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Pancreatic cystic neoplasms and post-inflammatory cysts: interobserver agreement and diagnostic performance of MRI with MRCP

Temel Tirkes[1], **Aashish A. Patel**[1], **Bilal Tahir**[1], **Rachel C. Kim**[2], **C. Max Schmidt**[2], **Fatih M. Akisik**[1]

[1]Department of Radiology and Imaging Sciences, Indiana University School of Medicine, 550 N. University Blvd UH 0663, Indianapolis, IN 46202, USA

[2]Department of Surgery, Indiana University School of Medicine, Indianapolis, IN, USA

Abstract

Purpose—We aimed to answer several clinically relevant questions; (1) the interobserver agreement, (2) diagnostic performance of MRI with MRCP for (a) branch duct intraductal papillary mucinous neoplasms (BD-IPMN), mucinous cystic neoplasms (MCN) and serous cystic neoplasms (SCN), (b) distinguishing mucinous (BD-IPMN and MCN) from non-mucinous cysts, and (c) distinguishing three pancreatic cystic neoplasms (PCN) from post-inflammatory cysts (PIC).

Methods—A retrospective analysis was performed at a tertiary referral center for pancreatic diseases on 71 patients including 44 PCNs and 27 PICs. All PCNs were confirmed by surgical pathology to be 17 BD-IPMNs, 13 MCNs, and 14 SCNs. Main duct and mixed type IPMNs were excluded. Two experienced abdominal radiologists blindly reviewed all the images.

Results—Sensitivity of two radiologists for BD-IPMN, MCN and SCN was 88–94%, 62–69% and 57–64%, specificity of 67–78%, 67–78% and 67–78%, and accuracy of 77–82%, 65–75% and 63–73%, respectively. There was 80% sensitivity, 63–73% specificity, 70–76% accuracy for distinguishing mucinous from non-mucinous neoplasms, and 73–75% sensitivity, 67–78% specificity, 70–76% accuracy for distinguishing all PCNs from PICs. There was moderate-to-substantial interobserver agreement (Cohen's kappa: 0.65).

Conclusion—Two experienced abdominal radiologists had moderate-to-high sensitivity, specificity, and accuracy for BD-IPMN, MCN, and SCN. The interobserver agreement was moderate-to-substantial. MRI with MRCP can help workup of incidental pancreatic cysts by distinguishing PCNs from PICs, and premalignant mucinous neoplasms from cysts with no malignant potential.

✉Temel Tirkes, atirkes@iupui.edu.

Conflicts of interest All authors declared that they have no conflict of interest.

Ethical approval A waiver status was obtained from the institutional review board.

Keywords

Pancreas; Cyst; Magnetic resonance imaging; Magnetic Resonance Cholangiopancreatography

Introduction

The high incidence of pancreatic cysts detected by cross-sectional imaging poses a challenge to radiologists and clinicians considering appropriate management. The prevalence of incidental pancreatic cysts has been reported to be 2.3% for multi-detector computerized tomography (MDCT) [1] and 19% for magnetic resonance imaging (MRI) studies [2]. Cystic lesions of the pancreas constitute a diverse category of abnormalities that can be malignant, precancerous, benign, or post-inflammatory in origin [3]. Together with the increased detection rates, the number of pancreatectomies for pancreatic cysts has also increased by 189% since 2006 [4]. However, a significant portion of PCNs are low-grade indolent neoplasms [5]. With the correct diagnosis, these cysts may be safely managed at least initially with surveillance and avoid repetitive invasive tests and surgery [6, 7]. Final recommendations to the patient are optimally made by an interdisciplinary team consisting of abdominal radiologists, pancreatologists, and pancreatic surgeons.

MRI with MR cholangiopancreatography (MRCP) is favored over CT for evaluation and follow-up of pancreatic cystic neoplasms (PCNs) [8, 9] due to higher soft tissue contrast and sensitivity for delineating connections of pancreatic cysts with the main pancreatic duct [10–12]. As these cysts are most often detected by cross-sectional imaging, a radiologists' level of confidence in the diagnosis plays a vital role. In the absence of high-risk stigmata and worrisome features [13, 14], radiologists recommend surveillance for incidentally found cysts [7]. On the other hand, the presence of these features should trigger an endoscopic evaluation with fine-needle aspiration for cytology, biochemical and DNA markers [7]. Radiologists should be aware that, even with the highest quality images, features of different pancreatic cysts can overlap, and distinguishing PCNs from other cysts is challenging. As a non-mucinous cyst, serous cystic neoplasm (SCN) is almost never malignant, and post-inflammatory cyst (PIC) is always benign. In contrast, mucinous neoplasms (mucinous cystic neoplasm [MCN] and intraductal papillary mucinous neoplasm [IPMN]) carry a variable (low to high) degree of potential for malignancy [3, 15]. Mucinous neoplasms should be identified and undergo a more aggressive workup. The cross-sectional imaging features of pancreatic cysts and differential diagnosis have been reported in the literature [15–17]. To the best of our knowledge this study presents the largest MRI/MRCP comparative case population that is confirmed with surgical pathology. We aimed to answer several clinically relevant questions; (a) the interobserver agreement, (b) performance of MRI/MRCP for diagnosis of PCNs (brand duct IPMN, MCN, and SCN), (c) performance of distinguishing mucinous (branch duct IPMN and MCN) from non-mucinous cysts, and (d) distinguishing PCNs from PIC.

Methods

Institutional review board approval was obtained for this retrospective analysis, and requirement for informed patient consent was waived. In our tertiary referral center for pancreatic diseases, we searched the electronic pathology archives to identify PCNs and PICs between 2010 and 2019. Inclusion criteria were to consecutively select the adult patients who had pre-operative abdominal MRI/MRCP within three months of the pancreatic surgery and were found to have MCN, SCN, BD-IPMN or PIC. PICs were confirmed either by surgical pathology or spontaneous regression on follow-up studies. Our study focused on parenchymal cysts; therefore, exclusion criteria included presence of main duct and mixed type IPMNs and acute pancreatitis which was determined by checking clinical history and serum pancreatic enzyme levels.

Examinations were performed on either a 1.5 T or 3.0 T MR scanner in the same institution using the same imaging protocol. Details of our institutional imaging parameters can be found in a recent publication [18]. Per protocol, all patients were fasting for 4 h before the examination. Two patients who had MCN and PIC did not receive intravenous contrast agent due to pregnancy and poor renal function. The post-contrast phase was performed using the manufacturer recommended dosage (0.1 mM/kg) of gadobenate dimeglu-mine (MultiHance®, Monroe Township, NJ, USA) and the images were obtained at arterial, venous and 5-min delayed phases. Secretin (ChiRhoStim®, ChiRhoClin, Inc, Burton-sville, MD) was utilized in 59 MRCP examinations.

Two abdominal radiologists with 13 and 15 years of experience reviewed MRI and MRCP images using a third-party DICOM viewer (OsiriX, Pixmeo, Switzerland). Readers were blinded to the clinical information, and all patient health identifiers were removed from the images. Each reader recorded number, location, size, shape, structure, border, internal debris, septations, enhancing soft tissue component of the cysts, and associated pancreatic duct dilation. The presence of a ductal connection between the cyst and the main pancreatic duct was assessed on both thick slab MRCP and S-MRCP, by a rating scale of “No”, “Possibly”, “Probably” and “Definitely”. Finally, readers made a final diagnosis of BD-IPMN, MCN, SCN or PIC.

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rates were calculated using MedCalc software (MedCalc Software Ltd, Belgium). Cohen’s kappa coefficient was used to evaluate the interobserver agreement.

Results

The average age of patients was 54 years (range 20–84). There were 24 males and 47 females. All 14 branch duct IPMN (BD-IPMN) (3 high-grade, 3 intermediate-grade, and 11 low-grade), 13 MCN (1 intermediate-grade and 12 low-grade) and 14 SCN were confirmed with surgical pathology. The interobserver agreement between the two readers was moderate-to-substantial (Cohen’s kappa: 0.65). Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for both readers are listed in Table 1. Readers’ accuracy for BD-IPMN, MCN, and SCN was 77–82%, 65–75%, and 63–73%. The accuracy

for distinguishing mucinous from non-mucinous neoplasms and all PCNs from PICs was both 70–76%. Morphologic features of pancreatic cysts are summarized in Table 2.

Discussion

Morphologic features of the PCNs can be summarized in four categories: unilocular, polycystic microcystic, oligocystic macrocystic, and cysts with a solid component [15]. Although a few publications have described the findings of the pancreatic cysts by CT, reports of MRI/MRCP findings are scarce. This study aimed to determine the interobserver agreement, performance of MRI/MRCP for diagnosis of PCNs, distinguish precancerous mucinous (BD-IPMN and MCN) from non-mucinous cysts and distinguish all PCNs from PIC. We evaluated 44 PCNs together with 27 PICs. Before this, the largest population comparative study reported MRI imaging features in 18 PCNs [19]. The remainder of the MRI/MRCP publications were review articles.

IPMNs arise from the pancreatic ductal epithelium and produce mucin that results in dilatation of the main pancreatic duct or secondary branch ducts. IPMN is considered a multifocal disease, unlike other cystic neoplasms [12]. In fact, multifocality in and of itself is almost diagnostic of BD-IPMN. In our study, readers had higher sensitivity, specificity and accuracy for BD-IPMN (AUC 0.80–0.83) compared to MCN (AUC 0.64–0.73) and SCN (AUC 0.62–0.71). These cysts favored the head but could be seen anywhere in the gland. BD-IPMNs appeared as well-defined cysts without a visible capsule, contours were mostly lobulated (grape-like) or ovoid, septations were not common but may be enhancing if present. A distinctive feature for BD-IPMN is the presence of the branch duct's communication with the main pancreatic duct, although the absence of this finding would not exclude the diagnosis [15, 20, 21]. In this regard, MRCP is considered superior to CT since the direct connection is seen in 73% by MRCP but only 18% by CT studies [12]. The MRCP with secretin (S-MRCP) is regarded as a refinement of MRCP in which the secretin effect can improve visualization of the pancreatic ducts, including the branch ducts [20, 22, 23]. In this study, readers' confidence level to diagnose BD-IPMN increased from "Probably" to "Definitely" in 12% of cases by S-MRCP. This was due to better visualization of the connecting branch duct (Fig. 1). This result is in concordance with the prior publications suggesting that S-MRCP facilitated the depiction of the connection between the BD-IPMN and pancreatic ducts [20, 24].

MCNs have a thickened wall underlined by a mucin-producing columnar epithelium, and the surrounding tissue is characterized by the presence of ovarian-type stroma [25]. In our study, these cysts were predominantly found in females, exclusively solitary and encapsulated, primarily round, favoring the tail, and septations were less common than SCNs. MCNs were the largest cysts in this study, with an average size of 5.5 cm (range 1.5–20 cm). Our readers were moderately sensitive, specific, and accurate for MCN, likely due to overlapping imaging features. A few of these cysts showed non-enhancing internal nodularity, which could be confused with internal debris seen in PICs. This overlapping imaging feature probably led to MCNs being misdiagnosed as PICs in our study (Fig. 2).

SCNs are lined by a simple, glycogen-rich cuboidal epithelium. These neoplasms are usually small and microcystic, but they may grow to be quite large. Partial pancreatic resection depending on the tumor's location is considered for symptomatic tumors larger than 4 cm in size [26]. In our study, SCNs were predominantly found in females (although may less commonly be found in males), located in the tail, appeared as a lobulated, solitary, well-defined cyst with no visible capsule. Two readers had moderate-to-high sensitivity, specificity and accuracy for SCN. Enhancement of multiple septa or enhancing "stellate" central scar can differentiate SCN from other neoplasms [27] but is only seen in 20–30% of the patients [28]. In agreement with prior reports, the enhancing central scar was not commonly seen in our study (21%) but was a distinguishing feature when present (Fig. 3). Septations seen with the polycystic pattern were more frequently enhancing compared to other cysts. MRI with contrast is thought to be more sensitive to show septal and nodular enhancement than CT due to its superior soft tissue contrast on T2-weighted images and utilization of fat-suppression technique on dynamic post-contrast T1-weighted series [29, 30]. This notion is particularly true when the microcystic variant of SCN is small enough to appear as a solid mass on CT.

Mucinous cysts (IPMN and MCN) are considered premalignant and carry a low, intermediate, or high malignant potential. The malignant transformation from SCNs is exceedingly rare [31, 32], and many question whether this truly does occur. In general, SCN's polycystic variants have a characteristic appearance, and a definite diagnosis does not require a further invasive diagnostic procedure. The difficulty arises when SCN or PIC presents itself as a unilocular or macrocystic pattern mimicking other cysts [26]. In our study, readers were 80% sensitive, 63–73% specific, and 70–76% accurate for distinguishing mucinous neoplasms from SCN and PIC. Sainani et al. reported a slightly higher 79–82% accuracy for differentiating mucinous from non-mucinous cysts [33]. Another investigation including 5 SCNs and 20 BD-IPMNs, reported combining four CT/MRI features to be very helpful; the presence of five or more cysts, clustered small peripheral cysts, presence of cyst calcifications, and absence of communication with the main pancreatic duct [34]. Two or three of these imaging features helped to diagnose SCN with a sensitivity of 80–100% and specificity of 85–100%, respectively. If MDCT was used as the imaging modality, the accuracy for stratifying lesions into mucinous and non-mucinous subtypes was reported to be up to 85% [35].

PIC is the most common pancreatic cyst [36] and therefore the initial consideration for an incidental pancreatic cyst should be directed toward exclusion of a PIC. PICs have no epithelialized wall; however, the cyst's periphery evolves from an inflammatory process toward a granular and fibrotic tissue that corresponds to the T2 hypointense border seen on MR imaging. After 4–6 weeks of evolution, subacute or chronic PICs may be confused with PCNs due to overlapping imaging characteristics. All the PICs in our study were selected explicitly in the mature stage; therefore, they appeared well-formed with a fibrous wall 75% of the time. Despite this confounding (real-life) scenario, our readers were 73–75% sensitive, 67–78% specific, and 70–76% accurate in distinguishing PIC from PCNs. They were primarily solitary, ovoid/round, commonly showed internal debris, but very few septations.

Interobserver agreement was moderate-to-substantial (Cohen's kappa of 0.65). This is lower than a study including 30 patients reported interobserver agreement to be good to perfect (kappa of 0.70 to 1.0) [37]. A less than satisfactory agreement is probably due to overlapping imaging features and including PICs to present a more real-life scenario to the readers. One example of overlapping features is that BD-IPMN, SCN, and MCN can present as unilocular cysts [15, 38]. We encountered unilocular presentation in 59% of BD-IPMN, 92% of MCN, 96% of PIC and 7% of SCN.

Herein, we present an MRI/MRCP study with the highest case population. Our study was limited by not including an equal proportion of low, intermediate, or high-grade neoplasms. The intermediate and high-grade mucinous lesions present with more aggressive features, therefore undergo surgery without a need for further evaluation by MRI/MRCP. Our study focused on parenchymal cysts; therefore, main duct type IPMNs were excluded from the analysis. We included three types of neoplasms: SCN, MCN, and IPMNs, which account for 90% of all primary cystic pancreatic neoplasms [3]. We refrained from discussing the incidence of age, sex, and other demographics as these can be quite helpful in improving the prediction accuracy regardless of imaging and have been previously reported in larger population studies [21].

In conclusion, MRI/MRCP is a helpful imaging modality with moderate-to-high sensitivity, specificity and accuracy for cystic pancreatic neoplasms. In the hands of experienced abdominal radiologists, MRI/MRCP can change clinical management by distinguishing post-inflammatory cysts from cystic neoplasms and premalignant mucinous cysts from non-malignant cysts. Interobserver variability is moderate-to-substantial.

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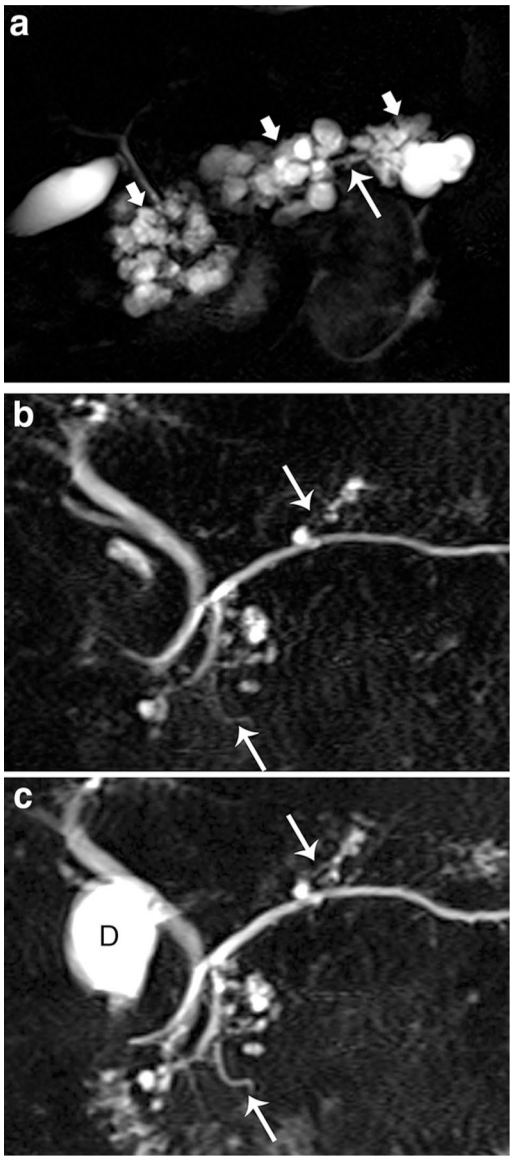

Fig. 1.

Branch duct type intraductal papillary mucinous neoplasm (BD-IPMN). **a** This is a coronal thick slab MRCP image of a 48-year-old female. The pancreas has multiple, clustered cysts throughout the head, body, and tail (thick arrows). The main pancreatic duct is not dilated (long arrow). **b** This is a coronal MRCP image of a 68-year-old male. There are scattered tubular structures in the head and body (arrows). It is not clear if the cyst in the body is communicating with the main pancreatic duct. **c** S-MRCP was also performed on the same patient. Secretin effect increased the diameter of these branch ducts, delineating the connection of the BD-IPMN with the main pancreatic duct. Excreated pancreatic fluid filled the first portion of the duodenum (D)

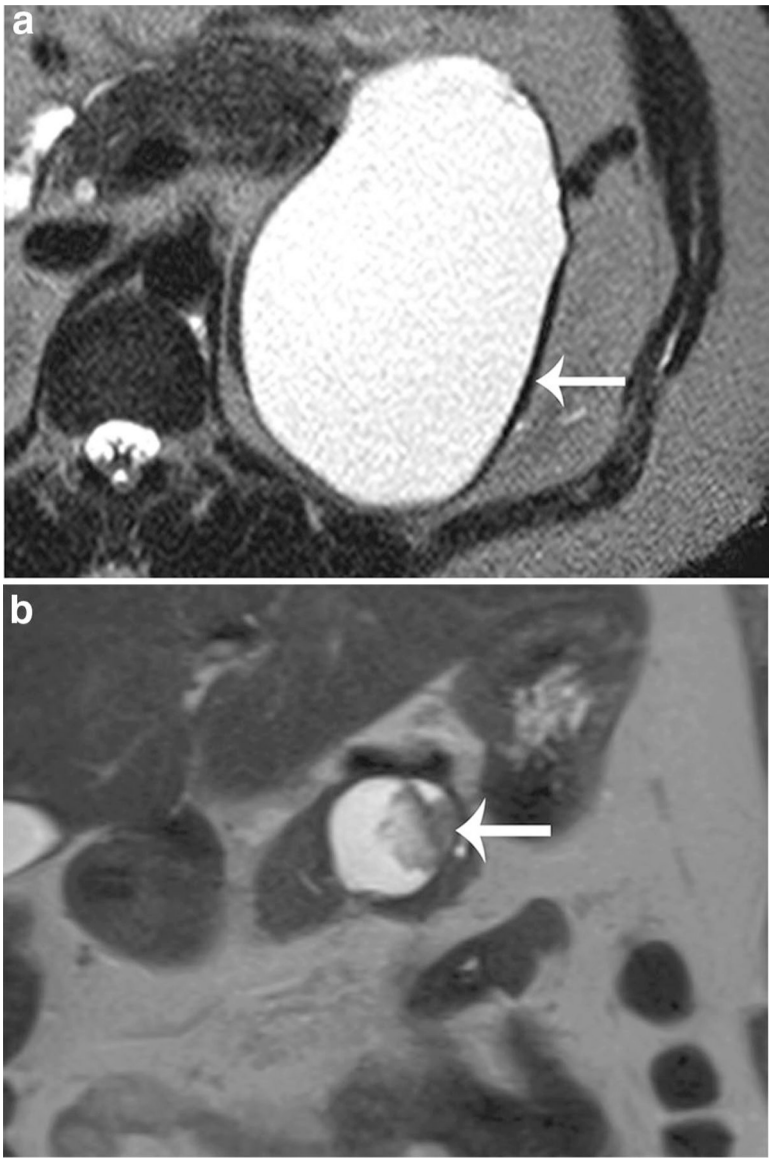

Fig. 2.

Mucinous cystic neoplasm (MCN) of the pancreas. **a** This is an axial T2-weighted image in a 42-year-old female. This unilocular 22 cm cyst arising from the pancreatic tail has a well-defined capsule (arrow). **b** A coronal T2-weighted image in a 46-year-old woman showing a unilocular, round, and well-defined MCN located in the body. Lobulated T2 hypointensity (arrow) was interpreted as debris leading to a misdiagnosis of PIC. This type of internal signal abnormality was seen in 38% of MCNs and 59% of PICs

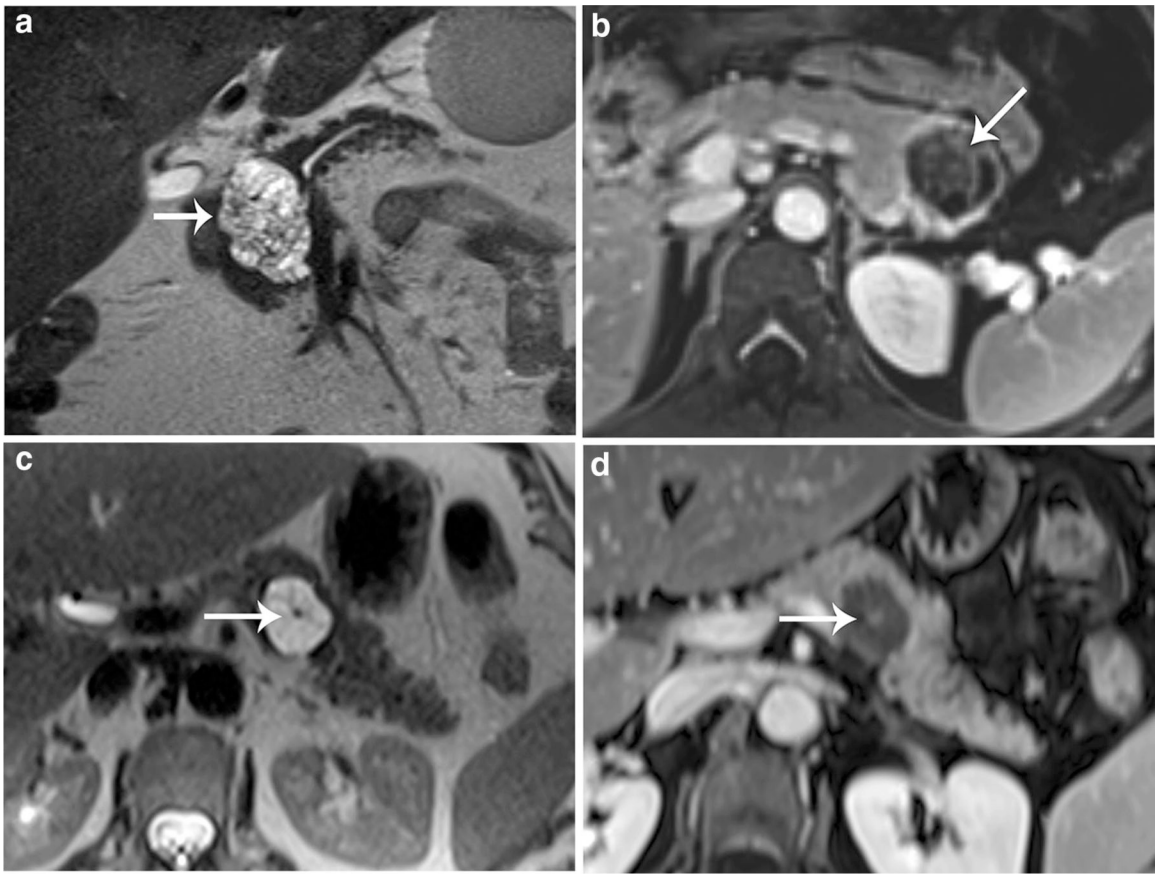

Fig. 3.

Serous cystic neoplasm (SCN) of the pancreas. **a** This coronal T2-weighted image in a 75-year-old male shows a well-circumscribed cyst with a polycystic microcystic architecture (arrow). **b** This is an axial T1-weighted fat-suppressed post-contrast image in a 55-year-old female presented with a SCN in the tail. This oligocystic macrocystic SCN shows septal enhancement (arrow), a common finding seen in 86% of our cases. **c** This is an axial T2-weighted image in a 62-year-old female with a SCN located in the pancreatic body. This cyst has a unique central hypoechoic nodule (arrow). **d** Axial post-contrast fat-suppressed T1-weighted image shows that this central nodule, i.e., the stellate scar, is enhancing

Table 1

Diagnostic performance of MRI/MRCP for cystic neoplasms, including distinguishing mucinous and non-mucinous lesions

	BD-IPMN ***n*** **= 17**		**MCN** ***n*** **= 13**		**SCN** ***n*** **= 14**		**Mucinous vs Non-mucinous Cysts** ***n*** **= 30 vs 41**		**All Neoplasms vs PIC** ***n*** **= 44 vs 27**	
Reader	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**
Sensitivity	94% (71–100)	88% (63–98)	62% (32–86)	69% (39–91)	57% (29–82)	64% (35–87)	80% (61–92)	80% (61–92)	73% (57–85)	75% (60–87)
Specificity	67% (46–84)	78% (58–91)	67% (46–84)	78% (58–91)	67% (46–84)	78% (58–91)	63% (47–78)	73% (57–86)	67% (46–83)	78% (58–91)
AUC	0.80 (0.66–0.91)	0.83 (0.69–0.93)	0.64 (0.47–0.79)	0.73 (0.57–0.87)	0.62 (0.45–0.77)	0.71 (0.55–0.84)	0.72 (0.60–0.82)	0.77 (0.65–0.86)	0.70 (0.58–0.80)	0.76 (0.65–0.86)
Positive predictive value	64% (51–75)	71% (55–84)	47% (31–66)	60% (40–77)	47% (31–64)	60% (40–77)	62% (51–71)	69% (56–79)	78% (67–86)	85% (73–92)
Negative predictive value	95% (72–99)	91% (74–97)	78% (63–88)	84% (69–92)	75% (61–85)	81% (67–90)	81% (67–90)	83% (70–91)	60% (46–72)	66% (52–77)
Accuracy	77% (62–88)	82% (67–92)	65% (48–79)	75% (59–87)	63% (47–78)	73% (57–86)	70% (58–81)	76% (64–85)	70% (58–81)	76% (64–85)

Numbers in parenthesis are 95% confidence intervals

BD-IPMN branch duct type intraductal papillary mucinous neoplasm, *MCN* mucinous cystic neoplasm, *SCN* serous cystic neoplasm, *PIC* post-inflammatory cyst. Mucinous neoplasms include BD-IPMN and MCN. Non-mucinous neoplasms include SCN and PIC. All neoplasms group include BD-IPMN, MCN and SCN. *AUC* area under the curve

Table 2

Incidence of standard morphologic features of cystic pancreatic neoplasms observed by MRI/MRCP (consider including multiple or multifocal cysts as category to distinguish BD-IPMN from other PCLs

	BD-IPMN	MCN	SCN	PIC
n	17	13	14	27
Size (range)	2.5 cm (1–7)	5.5 cm (1.5–20)	3.6 cm (1.5–8.7)	4.3 cm (0.9–12)
Sex				
Male|Female	59 | 41	8 | 92	14 | 86	44 | 56
Age (mean)	64	45	49	56
Location				
Head	88%	8%	21%	26%
Body	65%	23%	29%	33%
Tail	59%	92%	57%	59%
Solitary cyst	35%	92%	79%	70%
Main duct dilatation (> 4 mm)	24%	–	–	4%
Internal debris	–	38%	–	59%
Border				
Well-defined (encapsulated)	12%	77%	7%	74%
Well-defined, but no visible capsule	88%	23%	93%	26%
Very irregular	–	–	–	–
Shape				
Ovoid	29%	15%	29%	52%
Round	–	69%	–	41%
Tubular	18%	–	–	4%
Lobulated (grape-like)	47%	8%	71%	–
Irregular	6%	–	–	4%
Structure				
Unilocular	59%	92%	7%	96%
Oligocystic and macrocystic	35%	–	79%	4%
Polycystic and microcystic	6%	–	14%	–
Septations				

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	BD-IPMN	MCN	SCN	PIC
Thin (< 2 mm)	24%	31%	57%	7%
Thick	–	2%	3%	2%
Enhancing	24%	17%	86%	8%
Nodular enhancement	–	8%	21%	–

BD-IPMN branch duct type intraductal papillary mucinous neoplasm, *MCN* mucinous cystic neoplasm, *SCN* serous cystic neoplasm, *PIC* post-inflammatory cyst