

Clinicoradiological features of resected serous cystic neoplasms according to morphological subtype and preoperative tentative diagnosis: can radiological characteristics distinguish serous cystic neoplasms from other lesions?

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Purpose: Serous cystic neoplasm (SCN) of the pancreas is considered benign in most cases. However, some SCN patients undergo surgical resection because lesions could not be differentiated preoperatively. This study evaluated causes of resection for SCN, investigated clinical and radiological features of surgically resected SCNs, and compared characteristics of SCNs diagnosed accurately and those misdiagnosed.

Methods: One hundred patients, who underwent surgery for pancreatic cystic tumors with pathological confirmation of SCN between 2000 and 2014 were retrospectively analyzed.

Results: The mean patient age was 52.9 years, 67 (67%) were female, and most lesions (72%) were located in the pancreatic body or tail. Fifty-one (51%) pathologically confirmed SCNs were preoperatively diagnosed as non-SCNs. Patients underwent surgery due to uncertain diagnosis (58%) or symptomatology (18%). According to radiological examination, most lesions were macrocystic (85%), exhibited septation (58%), or were enhancing lesions (48%). Compared with preoperatively diagnosed non-SCNs, accurately diagnosed SCNs exhibited septation (75.5% vs. 41.2%, $P = 0.001$) and central scar (36.7% vs. 11.8%, $P = 0.003$) more frequently in radiological examinations. In terms of macrocystic tumors ($n = 85$), most parameters did not differentiate preoperative diagnoses, although lesions accurately diagnosed as SCN exhibited septation more frequently than those preoperatively misdiagnosed as mucinous cystic neoplasm or intraductal papillary mucinous neoplasm (70.7% vs. 38.9% vs. 33.3%, respectively, $P = 0.009$).

Conclusion: It is difficult to accurately distinguish macrocystic SCNs from other cystic tumors using conventional radiological methods. For more accurate diagnosis, new biomarkers and/or other diagnostic modalities are needed and warrant further investigation.

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INTRODUCTION

Pancreatic cystic neoplasms (PCNs) account for approximately 30% of resected pancreatic tumors [1-3]. Due to the increased use of sophisticated imaging modalities and advances in imaging techniques, detection rates for PCNs have gradually increased [4]. There are 4 common categories of PCN including: intraductal papillary mucinous neoplasm (IPMN); serous cystic neoplasm (SCN); mucinous cystic neoplasm (MCN); and solid pseudopapillary neoplasm [1]. Of these, IPMN, MCN, and SCN are recommended to be surgically removed due to their malignant potential [5-8].

Although symptomatic SCNs should be surgically removed, regular surveillance of asymptomatic SCNs is generally recommended due to lower malignant potential compared with other PCNs [9]. However, some SCNs do not exhibit the typical honeycomb pattern, and their atypical appearance makes it difficult to discriminate SCNs from other potentially malignant PCNs and to decide whether to perform the surgery [10]. If surgeons could accurately distinguish SCNs from other PCNs, unnecessary operations would be decreased. Therefore, the aim of this study was to evaluate the causes of resection for SCN, to investigate the clinical and radiological features of SCNs that are surgically resected, and to compare the characteristics of SCNs that were diagnosed accurately and those misdiagnosed.

METHODS

Patients and materials

This was a retrospective study that analyzed prospectively collected medical data. Between 2000 and 2014, patients who underwent surgical resection and were diagnosed with

pathologically confirmed SCN were included. Patients with incomplete radiological data were excluded. All patients underwent preoperative multidetector CT using either the Brilliance 64 (Philips Medical Systems, Cleveland, OH, USA) or LightSpeed Ultra (GE Healthcare, Little Chalfont, UK) instruments. Additional MRI using the Magnetom Verio (Siemens Healthcare, Erlangen, Germany) system was performed as required.

Clinical factors included age, sex, roots of detection of the lesions, preoperative diagnosis, tumor location, reason(s) for surgery, and operation type. The department of radiology of the authors' institution provided the reporting form for PCNs, which included radiological characteristics including type of cyst (microcystic or macrocystic), tumor size, calcification, central scar, solid component(s), cystic wall thickening, septation in the cyst, enhancing lesion, pancreatic duct dilatation, bile duct dilatation and pancreas atrophy, and suggested all possible diagnoses according to these radiological characteristics. Type of cyst, and other radiological characteristics were defined based on the authors' previous report [10]. Briefly, cysts were classified as microcystic if they were < 2 cm in size, and macrocystic when ≥ 2 cm. The typical "honeycomb" appearance was included among the microcystic features. All radiological images were reviewed by one specialized pancreatobiliary radiologist.

This study was approved by the Institutional Review Board of Seoul National University Hospital (No. 1606-086-771), and all patients consented to participate in this study.

Statistical analysis

Categorical variables were compared using the chi-square test and continuous variables were compared using Student t-test. Differences were considered to be statistically significant at $P <$

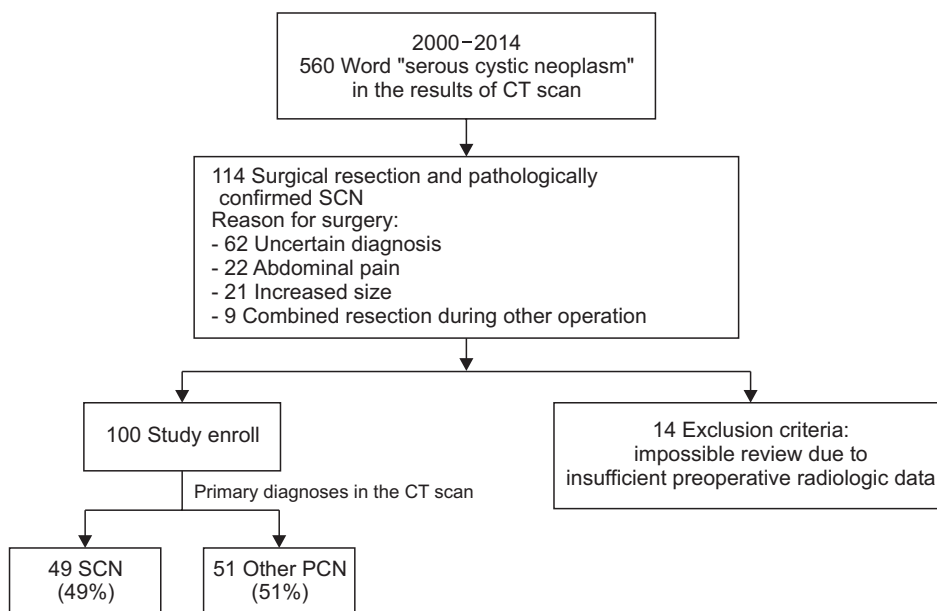


Fig. 1. Study design and patient enrollment. Finally, one hundred consecutive patients underwent surgical resection and had pathologic confirmation of serous cystic neoplasm (SCN). In regards to preoperative diagnoses, 49 patients were accurately diagnosed of SCN, and 51 patients were misdiagnosed of other pancreatic cystic neoplasm. SCN serous cystic neoplasm.

0.05 in 2-tailed testing. All statistical analyses were performed using IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA).

RESULTS

Clinical variables and radiological features

A flowchart illustrating patient enrollment is presented in Fig. 1. Overall, 560 patients were potentially diagnosed with SCN, which was described in the CT scan reports. Most patients underwent regular surveillance, and 114 underwent surgical resection and SCN was pathologically confirmed. All of the excluded patients (n = 14) underwent preoperative radiological examinations in another hospital; therefore, imaging data were not recorded in the medical database and could not be reviewed. Ultimately, 100 patients were included in the present study. There were no cases of serous cystadenocarcinoma.

The mean age of the patients was 52.9 years and 67 (67%) were female (Table 1). Seventy-one patients (71%) had their PCNs incidentally detected at a regular health check-up, 27 (27%) were due to abdominal pain, 1 (1%) due to jaundice, and 1 (1%) due to a palpable mass. Seventy-two patients (72%) had the PCN in the pancreatic body and tail. Reasons for surgery included uncertain diagnosis (n = 58, 58%), symptomatology (n = 18, 18%), and combined resection during other surgery (n = 8, 8%). Of patients with an uncertain diagnosis, 10 were preoperatively diagnosed with possible malignant lesions, in which the most probable preoperative diagnoses were: IPMN with invasive carcinoma (n = 5); pancreatic head cancer (n = 2); pancreatic

tail cancer (n = 2); and multiple metastases from renal cell carcinoma (n = 1). The preoperative diagnoses were SCN (n =

Table 1. Clinical variables in total patients (n = 100)

Variable	Value
Age (yr)	52.9 ± 13.9
Sex, male:female	33:67
How to detect	
Incidental detection by health check-up	71 (71)
Abdominal pain	27 (27)
Jaundice	1 (1)
Palpable mass	1 (1)
Tumor location	
Head	23 (23)
Body and tail	72 (72)
Entire pancreas	5 (5)
Reasons for surgery	
Uncertain diagnosis	58 (58)
Presence of abdominal pain	18 (18)
Increased size	18 (18)
Combined resection during other surgery	6 (6)
Preoperative diagnosis	
Serous cyst neoplasm	49 (49)
Mucinous cyst neoplasm	22 (22)
Intraductal papillary mucinous neoplasm	18 (18)
Pancreatic pseudocyst	3 (3)
Solid pseudopapillary neoplasm	2 (2)
Neuroendocrine tumor	1 (1)
Others	5 (5)

Values are presented as mean ± standard deviation or number (%).

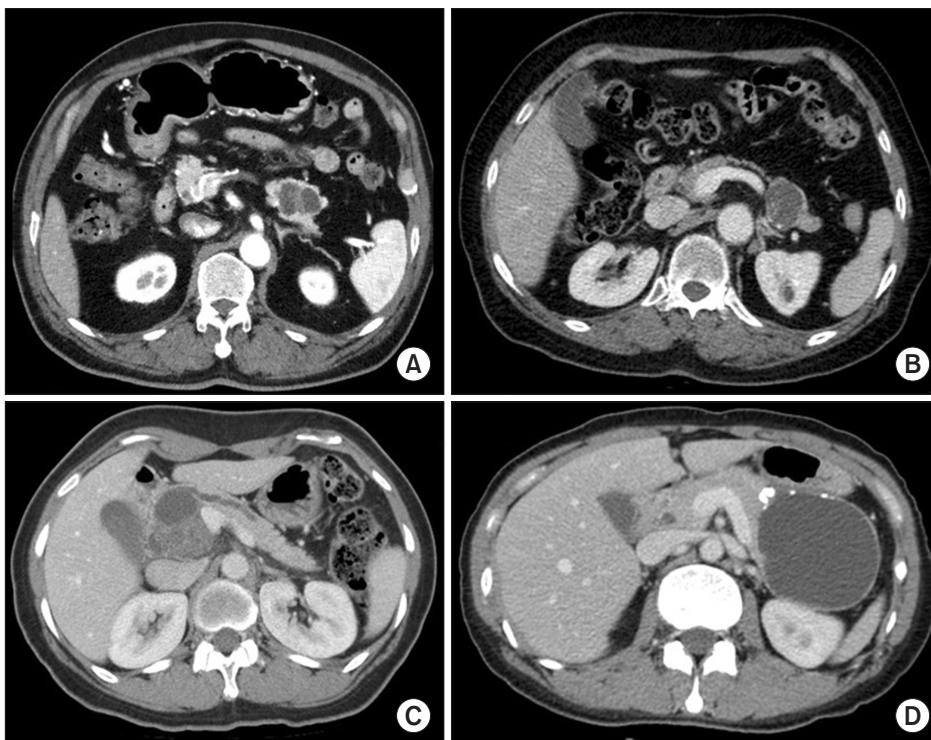


Fig. 2. Preoperative image according to the preoperative diagnoses. All these lesions were pathologically confirmed with serous cystic neoplasm (SCN) after surgical resection. (A) SCN. 3.8-cm-sized cystic lesion with internal septation in pancreas tail. (B) Preoperatively misdiagnosed mucinous cystic neoplasm. 3.8-cm-sized well-defined septated cystic lesion with wall calcification. (C) Preoperatively misdiagnosed intraductal papillary mucinous neoplasm. 6.3-cm-sized multi-loculated cystic mass with solid component and the presence of upstream pancreatic duct dilatation. (D) Preoperatively misdiagnosed pseudocyst. 9-cm-sized loculated cystic lesion with evenly-thickened wall with multiple calcification.

49, 49%) (Fig. 2A), misdiagnosed MCN (n = 22, 22%) (Fig. 2B), misdiagnosed IPMN (n = 18, 18%) (Fig. 2C), and misdiagnosed pancreatic pseudocyst (n = 3, 3%) (Fig. 2D).

The radiological characteristics of all patients are summarized

Table 2. Radiologic features in total patients (n = 100)

Variable	Value
Tumor size (cm)	4.1 ± 2.9
Cyst type	
Macrocystic:microcystic	85 (85):15 (15)
Septation	58 (58)
Enhancing lesion	48 (48)
Calcification	38 (38)
Solid portion	31 (31)
Main pancreatic duct dilatation	26 (26)
Central scar	24 (24)
External wall thickening	12 (12)
Bile duct dilatation	10 (10)
Pancreas atrophy	8 (8)

Values are presented as mean ± standard deviation or number (%).

in Table 2. The mean tumor size was 4.1 cm. Because only patients with surgically resected SCNs were enrolled in this study, most lesions exhibited macrocystic features (n = 85, 85%), followed by microcystic appearance (n = 15, 15%). Septation in the cyst was evident in 58 (58%) patients, enhancing lesions in the cyst in 48 (48%), and calcification in the cyst in 38 (38%).

Comparisons of clinical and radiological features according to preoperative diagnoses

Patients were divided into 2 groups: those preoperatively diagnosed with SCN (n = 49, 49%); and those who were diagnosed with lesions other than SCN (n = 51, 51%). The clinical and radiological characteristics of the 2 groups are compared in Table 3. There were no significant differences in clinical features between the 2 groups. In terms of radiological features, septation (75.5% vs. 41.2%, P = 0.001) and central scar (36.7% vs. 11.8%, P = 0.003) were more prevalent in patients preoperatively diagnosed with SCN.

A comparison of radiological features according to preoperative diagnoses for those with macrocystic neoplasms

Table 3. Comparisons of characteristics between preoperatively diagnosed serous cystic neoplasm (SCN) patients and non-SCN patients

Variable	SCN patients (n = 49)	Non-SCN patients (n = 51)	P-value
Age (yr)	55.0 ± 16.1	50.9 ± 15.6	0.145
Sex, male:female	16:33	17:34	0.942
How to detect			0.460
Incidental detection by health check-up	34 (69.4)	37 (72.5)	
Abdominal pain	15 (30.6)	12 (23.5)	
Jaundice	0 (0)	1 (2.0)	
Palpable mass	0 (0)	1 (2.0)	
Tumor location			0.774
Head	13 (26.5)	10 (19.6)	
Body and tail	34 (69.4)	38 (74.5)	
Entire pancreas	2 (4.1)	3 (5.9)	
Reasons for surgery			0.056
Uncertain diagnosis	23 (46.9)	35 (68.6)	
Presence of symptoms	13 (26.5)	5 (9.8)	
Increased size	11 (22.5)	7 (13.7)	
Combined resection during other surgery	2 (4.1)	4 (7.8)	
Tumor size (cm)	4.4 ± 3.4	3.9 ± 2.3	0.433
Cyst type			0.845
Macrocystic:microcystic	42 (85.7):7 (14.3)	43 (84.3):8 (15.7)	
Septation	37 (75.5)	21 (41.2)	0.001
Central scar	18 (36.7)	6 (11.8)	0.003
Enhancing lesion	27 (55.1)	21 (41.2)	0.164
Calcification	21 (42.9)	17 (33.3)	0.327
Solid portion	16 (32.7)	16 (31.4)	0.591
Main pancreatic duct dilatation	12 (24.5)	14 (27.5)	0.736
External wall thickening	7 (14.3)	5 (9.8)	0.491
Bile duct dilatation	6 (12.2)	4 (7.8)	0.463
Pancreas atrophy	4 (8.2)	4 (7.8)	0.953

Values are presented as mean ± standard deviation or number (%).

Table 4. Radiologic features according to the preoperative diagnoses in the macrocystic tumor

Variable	SCN (n = 41)	MCN (n = 18)	IPMN (n = 18)	P-value
Septation	29 (70.7)	7 (38.9)	6 (33.3)	0.009
Central scar	14 (34.1)	4 (22.2)	3 (16.7)	0.691
Enhancing lesion	21 (51.2)	8 (44.4)	9 (50.0)	0.831
Calcification	17 (41.5)	7 (38.9)	5 (27.8)	0.688
Solid portion	12 (29.3)	5 (27.8)	6 (33.3)	0.875
MPD dilatation	9 (22.0)	3 (16.7)	4 (22.2)	0.691
External wall thickening	4 (9.8)	4 (22.2)	3 (16.7)	0.167
Bile duct dilatation	4 (9.8)	2 (11.1)	0 (0)	0.381
Pancreas atrophy	4 (9.8)	3 (16.7)	0 (0)	0.173

Values are presented as number (%).

SCN, serous cystic neoplasm; MCN, mucinous cystic neoplasm; IPMN, intraductal papillary mucinous neoplasm; MPD, main pancreatic duct.

is shown in Table 4. Macrocystic lesions did not exhibit different radiological features among the preoperative diagnoses, although septation in the cyst was more prevalent in those accurately diagnosed with SCN compared with those preoperatively misdiagnosed with MCN or IPMN (70.7 vs. 38.9 vs. 33.3%, respectively, $P = 0.009$).

DISCUSSION

PCNs are increasingly being detected due to increased use of radiological examinations [4,11]. Whereas IPMNs and MCNs consist of columnar epithelium, which produces mucin, and have a relatively high malignant potential, SCNs have a single layer of either cuboidal or flattened cells, and malignant SCNs have been reported in a very limited number of cases [2,7,12-14]. Therefore, surgical indications for SCNs have not been based on oncological potential, but generally on large size, symptomatology, and difficult or impossible discrimination from other potentially malignant lesions [15,16]. However, because pancreatectomies are associated with a high morbidity rate, surgical resections of benign SCNs have also caused postoperative complications that would be preventable if the benign SCNs had been initially accurately diagnosed [17-19].

The present study investigated 100 consecutive patients who were diagnosed with pathologically confirmed benign SCN after complete surgical resection. Most lesions were discovered incidentally at health check-up (71%) or due to abdominal pain (27%) (Table 1). Most patients underwent surgical resection due to uncertain preoperative diagnosis (58%), with 51 lesions (51%) preoperatively diagnosed as non-SCNs. In other words, if the benign SCNs had been accurately diagnosed, more than one-half of patients could have undergone close observation instead of surgical resection.

In our previous report, we mentioned that the opposite of "microcystic" was "macrocystic," not "oligocystic," and proposed that the "oligocystic SCN" according to the World Health

Organization classification should be revised to "macrocystic SCN" [10,20]. We also suggested that macrocystic SCN could be divided into 2 subtypes: "unilocular" and "multilocular." The most representative radiological feature of SCN (i.e., honeycomb appearance) was included in the microcystic SCN [16]. Generally, macrocystic SCNs are detected in <10% of all SCN patients [16,21]. However, one large-scale study recently reported that macrocystic SCNs were detected in 32% of cases, and mixed macrocystic/microcystic in 18% [22]. In this study, 85% of SCNs exhibited macrocystic features (Table 2). This was because the present study enrolled surgically resected SCNs, not those that had undergone regular surveillance. Although we attempted to evaluate radiological differences in macrocystic tumors among the preoperative diagnoses, no significant difference was revealed, except for septation (Table 4). This result was in accordance with our previous study, in which CT could differentiate macrocystic unilocular SCN with low diagnostic accuracy [10].

Furthermore, the enrolled SCNs exhibited other radiological features such as enhancing lesions (48%), calcification (38%), solid component (31%), and main pancreatic duct dilatation (26%) that were representative of other PCNs including MCN, IPMN, and pseudocyst (Table 2). Microcystic honeycomb appearance is a representative feature of typical SCNs (Fig. 2A). However, some radiological features, such as a macrocystic lesion with calcification (Fig. 2B), a cystic lesion with a solid component and the presence of main pancreatic duct dilatation (Fig. 2C), and a cystic lesion with evenly-thickened wall with multiple calcifications (Fig. 2D), made it difficult to distinguish between SCN and other PCNs. Although 49 patients were preoperatively diagnosed with SCN, 23 (46.9%) underwent surgical resection due to uncertain diagnoses (Table 3). Conventional radiological examination provides fundamental information to the clinician, but cannot exactly diagnose atypical SCNs, which can mimic other PCNs.

As mentioned earlier, surgical indications for SCNs remain

controversial. Tumor size > 4 cm has been generally accepted because larger lesions tend to cause symptoms [14,23]. Furthermore, laparoscopic surgery becomes more difficult if tumors grow larger than a specific size due to small available operation field [24,25], or chronic inflammation around the cystic mass. Hwang et al. [24,25] suggested the timely and active surgery, especially for pancreatic body or tail SCN of more than 3 cm at detection, because laparoscopic distal pancreatectomy already proved to be safe and feasible. Two studies reported that cyst growth rate was not related to initial cyst size [26,27]. Recently, one large-scale European study reported that cyst size \geq 4 cm exhibited a faster cyst growth rate than those < 4 cm [22]. Despite these results, the authors argued that whether size or growth rate criteria was an appropriate surgical indication remained questionable [22,27,28]. Although symptom resolution is also an essential goal of surgery, not all SCNs are associated with abdominal pain [22]. Therefore, surgical resection could be considered if SCNs are associated with abdominal symptoms or growth into a large cyst, even if the diagnosis of SCN is highly suspected.

The distinction between SCNs and other PCNs is worldwide, long-term task. Recently, endoscopic ultrasonography (EUS) or EUS-guided fine-needle aspiration (FNA) biopsy has been performed to diagnose PCNs accurately. However, EUS or EUS-guided FNA biopsy was not helpful in diagnosing benign SCNs that it had low sensitivity with high specificity that was not superior to CT or MRI [22,28,29]. In addition, EUS-guided FNA biopsy had always potential peritoneal dissemination in case of malignant tumor [30]. Therefore, EUS or EUS-guided biopsy would be helpful for selected lesions that could not be distinguished from other potentially malignant diseases.

In conclusion, it is difficult to accurately distinguish atypical SCNs from other PCNs using conventional radiological examinations, especially macrocystic SCNs. For more accurate diagnosis, new biomarkers and/or other diagnostic modalities are needed and, thus, warrant further investigation.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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