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MAGNETIC RESONANCE

Added value of apparent diffusion coefficient in distinguishing between serous and mucin-producing pancreatic cystic neoplasms

Pallavi Pandey[1] · Ankur Pandey[1] · Nannan Shao[1] · Farnaz Najmi Varzaneh[1] · Mounes Aliyari Ghasabeh[1] · Manijeh Zharghampour[1] · Pegah Khoshpouri[1] · Daniel Fouladi[1] · John Eng[1] · Anne Marie O'Broin-Lennon[2] · Marcia Canto[2] · Ralph H. Hruban[3] · Ihab R. Kamel[1]

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Abstract

Objectives To evaluate the added value of diffusion-weighted imaging (DWI) on MRI in differentiating serous from mucin-producing pancreatic cystic neoplasms (PCNs).

Methods One hundred seventeen patients with PCN measuring ≥ 10 mm were included. Three readers independently evaluated MRI with and without the use of apparent diffusion coefficient (ADC). Logistic regression was used to analyze whether confidence scores were different with the use of different image sets. Diagnostic performance with and without ADC was compared.

Results DWI/ADC improved confidence in 44.8%, 73.6%, and 78.2% of patients by the three readers in distinguishing serous from mucin-producing PCNs. The use of ADC increased the probability of a higher confidence in the differentiation as compared to morphological imaging for all three readers ($p < 0.001$). Odds ratio for increase in the diagnostic confidence with the use of ADC for the three readers with decreasing years of experience were 5.8, 6.8, and 12.7. The diagnostic accuracy of morphological MRI with ADC was higher than that without ADC for two of three readers with lesser experience (87.2% vs. 80.8%; 91.5% vs. 80.8%).

Conclusion DWI may have added value as a complementary tool to conventional morphological MRI in differentiating between serous and mucin-producing PCNs with possibly greater value for readers with less experience in reading abdominal MRI.

Key Points

- *Optimal management of PCNs requires differentiation of serous from mucin-producing PCNs.*
- *ADC measurements allow increased confidence in differentiating serous from mucin-producing PCNs.*
- *ADC measurements increase the accuracy in diagnosing serous versus mucin-producing PCNs.*

Keywords Magnetic resonance imaging · Diffusion MRI · Pancreas · Cysts · Mucin

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✉ Ihab R. Kamel
ikamel@jhmi.edu

[1] Russell H. Morgan Department of Radiology and Radiological Sciences, Central Radiology, Johns Hopkins University School of Medicine, 600 N Wolfe St, Room 143, Baltimore, MD 21287, USA

[2] Division of Gastroenterology, Johns Hopkins Medical Institutions, Baltimore, MD, USA

[3] Department of Pathology, Johns Hopkins Medical Institutions, 1550 Orleans Street, Baltimore, MD 21231, USA

Abbreviations

ADC	Apparent diffusion coefficient
BD-IPMN	Branch duct intraductal papillary mucinous neoplasm
CE-MRI	Contrast-enhanced magnetic resonance imaging
CT	Computed tomography
DWI	Diffusion-weighted imaging
FNA	Fine needle aspiration
FS	Fat saturation
GRE	Gradient echo
IPMN	Intraductal papillary mucinous neoplasm
MCN	Mucinous cystic neoplasm

MD-IPMN	Main duct intraductal papillary mucinous neoplasm
MRCP	Magnetic resonance cholangiopancreatography
MRI	Magnetic resonance imaging
PCN	Pancreatic cystic neoplasm
SCA	Serous cystadenoma
SD	Standard deviation

Introduction

Pancreatic cystic neoplasms (PCNs) including serous cystadenomas (SCAs) as well as mucin-producing PCNs (intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystic neoplasms (MCNs)) need careful imaging analysis for their characterization to allow optimal management strategy. SCAs are almost never malignant, and asymptomatic patients may only require surveillance [1, 2]. On the other hand, IPMNs and MCNs (mucin-producing PCNs) contribute to 80% of pancreatic cysts seen in multidisciplinary clinics [3]. Mucin-producing PCNs have a moderate to significant malignant potential. Resection is recommended for all surgically fit patients having MCN, main duct IPMN (MD-IPMN), or branch duct IPMN (BD-IPMN) associated with certain *high-risk stigmata* including obstructive jaundice with cystic lesion of the head of the pancreas, enhancing solid component within the cyst and main pancreatic duct > 10 mm in size, or certain *worrisome features* including cyst > 3 cm, thickened/enhancing cyst walls, main duct size 5–9 mm, non-enhancing mural nodule, and abrupt change in caliber of the pancreatic duct with distal pancreatic atrophy [4]. It is therefore important to differentiate among various types of PCNs. Magnetic resonance imaging (MRI) takes lead in definitive PCN characterization due to superior soft tissue contrast [5, 6]. While morphologic imaging is able to differentiate between these neoplasms in a majority of cases, significant overlap still exists among morphological imaging features [7–10] that prevents accurate characterization in a significant number of PCNs. Thus, a large number of PCNs detected at imaging remain indeterminate [11, 12] with limited preoperative diagnostic accuracy [13, 14] and thus may require the entire MRI toolkit including diffusion-weighted imaging (DWI).

DWI has been found useful to distinguish between different types of PCNs in difficult cases [15] and is quantifiable as apparent diffusion coefficient (ADC) maps [16]. A study from a high-volume center concluded that DWI is a helpful tool in distinguishing between mucin-producing and serous PCNs [17]. This study showed that an ADC of 3×10^{-3} mm^2/s resulted in correct classification of cysts in 77% to 81% of cases by three readers, with sensitivity and specificity ranging between 84 and 88% and between 66 and 72%, respectively, among the three readers. Previous studies, however, have not compared the performance of DWI with conventional morphological MRI alone, and the added value of DWI (over morphological imaging sequences) in differentiating between serous and mucin-producing PCNs remains unknown. Therefore, the purpose of our study was to evaluate the added value of DWI as a complementary tool to a routine morphological MRI protocol in differentiating between serous and mucin-producing PCNs.

Materials and methods

This was a retrospective study approved by our institutional review board and performed in compliance with the Health Insurance Portability and Accountability Act. Informed consent was waived.

Study population

We reviewed patients with PCNs measuring ≥ 10 mm who underwent MRI at our institution between July 2009 and September 2016. Out of the 307 identified patients, we selected patients with a complete MRI study including gadolinium administration and DWI/ADC mapping ($n = 201$). Of these, the diagnosis and type of PCN were confirmed in 117 patients on either histology following surgery ($n = 49$) or multidisciplinary pancreatic cyst clinic (MPCC) evaluation ($n = 68$). The MPCC dedicated exclusively to patients with pancreatic cysts was established at our institution in 2010 with the purpose of providing a comprehensive multispecialty evaluation for patients with pancreatic cysts, and its usefulness in the diagnosis and management of patients with pancreatic cysts has been shown in a previous study [3]. The MPCC evaluation is conducted on a weekly basis where patients are first assessed by a gastroenterologist and pancreatic surgeon. Each case is then presented at a multidisciplinary conference consisting of pancreatic surgeons, CT and MRI radiologists, pancreatic pathologists, a cytopathologist, and a gastroenterologist who is an expert pancreatic endosonographer. The patients' clinical history, imaging, endoscopic ultrasound, cytology, and cyst fluid analysis are reviewed. The CT/MRI images are reviewed by a pancreatic CT and MRI radiologist, while a cytopathologist presents any cases in which there is marked atypia or a suspicion of malignancy. A consensus diagnosis is made after a review of the imaging features, cyst fluid analysis, and cytology, and treatment recommendations are provided. The histological or multidisciplinary diagnosis was considered as reference. Thus, a total of 117 patients, 40 men (mean age, 70 ± 10 years; range, 40–87 years) and 77 women (mean age, 66 ± 13 years; range, 34–89 years) were included. Besides serous and mucin-producing PCNs, uncommon PCNs were also included so that readers consider these in their differential to simulate real-world scenario. Figure 1 shows a summary of the patient selection algorithm.

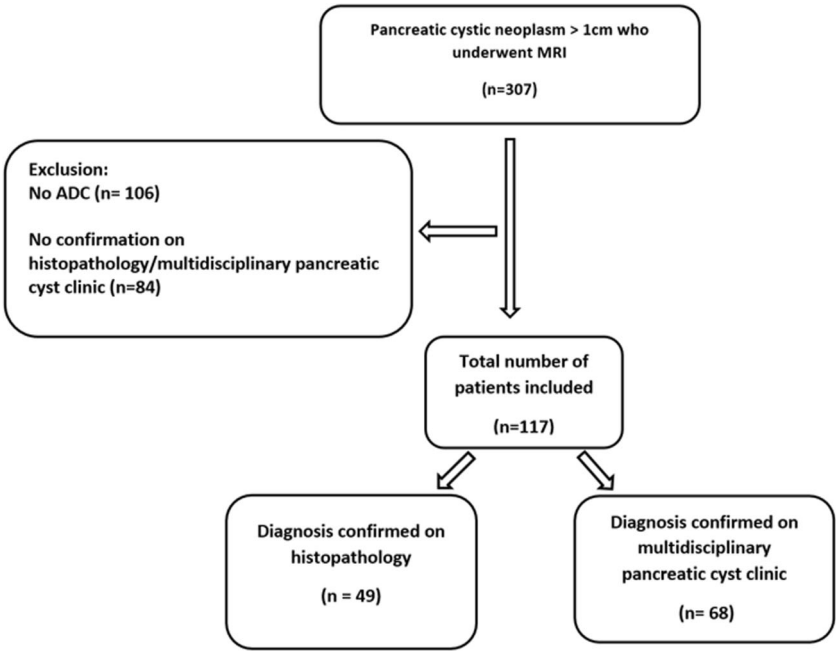

Fig. 1 Flow chart depicting the patient selection algorithm

MRI acquisition protocol and contrast

All MRI studies were performed on Siemens (Siemens Healthcare) 3-T Magnetom Trio Tim ($n = 52$) or 1.5-T Magnetom Avanto ($n = 65$) using a phased-array torso coil. The imaging protocol is summarized in Table 1.

Image analysis

Initially, one investigator not involved in the image analysis reviewed all the MRI studies to record the presence, number, and size of the PCNs in each study and recorded the index PCN (in cases with multiple cystic lesions) as the lesion with the largest diameter on axial image. Next, MRI studies were de-identified, including the age and gender, and were shuffled for a randomly ordered viewing list.

Three other radiologists with 20 years, 7 years, and 4 years of experience in reading abdominal MRI with specific interest and expertise in pancreatic cyst imaging, and blinded to clinical information/pathologic diagnosis, independently reviewed the MRI studies. Each reader evaluated the same index PCN in two stages, recording his/her diagnosis of the PCN type (SCA vs. mucin-producing vs. indeterminate) and the confidence in that diagnosis during each stage of image analysis. The first stage involved using a first image set including T2WI, T1WI, CE-T1WI, and magnetic resonance cholangiopancreatography (MRCP). The second stage of image analysis was performed 6 weeks later to minimize any recall bias. During this, a second image set including DWI

Table 1 MRI pulse sequences and the parameters used to perform imaging of the pancreas in the study

Technical parameters (Siemens, 1.5 T and 3 T)	Axial T2W turbo spin echo	T2W fast spin echo sequence (coronal 3-D MRCP)	DWI echo planar images[#]	Axial T1W 3-D FS-spoiled GRE unenhanced and CE-MRI*
Repetition time (TR) (ms)	3000	3000–4000	5000	4.77
Echo time (TE) (ms)	90	600–800	70	1.77
Section thickness (mm)	5	1	7	3
Intersection gap (mm)	2	1	2	NA
Matrix size	256 × 256	256 × 128	128 × 128	192 × 160
Receiver bandwidth (kHz)	32	NA	64	64
b value (s/mm^2)	NA	NA	50 and 750	NA

NA not available

[#] Acquired using breath-hold technique; number of averages, 1; and acquisition time, 15–30 s

*Twenty seconds (arterial), 70 s (portal venous), and 3 min (delayed) after intravenous contrast bolus (0.1 mmol/kg gadobutrol [Gadavist; Bayer HealthCare Pharmaceuticals])

with ADC map was utilized in addition to the first image set. The diagnosis of each PCN from the first stage of analysis but not the confidence rating in the diagnosis was made available to the readers during the second stage of analysis. This was done to allow assessment of any change in the confidence in the diagnosis made during the first stage. Based on the results of previous studies [17, 18], ADC values $< 2.8 \times 10^{-3}$ mm^2/s, 2.8–3.0 $\times 10^{-3}$ mm^2/s, and $\geq 3.0 \times 10^{-3}$ mm^2/s were considered as favoring a diagnosis of serous cyst, indeterminate PCN, and mucin-producing PCN, respectively. The MRI machines and MRI acquisition protocol used for pancreatic imaging in the study were the same as that used in the study by Pozzessere et al [17], and this further ensured the credibility of ADC cutoff values used in this study. All three readers were made aware of the ADC cutoff values and were free to utilize it in their process of making a diagnosis as well as recording confidence in that diagnosis. For consistency, all three readers had previously agreed by consensus upon the typical morphological imaging features favoring different types of PCNs as well as the ADC measurement technique using an elliptical region of interest (≥ 5 mm in diameter, covering the largest possible area of the cyst on the axial ADC map while avoiding cyst wall, as confirmed on T2WI and DWI-b50 images). The morphological imaging features of cyst considered by readers to be consistent with serous PCN included the following: (1) cluster of small cysts within the pancreas, (2) no visible ductal communication, (3) thin fibrous septa enhancing on delayed contrast-enhanced magnetic resonance imaging (CE-MRI), and (4) central scar. Features considered consistent with mucin-producing PCN (including BD-IPMN and MCN) included the following: (1) unilocular or mildly septate cystic lesion, (2) thickened walls with enhancement at delayed CE-MRI, (3) internal enhancing soft tissue, and (4) ductal communication. The degree of confidence in the diagnosis was scored on a 5-point scale: 1 (≤ 20%), 2 (> 20–≤ 40%), 3 (> 40–≤ 60%), 4 (> 60–≤ 80%), and 5 (> 80%). A confidence rating of 5 was given when at least two of the characteristic features of one PCN type were noted unequivocally; a rating of 4 was given when at least one of the characteristic features of one PCN type was noted unequivocally; a rating of 3 was given when at least two of the characteristic features of one PCN type along with a feature from another type was noted; ratings of 2 and 1 were given when one and two or more features were noted from both PCN types simultaneously within a cyst, respectively.

To assess the incremental role of ADC on the diagnostic accuracy, a sub-analysis was performed on the patients with pathology-proven diagnosis of serous and mucin-producing PCNs. Since the use of ADC in deciding the diagnosis of serous versus mucin-producing PCNs is not clinically established and the aim of the study was to evaluate its complementary role, it was decided for the sub-analysis to change the readers' initial morphological diagnosis based on the ADC cutoff only when the confidence rating for morphological diagnosis from the first stage of analysis was < 5.

Statistical analysis

An ordered logistic regression model was used to analyze whether confidence scores in diagnosing serous versus mucin-producing PCNs were different with the use of different image sets among the three readers. In our ordered logistic regression model, the ordinal dependent variable was the confidence score using each of the image sets while the independent variable was the image set used for each stage of analysis. For the sub-analysis of pathologically confirmed PCN subgroup, the correct diagnoses given before and after the use of ADC were tallied. Sensitivity, specificity, and diagnostic accuracy of morphology with and without DWI were calculated for each reader. The ADC reproducibility between 1.5 and 3-T MRI scanners was assessed using intraclass correlation coefficient (ICC) and the Bland-Altman analysis. For this, 15 PCNs with DWI and ADC mapping performed on both 1.5-T and 3-T scanners were analyzed. One reader performed ADC measurements on each of these 15 PCNs on both 1.5-T and 3-T MRI scanners. ICC was interpreted as follows: less than 0.40, poor; 0.40–0.59, fair; 0.60–0.74, good; and 0.75–1.00, excellent [19]. Stata (version 14) was used for statistical analyses. A p value < 0.05 was considered significant.

Results

Demographics and cyst characteristics

Table 2 shows the demographics and clinical information of the study cohort along with PCN characteristics. Fifty (42.7%) patients had solitary while 67 (57.3%) had multiple PCNs. The mean size of the analyzed lesions was 24 mm ± 13 mm (range, 10–70). Surgical resection (Whipple's or distal pancreatectomy) was carried out in 49 (42%) patients with the final histological diagnosis available. For the remaining 68 (58%) patients, the diagnosis of cyst type was confirmed at the MPCC evaluation combined with follow-up imaging (median, 33; range, 18–126 months). The reference diagnosis in the study cohort included SCA ($n = 33$), MCN ($n = 10$), IPMN ($n = 72$), lymphoepithelial cyst ($n = 1$), and solid pseudopapillary neoplasm ($n = 1$). Among 49 patients with pathology-proven diagnosis of PCNs, 8 were SCAs, 7 were MCNs, 32 were IPMNs, and 1 each was lymphoepithelial cyst and solid pseudopapillary neoplasm.

Table 2 Demographics and cyst characteristics

Characteristics	All cysts
Patients, *n*	117
Mean age (years)[a]	68 (34–89)
Gender (*n*)	
Female	77 (65.8)
Male	40 (34.2)
Ethnicity (*n*)	
White or Caucasian	96 (82.0)
African American or black	12 (10.3)
Other	8 (6.8)
Hispanic	1 (0.9)
Number of cysts (*n*)	
Solitary	50 (42.7)
Multiple	67 (57.3)
Mean size (mm)[a]	24 (10–70)
Location (*n*)	
Head	33 (28.2)
Uncinate process	14 (12)
Neck	2 (1.7)
Body	37 (31.6)
Tail	31 (26.5)
Reference diagnosis	
Serous cystadenoma	33 (28.2)
Mucinous cystic neoplasm	10 (8.6)
Intraductal papillary mucinous neoplasm	72 (61.5)
Lymphoepithelial cyst	1 (0.85)
Solid pseudopapillary neoplasm	1 (0.85)

Numbers in parentheses are percentages except where otherwise indicated

[a] Numbers in parentheses are range

Role of DWI/ADC in improving confidence in diagnosis

ADC reproducibility between 1.5 and 3-T scanners

The ICC between ADC measurements performed on 15 PCNs with DWI and ADC mapping on both 1.5-T and 3-T scanners (Figure 1-appendix) was 0.961 (95% CI, 0.892–0.987), suggesting excellent reproducibility of ADC measurements between the two magnet strengths. The Bland-Altman analysis revealed no significant bias between ADC measured on a 1.5-T scanner and that measured on a 3-T scanner (mean bias, -36.5×10^{-6} mm^2/s; $p = 0.317$ [Figure 2-appendix]).

For assessing the added value of ADC in increasing confidence in morphological diagnosis, 90 out of total 117 cases in which the measured ADC by all three readers was consistent with the reference diagnosis were evaluated. The remaining 27 cases were analyzed separately and are discussed later. In three of these 90 cases, radiologist/s diagnosis using T2WI, T1WI, CE-TIWI, and MRCP (first image set) did not match with reference diagnosis. Despite the ADC map (second image set) suggesting an alternate diagnosis, none of the readers changed their diagnosis or confidence level. Thus, improvement in confidence was amenable for assessment in 87 patients. The confidence scores in correctly distinguishing serous versus mucin-producing PCNs by the three readers during the first stage (using T2WI, T1WI, CE-T1WI, and MRCP) and the second stage (using an ADC map with the suggested ADC cutoff, in addition to T2WI, T1WI, CE-T1WI, and MRCP) of image analysis are shown in Table 3. The additional use of DWI/ADC allowed an increase in diagnostic confidence in 39 (44.8%), 64 (73.6%), and 68 (78.2%) patients by readers 1, 2, and 3, respectively, in distinguishing between serous and mucin-producing PCNs. Representative examples of such cysts are shown in Figs. 2, 3, and 4. Assessment of the incremental value with the use of ADC map in the form of confidence improvement for all three readers is shown in Table 4. None of the cases were diagnosed with a lower level of confidence score after utilizing DWI/ADC by any of the readers. Using the ordered logistic regression model, the use of ADC map was associated with a significant increase in the probability of a higher level of confidence in differentiating between serous and mucin-producing PCNs than only using T2WI + T1WI + CE-T1WI + MRCP for all three readers ($p < 0.001$). The corresponding odds ratios of increase in the level of diagnostic confidence with the use of ADC were 5.8 (95% CI, 3.4–9.8), 6.8 (95% CI, 3.6–13), and 12.7 (95% CI, 6.8–23.4) for the three readers, respectively.

As compared to the reference diagnosis, the overall accuracy of the ADC cutoff used was 76.9% for differentiating between serous and mucin-producing PCNs by all three readers.

In 27 cases, the measured ADC by all three readers suggested a diagnosis in discordance with the reference diagnosis. However, on review, 10 of these patients had fine needle aspiration (FNA) performed on the index cystic lesion prior to DWI. In three of these, MRI study with DWI performed prior to FNA was available and re-measurement of ADC values by one of the readers revealed concordance of ADC with the reference diagnosis when using the suggested ADC criteria. When patients with FNA ($n = 10$) prior to MRI were excluded, the overall accuracy of the used ADC cutoff improved from 76.9% (90/117) to 84.1% (90/107).

Role of DWI/ADC in improving diagnostic accuracy

The diagnostic performance of morphological MRI with and without DWI for the differentiation of serous PCNs ($n = 8$) from mucin-producing PCNs ($n = 39$) among the

Table 3 Confidence scores in correctly distinguishing serous versus mucin-producing PCNs in 87 out of 117 total cases by the three readers during two stages of image analysis

Confidence score in distinguishing serous versus mucin-producing PCNs*	Using the first image set (T2WI, T1WI, CE-TIWI, and MRCP)			Using the second image set (first image set + ADC map)		
	Reader 1	Reader 2	Reader 3	Reader 1	Reader 2	Reader 3
3	8 (9.2)	24 (27.6)	19 (21.8)	0 (0)	0 (0)	0 (0)
4	31 (35.6)	40 (46.0)	48 (55.2)	1 (1.1)	21 (24.1)	4 (4.6)
5	48 (55.2)	23 (26.4)	20 (23.0)	86 (98.9)	66 (75.9)	83 (95.4)

Numbers in parentheses are percentages

PCNs pancreatic cystic neoplasms, *MRCP* magnetic resonance cholangiopancreatography, *ADC* apparent diffusion coefficient

*None of the cases were diagnosed with a confidence score of 1 or 2 by any of the readers on either of the two image sets

pathologically confirmed subgroup of PCNs is shown in Table 5. The diagnostic accuracy did not change for reader 1 with or without the use of ADC (91.5%). However, diagnostic accuracy of morphological MRI with ADC was higher than that without ADC for reader 2 (80.8% vs. 87.2%) and reader 3 (80.8% vs. 91.5%). The three cases by reader 2 that were correctly diagnosed with the additional use of ADC were one SCA and two mucin-producing PCNs. The five cases by reader 3 that were correctly diagnosed with the additional use of ADC were two SCAs and three mucin-producing PCNs (these five cases included the three cases by reader 2 that were correctly diagnosed with the additional use of ADC).

Discussion

DWI provides functional information and may allow increased accuracy and confidence in PCN characterization [17]. Thus, we undertook this study to evaluate the added value of DWI-derived ADC maps in complementing routine MRI involving T1WI, T2WI, CE-T1WI, and MRCP in differentiating serous from mucin-producing PCNs. Our results involving three readers with different levels of experience in reading abdominal MRI images are interesting. First, the use of ADC maps was associated with an increase in readers' confidence in making a diagnosis of serous versus mucin-producing PCNs. Second, the increase in readers' confidence

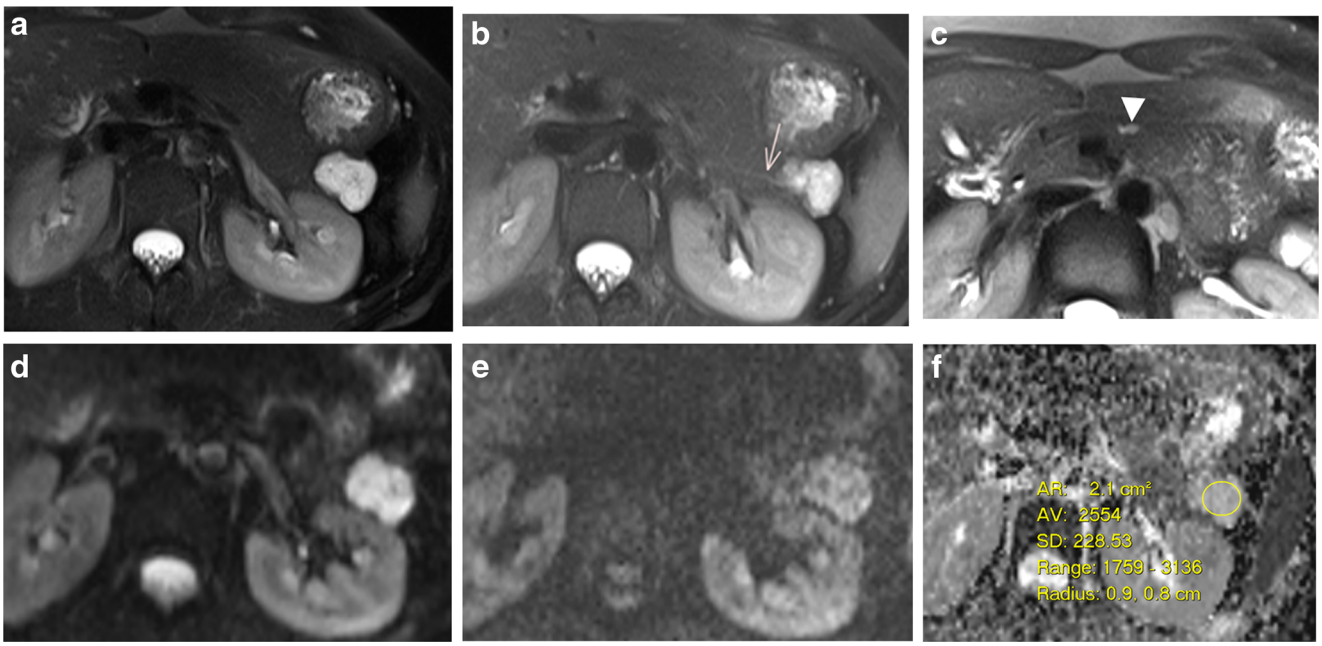

Fig. 2 Axial T2WI (**a**) shows a microcystic lesion arising within the pancreatic tail suggesting a serous cystic neoplasm. However, probable ductal communication (arrow, **b**) along with lesion multiplicity as evident by the presence of another small cystic lesion within the pancreatic body (arrowhead, **c**) lowered the confidence in diagnosing serous cyst. DWI-b50 (**d**), DWI-b750 (**e**), and ADC map (**f**) revealed an ADC of $< 2.8 \times 10^{-3}$ mm^2/s favoring serous cyst and allowed higher confidence in this diagnosis. Histopathology on surgically resected specimen confirmed the diagnosis of serous cyst

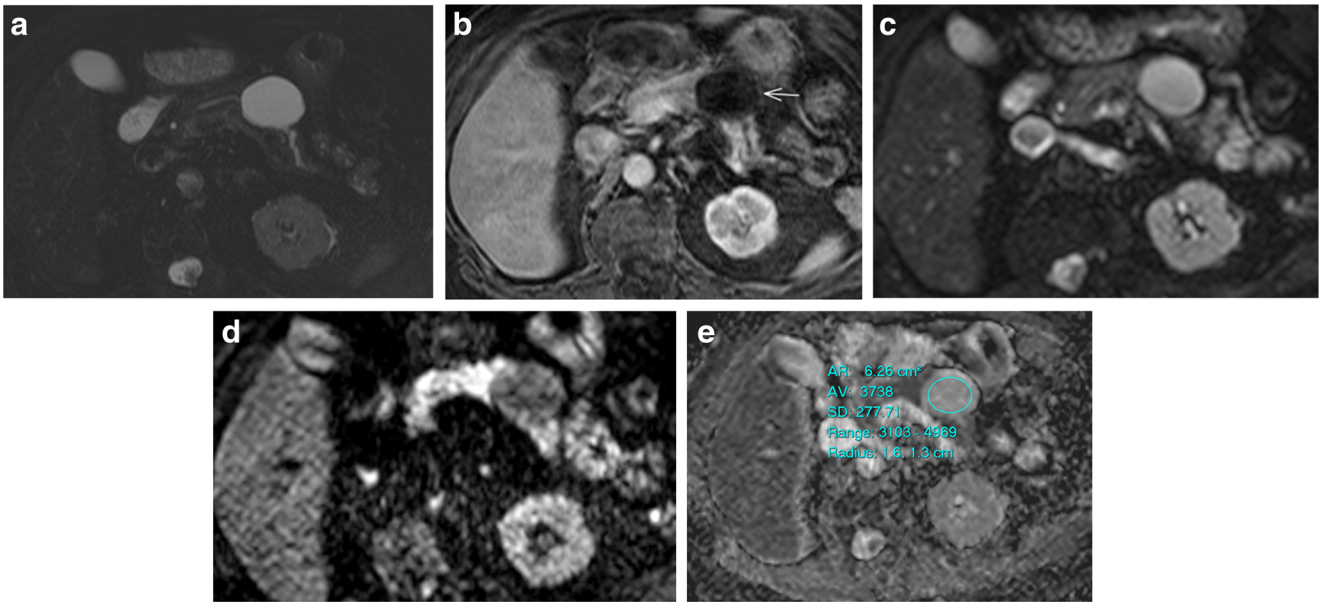

Fig. 3 Axial T2WI (**a**) and axial contrast-enhanced T1WI in the venous phase (**b**) show a unilocular cystic lesion (arrow) within the pancreatic body with equivocal ductal communication. The cyst wall was not thickened, and no mural nodule was visualized. A diagnosis of mucinous cystic neoplasm was suspected. DWI-b50 (**c**), DWI-b750 (**d**), and ADC map (**e**) of the cyst revealed an ADC value of $> 3.0 \times 10^{-3}$ mm^2/s which increased the confidence in diagnosing a mucin-producing PCN. Post-surgical histopathology analysis of the cyst confirmed the diagnosis of MCN

score may be related to the reader's level of experience in reading abdominal MRI images. While reader 1 with the maximum experience of 20 years showed an increase in confidence in 44.8% cases, reader 2 (7 years of experience) and reader 3 (4 years of experience) showed an increase in confidence in 73.6% and 78.2% of cases, respectively. The odds ratios for an increase in the level of diagnostic confidence with the use of ADC maps were 5.8, 6.8, and 12.7 for the three readers with 20 years, 7 years, and 4 years of experience, respectively.

With regard to diagnostic accuracy, our subgroup analysis of pathologically confirmed PCNs showed no improvement in

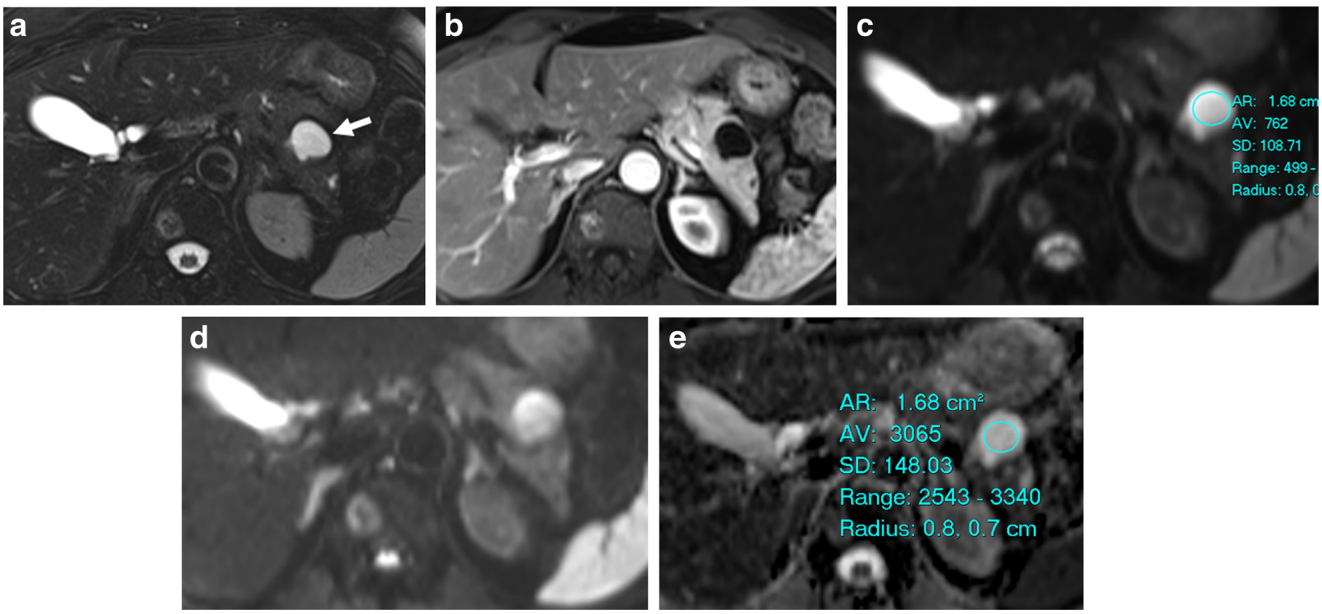

Fig. 4 Axial T2WI (**a**) and axial contrast-enhanced T1WI (**b**) show a cystic lesion (arrow) with few septations within. Probable ductal communication was noted. However, the confidence in the ductal communication was low for two readers. A diagnosis of IPMN was entertained. DWI-b50 (**c**), DWI-b750 (**d**), and ADC measurements within the cyst (**e**) revealed an ADC value of $> 3.0 \times 10^{-3}$ mm^2/s. This allowed the two readers to increase their confidence in diagnosing the cyst as mucin-producing. Cyst was surgically resected, and histopathology analysis of the cyst confirmed the diagnosis of IPMN

Table 4 Increase in confidence in diagnosis using an ADC map in 87 out of 117 total cases

Confidence change after DWI/ADC	Reader 1	Reader 2	Reader 3
No increase in confidence (*n*)	48 (55.2)	23 (26.4)	19 (21.8)
Confidence increase by 1 point (*n*)	32 (36.8)	60 (69.0)	47 (54.0)
Confidence increase by 2 points (*n*)	7 (8.0)	4 (4.6)	21 (24.2)
Total (*n*)	87 (100)	87 (100)	87 (100)

Numbers in parentheses are percentages

diagnostic accuracy for reader with most years of experience while there was an increase in the diagnostic accuracy of morphological MRI when combined with ADC for the other two readers with less experience. For both these readers, the combined use of morphologic imaging and ADC allowed correct classification of serous versus mucin-producing PCNs in three (reader 2) and five (reader 3) additional cases as compared to morphologic imaging alone. Among the SCAs that were wrongly diagnosed by morphologic MRI as mucin-producing PCNs, probable ductal communication made the readers favor the diagnosis of mucin-producing PCNs. However, the confidence in the diagnosis was low (3 or 4). The ADC measurements in both the cases were $< 2.8 \times 10^{-3}$ mm^2/s and correctly diagnosed the cases as SCAs. Among the mucin-producing PCNs that were wrongly diagnosed by morphologic MRI as SCAs, the appearance of cluster of small cysts (microcystic appearance) prompted the diagnosis of SCA by the readers. However, due to equivocal ductal communication, the confidence in this diagnosis was low (3 or 4). The ADC measurements in both the cases were $\geq 3.0 \times 10^{-3}$ mm^2/s and correctly diagnosed the cases as mucin-producing PCNs. Considering the morbidity/mortality associated with misdiagnosis of serous versus mucin-producing PCNs, this may justify further studies with larger sample size.

These findings suggest that DWI could be a valuable tool in increasing the confidence and diagnostic accuracy in differentiating between serous and mucin-producing PCNs. Also, this value of DWI is possibly more likely in radiologists with less experience. MRI is used routinely for characterization and follow-up of PCNs. The addition of DWI to the routine protocol is feasible since it is a rapid, non-invasive sequence without the need for contrast administration. Furthermore, ADC provides an easily quantifiable parameter that is reproducible with excellent inter- and intra-observer agreement [17]. Studies on the utility of DWI in characterization of cystic pancreatic lesions have reported varying degrees of success [15, 17, 18, 20–24]. The most recent study from a high-volume center and the only study using histopathology as the gold standard for all cases reported DWI to be a helpful tool in distinguishing between mucin-producing and serous PCNs [17]. Here, we show the added value of DWI/ADC in differentiating between the two most clinically relevant groups of pancreatic cysts (serous and mucin-producing PCNs).

While our study highlights the role of DWI/ADC in increasing the confidence in the distinction of serous versus mucin-producing PCNs, it also highlights some limitations in its use. The ADC cutoff used by us and validated by a previous study showed an overall accuracy of 76.9% in our study cohort as compared to the reference diagnosis. Thus, there were a significant number of cases where this ADC pointed towards a wrong diagnosis. In 10 cases, the ADC measurements were on a scan performed post FNA of the index cystic lesion. Intracystic bleeding and other post-FNA changes may have altered the ADC values, though none of these cases demonstrated high signal intensity on T1WI suggestive of bleeding. Until further studies are able to analyze the effect of FNA on ADC values in pancreatic cystic lesions, we suggest to be

Table 5 Comparison of diagnostic performance of morphological MRI with and without DWI/ADC in differentiating serous versus mucin-producing PCNs

Diagnostic parameters	Morphological MRI	Morphological MRI + DWI/ADC
Reader 1		
Sensitivity (%)	50 (4/8)	87.5 (7/8)
Specificity (%)	100 (39/39)	94.9 (37/39)
Accuracy (%)	91.5 (43/47)	91.5 (43/47)
Reader 2		
Sensitivity (%)	37.5 (3/8)	75 (6/8)
Specificity (%)	89.7 (35/39)	89.7 (35/39)
Accuracy (%)	80.8 (38/47)	87.2 (41/47)
Reader 3		
Sensitivity (%)	50 (4/8)	75 (6/8)
Specificity (%)	87.2 (34/39)	94.9 (37/39)
Accuracy (%)	80.8 (38/47)	91.5 (43/47)

Numbers in parentheses are those used to calculate the percentage

careful while interpreting ADC measurements on cysts with previous FNA.

Our study has limitations. First, in order to maximize the sample size, we included both cases with histologically confirmed diagnosis ($n = 48$), as well as those in whom the diagnosis was based on MPCC evaluation ($n = 69$) [3]. However, this was reasonable since most patients with SCAs and small IPMNs do not undergo surgical resection of their cyst(s). The usefulness of MPCC in managing PCNs at our center has been shown [3]. Moreover, EUS-FNA has been shown to provide 36% and 54% incremental increases over CT and MRI, respectively, for diagnosis of PCNs [25, 26]. Second, ADC variability may arise in relation to technical or other factors [27–29]. However, studies have shown good intra- and interscanner reproducibility using data from multiple scanners [30]. With respect to the pancreas, a study demonstrated good reproducibility between different MR systems [31]. Another recent study that assessed whether normalized ADC would perform better than absolute ADC by limiting the inter- and intrascanner variability found that both absolute and normalized ADCs allowed clinically relevant differentiation of pancreatic NET and IPAS [32]. In our study also, there was excellent reproducibility without significant bias between ADC measurements performed on 1.5-T and 3-T MRI scanners. The ADC threshold used was thus applicable to scans performed with both 1.5-T and 3-T MRI scanners, thus demonstrating the applicability and incremental value of the ADC values in a real-world scenario where patients often are imaged on different scanners. Another study reported a median ADC value of 2.99 versus 2.31 ($\times 10^{-3}$ mm^2/s) for mucin-producing versus serous tumors, though not reaching statistical significance ($p = 0.12$) [18], further supporting the ADC threshold used in the current study. The MRI machines and protocol in our study were similar to those used in a previous study [17]. Third, this is a retrospective study. However, it is unlikely that a prospective study performed at a single institution would recruit a large patient population in a short time interval. Fourth, we did not assess the value of ADC in differentiating between IPMN and MCN which was beyond the scope of this study. However, the current study focused on the added value of ADC in differentiating serous from mucin-producing PCNs (IPMN and MCN). This differentiation has significant implications for optimal management before even considering further differentiation between IPMN and MCN [33]. Nevertheless, future studies can explore the role of DWI in further differentiating between IPMNs and MCNs.

In summary, our study shows that DWI may have added value as a complementary tool to conventional morphological MRI in differentiating between serous and mucin-producing PCNs with possibly greater value for readers with less experience in reading abdominal MRI. Additional findings suggest that one should be careful while interpreting ADC measurements on cysts that have undergone FNA assessment.

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Compliance with ethical standards

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Ethical approval Institutional review board approval was obtained.

Methodology
- retrospective
- diagnostic study
- performed at one institution

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