

Solid Pancreatic Tumors with Unilocular Cyst-Like Appearance on CT: Differentiation from Unilocular Cystic Tumors Using CT

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Objective: To describe the computed tomography (CT) features of neuroendocrine tumors (NETs) and solid pseudopapillary tumors (SPTs) with unilocular cyst-like appearance, and to compare them with those of unilocular cystic tumors of the pancreas.

Materials and Methods: This retrospective study was approved by our Institutional Review Board, and informed consent was waived. We included 112 pancreatic tumors with unilocular cyst-like appearance on CT (16 solid tumors [nine NETs and seven SPTs] and 96 cystic tumors [45 serous cystadenomas, 30 mucinous cystic neoplasms, and 21 branch-duct intraductal papillary mucinous neoplasms]). Two radiologists reviewed the CT images in consensus to determine tumor location, long diameter, morphological features, wall thicknesses, ratio of wall thickness to tumor size, wall enhancement patterns, intratumoral contents, and accompanying findings. Fisher's exact test was used to analyze the results.

Results: All 16 solid tumors had perceptible walls (mean thickness, 2.7 mm; mean ratio of wall thickness to tumor size, 7.7%) with variable enhancement. Four NETs and seven SPTs had hemorrhage, calcifications, and/or mural nodules. Six CT findings were specific for solid tumors with unilocular cyst-like appearance: a thick (> 2 mm) wall, uneven thickness of the wall, high ratio of wall thickness to tumor size, hyper- or hypo-attenuation of the wall in the arterial and portal phase, and heterogeneous internal contents. When three or more of the above criteria were used, 100% specificity and 87.5–92% accuracy were obtained for solid tumors with unilocular cyst-like appearance.

Conclusion: A combination of CT features was useful for distinguishing solid tumors with unilocular cyst-like appearance from unilocular cystic tumors of the pancreas.

Index terms: Pancreatic neoplasm; Neuroendocrine tumor; Solid pseudopapillary tumor; Contrast-enhanced CT

INTRODUCTION

Cystic neoplasms of the pancreas are rare, representing 1%

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of pancreatic neoplasms (1). However, recent developments in imaging techniques and the increasing number of diagnostic examinations enable more often detect cystic lesions of the pancreas, and their diagnosis is challenging. Pancreatic cystic lesions can be classified as cystic neoplasms, solid neoplasms with cystic change, or non-neoplastic cysts. Relatively common cystic tumors are serous cystadenomas (SCAs), mucinous cystic neoplasms (MCNs), and intraductal papillary mucinous neoplasms (IPMNs) (2). Solid pancreatic tumors with cystic changes, while rare, have also been reported (3-6). Among solid pancreatic tumors with cystic changes, neuroendocrine tumors (NETs) and solid pseudopapillary tumors (SPTs), both of which

arise with intratumoral cystic changes, are relatively common. When solid tumors have large intratumoral cystic changes, they have a cyst-like appearance on computed tomography (CT), are not true physical cysts, and can mimic cystic tumors in daily clinical practice. Most cystic tumors are benign and can be observed, whereas solid tumors with intratumoral cystic changes have malignant potential and require surgical resection. Due to the risk of malignancy, solid tumors with intratumoral cystic changes should be distinguished from cystic tumors for appropriate management.

Cystic solid tumors of the pancreas (i.e., solid tumors with a large intratumoral cystic change) have been reported but few reports (7, 8) are available regarding the CT features of cystic pancreatic NETs and a comparison with other cystic neoplasms. However, the number of cystic pancreatic NETs was small (less than five) and the CT features evaluated were not detailed. Furthermore, a comparison of CT features between solid tumors with a unilocular cyst-like appearance and unilocular cystic tumors of the pancreas has not been

reported. Therefore, we performed this study to describe the CT features of NETs and SPTs with unilocular cyst-like appearance and to compare them with those of unilocular cystic tumors of the pancreas.

MATERIALS AND METHODS

Subjects

This retrospective study was approved by the Institutional Review Board of Asan Medical Center, and informed consent was waived. A total of 1921 tumors of the pancreas were surgically resected or excised at Asan Medical Center between January 2001 and May 2011 (Fig. 1). Because relatively common pancreatic solid tumors with intratumoral cystic change are either NETs or SPTs, and common cystic tumors are either SCAs, MCNs, or IPMNs (2, 5, 9), an investigator searched the NET and SPT pathological database for solid tumors and the SCA, MCN, and IPMN pathological database for cystic tumors. We excluded pancreatic ductal adenocarcinomas (n = 1171), because

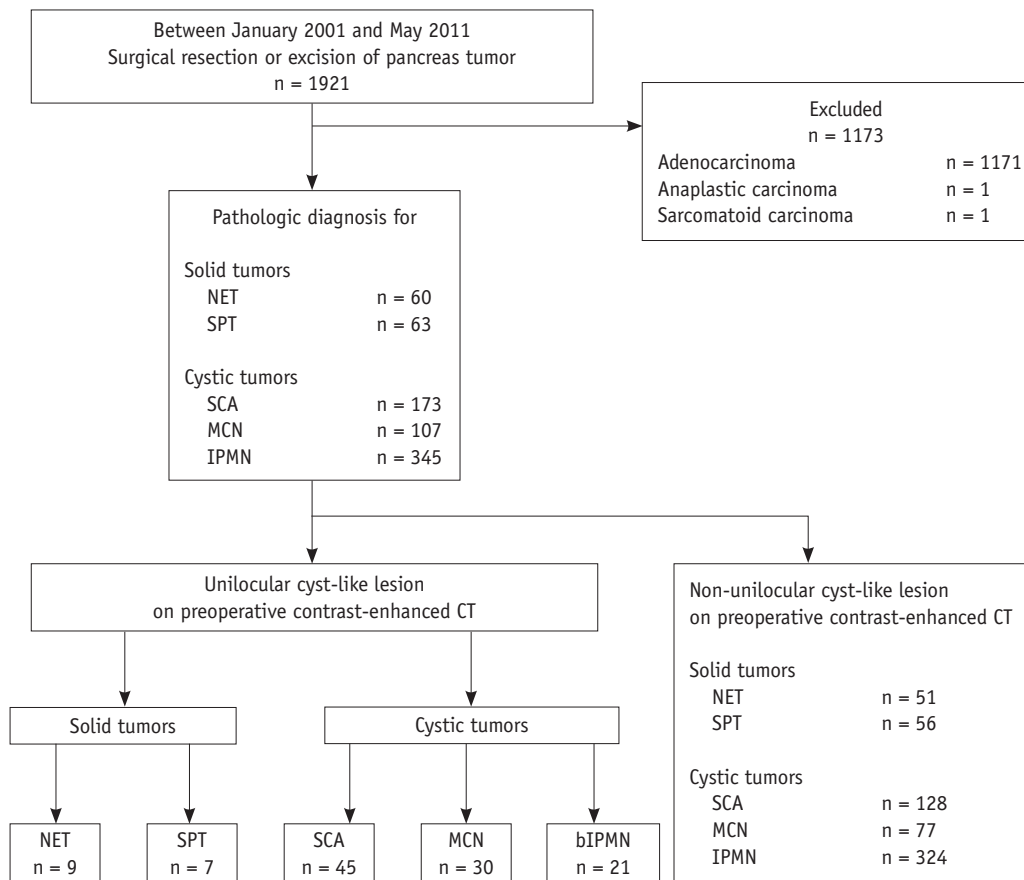


Fig. 1. Flow diagram of study patients. Data are numbers of tumors. bIPMN = branch-duct intraductal papillary mucinous neoplasm, MCN = mucinous cystic neoplasm, NET = neuroendocrine tumor, SCA = serous cystadenoma, SPT = solid pseudopapillary tumor

they are frequently associated with secondary findings, such as proportional dilatation of the upstream pancreatic duct, parenchymal atrophy, and/or invasiveness of vascular or adjacent structures. Therefore, most pancreatic ductal adenocarcinomas are easily differentiated from other solid tumors. Pancreatic miscellaneous rare solid tumors ($n = 2$) were also excluded due to their extreme rareness. We identified 60 NETs, 63 SPTs, 173 SCAs, 107 MCNs, and 345 IPMNs.

A board-certified abdominal radiologist (9 years of experience in abdominal radiology) reviewed preoperative contrast-enhanced CT scans of all 748 tumors, and selected tumors determined to be unilocular cyst-like lesions with a diagnostic challenge. Solid tumors that mimicked unilocular cystic lesions were defined as having an intratumoral cyst-like portion that comprised $> 90\%$ of the tumor. Cystic tumors with unilocular cystic lesions were identified by their resemblance to unilocular cysts without ancillary findings for diagnosis, such as a honeycomb appearance or the presence of grape-like cystic lesions. Nine NETs and seven SPTs with a unilocular cyst-like appearance, which mimicked unilocular cystic neoplasms, and 45 SCAs, 30 MCNs, and 21 branch-duct IPMNs with a unilocular cystic appearance, were identified. Finally, we enrolled all 112 tumors from 111 patients including 16 solid tumors in 15 subjects (five men and 10 women; mean age \pm standard deviation [SD], 42 ± 14.7 years) and 96 cystic tumors in 96 subjects (24 men and 72 women; mean age \pm SD, 48 ± 12.8 years). The types of surgery of the 15 patients with solid tumors were segmentectomy ($n = 10$), excision ($n = 1$), total pancreatectomy ($n = 1$), Whipple's operation ($n = 2$), and pylorus-preserving pancreaticoduodenectomy ($n = 1$). Those of the 96 patients with cystic tumors were segmentectomy ($n = 72$), excision ($n = 13$), subtotal pancreatectomy ($n = 1$), Whipple's operation ($n = 5$), and pylorus-preserving pancreaticoduodenectomy ($n = 5$).

CT Examinations

All CT examinations were performed on 4- or 16-detector row CT scanners (LightSpeed QX/i or LightSpeed 16, GE Healthcare, Milwaukee, WI, USA; Somatom Sensation 16, Siemens Medical Systems, Erlangen, Germany). Both arterial and portal phase scans were obtained with pre-enhanced scans in the 11 patients with solid tumors and the 86 patients with cystic tumors, whereas single portal-phase scans were performed with pre-enhanced scans in four with solid tumors and 10 with cystic tumors. Arterial and

portal phase scans were obtained using a fixed 15-second delay after attenuation of the aorta at the thoracolumbar junction had reached 100 Hounsfield units and a 72- to 80-second delay, respectively, after intravenous injection of 120–150 mL (2–2.5 mL/kg) iopromide (Ultravist 370; Bayer Healthcare, Berlin, Germany) administered at a rate of 3 mL/sec with an automatic injector (LF CT 9000; Liebel-Flarsheim, Cincinnati, OH, USA). The imaging parameters of the 16-multidetector CT (MDCT) systems were beam collimation of 16×0.75 mm, beam pitch of 1, gantry rotation time of 0.5 second, voltage of 120 kV, automated dose modulating using the maximum allowable tube current set to 200 mAs, and a reconstructed slice thickness of 3 mm for the Siemens system. The corresponding parameters for the 16-MDCT GE system were beam collimation of 16×1.25 mm, beam pitch of 0.938, gantry rotation time of 0.6 second, voltage of 120 kV, maximum allowable tube current set to 200 mAs, and slice thickness of 2.5 mm, whereas those for the 4-MDCT were beam collimation of 4×1.25 mm, beam pitch of 1.5, and gantry rotation time of 0.8 second with the same voltage, tube current, and slice thickness.

Image Analysis

All images were reviewed using a local picture archiving and communications system monitor and digital imaging and communications in medicine image viewing software. All CT images were reviewed by two board-certified abdominal radiologists (3 and 12 years of experience in abdominal radiology, respectively), who were blinded to the pathological diagnosis. Differences in assessments by the two radiologists were resolved by consensus, including the opinion of a third board-certified abdominal radiologist (26 years of clinical experience in abdominal radiology). The size, location (head, body, or tail), and contour (round, oval, or lobulated) of each pancreatic tumor was noted. Lobulation was defined as the presence of rounded contours that could not be described as borders of the same circle. The wall of the lesion was considered to be thick if it was > 2 mm in diameter for at least 25% of the lesion circumference (10). When thickness of the tumor wall was not equal, it was considered uneven. The ratio of wall thickness to tumor size was calculated as the thickest portion of the tumor wall divided by axial diameter of the tumor. Enhancement of the wall was regarded as low-, iso-, or high-attenuation compared with the pancreatic parenchyma in the portal phase and the available arterial phase.

Lesion content was classified as either homogeneous or heterogeneous. The presence of mural nodules, incomplete septa-like structures, calcification, and hemorrhage was evaluated. Accompanying findings, such as dilatation of the main pancreatic duct or parenchymal atrophy, were also reported.

Statistical Analysis

Fisher's exact test was used to compare differences in the numbers of CT features between solid tumors and cystic tumors, and a *p* value < 0.05 was considered significant. Sensitivity and specificity values of each CT feature and

the combined CT findings for differentiating solid tumors from cystic tumors were calculated. Statistical analyses were performed using the IBM SPSS statistics 19 software package (IBM Corp., New York, NY, USA).

RESULTS

The 16 solid tumors with a unilocular cyst-like appearance comprised nine NETs and seven SPTs in 15 patients, including one patient with two SPTs. The CT features of these solid tumors are summarized in Table 1. The mean long diameter of the nine NETs was 3.5 cm

Table 1. CT Features of Pancreatic Unilocular Cyst-Like Lesions, Including Solid Tumors and Cystic Tumors

CT Finding	Solid Tumors		Cystic Tumors			<i>P</i> *
	NET (n = 9)	SPT (n = 7)	SCA (n = 45)	MCN (n = 30)	IPMN (n = 21)	
Mean size (cm)	3.5	4.8	3.7	3.8	3.0	
Location						0.103
Head	3	3	13	1	6	
Body or tail	6	4	32	29	15	
Contour						0.265
Round or oval	4	4	11	20	6	
Lobulated	5	3	34	10	15	
Wall						
Thin (≤ 2 mm)	2	3	45	30	21	
Thick (> 2 mm)	7	4	0	0	0	< 0.001
Even thickness	5	1	44	25	20	
Uneven thickness	4	6	1	5	1	< 0.001
Wall thickness to tumor size ratio (%)	9.5	5.4	3.2	3.9	1.9	< 0.001
Wall attenuation in portal phase						< 0.001
High	2	0	0	1	0	
Iso	7	5	45	29	21	
Low	0	2	0	0	0	
Wall attenuation in arterial phase [†]						< 0.001
High	5	0	0	0	0	
Iso	1	2	42	26	18	
Low	1	2	0	0	0	
Content						
Homogeneous	5	0	43	28	21	
Heterogeneous	4	7	2	2	0	< 0.001
Mural nodules	1	4	0	0	0	
Septa-like	3	3	1	0	0	
Calcification	0	4	1	2	0	
Hemorrhage	2	1	0	1	0	
Dilatation of main pancreatic duct	1	0	1 [‡]	2 [§]	0	0.565
Parenchymal atrophy	0	0	0	0	0	

Note.— Data are numbers of tumors. *Fisher's exact test was used to compare differences in each finding between solid tumors and cystic tumors, [†]Arterial phase CT was available in 7 NETs, 4 SPTs, 42 SCAs, 26 MCNs, and 18 IPMNs, [‡]Dilatation of main pancreatic duct developed with increase of tumor size, [§]Downstream main pancreatic duct was mildly dilated, ^{||}Reference value was 4.4%, mean ratio of wall thickness to tumor size in all 112 tumors. IPMN = intraductal papillary mucinous neoplasm, MCN = mucinous cystic neoplasm, NET = neuroendocrine tumor, SCA = serous cystadenoma, SPT = solid pseudopapillary tumor

(range, 1.9–5.3 cm) and that of the seven SPTs was 4.8 cm (range, 3.4–9.2 cm). Ten of 16 solid tumors were located in the body or tail of the pancreas. All 16 solid tumors had well-defined margins with round or oval ($n = 8$), or lobulated ($n = 8$) contours, and had perceptible walls (mean wall thickness, 2.7 mm; range, 1.5–5.6 mm; mean ratio of wall thickness to tumor size, 7.7%). Five of nine NETs showed high attenuation of the wall in the arterial phase. Two of these five NETs showed persistent high attenuation, and the remaining three NETs showed iso-attenuation in the portal phase (Fig. 2). Internal content

appeared homogeneous in five of nine NETs. Solid nodules, incomplete subtle septa-like structures, or hemorrhage were noted in the other four NETs. All seven SPTs had low- or iso-attenuated walls and had heterogeneous contents, which consisted of mural nodules, incomplete subtle septa-like structures, calcification, and/or hemorrhage (Fig. 3). The histopathological findings of internal contents of the solid tumors were tumor necrosis, cystic degeneration, and/or hemorrhage.

All cystic tumors had thin walls (mean wall thickness, 0.9 mm; range, 0–1.7 mm; mean ratio of wall thickness to



Fig. 2. Pancreatic neuroendocrine tumor in 54-year-old woman.

A, B. Transverse contrast-enhanced arterial (**A**) and portal (**B**) phase computed tomography images demonstrate 2-cm round cyst-like mass in pancreatic tail. Thick (3.3 mm) uneven wall (white arrows) shows high attenuation in arterial phase and iso-attenuation in portal phase.

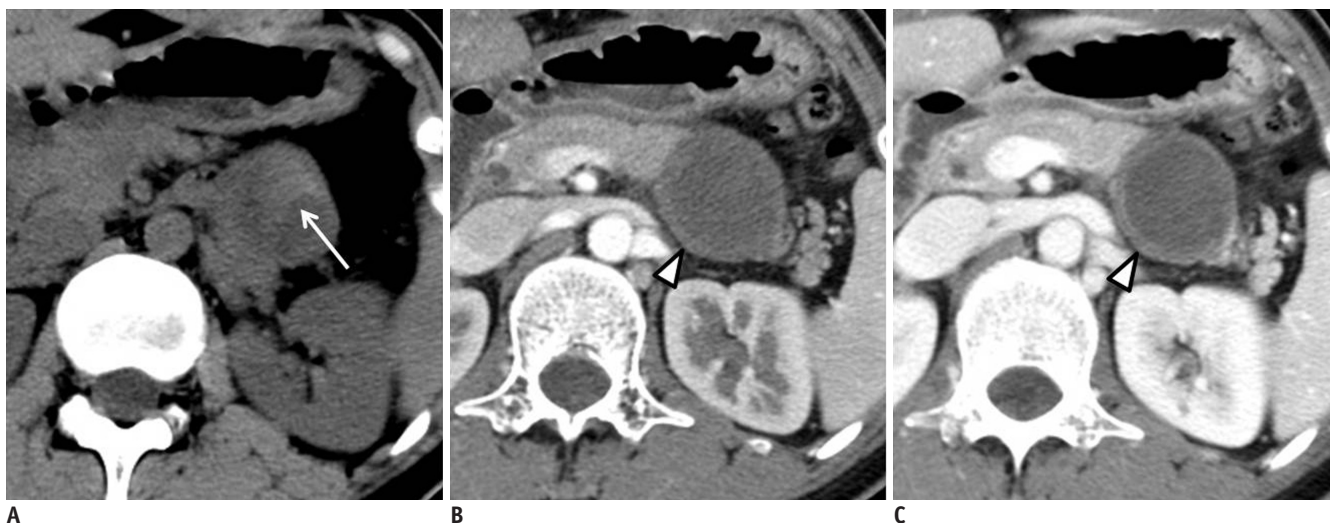


Fig. 3. Solid pseudopapillary tumor in 33-year-old-woman.

A. Transverse precontrast computed tomography (CT) image shows 3.5-cm round mass with intratumoral high attenuated lesions (white arrow), suggesting internal hemorrhage. **B, C.** Transverse contrast-enhanced arterial (**B**) and portal (**C**) phase CT images show unilocular cyst-like mass with low-attenuating, thick (3.4 mm) uneven wall (white arrowheads).

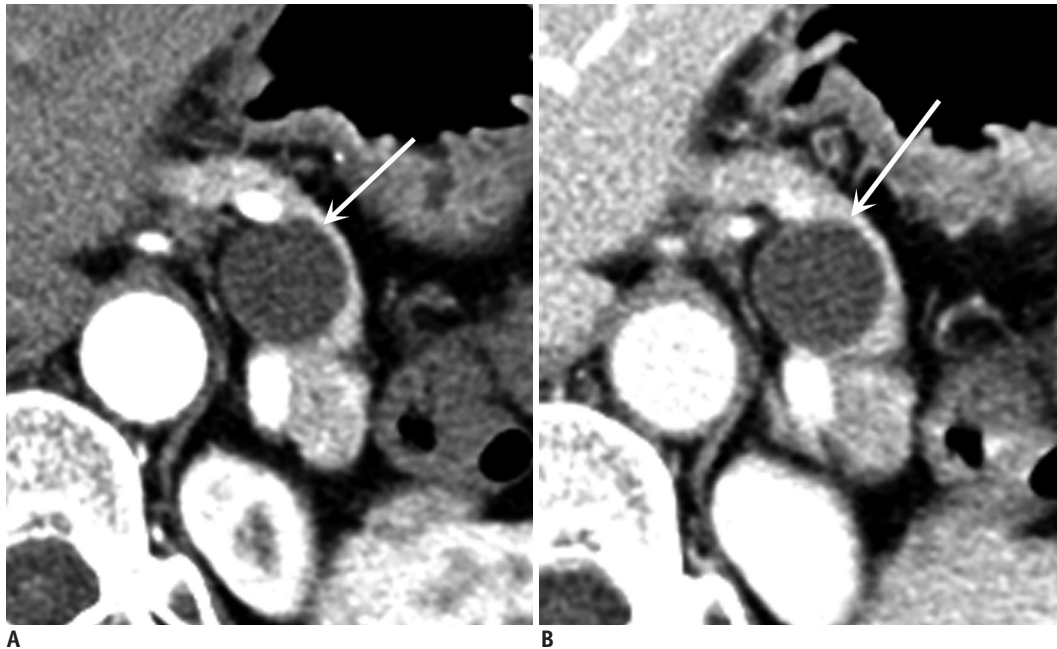


Fig. 4. Mucinous cystadenoma in 54-year-old woman.

A, B. Transverse contrast-enhanced arterial (A) and portal (B) phase computed tomography images demonstrate 2.3-cm round cystic mass (white arrows) in pancreatic tail. Even thin (1 mm) wall shows iso-attenuation in arterial and portal phases.

Table 2. Sensitivity and Specificity Values for CT Features in Diagnosis of Pancreatic Solid Tumors with Unilocular Cyst-Like Appearance

Finding	Sensitivity (%)	Specificity (%)
Thick wall (> 2 mm)	68.8 (11/16)	100 (96/96)
Uneven thickness of wall	62.5 (10/16)	92.7 (89/96)
High ratio of wall thickness to tumor size*	81.3 (13/16)	75 (72/96)
Variable (high or low) attenuation of wall		
In portal phase	31.3 (5/16)	99 (95/96)
In arterial phase	72.7 (8/11)	100 (86/86)
Heterogeneous internal content	68.8 (11/16)	95.8 (92/96)

Note.— Data in parentheses are numbers of tumors. *More than 4.4%, mean ratio of wall thickness to tumor size in all 112 tumors

Table 3. Diagnostic Performance of CT in 112 Patients with Pancreatic Unilocular Cyst-Like Lesions, Including Solid Tumors and Cystic Tumors

No. of CT Findings*	Sensitivity (%)	Specificity (%)	Accuracy (%)
2	62.5 (10/16)	97.9 (94/96)	92.9 (104/112)
3	43.8 (7/16)	100 (96/96)	92.0 (103/112)
4	31.3 (5/16)	100 (96/96)	90.2 (101/112)
5	18.8 (3/16)	100 (96/96)	88.4 (99/112)
6	12.5 (2/16)	100 (96/96)	87.5 (98/112)

Note.— Data in parentheses are numbers of tumors. *Numbers of following CT findings: wall thickness of more than 2 mm, uneven thickness of wall, high ratio of wall thickness to tumor size (> 4.4%), high or low attenuation of the walls in the arterial and portal phases, and heterogeneous internal contents

tumor size, 3.1%) with iso-attenuation in both the portal and available arterial phases (Fig. 4), except one MCN. Most walls of the cystic tumors had an even thickness. Cystic tumors had mainly homogeneous internal contents. Dilatation of the main pancreatic duct was seen in one SCA and two MCNs. As shown in Table 1, solid tumors

with a unilocular cyst-like appearance had a significantly higher likelihood of having thick walls ($p < 0.001$), uneven thickness of walls ($p < 0.001$), high ratios of wall thickness to tumor size ($p < 0.001$), high or low attenuation of the walls in the arterial and portal phases ($p < 0.001$), and heterogeneous internal contents ($p < 0.001$) compared with

those of unilocular cystic tumors.

The sensitivity and specificity values for the diagnosis of the solid tumors were based on the six significant CT findings mentioned above (Table 2). The highest sensitivity and specificity values for the solid tumors were 81.3% and 100%, respectively. When three or more of above criteria were used in combination, specificity of 100% and accuracy of 87.5–92% for solid tumors were obtained (Table 3).

DISCUSSION

We showed that a combination of CT features can help differentiate solid tumors with a unilocular cyst-like appearance from unilocular cystic tumors of the pancreas. In our present analyses, 13% (16/123) of NETs and SPTs had a unilocular cyst-like appearance on CT. Although several studies (5, 7, 11) have shown that cystic pancreatic NETs represent 5–10% of pancreatic NETs, the accurate percentage frequency of these two solid tumors with a unilocular cyst-like appearance, not just cystic appearance, has not been reported. Furthermore, the frequency reported in our study was higher than expected. Only visual assessment of CT features, not true physical cysts, may be one of the causes for the unexpected high prevalence of NETs and SPTs with a unilocular cyst-like appearance in our study. Hence, accurate diagnosis and distinguishing these solid tumors with a unilocular cyst-like appearance from unilocular cystic tumors of the pancreas is important for proper management and treatment.

Our results show that CT features of wall of solid tumors with a unilocular cyst-like appearance are important clues to differentiate them from unilocular cystic tumors of the pancreas on CT. Adsay et al. (9, 11) reported that cystic NETs are lined by a ragged cuff of well-preserved neoplastic endocrine cells. Therefore, the walls of cystic NETs appear hypervascular on CT. Characteristic morphological features of the SPT cavity wall include pseudopapillary architecture (which creates an ependymoma-like appearance), hyaline globules, clusters of uniform cells that mimic those found in NETs (although they lack neuroendocrine chromatin), and grooved nuclei (9, 12). Although histological findings differ between NETs and SPTs, the walls of NETs and SPTs with unilocular cyst-like appearances are parts of solid tumors. Therefore, they have perceptible uneven thick walls and variable enhancement, similar to the enhancement pattern of the original tumor in this study. In contrast, unilocular cystic tumors of the pancreas, including SCAs,

MCNs, and IPMNs, tended to have even thin walls without enhancement in our study. Cystic tumors of the pancreas commonly show a thin wall without enhancement on CT, unless they have complications or are malignant. Due to these differences in mural features on CT between solid tumors with unilocular cyst-like appearance and unilocular cystic tumors, the combination of CT features of their walls is helpful for their differential diagnosis.

In our study, the other important CT feature for differentiating solid tumors with a unilocular cyst-like appearance from unilocular cystic tumors of the pancreas was heterogeneous internal content. Adsay et al. (9, 11) reported that cystic NETs are filled with clear fluid instead of necrotic debris. It is well known that the cavities of SPTs are formed by a necrotic or degenerative process (9, 12). Therefore, the cystic areas often contain blood, necrotic debris, and clusters of foamy macrophages. These observations support our present findings that cystic NETs are more likely to have relatively homogenous internal contents, compared with those of SPTs. Due to the greater incidence of tumor necrosis or degeneration, SPTs had more heterogeneous internal contents than those of cystic NETs. In contrast, most common unilocular cystic tumors of the pancreas had homogeneous internal contents on CT in our study. Cystic tumors of the pancreas usually show homogeneous cystic attenuation on CT, unless they have a complication.

The most common cystic lesion in the pancreas is the pseudocyst. Pseudocysts are usually seen as unilocular round or oval shaped cystic lesions with a barely perceptible wall. Therefore, distinguishing between pseudocysts and any unilocular cystic lesions including solid tumors with unilocular cyst-like appearances is very important in daily practice. However, most pseudocysts are easily diagnosed with clinical findings, laboratory results, prior history of pancreatitis, and CT findings of chronic pancreatitis (13). Furthermore, isolated pseudocysts without these typical collateral findings are very rare.

Radiologists and physicians often find it difficult to distinguish unilocular cystic lesions of the pancreas. Although SCAs are usually composed of numerous small cysts with a honeycomb appearance, they may also exist as macrocystic variants that mimic unilocular cystic lesions (10, 14). Given that MCNs often have thickened walls and frequently appear as unilocular or septated cystic lesions with/without peripheral curvilinear calcification or calcified contents (15), macrocystic forms of SCAs are

occasionally misdiagnosed as MCNs or pseudocysts (10). One study (10) reported that CT findings of the location in the pancreatic head, a lobulated contour, and the absence of wall enhancement are specific for macrocystic SCAs in comparison with those of MCNs. In our study, SCAs showed lobulated contours more frequently than that of MCNs. However with the exception of one MCN, all SCAs and MCNs had thin walls without enhancement. Branch-duct IPMNs have characteristic findings of grape-like lobulated contours and a close proximity to the pancreatic duct (16). However, the segmental cystic appearance of branch-duct IPMNs may mimic unilocular cystic lesions, creating difficulty for a differential diagnosis from MCNs or macrocystic SCAs. In our study, most branch-duct IPMNs with unilocular features had merely imperceptible thin walls and all had homogeneous contents.

This study had several limitations. First, the number of cases was small due to the rarity of solid pancreatic tumors with a unilocular cyst-like appearance. Second, we did not compare the features of CT and magnetic resonance imaging (MRI), because only a subset of patients underwent MRI examinations. Although CT is a more commonly used diagnostic imaging tool, MRI can be helpful. Third, a quantitative analysis using wall enhancement region-of-interest (ROI) was not performed. However, the thin walls of the majority of the cystic tumors complicate precise ROI measurements of wall enhancement. Furthermore, in daily practice, a visual assessment of wall enhancement on CT is used instead of quantitative analysis. Fourth, we compared only the CT findings of solid tumors with unilocular cyst-like appearance with those of unilocular cystic tumors of the pancreas. However, in daily practice, pancreatic tumor characterization relies not only on image features but also on demographic, clinical and biological data of patients. Therefore, a further comparative study regarding imaging features as well as demographic, clinical and biological data will be more helpful for clinical practice.

In conclusion, NETs and SPTs with large intratumoral cystic changes can mimic unilocular cystic tumors of the pancreas. Several CT findings, including an uneven thick (> 2 mm) wall with variable enhancement, high ratio of wall thickness to tumor size, and heterogeneity of internal contents, are helpful to distinguish solid pancreatic tumors with unilocular cyst-like appearance. A combination of these CT findings is suggestive of solid tumors with unilocular cyst-like appearance rather than unilocular cystic tumors of the pancreas.

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