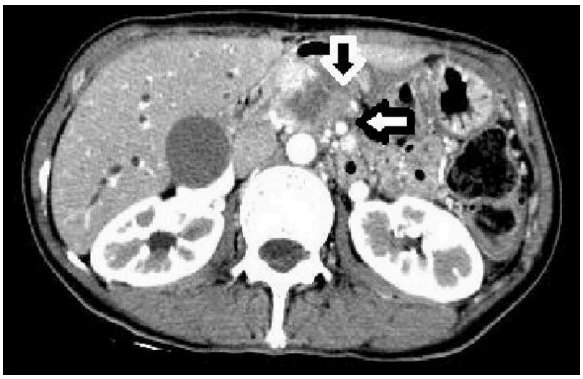

Fig. 7. Pancreatic ductal adenocarcinoma with an unclear border of a cystic lesion (black arrow) and no septation, and a solid component (white arrow) within the head of the pancreas.

some patients have a long history of repeated acute or chronic erythema from intermittent obstruction of the pancreatic duct with mucus plugs. Previously, >80 % of patients with solid pseudopapillary neoplasms (SPNs) were symptomatic. However, incidental detection of SPNs is increasing with the widespread use of cross-sectional imaging, which currently accounts for up to 50 % of cases [65]. The most common symptom is abdominal pain, followed by nausea, vomiting, and weight loss [65].

This study included 53 patients with pancreatic cystic lesions [Table 1]; 47 had physical symptoms on examination and among them, 23 had benign and 24 had premalignant or malignant cysts. Seven

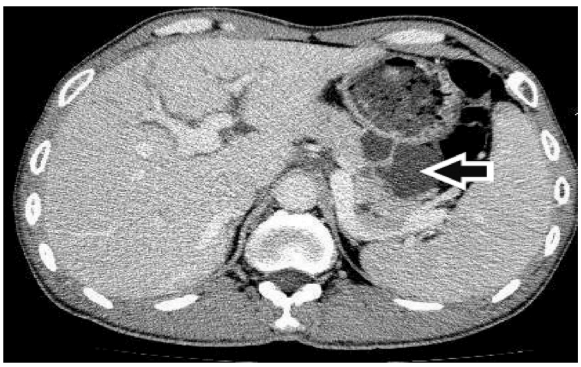

Fig. 8. SCA of the pancreas with uniform homogeneity (black arrow), a lobulated shape, and septation in the tail of the pancreas.

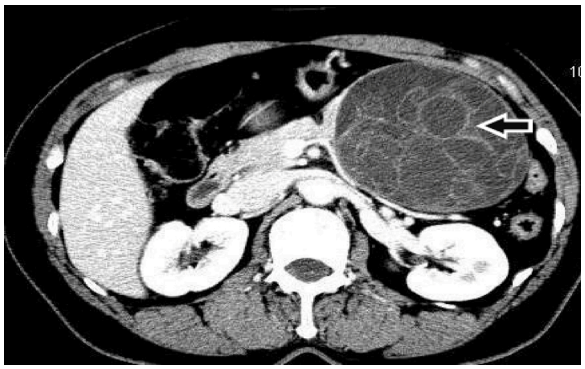

Fig. 9. Pancreatic MCA with septation (arrow), lack of solid component, thin cystic walls, and a clear border in the tail of the pancreas.

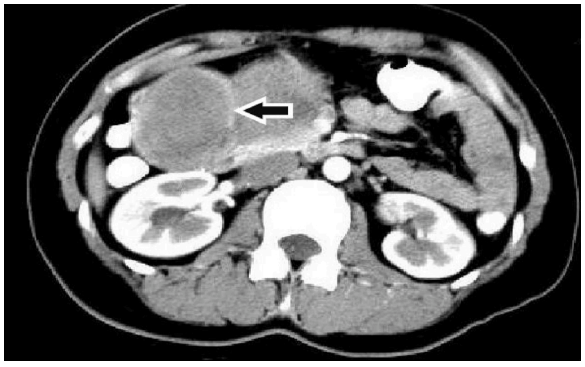

Fig. 10. Pancreatic solid pseudopapillary tumor with wall enhancement (arrow), a lobulated shape, and thin cystic walls in the tail of the pancreas.

displayed abdominal discomfort and pain, and 15 had other physical symptoms that were present before the preoperative examination, including gallstones and abdominal masses. Clinical examination was not particularly useful; imaging studies were more helpful in differentiating and characterizing pancreatic lesions.

4.2. Age and sex

In this outpatient population, the prevalence of unsuspected pancreatic cysts identified on 16-MDCT was 2.6 %. Cyst presence was strongly correlated with increasing age and Asian race [55]. We assessed 53 patients with 26 benign cysts [Table 2,3] (age range, 19–76 years; mean 52 years; 12 men and 15 women) and 27 premalignant or malignant cysts (age range 13–71 years; mean 46 years; six men and 20

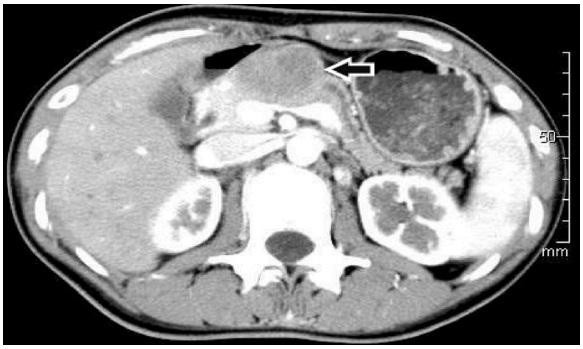

Fig. 11. Pancreatic solid pseudopapillary tumor with wall enhancement (arrow), an oval or round shape, thick cystic walls, and a solid component in the neck of the pancreas.

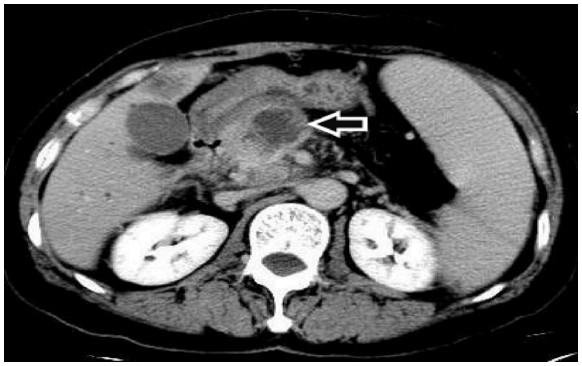

Fig. 12. Head of the pancreas, Pancreatic ductal carcinoma with thick cystic walls (arrow) and a lobulated shape in the body of pancreas.

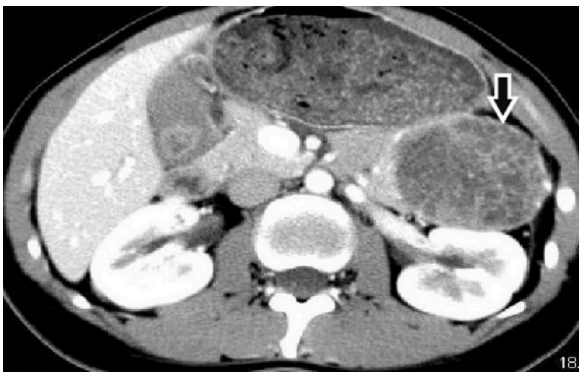

Fig. 13. Pancreatic SCA with an oval or round lobulated shape (arrow) in the tail of pancreas.

women). The risk of developing pancreatic lesions increased with age, and lesions mostly developed in women.

4.3. Principles of management

Patients with cystic pancreatic lesions tend to survive a long time, resulting in changes in their management. This contrasts with patients with pancreatic adenocarcinoma, where an aggressive approach, including surgical resection, is usually recommended [50].

Resection of all cystic lesions would be inappropriate because over one-third of them are identified incidentally [33]. Adopting this policy would lead to the resection of innocuous benign lesions, along with some potentially malignant mucin-producing cystic neoplasms, and unnecessarily subject patients to the risks associated with aggressive pancreatic surgery. However, surgical resections are indicated for most symptomatic patients [33]. Other factors influencing the choice of treatment include the tumor's histological features, the patient's age and surgical risk, and tumor size and location.

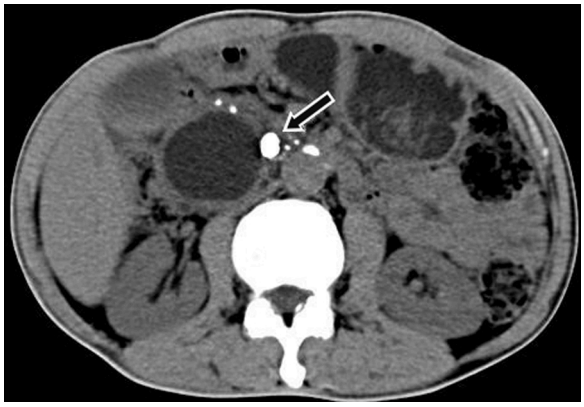

Fig. 14. Pancreatic SCA in the head of the pancreas with thin-walled cystic lesions, a clear border, small nodular calcifications (arrow), and no solid component.

Table 1
Symptoms associated with pancreatic cystic lesions.

Clinical Symptoms	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Present	23 (85.2)	24 (92.3)	47	0.67**	0.67
None	4 (14.8)	2 (7.7)	6		

4.4. Size

Fernandez-del Castillo et al. [56] recommend that patients with incidental pancreatic cystic lesions <2 cm should be observed, whereas those with cystic lesions >2 cm should be managed according to age, with young and middle-aged patients undergoing resection. In this study, the maximum dimension of benign cysts ranged [Tables 4,5] from 3.7–26 cm (IQR, 5.0–8.7 cm), similar to premalignant or malignant cysts, which ranged from 2.8–11.9 cm (IQR5.4–8.9 cm).

4.5. Location

An SPN located in the pancreatic tail may suggest malignancy [41], and serous cystadenomas and benign MCNs are more likely to be found in the body or tail [42–44]. We found premalignant or malignant cysts more frequently in the head and body [Table 6], whereas benign cysts were equally distributed throughout the pancreas.

4.6. Shape

Kim et al. have reported that lesion shape is a significant CT feature [58] for differentiating benign from premalignant or malignant macrocystic pancreatic lesions [58]. However, in this study [Table 7], there

Table 2
Patient age.

Age Sex	Benign Mean ± SD, N (%)	Premalignant or Malignant Mean ± SD, N (%)	Total	t/χ^2	p
Male	51.7 ± 16.0	45.9 ± 16.3	48.9 ± 16.2	1.30	0.2
Female	12 (44.4)	6 (23.1)	18	2.69	0.10
	15 (55.6)	20 (76.9)	35		

Table 3
Comparison of cystic lesions by age.

Age (Years)	Benign	Premalignant or Malignant	t/χ^2	p
	51.7 ± 15.99	45.92 ± 16.28	1.30	0.2

Table 4
Lesion size.

Size (mm)	Benign (range)	Premalignant or Malignant (range)	Total	t/χ^2	p
	79 (50–87)	76 (54–89)	77 (50–88)	−0.34*	0.73

were nine oval or round and 18 lobulated benign cysts, which was similar to the nine oval and 17 lobulated premalignant or malignant cysts.

4.7. Cyst wall thickness and enhancement

Previous studies have found cyst wall thickness to be a significant CT feature for differentiating benign from malignant lesions. However, mucinous cystic tumors have often been misdiagnosed as pseudocysts [34,16], and to a lesser extent, benign lesions have been misdiagnosed as microcystic adenomas or other tumors [10,32,29,66]. The most serious problem is misdiagnosing a mucinous cystic tumor as a benign microcystic adenoma. We have encountered several patients with mucinous tumors who had a nondescript small cystic pancreatic lesion but underwent surgery because there was no history of pancreatitis that might have led to pseudocysts. Some previous studies have noted that benign cysts, including macrocystic SCAs, had a thin wall 0.1 cm in thickness [38,39], and no predominant enhancement of this wall was noted [7,9]. In our study, [Table 8] we often found the wall of benign cysts to be almost imperceptible (≤2 mm in diameter) compared to premalignant or malignant cysts, which were thick-walled on thin-section CT.

The lack of cyst wall enhancement of pancreatic neoplasms indicates SCA [7]. We observed wall enhancement most commonly in premalignant or malignant cysts [Table 9]. This may be a helpful CT feature for differentiation.

4.8. Septation

The presence of septation has been reported as useful for predicting malignancy on MSCT [16]. In our study, [Table 10] septation was a common CT feature among benign cysts and unusual in premalignant or malignant lesions.

Table 5
Size comparison of lesions.

Benign	Premalignant or Malignant	t/χ^2	p
7.9 (5.0–8.7)	7.6 (5.4–8.9)	−0.34*	0.73

Table 6
Location of lesions.

Location	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Head	8 (29.6)	13 (50.0)	21	10.94**	<0.01
Body	6 (22.2)	11 (42.3)	17		
Tail	8 (29.6)	2 (7.7)	10		
Throughout	5 (18.5)	0 (0)	5		

Table 7
Lesion shape on CT.

Shape	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Oval / Round	9 (33.3)	9 (34.6)	18	0.01	0.92
Lobulated	18 (66.7)	17 (65.4)	35		

Table 8
Cystic wall CT features.

Cystic wall	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Thick	10 (37.0)	21 (80.8)	31	10.43	<0.01
Thin	17 (63.0)	5 (19.2)	22		

4.9. Homogeneity

Homogeneity is not useful for differentiating benign from malignant lesions [58]. However, we frequently found uniform homogeneity in benign cysts and asymmetrical homogeneity in premalignant or malignant cysts. Thus, uniform homogeneity may be helpful for differentiation [Table 11]

4.10. Calcification

Wall calcification has been found more frequently in serous cystic tumors than mucinous cystadenomas [34,29]. Similarly, this study found nine cases with calcification—six benign and three malignant or premalignant [Table 12].

4.11. Pancreatic atrophy and duct dilatation

A prior study reported no difference in the presence of pancreatic atrophy between benign and malignant lesions [45]. We found pancreatic atrophy to be more common in benign cysts [Table 14], which may help with differentiation.

Yoshihiko et al. reported that bulging papilloma was observed more often in malignant lesions [58], whereas Kimura et al. reported that some IPMTs are not malignant and can be simply followed up [59]. Our study found seven (25.9 %) benign lesions causing dilation of the pancreatic duct, whereas eight (30.8 %) premalignant or malignant lesions caused dilatation [Table 15]. Thus, this is not a useful feature for differentiating lesions. However, our study only included a limited number of patients and the findings must be validated by larger studies.

Table 9
Wall enhancement on CT.

Wall enhancement	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Yes	20 (74.1)	26 (100)	46	7.76	0.01
No	7 (25.9)	0 (0)	7		

Table 10
Septation on CT.

Septation	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Yes	20 (74.1)	7 (26.9)	27	11.78	<0.01
No	7 (25.9)	19 (73.1)	26		

Table 11
Homogeneity on CT.

Homogeneity	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Asymmetric	15 (55.6)	24 (92.3)	39	9.20	<0.01
Uniform	12 (44.4)	2 (7.7)	14		

Table 12
Calcification on CT.

Calcification	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Yes	6 (22.2)	3 (11.5)	9	1.07**	0.47
No	21 (77.8)	23 (88.5)	44		

4.12. Border

Clear borders [Table 16] were significantly more common in benign cysts, which may help with differentiation [Table 17].

4.13. Solid component

A solid component within a pancreatic cyst is a strong indicator of malignancy [36,47]. This was confirmed in our study, where 96.2 % cysts with a solid component were either malignant or premalignant [Table 13].

In this study, septation and a solid component were the main CT features that could differentiate between lesions of the pancreas. Kim et al. noted that shape and wall thickness are significant in differentiation [57], and we believe that septation and a solid component may also aid in the differential diagnosis and management of these lesions before surgery.

Additionally, size, shape, calcification, and dilation of the pancreatic duct help differentiate benign from malignant cystic neoplasms [5,11,12,16,29,30]. Lesion, location, age, and sex may also be helpful distinguishing features [9,7,69].

4.14. Limitation and strengths

The strengths of this study were that the CT images were reviewed in a double-blind manner, with the radiologists unaware of the patients' clinical outcomes. Moreover, both radiologists had >5 years of experience in abdominal imaging, and they reviewed the images together.

This study has several limitations. Although the radiologists were blinded to the clinical outcomes, they were aware of the patients' sex and age. Additionally, this was a retrospective study, with imaging obtained over a period of 5 years from different hospitals with a relatively small sample size. Considering the small sample size, there may have been selection bias. Additionally, only CT images with optimal quality were included, which may have influenced the image parameters reported.

We only reviewed patients who underwent MDCT and had pathological confirmation of their lesion. The exclusion of cases without pathological confirmation may be an explanation for the paucity of pseudocysts in this report, although pseudocysts are the most abundant cystic lesion of the pancreas. Finally, the lack of established imaging criteria in the literature may have been a major factor for the poor to fair agreement between our study and prior studies.

Table 13
Solid components on CT.

Solid component	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Yes	13 (48.1)	25 (96.2)	38	15.04	<0.01
No	14 (51.9)	1 (3.8)	15		

Table 14
Pancreatic atrophy on CT.

Atrophy	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Yes	11 (40.7)	4 (15.4)	15	4.20	0.04
No	16 (59.3)	22 (84.6)	38		

Table 15
Dilatation of the Pancreatic Duct.

Pancreatic duct dilatation	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Yes	7 (25.9)	8 (30.8)	15	0.15	0.70
No	20 (74.1)	18 (69.2)	38		

Table 16
Border features on CT.

Border	Benign N (%)	Premalignant or Malignant N (%)	Total	t/χ^2	p
Clear	25 (92.6)	14 (53.8)	39	10.23	<0.01
Not Clear	2 (7.4)	12 (46.2)	14		

5. Conclusion

A solid component and septation are significant independent CT features for differentiating benign from premalignant and malignant pancreatic lesions. The absence of a solid component and presence of septation within cystic lesions are more frequently observed in benign pancreatic lesions, whereas a solid component without septation is more frequently observed in premalignant or malignant pancreatic lesions.

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Ethical statement for solid state ionics

This material is the authors' own original work, which has not been previously published elsewhere.

The paper is not currently being considered for publication elsewhere.

The paper reflects the authors' own research and analysis in a truthful and complete manner.

The paper properly credits the meaningful contributions of co-authors and co-researchers.

The results are appropriately placed in the context of prior and

Table 17
Multivariate analysis of CT features (n = 53).

Multivariate analysis	β	S.E.	Wald	P	Exp. (B)	95% CI for Lower	EXP(B) Upper
Septation	2.27	0.77	8.64	<0.01	9.71	2.13	44.22
Solid Component	−3.52	1.19	8.80	<0.01	0.03	0	0.30
Constant	0.84	1.53	0.30	0.58	2.32		

existing research.

All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.

All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

Disclosures

There are no conflicts of interest to disclose.

Human rights statements and informed consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and its later amendments. Informed consent was obtained from all patients for being included in the study.

CRediT authorship contribution statement

RKY and JC designed the experiments. RKY, XJ, LL, and LZ executed the experiments and analysis. RKY and JC wrote the manuscript.

Declaration of Competing Interest

The authors have no potential conflict of interest.

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