Original Article

The differential diagnosis of pancreatic cystic neoplasms with conventional ultrasound and contrast-enhanced ultrasound

Zhiqiang Yuan, Jiawu Li, Lulu Yang, Yingyu Shi, Yan Luo

Department of Medical Ultrasound, West China Hospital, Sichuan University, Chengdu, China

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Correspondence to: Yan Luo, MD. Department of Medical Ultrasound, West China Hospital, Sichuan University, No. 37, Guoxue Alley, Chengdu 610041, China. Email: yanluo@scu.edu.cn.

Background: Advances in imaging have improved the detection rate of pancreatic cystic neoplasms (PCNs), but clinical management varies depending on the pathological type of PCNs, and thus accurate differential diagnosis is of considerable clinical significance. We conducted this study to identify the clinical and sonographic features of PCNs with significance for differential diagnosis and to compare the diagnostic accuracy of conventional ultrasound and conventional ultrasound combined with contrast-enhanced ultrasound (CEUS) for PCNs.

Methods: From January 1, 2011, to December 31, 2022, a total of 100 patients with PCNs who underwent CEUS examination and were confirmed to have PCNs by postoperative pathology in West China Hospital of Sichuan University were included in this study.

Results: Of the clinical characteristics of PCNs, age and gender were found to be important differential diagnostic features. Moreover, communication of the lesion with the main pancreatic duct on conventional ultrasound and CEUS images was a critical feature in the differential diagnosis of intraductal papillary mucinous neoplasm (IPMN). The size of the lesion, the thickness of the cyst wall and the number of septa in conventional ultrasound images, the uniformity of the cyst wall thickness in CEUS images, and the enhancement pattern in the arterial phase were significant features for the differential diagnosis of serous cystic neoplasm (SCN). Cyst wall thickness and uniformity of the cyst wall thickness in conventional ultrasound images and cyst wall thickness and septa thickness in CEUS images were important features in the differential diagnosis of mucinous cystic neoplasm (MCN). The size and internal components of the lesion on conventional ultrasound images, internal components of the lesion, and the enhancement pattern in the arterial phase and rim enhancement on CEUS images were the key features in the differential diagnosis of solid pseudopapillary neoplasm (SPN). Conventional ultrasound combined with CEUS demonstrated significantly greater accuracy than did conventional ultrasound alone in the differential diagnosis of PCNs (66% *vs.* 79%; P=0.002).

Conclusions: PCN types differ in their clinical and ultrasound features. Conventional ultrasound combined with CEUS can better distinguish between different pathological types of PCNs than can conventional ultrasound alone.

Keywords: Pancreatic cystic neoplasms (PCNs); differential diagnosis; contrast-enhanced ultrasound (CEUS); ultrasound

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Introduction

Pancreatic cystic neoplasms (PCNs) account for about 10–15% of pancreatic cystic diseases (1). PCNs primarily include intraductal papillary mucinous neoplasm (IPMN), serous cystic neoplasm (SCN), mucinous cystic neoplasm (MCN), and solid pseudopapillary neoplasm (SPN), with these four tumor types accounting for about 90% of PCNs (2-6). The malignant transformation rate of the different types of PCNs varies (7): IPMN has the highest rate, that of main pancreatic duct IPMN and mixed pancreatic duct IPMN is 33–60%, that of branch pancreatic duct IPMN is 11–30%, that of SCN is nil or negligible, that of MCN is 10–15%, and that of SPN is 10–16%. Therefore, the accurate differential diagnosis of these four PCNs is of critical significance to the clinical management decision of patients.

At present, imaging examinations for PCNs include conventional ultrasound, contrast-enhanced ultrasound (CEUS), computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasound (EUS), among others. CT can clearly show the lesions and is sensitive to calcification. However, CT involves ionizing radiation, and multiple follow-ups with CT may increase the risk of the malignant transformation of lesions (4,8). The high soft tissue resolution of MRI can improve the ability to display the wall nodules and septa of the lesions and whether the lesions communicate with the pancreatic duct, and thus MRI is the current imaging gold standard for the diagnosis of PCNs (9,10). However, MRI scans are time-consuming, and the ability to conduct follow-up examinations of patients with this modality is limited. Meanwhile, although EUS has certain accuracy in identifying the resection ability of lesions (3), its invasiveness limits its application in the diagnosis and follow-up of PCNs to a degree.

Conventional ultrasound is cost-effective, convenient, and fast and is thus the first choice for examining pancreatic diseases (11). It is used in the initial detection and preliminary characterization of PCNs but has limited value in the differential diagnosis of some PCNs. CEUS can assess normal perfusion of a variety of organs noninvasively without ionizing radiation and has a higher temporal resolution than does CT and MRI (12-14). CEUS can further improve the ability of conventional ultrasound to display the lesion structure and can clearly distinguish solid and cystic pancreatic lesions (15). The related guidelines (16) strongly recommend the use of CEUS for the differential diagnosis of pancreatic pseudocysts and cystic tumors, as well as for the follow-up of PCNs of uncertain nature. Research in this area (17) suggests that for patients with nonsurgical PCNs, follow-up monitoring by ultrasound can delay and reduce the number of MRI examinations, thereby reducing costs. To the best of our knowledge, no previous study has examined the clinical and ultrasound differential diagnostic features of the four types of PCNs. Therefore, this study aimed to characterize the clinical and ultrasonographic features of PCNs, identify those features with differential diagnostic value, and compare the differential diagnostic ability of conventional ultrasound to that of conventional ultrasound combined with CEUS.

Methods

Study design

This study was approved by the ethics committee of West China Hospital, Sichuan University (No. 2023[2096]) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was waived for all patients due to the retrospective nature of this study. This study first identified the clinical and ultrasonographic features of the four types PCNs, the differential features of clinical and ultrasound features were then screened, and the diagnostic accuracy of conventional ultrasound combined with CEUS was compared with that of conventional ultrasound alone.

Patients

Patients admitted to West China Hospital of Sichuan University from January 1, 2011, to December 31, 2022, were included in this study. The inclusion criteria for patients were as follows: (I) a postoperative pathological diagnosis of IPMN, SCN, MCN, or SPN; (II) CEUS examination performed 1 week before surgery; and (III) complete clinical data. Meanwhile, the exclusion criteria of this study were as follows: (I) no tumor lesion found on ultrasound examination, (II) the presence of two tumor pathological types in the same lesion, and (II) difficulty in reanalysis due to the incomplete and poor quality of the ultrasound image.

Ultrasound examination

Equipment and contrast agents

The equipment used included the iU22 (Philips, Amsterdam, the Netherlands), the Resona 7 (Mindray, Shenzhen, China), and the Resona 9 (Mindray). SonoVue

(Bracco, Milan, Italy) was used as the contrast agent in all examinations.

Ultrasonographic procedures

For ultrasonographic procedures, the patient fasted for more than 8 hours and assumed the lateral or supine position according to clinical need. First, conventional ultrasound was used to comprehensively scan the pancreas, observe the lesion in detail, and record the location, margin, shape, internal components, number of cysts, septa, calcification, main pancreatic duct dilation, communication with the main pancreatic duct, and blood flow. CEUS examination was then performed. The CEUS mode was selected, and 1.2–2.4 mL of SonoVue suspension was rapidly bolus injected through the cubital vein, and the tube was flushed with 5 mL of normal saline. All examinations were performed by sonographers with more than 5 years experience in CEUS in the Department of Medical Ultrasound, West China Hospital of Sichuan University.

Analysis of images

The features of the lesions were independently analyzed by two radiologists with more than 5 years of experience in abdominal CEUS. When there was a discrepancy between the two radiologists, a consensus reached after discussion was regarded as the final result. In the study, the cutoff values were 6, 20, 3, 2, and 3 mm, respectively, for the number of cysts, the size of a single cyst, the thickness of the cyst wall, the thickness of the septa, and main pancreatic duct dilatation (18-22). CEUS was divided into the arterial phase (10 to 30 seconds) and venous phase (30 to 120 seconds) according to the standards recommended by the guidelines of the Federation of European Ultrasound Societies in Medicine and Biology (16).

Statistical analysis

All the data of the patients included in this study were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA), and a P value <0.05 (two-tailed) indicated a statistical difference. Measurement data are expressed as the mean ± standard deviation. For the r-analysis of the sonographic features of the lesions, the weighted kappa consistency test was used for interreader consistency analysis. The basic clinical data of the four groups were compared, with the measurement data being analyzed with the one-way analysis of variance or Kruskal-Wallis test and the count data being analyzed with R × C contingency table chi-square test or Fisher exact probability test. Univariate and multivariate logistics regression were used to screen the differential diagnostic features. The McNemar test was used to compare the differential diagnostic accuracy of conventional ultrasound and conventional ultrasound combined with CEUS.

Results

Basic clinical data of patients with PCNs

A total of 100 patients were included in this study, including 21 with IPMN, 36 with SCN, 15 with MCN, and 28 with SPN. The basic clinical data of the patients are shown in *Table 1*.

Consistency test of the ultrasonic image features of the patients

In this study, a consistency test was carried out on the rereading results of two doctors. In the consistency test of conventional ultrasound features, the Cohen kappa coefficient was between 0.663 and 0.932. In the consistency test of CEUS features, the Cohen kappa coefficient ranged from 0.672 to 0.932.

The data on the conventional ultrasound and CEUS images of PCNs are summarized in the *Tables 2*,*3*.

Regression model of conventional ultrasound and conventional ultrasound combined with CEUS for IPMN

Univariate logistics regression was used to screen the differential characteristics in conventional ultrasound images with presence of IPMN as the outcome variable. The minimum P value of dummy variable was selected for the setting of the dummy variable for multiple categorical variables, and the results are shown in *Table 4*. Variables with a P value less than 0.1 in univariate analysis were included in the multivariate regression along with age and gender. Multivariate analysis showed that older age [odds ratio (OR) =1.058; P=0.04), male gender (OR =5.765; P=0.03), and communication between the lesion and the main pancreatic duct (OR =37.939; P=0.002) were correlated. In other words, the older the age, the higher the risk of PCN being diagnosed as IPMN, the risk of being diagnosed with IPMN is higher in males than in females, and the risk of being diagnosed with IPMN is higher in patients with lesions communicating with the main pancreatic duct. The results

Table 1 Basic clinical data of patients with PCNs

Characteristics of patients	IPMN	SCN	MCN	SPN	P
Age (years)	59.67±8.48	50.28±14.61	54.13±15.93	23.57±13.92	<0.001
Gender					<0.001
Male	13	4	3	3	
Female	8	32	12	25	
Symptoms					0.54
No	11	16	6	9	
Yes	10	20	9	19	
CEA (ng/mL)					0.07
<3.4	15	34	13	26	
≥3.4	6	2	2	2	
CA19-9 (U/mL)					0.15
<22	12	28	9	23	
≥22	9	8	6	5	
CA125 (U/mL)					0.76
<35	21	35	14	27	
≥35	0	1	1	1	
Total	21	36	15	28	

Data are presented as mean ± standard deviation or number. PCN, pancreatic cystic neoplasm; IPMN, intraductal papillary mucinous neoplasm; SCN, serous cystic neoplasm; MCN, mucinous cystic neoplasm; SPN, solid pseudopapillary neoplasm; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CA125, carbohydrate antigen 125.

from the univariate logistics regression of CEUS images are shown in *Table 5*. The abovementioned characteristics and the statistically different features of the conventional ultrasound prediction model were included in the prediction model of conventional ultrasound combined with CEUS via the stepwise forward method. The multivariate analysis showed that older age (OR =1.075; P=0.03) and a lesion communicating with the main pancreatic duct under CEUS (OR =209.813; P<0.001) were correlated. The combined prediction model showed that the older the age is, the higher the risk of PCNs being diagnosed as IPMN and that the risk of IPMN diagnosis is higher in patients with lesions communicating with the main pancreatic duct on CEUS (*Figure 1*).

Regression model of conventional ultrasound and conventional ultrasound combined with CEUS for SCN

The univariate logistics regression results of conventional ultrasound features are shown in *Table 4*. Variables with the P value less than 0.1 in univariate analysis were included in the multivariate regression along with age and gender. Multivariate analysis showed that female gender (OR =8.725; P=0.004), lesion size (OR =0.388; P=0.001), thin cyst wall (OR =39.655; P=0.005), and multiple septa (OR =7.574; P=0.01) were correlated. The model predicted the following: females have a higher risk of being diagnosed with SCN than do males; the larger the PCN lesion is, the lower the risk of being diagnosed with SCN; patients with PCNs with a thin wall have a higher risk of being diagnosed with SCN than do those with a thick wall; and patients with PCNs with more septa have a higher risk of being diagnosed with SCNs than do those with few septa. The univariate logistics regression results of CEUS images are shown in *Table 5*. The abovementioned CEUS features and conventional ultrasound features were included in the binary multivariate logistics regression. The results showed that female gender (OR =11.115; P=0.005), lesion size (OR =0.315; P=0.001), no cyst wall on conventional ultrasound (OR =101.026; P=0.01), a thin cyst wall on conventional ultrasound (OR =28.967; P=0.03), a uniform thickness

Table 2 The conventional ultrasound features of PCNs

Characteristics of lesions	IPMN	SCN	MCN	SPN
Tumor size (cm)	3.5±2.3	2.5±1.1	4.2±2.3	4.4±2.0
Location				
Head/neck	11	11	3	14
Body	6	8	4	6
Tail	4	17	8	8
Margin				
Clear	12	25	14	22
Not clear	9	11	1	6
Shape				
Regular	8	20	12	23
Irregular	13	16	3	5
Calcification				
No	20	34	12	23
Yes	1	2	3	5
Components				
Cystic	16	26	13	2
Solid	3	7	0	21
Mixed cystic and solid	2	3	2	5
Number of cysts				
No	5	10	2	26
≥1, <6	14	25	9	2
≥6	2	1	4	0
A single cyst size				
No	5	10	2	26
<20 mm	6	18	2	0
≥20 mm	10	8	11	2
Cyst wall thickness				
No wall	5	10	2	26
<3 mm	14	25	4	0
≥3 mm	2	1	9	2
Uniformity of cyst wall thickness				
No wall	5	10	2	26
Uniform	12	23	2	1
Not uniform	4	3	11	1
Mural nodules				
No	20	36	13	28
Yes	1	0	2	0
The number of septa				
<2	17	23	9	27
≥2	4	13	6	1
Thickness of septa				
No	10	16	5	27
<2 mm	7	19	5	1
≥2 mm	4	1	5	0
Dilation of the main pancreatic duct				
≤3 mm	9	34	13	27
>3 mm	12	2	2	1
Communication with the main pancreatic duct				
No	8	36	14	28
Yes	9	0	1	0
Undefined	4	0	0	0
Color				
No	20	36	14	21
Yes	1	0	1	7

Data are presented as mean ± standard deviation or number. PCN, pancreatic cystic neoplasm; IPMN, intraductal papillary mucinous neoplasm; SCN, serous cystic neoplasm; MCN, mucinous cystic neoplasm; SPN, solid pseudopapillary neoplasm.

of the cyst wall on CEUS (OR =17.292; P=0.01), and hypoenhancement pattern in the arterial phase (OR =0.014; P=0.02) were correlated. In other words, the combined model predicted the following: females are at higher risk of being diagnosed as SCN than are males; the larger the lesion is, the lower the risk of SCN; patients with PCNs with no cyst wall and a thin wall on conventional ultrasound have a higher risk of being diagnosed as SCNs than do those with a thick wall; patients with PCNs with a uniform cyst wall on CEUS have a higher risk of being diagnosed with SCNs than do those with an uneven cyst wall; and patients with PCNs with hypoenhancement pattern in the arterial phase have a lower risk of being diagnosed with SCNs than do those with a hyperenhancement pattern (*Figure 2*).

Regression models of conventional ultrasound and conventional ultrasound combined with CEUS for MCN

The univariate logistics regression results of conventional

Table 3 The CEUS features of PCNs

Characteristics of lesions	IPMN	SCN	MCN	SPN
Components				
Cystic	18	33	15	9
Solid	1	2	0	9
Mixed cystic and solid	2	1	0	10
Number of cysts				
No	3	3	0	19
≥1, <6	13	24	12	7
≥6	5	9	3	2
A single cyst size				
No	3	3	0	19
<20 mm	7	24	2	3
≥20 mm	11	9	13	6
Cyst wall thickness				
No wall	3	3	0	19
<3 mm	15	24	3	2
≥3 mm	3	9	12	7
Uniformity of cyst wall thickness				
No wall	3	3	0	19
Uniform	11	30	2	4
Not uniform	7	3	13	5
Mural nodules				
No	18	33	12	27
Yes	3	3	3	1
The number of septa				
<2	12	17	8	27
≥2	9	19	7	1
Thickness of septa				
No	5	12	3	27
<2 mm	11	23	3	1
≥2 mm	5	1	9	0
Dilation of the main pancreatic duct				
≤3 mm	9	34	13	27
>3 mm	12	2	2	1
Communication with the main pancreatic duct				
No	5	36	14	28
Yes	16	0	1	0
Enhancement pattern in arterial phase				
Hypo	0	1	0	15
Iso	16	33	10	8
Hyper	5	2	5	5
Enhancement pattern in venous phase				
Hypo	7	8	6	26
Iso	14	28	9	2
Rim enhancement				
No	21	36	14	9
Yes	0	0	1	19

Data are represented as number. CEUS, contrast-enhanced ultrasound; PCN, pancreatic cystic neoplasm; IPMN, intraductal papillary mucinous neoplasm; SCN, serous cystic neoplasm; MCN, mucinous cystic neoplasm; SPN, solid pseudopapillary neoplasm.

ultrasound features are shown in *Table 4*. Variables with a P value less than 0.1 in the univariate analysis were included in the multivariate regression along with age and gender. The results of multivariate analysis showed that a thick wall (OR =8.873; P=0.01) and an uneven cyst wall (OR =14.409; P=0.004) were correlated. In other words, PCNs with thick cyst wall predicted a higher risk of MCN diagnosis than did a thin cyst wall, and the risk of MCN diagnosis is higher in patients with PCNs and an uneven cyst wall than in those with a uniform cyst wall. The univariate logistics regression results of CEUS images are shown in *Table 5*. The abovementioned CEUS features and conventional ultrasound related features were included in the binary multivariate logistics regression. The results showed that an uneven thickness of the cyst wall on conventional ultrasound (OR =9.385; P=0.04), a thick cyst wall on CEUS (OR =38.746; P=0.006), and a thick septa on CEUS (OR =29.489; P=0.02) were correlated. The combined model predicted the following: patients with PCNs with an uneven cyst wall under conventional ultrasound have a higher risk of being diagnosed with MCN than do those with PCNs with a uniform cyst wall, patients with PCNs with a thick cyst wall under CEUS have a higher risk of being diagnosed with MCN than do those with a thin cyst wall; and patients with PCNs with a thick septa on CEUS have a higher risk of being diagnosed with MCN than do those with a fine

Table 4 Results of the conventional ultrasound univariate regression of PCNs

Characteristics of lesions	P (IPMN)	P (SCN)	P (MCN)	P (SPN)
Tumor size (cm)	0.97	<0.001	0.16	0.007
Location (head/neck *vs*. body *vs*. tail)	0.07	0.11	0.09	0.17
Margin (clear *vs*. not clear)	0.07	0.55	0.09	0.44
Shape (regular *vs*. irregular)	0.01	0.25	0.15	0.02
Calcification (no *vs*. yes)	0.32	0.21	0.24	0.18
Components (cystic *vs*. solid *vs*. mixed cystic and solid)	0.06	0.04	0.64	<0.001
Number of cysts (no *vs*. ≥1, <6 *vs*. ≥6)	0.06	0.009	0.002	<0.001
A single cyst size (no *vs*. <20 *vs*. ≥20 mm)	0.04	<0.001	0.003	<0.001
Cyst wall thickness (no wall *vs*. <3 *vs*. ≥3 mm)	0.02	0.001	<0.001	0.007
Uniformity of wall thickness (no wall *vs*. uniform *vs*. not uniform)	0.03	0.001	<0.001	<0.001
Mural nodules (no *vs*. yes)	0.60	>0.99	0.04	>0.99
The number of septa (<2 *vs*. ≥2)	0.55	0.04	0.12	0.02
Thickness of septa (no *vs*. <2 *vs*. ≥2 mm)	0.11	0.004	0.003	>0.99
Dilation of the main pancreatic duct (≤3 *vs*. >3 mm)	<0.001	0.04	0.68	0.05
Communication with the main pancreatic duct (no *vs*. yes *vs*. undefined)	<0.001	>0.99	0.61	>0.99
Color (no *vs*. yes)	0.46	>0.99	0.73	0.003

PCNs, pancreatic cystic neoplasms; IPMN, intraductal papillary mucinous neoplasm; SCN, serous cystic neoplasm; MCN, mucinous cystic neoplasm; SPN, solid pseudopapillary neoplasm.

Table 5 Results of univariate regression for the CEUS of PCNs

Characteristics of lesions	P (IPMN)	P (SCN)	P (MCN)	P (SPN)
Components (cystic *vs*. solid *vs*. mixed cystic and solid)	0.25	0.04	>0.99	<0.001
Number of cysts (no *vs*. ≥1, <6 *vs*. ≥6)	0.23	0.01	0.60	<0.001
A single cyst size (no *vs*. <20 *vs*. ≥20 mm)	0.38	<0.001	>0.99	<0.001
Cyst wall thickness (no wall *vs*. <3 *vs*. ≥3 mm)	0.05	0.002	0.002	<0.001
Uniformity of wall thickness (no wall *vs*. uniform *vs*. not uniform)	0.24	<0.001	<0.001	<0.001
Mural nodules (no *vs*. yes)	0.47	0.68	0.18	0.21
The number of septa (<2 *vs*. ≥2)	0.46	0.01	0.35	0.002
Thickness of septa (no *vs*. <2 *vs*. ≥2 mm)	0.04	0.001	<0.001	>0.99
Dilation of the main pancreatic duct (no *vs*. yes)	<0.001	0.04	0.68	0.05
Communication with the main pancreatic duct (no *vs*. yes)	<0.001	>0.99	0.27	>0.99
Enhancement pattern in the arterial phase (hypo *vs*. iso *vs*. hyper)	0.64	0.01	>0.99	0.002
Enhancement pattern in the venous phase (hypo *vs*. iso)	0.16	<0.001	0.56	<0.001
Rim enhancement (no *vs*. yes)	>0.99	>0.99	0.19	<0.001

CEUS, contrast-enhanced ultrasound; PCN, pancreatic cystic neoplasms; IPMN, intraductal papillary mucinous neoplasm; SCN, serous cystic neoplasm; MCN, mucinous cystic neoplasm; SPN, solid pseudopapillary neoplasm.

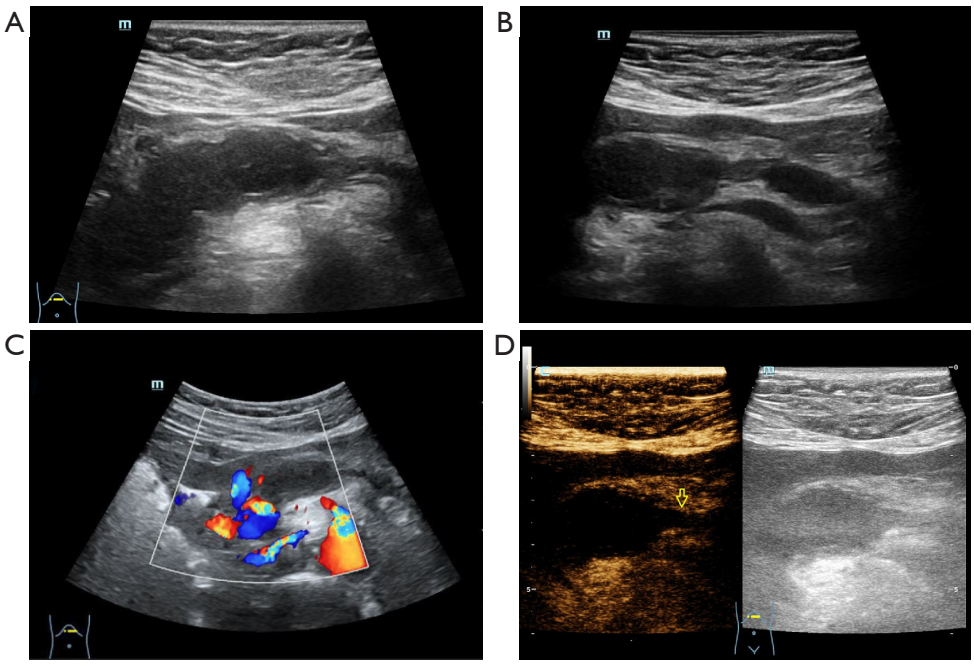

Figure 1 Conventional ultrasound and CEUS findings of IPMN. (A,B) Conventional ultrasound showing a cystic mass in the head of the pancreas and dilation of the main pancreatic duct, with the mass being closely involved with the main pancreatic duct. (C) Color Doppler flow imaging showing no obvious blood flow signal. (D) CEUS showing the mass communicating with the main pancreatic duct (yellow arrow). CEUS, contrast-enhanced ultrasound; IPMN, intraductal papillary mucinous neoplasm.

septa (*Figure 3*).

Regression model of conventional ultrasound and conventional ultrasound combined with CEUS for SPN

The univariate logistics regression results of conventional ultrasound features are shown in *Table 4*. Variables with the P value less than 0.1 in the univariate analysis were included in the multivariate regression along with age and gender. The results of multivariate analysis showed that age (OR =0.847; P<0.001), lesion size (OR =1.593; P=0.02), solid internal composition (OR =431.297; P<0.001), and mixed cystic and solid internal composition (P=0.01, OR =47.802) were correlated. In other words, the model predicted that younger patients with PCNs have a greater risk of being diagnosed with SPN, patients with PCNs with larger lesions have a greater risk of being diagnosed with SPN, and patients with PCNs with solid internal components or mixed cystic and solid components have a higher risk of being diagnosed with SPN than do those with cystic components. The univariate logistics regression results of CEUS images are shown in *Table 5*. The abovementioned CEUS features and conventional ultrasound features were included in the binary multivariate logistics regression using the stepwise forward method. The results showed that age (OR =0.871; P=0.03), mixed cystic and solid internal composition (OR =208.037; P=0.007), hypoenhancement pattern in the arterial phase (OR =6393.382; P=0.02), and rim enhancement (OR =5850.927; P=0.01) were correlated. In other words, the combined model predicted the following: the younger the patient with PCNs is, the higher the risk of being diagnosed as SPN; patients with PCNs with mixed cystic and solid components have a higher risk of being diagnosed with SPN than do those with cystic components; patients with PCNs with a hypoenhancement pattern in the arterial phase have a higher risk of being diagnosed with SPN than do those with a hyperenhancement pattern; and patients with PCNs with rim enhancement on CEUS have a higher risk of being diagnosed with SPN than do those with no rim enhancement (*Figure 4*).

Comparison of the differential diagnostic efficacy of conventional ultrasound and conventional ultrasound combined with CEUS

According to the results of the regression prediction

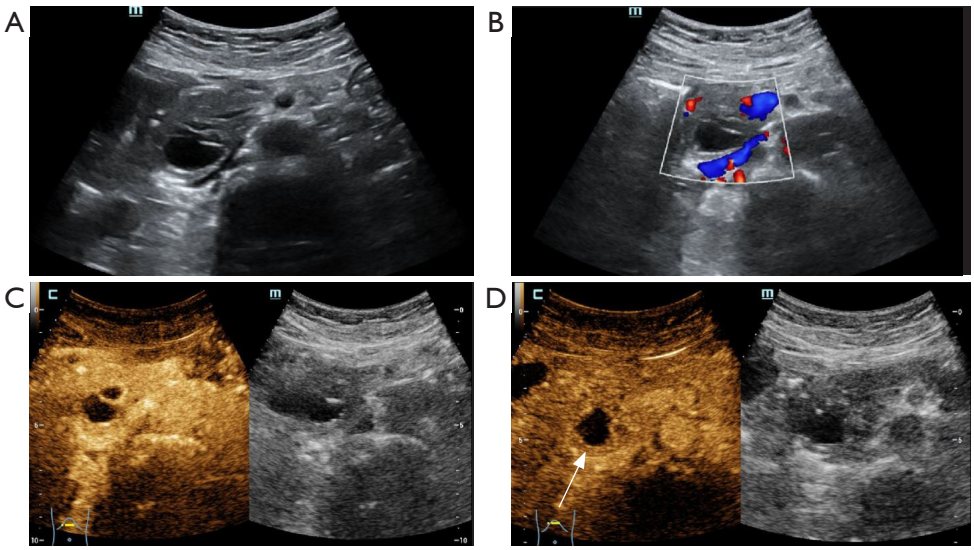

Figure 2 Conventional and CEUS findings of SCN. (A,B) Conventional ultrasound showing a cystic mass with a thin cyst wall in the head and neck of the pancreas without obvious blood flow signals. (C,D) CEUS showing uniform thickness of the cyst wall (white arrow) with iso enhancement both in the arterial phase and venous phase. CEUS, contrast-enhanced ultrasound; SCN, serous cystic neoplasm.

model, the four types of PCNs were differentiated in turn. Through comparison with the pathological results, it was determined that the diagnostic accuracy of conventional ultrasound was 66% and that the accuracy of conventional ultrasound combined with CEUS was 79%. The McNemar test was performed on the two diagnostic results, and the difference between them was statistically significant (P=0.002) (*Figure 5*).

Discussion

The biological behavior of PCN type varies, and therefore accurate differential diagnosis is critical to informing clinical management decisions. In this study, the clinical features and conventional ultrasound and CEUS characteristics of four types of PCNs were analyzed to identify the clinical features and differential diagnostic characteristics of conventional ultrasound and CEUS. The diagnostic accuracy of conventional ultrasound combined with CEUS was higher than that of conventional ultrasound.

In this study, 58 patients with PCNs had clinical symptoms, including abdominal pain and abdominal distension. Other studies (23,24) have reported that the incidence of clinical symptoms in PCNs is 44–80%, but the data on symptomatic PCNs are primarily from surgical series, so selection bias may be an issue (7). In observational studies, the incidence of symptoms in patients with PCN decreased to 17% to 21% (25-27). In our study, the age of the IPMN, SCN, MCN, and SPN groups were 59.67±8.48, 50.28±14.61, 54.13±15.93, and 23.57±13.92 years, respectively. This is consistent with the results of another study (28) in which the age of the IPMN, SCN, and MCN groups was typically between 50 and 70 years old and that of the SPN group was between 20 and 30 years old, with the age distribution among the four groups of PCNs being statistically different. Other research (7) indicates that the proportion of men and women with IPMN was similar, while patients with SCN, MCN, or SPN were predominantly women. In this study, except for the IPMN group, in which there was a slightly higher proportion of men (61.9%) than women (48.1%), the other three groups were predominantly female. The reason for this distinction of IPMN may be the bias introduced by the small number of samples in IPMN group.

IPMN originates from the ductal epithelium of the main pancreatic duct or branch pancreatic duct and accounts for about 20–50% of PCNs (29). The conventional ultrasound manifestations of IPMN are various, and depending on the pathological type, main pancreatic duct IPMN can show dilatation of the main pancreatic duct, with hypoechoic nodules appearing on the dilated pancreatic duct (30). Branch duct IPMN is characterized by a multilocular cystic appearance accompanied by main pancreatic duct dilatation (21). IPMN was not classified according to

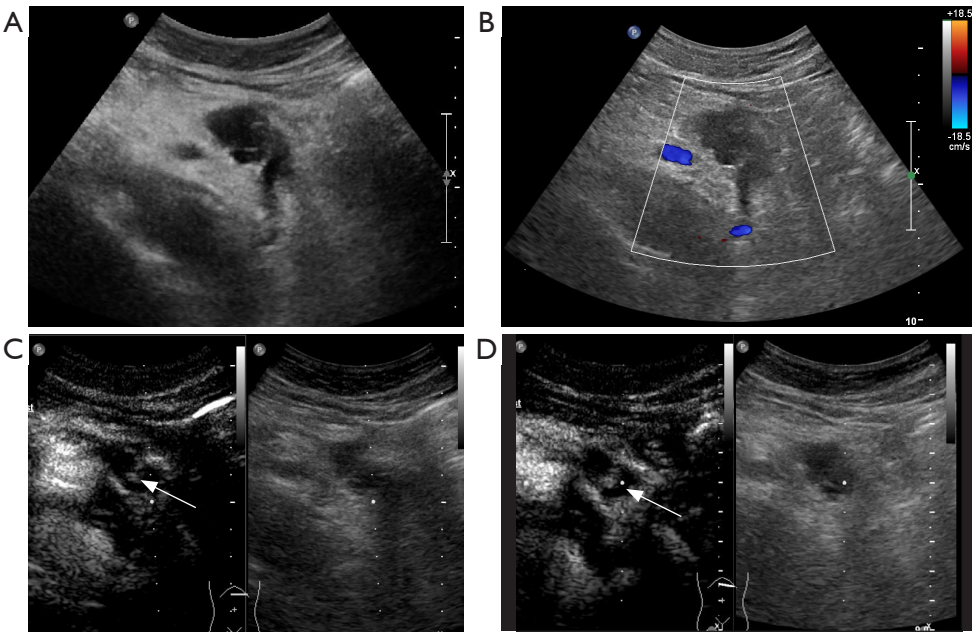

Figure 3 Conventional ultrasound and CEUS of MCN. (A,B) Conventional ultrasound showing a cystic mass with uneven thickness of the cyst wall in the tail of the pancreas without obvious blood flow signals. (C,D) A thick cyst wall on contrast-enhanced ultrasound with a thick septa (white arrow) appearing inside. CEUS, contrast-enhanced ultrasound; MCN, mucinous cystic neoplasm.

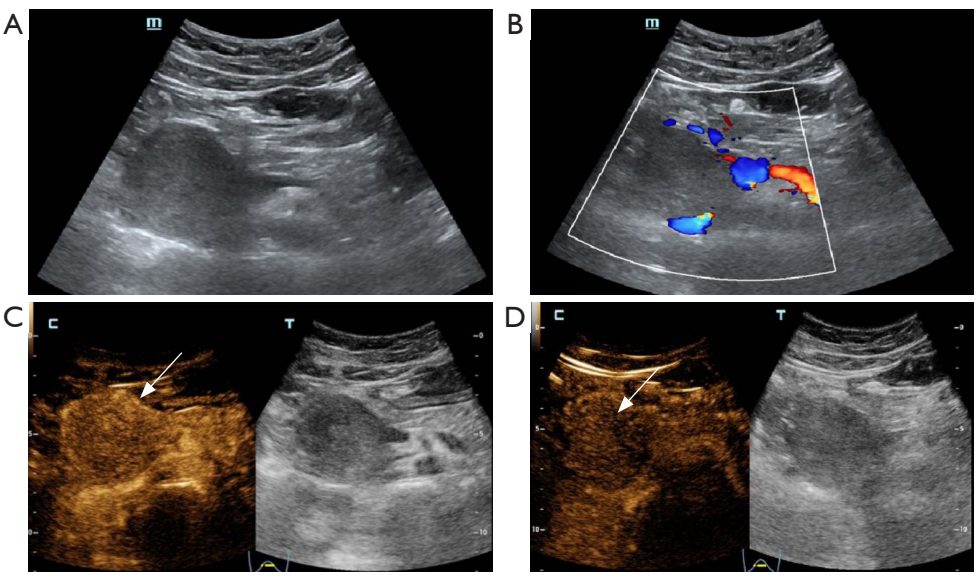

Figure 4 Conventional ultrasound and CEUS images of SPN. (A,B) Conventional ultrasound showing a solid mass in the head of the pancreas without obvious blood flow signal. (C,D) Hypoenhancement observed in the arterial phase of CEUS and rim enhancement (white arrow) observed in both the arterial phase and venous phase of CEUS. CEUS, contrast-enhanced ultrasound; SPN, solid pseudopapillary neoplasm.

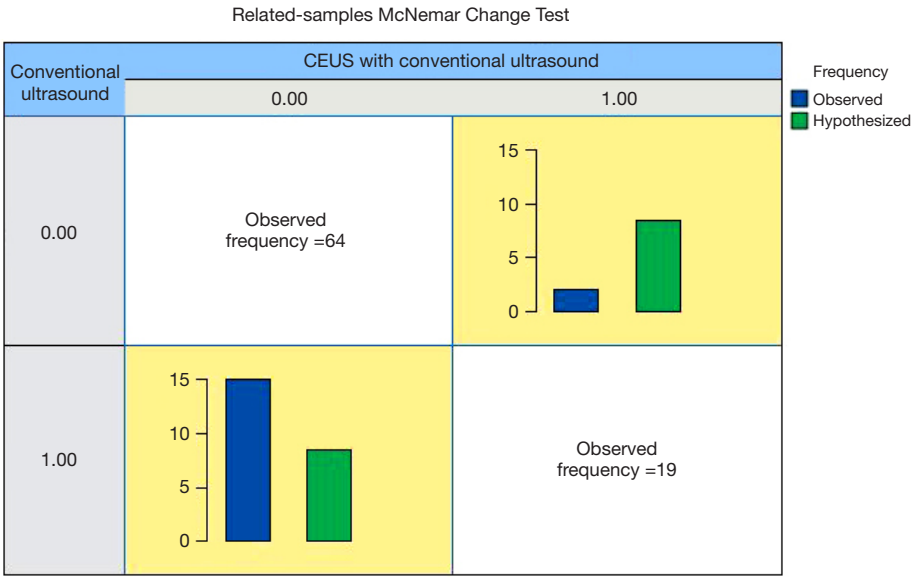

Figure 5 Comparison of the differential diagnosis between conventional ultrasound and conventional ultrasound combined with CEUS. CEUS, contrast-enhanced ultrasound.

conventional ultrasound and CEUS images because the pathological results of the patients included in this study had not been classified. Twelve patients with IPMN in this study had a dilated main pancreatic duct. Conventional ultrasound showed that nine lesions of IPMN communicated with the main pancreatic duct, and four lesions could not be clearly identified because of their close relationship with the main pancreatic duct. Conventional ultrasound shows that part of the main pancreatic duct is not communicated, which may be the mucin-blocked area, while the mucin-blocked area is not enhanced by CEUS (12,31), which can improve the visualization ability of the lesion and the main pancreatic duct and thus facilitate the diagnosis of IPMN. In a study (32) on the differentiation of branched IPMN and SCN, conventional ultrasound showed that four lesions of branched IPMN communicated with the main pancreatic duct, and CEUS showed that six lesions communicated with the main pancreatic duct, indicating that CEUS could further improve the ability to display the communication between the lesion and the main pancreatic duct. The results of previous study (32) also showed that the microcyst, the echo in the cyst, the dilatation of the main pancreatic duct in the conventional ultrasound image, the lesion in the CEUS image communicating with the main pancreatic duct, and the enhancement of the wall nodule had significance for differential diagnosis. Our study showed that a lesion in the CEUS image communicating with the main pancreatic duct had significance for differential diagnosis. The reason why the ultrasonographic differential diagnostic features are not exactly the same may be that our study differentiated IPMN and the other three PCNs, not only SCN.

SCN accounts for about 30% of all PCNs, and SCNs rarely undergo malignant transformation (33). SCNs can be divided into a microcystic type, macrocystic type, mixed type, and solid type, with the microcystic and macrocystic types accounting for 45% and 32% of the total number, respectively (34,35). Conventional ultrasound of SCNs typically shows that the cysts are microcystic (<20 mm) and have a thin wall and fine septa, with a portion appearing as a solid structure (21). In this study, convention ultrasound indicated that 72.2% (26/36) of the internal components of SCN were cystic, 69.4% (25/36) of the SCNs were oligocystic (number of cysts <6), 50% (18/36) were microcystic (<20 mm), 22.2% (8/36) were macrocystic (≥20 mm), 69.4% (25/36) had a thin wall, and 63.9% (23/36) had a uniform wall thickness. Moreover, the diagnostic value of cyst wall thickness and the septal thickness of the SCNs was consistent with previous studies (19). Meanwhile, CEUS showed that 91.7% (33/36) of SCNs were cystic, 66.7% (24/36) were microcystic (<20 mm), and 25% (9/36) had multiple cysts (the number of cysts ≥6). Thus, CEUS showed a superior ability to discern the internal components and the honeycomb

structure of microcystic SCNs. In the arterial phase, 91.7% (33/36) of SCNs showed isoenhancement and two of SCNs showed hyperenhancement, and in the venous phase, 77.8% (28/36) of SCNs showed isoenhancement.

MCN accounts for about 23% of PCNs (36), and the rate of malignancy is about 10–15% (7). MCN is usually unilocular or oligocystic, and conventional ultrasound usually shows the cyst wall as thick with visible septa (37). In our study, conventional ultrasound indicated that 56.2% (9/15) of MCNs had fewer than six cysts, 56.2% (9/15) had a thick wall, and 33.3% (5/12) MCN had a thick septa. Meanwhile, CEUS indicated 80% (12/15) of MCNs had fewer than six cysts, 80% (12/15) had a thick wall, and 60% (9/15) had a thick septa. The thickness of the cyst wall and septa of MCNs in our present study are generally consistent with the results of Sun *et al.* (19). Conventional ultrasound showed that the internal components of MCNs were cystic in 13 cases and mixed cystic and solid in 2 cases, while CEUS showed that the internal components of MCNs were cystic in 15 cases. CEUS can improve the ability to display the internal components of the lesions, thereby further improving the ability of the differential diagnosis of the lesions.

SPN is a low-grade malignant tumor, accounting for about 2% of PCNs (38). In this study, conventional ultrasound showed that SPNs had a clear margin and regular shape. The internal components were mainly solid and mixed cystic and solid, accounting for 92.9% of SPNs, a few SPNs showed calcification, and some SPNs could be seen with blood flow, which was consistent with the results of a previous study (39). CEUS can show liquefaction necrosis in some lesions, which are mixed cystic and solid or cystic lesions, and can also show cystic lesions with uniform or uneven thickness of the cyst wall. In this study, 53.6% (15/28) of SPNs showed hypoenhancement in the arterial phase, and all SPNs showed isoenhancement or hypoenhancement in the venous phase, with the latter being a significant feature, which is consistent with the results of a previous study (39). Moreover, we found that 67.9% (19/28) of SPNs showed rim enhancement, also representing a significant feature, which is in line with other studies (40).

In our study, the regression predictive model was used to conduct a retrospective study combining basic clinical characteristics with conventional ultrasound and CEUS findings of four types of PCNs. Conventional ultrasound and CEUS showed potential in the differential diagnosis of PCNs. However, we also need to recognize the role of EUS in the diagnosis of PCNs. Research has shown that contrast-enhanced EUS is helpful for the identification of malignant pancreatic wall nodules (41). EUS-guided fine needle aspiration biopsy is helpful for the diagnosis of PCNs through the acquisition of cytopathology (42), but it needs to be used selectively to avoid adverse events (43).

This study is a retrospective and exploratory study with some limitations. The sample size of PCNs was insufficient, and the distribution of SCN pathological types was not balanced, which might have introduced a degree of selection bias. The cutoff values of some categorical variables were selected by referring to previous literature, as there is no clear standard at present. Moreover, we did not compare the diagnostic accuracy of conventional ultrasound combined with CEUS to that of CT and MRI. In the future, we will increase the sample size, compare the diagnostic accuracy of the combined modality with CT and MRI, and clarify its role in predicting the different grades of malignant transformation of PCNs across various pathological types.

Conclusions

There exist certain differences in the basic clinical data and conventional ultrasound and CEUS image characteristics between the four types of PCNs. Conventional ultrasound combined with CEUS has a higher diagnostic accuracy than does conventional ultrasound in the differential diagnosis of PNC types.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-154/coif). All authors report that this research was supported by the National Natural Science Foundation of China (No. 82071940). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the ethics committee of West China Hospital,

Sichuan University (No. 2023[2096]) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was waived for all patients due to the retrospective nature of this study.

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