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Perspectives of Pancreatic Serous Cystadenoma Diagnostic Challenges and Management: Avoiding Irrelevant Surgery

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Abstract

Pancreatic cystic neoplasms (PCN) are divided into two types: inflammatory (pseudocysts) and genuine cysts, with an inflammatory pancreatic cyst being the most prevalent. True cysts are divided into three types: neoplastic (10–15%), congestive (10%), and congenital (5%). Cystic pancreatic neoplasms account for 1–5% of all primary pancreatic tumours. These include serous cystadenoma (SCA). Serous cystadenoma appears as a spherical, liquid-filled, clear cystic tumour with well-defined lobulated edges. They are mostly solitary lesions; however, they can have multiple lesions or multifocal and confluent neoplasms, particularly in von Hippel – Lindau patients (VHL). SCA often exhibits three different morphologic types: microcystic, macro-oligocystic, and solid. Serous cystadenomas account for 15–25% of all cases and present as unilocular or oligocystic lesions that can be diagnosed with cystic tumours. The "solid" variant could be the most perplexing and difficult to diagnose, since it might manifest as a solid hypervascular mass that actively increases on the arterial phase and seems remarkably similar to a pancreatic neuroendocrine tumour. Radiographic imaging is a powerful tool for identifying pancreatic serous cystadenoma, although it has limitations. With a clarified serous cystadenoma of small size, lack of symptoms, and no ductal or vascular engagement, conservative therapy is undoubtedly convenient.

Keywords: pancreatic cystic neoplasms, serous cystadenoma, post-operative pancreatic fistula, pseudocyst, pancreatic lesion

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Перспективы диагностики и лечения панкреатической серозной цистаденомы: избежание излишнего хирургического вмешательства

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Резюме

Кистозные образования поджелудочной железы делят на 2 типа: воспалительные (псевдокисты) и истинные кисты, причем наиболее распространенной является воспалительная киста поджелудочной железы. Истинные кисты разделяют на 3 типа: неопластические (10–15%), застойные (10%) и врожденные (5%). Кистозные новообразования поджелудочной железы составляют 1–5% всех первичных опухолей поджелудочной железы. К ним относят серозную цистаденому. Серозная цистаденома выглядит как сферическая, заполненная жидкостью, прозрачная кистозная опухоль с четко выраженными дольчатыми краями. Чаще встречается одиночное поражение, однако может иметь место мультифокальное поражение, когда со временем множественные очаги сливаются между собой. Это характерно для пациентов с болезнью фон Хиппеля – Линдау. Серозная цистаденома имеет 3 различных морфологических варианта: микрокистозный, макро-олигокистозный и солидный. Серозные цистаденомы представляют собой однокамерные или олигокистозные поражения, которые диагностируют как кистозные опухоли. Солидный вариант может быть наиболее затруднительным для диагностики, поскольку может проявляться в виде солидного гиперваскулярного образования, которое активно увеличивается в артериальную фазу и очень похоже на нейроэндокринную опухоль поджелудочной железы. Рентгенологическая визуализация является важным инструментом для выявления серозной цистаденомы поджелудочной железы, хотя и имеет некоторые ограничения. При установленном диагнозе серозной цистаденомы небольших размеров, отсутствии симптомов, поражения протоков и сосудов консервативная терапия, несомненно, предпочтительна.
Ключевые слова: кистозные новообразования поджелудочной железы, серозная цистаденома, послеоперационный свищ поджелудочной железы, псевдокиста, поражение поджелудочной железы

■ INTRODUCTION

Serous cystic neoplasms belong to the pancreatic cystic neoplasms group, which is diagnosed with the widespread use of modern imaging techniques including computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasonography (EUS). These neoplasms are becoming more frequently recognised incidentally. In accordance with the most recent WHO classification [1], pancreatic cystic lesions are classified into two main groups according to the nature of the cyst: inflammatory (pseudocysts) and true cysts. The most frequent type is an inflammatory pancreatic cyst, which is a local consequence of severe pancreatic inflammation. True cysts are classified as neoplastic (10–15%), congestive (10%), or congenital (5%). 1–5% of all primary pancreatic tumours are cystic pancreatic neoplasms [2]. Neoplastic cysts are thought to account for 10–15% of cystic lesions [3] and have different malignant potentials. The most prevalent cystic neoplasms of the pancreas are intra-ductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm (MCN), serous cystadenoma, solid pseudopapillary neoplasm (SPN), and cystic pancreatic endocrine neoplasm (CPEN) [3, 4]. IPMN and MCN are thought to be precursors of pancreatic ductal adenocarcinoma, while SCA is mostly benign, even though there have been a few cases reported in the literature that harbour malignant transformation [5]. Other types of PCNs are beyond the scope of this article; we will focus on the serous cystic neoplasm (SCN) genetic profile and diagnostic challenges.

SCN is a benign pancreatic lesion with a slow growth rate, a low risk of complications, and a low chance of malignant progression. In the international literature, around 30 cases of malignant transformation of SCA have been described, and these "malignant" SCA studies often describe locally invasive lesions rather than metastatic disease [6]. SCNs comprise approximately 16% of surgically removed PCNs and more than 30% of all clinically confirmed PCNs [7]. SCA occurs most frequently in females over the age of 60. The tumour ranges in size from less than 1 cm up to more than 10 cm. Inside the tumour, the diameter of cystic components can range from a few micrometers to several centimeters [7], and they can be pseudo-solid or unilocular. SCNs are often larger in male patients [8]. Management of pancreatic cystic neoplasms is difficult because it requires making decisions in the face of inadequate diagnostic information. If surgical resection is selected over radiographic monitoring, the risk of a major surgical procedure with detectable associated mortality must be balanced against the chance of malignant progression when radiographic observation is chosen. Surgical resection of all pancreatic cysts is no longer applicable. The overwhelming majority of newly detected lesions are asymptomatic, small (2 cm) and benign. In this group of patients, the risk of malignant progression is lower than the risk of surgical resection [9].

■ PATHOLOGY AND GENETIC PROFILE

Pancreatic serous neoplasms are cystic tumours characterised by the morphology of the neoplastic epithelial cells lining the cysts [10]. Most serous cystic neoplasms have a very slow growth rate of 0.28–0.56 cm/year on average, although growth rates vary substantially and larger SCNs grow quicker on average than smaller SCNs [11]. Serous cystadenoma often manifests as a spherical, liquid-filled, transparent cystic tumour with lobulated and well-defined borders. They are mainly solitary lesions; however, numerous lesions or multifocal and confluent neoplasms might be present, especially in von

Hippel – Lindau patients. There is no connection between the SCA and the primary pancreatic duct. Macroscopically, they are classified into three subtypes based on the number and size of cysts: microcystic, macrocystic and solid type [12]. Microcystic lesions have well-circumscribed lobulated borders in the typical form. The cysts are filled with a clear serous fluid. A distinctive central "star-shaped" scar formed of white nodules and fibrosis is seen in 30% of patients, and this scar commonly contains calcium deposits and can be seen on imaging as starry or punctuated calcifications. The second subtype is oligocystic (macrocystic), which is characterised by the presence of a small number (<6) of larger cysts (>1cm). The intracystic fluid might be clear and translucent, or it can be a brownish fluid that contains blood. The cutting surface reveals a countable number of cysts or, in certain cases, a single cyst (unilocular type) with a diameter ranging from 2 to 15 cm. The center scar is usually absent in this form. [13] SCA-targeted sequencing and full exome sequencing were studied by Wu et al. [14]. They demonstrated that DNA-neoplastic epithelium samples were collected from eight SCA patients. Each of the eight SCAs tested showed loss of heterozygosity (LOH) in at least one chromosomal location. They noticed that SCAs have 10±4.6 mutations per tumor. Only two mutations have been identified in more than one SCA. Four of the eight SCAs had a mutation in the von Hippel-Lindau gene. Three of the four showed LOH of the VHL chromosomal region. This is remarkable because SCAs are typically linked with individuals who have VHL syndrome, and VHL mutations have been documented in pancreatic cysts obtained from VHL syndrome patients [15]. The link between VHL mutations and SCNs has significant implications. For example, SCNs are detected in up to 15% of hereditary VHL syndrome patients, along with other tumours such as renal clear cell carcinoma. VHL mutations increase the expression of VEGF-1, hypoxia-inducible factor 1 alpha (HIF1-a), carbonic anhydrase IX (CAIX), and glucose transporter (GLUT)-1. TBC1 domain family member 3 (TBC1D3) was another gene in this series that was mutated in two of the eight samples. TBC1D3 belongs to the TBC1 domain family and encodes GTPase-stimulating proteins. While TBC1D3 has been shown to be useful in prostate cancer, its role in the aetiology of SCAs remains uncertain [14].

■ DIAGNOSTIC CHALLENGES AND BIOPSY ACCURACY

When a pancreatic lesion has been identified (either clinically or as a consequence of a previous imaging study), the image acquisition should be particularly adjusted for a targeted assessment of the pancreas. Patients are usually given around 1500 cc of water prior to the scan to dilate the stomach and duodenum and thus enhance our capacity to distinguish primary pancreatic lesions from duodenal or gastric lesions. Many lesions cannot be visualised (especially when small) without intravenous contrast, and the internal structure and morphology of larger cysts can't be properly evaluated without intravenous contrast. Serous cystadenomas frequently demonstrate three distinct morphologic types, which can be detected by CTs. As we mentioned above, SCAs frequently demonstrate three distinct morphologic types: 1) microcystic type, 2) macro-oligocystic type, and 3) solid type. Microcystic serous cystadenomas resemble a "honeycomb" or "sponge" pattern, with numerous (usually > 6 cysts) small (2 cm) cysts forming a bigger cystic mass. When multiphase imaging is implemented, the septations and periphery of the lesion display ardent enhancement on the arterial phase; however, the center scar may show delayed enhancement [16]. While this pattern provides for a definite diagnosis (which may allow the lesion to be managed conservatively without the need for additional

evaluation or surgical excision), it is only found in around ¼ of all instances [17]. The macrocystic variety accounts for 15–25% of all cases and manifests as a unilocular or oligocystic lesion that can be misdiagnosed for other common cystic tumours (such as an IPMN or MCN). While several studies have attempted to distinguish these macrocystic serous cystadenomas from other cystic lesions by using imaging features such as cyst location, wall thickness, wall enhancement, and external lobulation, the prospective diagnosis of this type of lesion is still challenging [18]. Finally, the "solid" variation might be the most confusing and difficult to detect in advance, since these lesions can present as a solid hypervascular mass that actively enhances on the arterial phase and seems nearly identical to a pancreatic neuroendocrine tumour. These lesions are hypothesised to be caused by the cystadenoma's aggressively vascularized septa predominating over the internal cystic component, leading the septa to appear as confluent, hyperenhancing solid tissue. While these lesions may show a central scar with calcification, this is extremely unusual and insufficiently specific to provide an accurate diagnosis [19]. Magnetic resonance imaging is an essential tool in the diagnosis of cystic tumours. Furthermore, the use of magnetic resonance cholangiopancreatography (MRCP) provides for a more accurate evaluation of the relation between the cystic mass and the main pancreatic duct, which helps in distinguishing serous cystadenoma from branch-duct intraductal papillary mucinous neoplasm [20]. Now let's talk about the radiological variants of the microcystic SCA visualised by MR imaging. T1-weighted images demonstrate hypointensity in comparison to the adjacent parenchyma. The information obtained on T1-weighted images after contrast administration is essentially comparable to images obtained by CT scans that show contrast enhancement of walls and septa in the arterial phase, allowing optimal visualisation of the "honeycomb" structure, which is even more noticeable in the portal venous phase. On T2-weighted images, it appears as a cluster of small cysts with hyperintense fluid content that have no relation to the main pancreatic duct and are separated by thin fibrous septa. A pathognomonic central fibrous scar may be present. T2-weighted images are crucial for assessing the cystic lesions content (fluid, existence of septa) and the pancreatic ductal system. On the other hand, endoscopic ultrasound or computed tomography guided needle aspiration is a diagnostic technique, and it's specifically beneficial to establish the diagnosis of SCAs with acceptable results. Jennifer et al. [21] described the usage of endoscopic ultrasonography and computed tomography CT-guided fine needle aspiration (FNA), which was performed in 21 cases as diagnostic testing. EUS, or CT-guided FNA, was considered diagnostic of serous cystadenoma in 10 of the 21 individuals. In the remaining 11 cases, the specimens were deemed insufficient, or a diagnosis other than serous cystadenoma had been proposed by EUS or CT-FNA, and serous cystadenoma was only discovered during surgical pathology. For pancreatic cystic lesions, EUS has been contemplated as an excellent imaging tool. Endoscopic ultrasound can easily characterise cysts and provide high-resolution imaging of the pancreas. Needle aspiration of pancreatic cystic lesions can be used for obtaining fluid for cytology, and tumour markers in cyst fluid can be used for diagnosis (fig. 1).

■ DISCUSSION

SCAs are benign cystic tumours consisting of a cuboidal epithelium that secretes serous fluid [22]. Although there have been a few cases of serous cyst adenocarcinoma recorded, the WHO estimates that the prevalence of malignant pancreatic SCAs is 1–3%

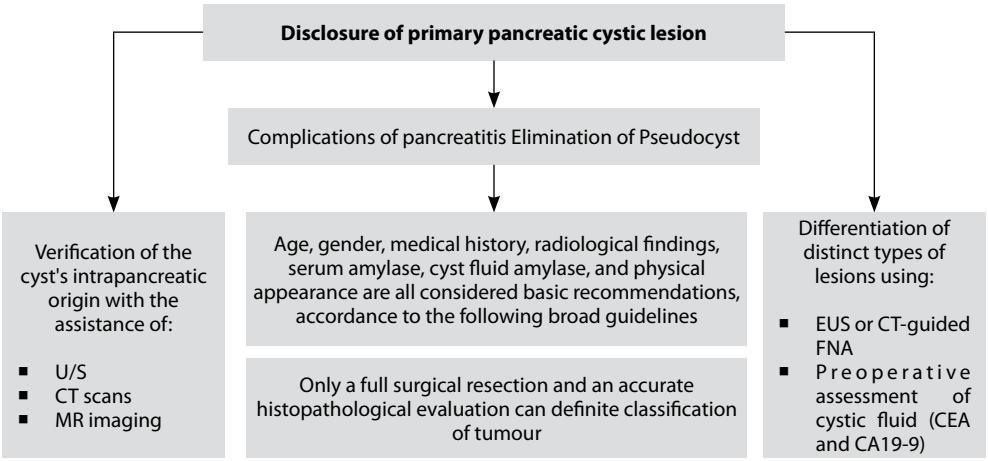

Fig. 1. Diagnostic algorithm of pancreatic cystic lesion

[6, 23]. SCA is commonly observed in women in their 6th decade of life within the body and tail of the pancreas [24]. To start with, a good differential diagnosis must be made to exclude mucin-producing cystic lesions along with other pancreatic cystic neoplasms with malignant potential. Secondly, although the diagnosis of serous cystadenoma is certain, there is no evidence to predict whether an asymptomatic tumour would grow large enough to produce symptoms over the individual's lifespan. This is an essential

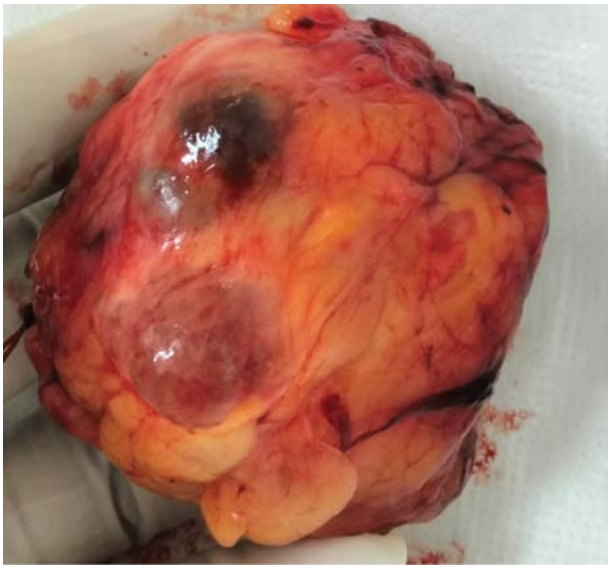

Fig. 2. First patient specimen central pancreatectomy

concern because, while the mortality rate after pancreatic resection has dropped significantly in experienced hands, the morbidity remains high, and the repercussions of pancreatic tissue loss are serious. Laboratory testing for serous cystadenoma generally finds no abnormally high levels of tumour markers unless the tumours develop malignant transformation or if the individual has simultaneously malignant tumours at other locations. Radiographic imaging is a powerful technique for diagnosing serous cystadenoma of the pancreas, but it has limits. At the moment, the most extensively used radiographic diagnostic is helical CT scanning with thin cuts towards the pancreas, which may often help distinguish between serous and mucinous neoplasms. A central scar with the "honeycomb" appearance of microcysts, present in the more frequent microcystic form of serous cystadenoma, is a classic CT finding indicative of serous cystadenoma. Magnetic resonance imaging with magnetic resonance cholangiopancreatography enables a more precise assessment of the relation between the cystic mass and the main pancreatic duct, which aids in differentiating between serous cystadenoma and branch-duct intraductal papillary mucinous neoplasm [20]. Because the cystic septa are well vascularized, they predominate throughout the internal cystic portion, making the septa appear as a confluent hyperenhancing solid lesion [19]. For pancreatic cystic lesions, EUS has been considered an excellent imaging tool. Endoscopic ultrasound can easily characterise cysts and provide high-resolution imaging of the pancreas. Needle aspiration of pancreatic cystic lesions can be used for collecting fluid for cytology, and tumour markers in cyst fluid can be used for diagnosis. Carcinoembryonic antigen (CEA) levels in cyst fluid are consistently low in serous cystadenomas, tend to be higher in mucinous lesions, and are typically even higher in mucinous cystadenocarcinomas [25]. Cytologic samples that have been collected from serous cystadenoma are diagnostic only in less than 50% of

Guideline for grading pancreatic fistulas international study group of pancreatic surgery classification blueprint (From Mark P. Callery, Manuel Castillo A., Tara S. Kent., Prevention and management of complications of pancreatic surgery. Shackelford's surgery if the alimentary tract. 8th ed. Philadelphia: Elsevier Publishing; 2019. P. 1239–48)

Criteria	No Fistula	Grade A Fistula	Grade B Fistula	Grade C Fistula
Drain amylase	<3 times normal	>3 times normal	>3 times normal	>3 times normal
	serum amylase	serum amylase	serum amylase	serum amylase
Clinical conditions	Well	Well	Often well	Ill appearing/bad
Specific treatment	No	No	Yes/No	Yes
U Itrasonog raphy/Computed tomography (if obtained)	Negative	Negative	Negative/positive	Positive
Persistent drainage (>3 weeks)	No	No	Usually yes	Yes
Signs of infection	No	No	Yes	Yes
Readmission	No	No	Yes/No	Yes/No
Sepsis	No	No	No	Yes
Reoperation	No	No	No	Yes
Death related to fistula	No	No	No	Yes

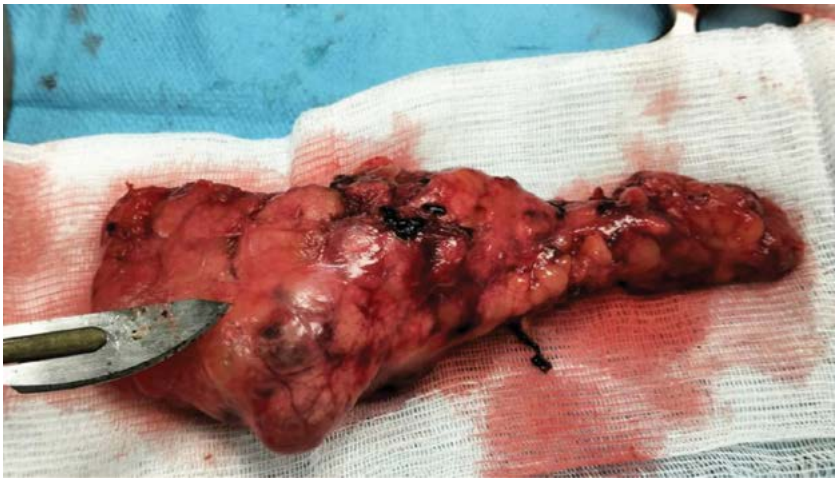

Fig. 3. Second patient subtotal pancreatectomy

cases; the specificity is excellent when such samples are affirmative. Clinical knowledge and radiologic evaluations are frequently used to distinguish cystic neoplasms from pseudocysts. When the difference between a serious and a mucinous cystic tumour is critical, cyst fluid examination using endoscopic ultrasonography or CT-guided aspiration and biopsy is very helpful [26].

In our discussion, we will be demonstrating two cases of SCAs, both of which are in the pancreatic body. The first patient was a female 54-year-old, asymptomatic, and had two uninformative biopsies underwent for operative resection to exclude other pancreatic cystic neoplasms. We performed a central pancreatectomy (fig. 2) with a duct-to-mucosa pancreatojejunostomy.

The postoperative period was complicated by a post-operative pancreatic fistula (POPF) grade C and was treated according to international guidelines (table).

The second patient was a symptomatic female 63-year-old who had a percutaneous biopsy under ultrasonography control. Underwent laparoscopic subtotal pancreatectomy (fig. 3).

The postoperative period was also complicated with post-operative pancreatic fistula Grade A; no treatment was indicated except for keeping the drain in place until the amylase level normalized. The final pathology for both cases was serous cystadenoma. Following surgical resection, survival is primarily influenced by operative mortality and post-operative complications, compared to the disease itself. Postoperative observation after the removal of a serous cystadenoma is often not recommended. There is no indication that this group of patients has an elevated risk of pancreatic cancer [27]. It is predicted that 6.2% of serous cystic pancreatic neoplasms are malignant. Because of the well-documented cases of serous cystadenocarcinoma and the diagnosis that can only be made post-operatively, surgical excision of all cystic tumours is recommended. Resection is always recommended when there are mass-related symptoms or when distinguishing

between MCN and side-branch IPMN is difficult [28]. A non-radical resection is preferred when resection is planned. No lymphadenectomy or extensive resection is indicated.

■ CONCLUSION

SCN is normally benign; non-surgical conservative therapy is completely appropriate for a well-documented serous cystadenoma with no symptoms and no ductal or vascular involvement. Endoscopic ultrasonography and MRI are powerful imaging modalities for diagnosing pancreatic cystic lesions. EUS is an effective technique for cyst identification, providing high-resolution imaging, detecting the relationship between cystic mass and pancreatic duct, and distinguishing between serous cystadenoma and branch-duct intraductal papillary mucinous neoplasm.

■ REFERENCES

1. Laffan T.A., Horton K.M., Klein A.P., Berlanstein B., Siegelman S.S., Kawamoto S., Johnson P.T., Fishman E K., Hruban R.H. Prevalence of unsuspected pancreatic cysts on MDCT. *AJR. American journal of roentgenology*. 2008;191(3):802–807. doi: 10.2214/AJR.07.3340
2. Spence R.A., Dasari B., Love M., Kelly B., Taylor M. Overview of the investigation and management of cystic neoplasms of the pancreas. *Digestive surgery*. 2011;28(5–6):386–397. doi: 10.1159/000334758
3. Dudeja V., Allen P.J. Premalignant cystic neoplasms of the pancreas. *Seminars in oncology*, 2015;42(1):70–85. doi: 10.1053/j.seminoncol.2014.12.007
4. Jabłońska B., Gudz A., Hinborch T., Bujała B., Biskup K., Mrowiec S. Pancreatic Cystic Tumors: A Single-Center Observational Study. *Medicina (Kaunas, Lithuania)*. 2023;59(2):241. doi: 10.3390/medicina59020241
5. Visser B.C., Muthusamay V.R., Mulvihill S.J., Coakley F. Diagnostic imaging of cystic pancreatic neoplasms. Surgical Oncology. 2004;13(1):27–39. doi: 10.1016/j.suronc.2004.01.002
6. Robinson S.M., Scott J., Oppong K.W., White S.A. What to do for the incidental pancreatic cystic lesion? *Surgical oncology*. 2014;23(3):117–125. doi: 10.1016/j.suronc.2014.04.001
7. Malleo G, Bassi C, Rossini R, et al. Growth pattern of serous cystic neoplasms of the pancreas: observational study with long-term magnetic resonance surveillance and recommendations for treatment. *Gut*. 2012 May;61(5):746–751. doi: 10.1136/gutjnl-2011-300297. PMID: 21940725
8. Tseng J.F., Warshaw A.L., Sahani D.V., Lauwers G.Y., Rattner D.W., Fernandez-del Castillo C. Serous cystadenoma of the pancreas: tumor growth rates and recommendations for treatment. *Annals of surgery*. 2005;242(3):413–421. doi: 10.1097/01.sla.0000179651.21193.2c
9. Gaujoux S., Brennan M.F., Gonen M., D'Angelica M.I., DeMatteo R., Fong Y., Schattner M., DiMaio C., Janakos M., Jarnagin W.R., Allen P.J. Cystic lesions of the pancreas: changes in the presentation and management of 1.424 patients at a single institution over a 15-year time period. *Journal of the American College of Surgeons*. 2011;212(4):590–603. doi: 10.1016/j.jamcollsurg.2011.01.016
10. Nagtegaal I.D., Odze R.D., Klimstra D., Paradis V., Rugge M., Schirmacher P., Washington K.M., Carneiro F., Cree I.A. WHO Classification of Tumours Editorial Board. The 2019 WHO classification of tumours of the digestive system. *Histopathology*. 2020;76(2):182–188. doi: 10.1111/his.13975
11. Chalian H., Töre H.G., Rezai P., Bentrem D.J., Yaghmai V. MDCT evaluation of the growth kinetics of serous and benign mucinous cystic neoplasms of the pancreas. *Cancer imaging: the official publication of the International Cancer Imaging Society*. 2011;11(1):116–122. doi: 10.1102/1470-7330.2011.0019
12. Adet A., Miquel R., Bombi J.A., Gines A., Fernández-Esparrach G., De Juan C., Ayuso J.R., Maurel J., Castells A., Fernández-Cruz L., Navarro S. Incidence and characteristics of pancreatic cystic neoplasms. *Gastroenterologia y hepatologia*. 2010;33(8):563–568. doi: 10.1016/j.gastrohep.2010.07.001
13. Sakorafas G.H., Smyrniotis V., Reid-Lombardo K.M., Sarr M.G. Primary pancreatic cystic neoplasms revisited. Part I: serous cystic neoplasms. *Surgical oncology*. 2011;20(2):e84–e92. doi: 10.1016/j.suronc.2010.12.002
14. Wu J., Jiao Y., Dal Molin M., Maitra A., de Wilde R.F., Wood L.D., Eshleman J.R., Goggins M.G., Wolfgang C.L., Canto M.I., Schulick R.D., Edil B.H., Choti M.A., Adsay V., Klimstra D.S., Offerhaus G.J., Klein A.P., Kopelovich L., Carter H., Karchin R., Vogelstein B. Whole-exome sequencing of neoplastic cysts of the pancreas reveals recurrent mutations in components of ubiquitin-dependent pathways. *Proceedings of the National Academy of Sciences of the United States of America*. 2011;108(52):21188–21193. doi: 10.1073/pnas.1118046108
15. Mohr V.H., Vortmeyer A.O., Zhuang Z., Libutti S.K., Walther M.M., Choyke P.L., Zbar B., Linehan W.M., Lubensky I.A. Histopathology and molecular genetics of multiple cysts and microcystic (serous) adenomas of the pancreas in von Hippel-Lindau patients. *The American journal of pathology*. 2000;157(5):1615–1621. doi: 10.1016/S0002-9440(10)64799-2
16. Choi J.Y., Kim M.J., Lee J.Y., Lim J.S., Chung J.J., Kim K.W., Yoo H.S. Typical and atypical manifestations of serous cystadenoma of the pancreas: imaging findings with pathologic correlation. *AJR. American journal of roentgenology*. 2009;193(1):136–142. doi: 10.2214/AJR.08.1309
17. Chu L.C., Singhi A.D., Hruban R.H., Fishman E.K. Characterization of pancreatic serous cystadenoma on dual-phase multidetector computed tomography. *Journal of computer assisted tomography*. 2014;38(2):258–263. doi: 10.1097/RCT.10.1097/RCT.0b013e3182ab1556
18. Kim SY, Lee JM, Kim SH, et al. Macrocystic neoplasms of the pancreas: CT differentiation of serous oligocystic adenoma from mucinous cystadenoma and intraductal papillary mucinous tumor. *AJR Am J Roentgenol*. 2006;187:1192–8.
19. Hayashi K., Fujimitsu R., Ida M., Sakamoto K., Higashihara H., Hamada Y., Yoshimitsu K. CT differentiation of solid serous cystadenoma vs endocrine tumor of the pancreas. *European journal of radiology*. 2012;81(3):e203–e208. doi: 10.1016/j.ejrad.2011.01.111
20. Kalb B., Sarmiento J.M., Kooby D.A., Adsay N.V., Martin D.R. MR imaging of cystic lesions of the pancreas. *Radiographics : a review publication of the Radiological Society of North America, Inc*. 2009;29(6):1749–1765. doi: 10.1148/rg.296095506
21. Tseng J.F., Warshaw A.L., Sahani D.V., Lauwers G.Y., Rattner D.W., Fernandez-del Castillo C. Serous cystadenoma of the pancreas: tumor growth rates and recommendations for treatment. *Annals of surgery*. 2005;242(3):413–421. doi: 10.1097/01.sla.0000179651.21193.2c

22. Klöppel G, Solcia E, Longnecker DS. World Health OrganizationInternational Histological Classification of Tumors. In Histologic Typing of Tumours of the Exocrine Pancreas. 2nd ed. Berlin: Springer-Verlag; 1996.
23. Bramis K., Petrou A., Papalambros A., Manzelli A., Mantonakis E., Brennan N., Felekouras E. Serous cystadenocarcinoma of the pancreas: report of a case and management reflections. *World journal of surgical oncology*. 2012;10:51. doi: 10.1186/1477-7819-10-51
24. Kim S.W., Song I.H., An S., Kim S.Y., Kim H.J., Song K.B., Hwang D.W., Lee S.S., Byun J.H., Seo D.W., Kim S.C., Yu E., Hong S.M. Pancreatic serous cystic neoplasms accompanying other pancreatic tumors. *Human pathology*. 2017;60:104–113. doi: 10.1016/j.humpath.2016.10.011
25. Brugge W.R. Role of endoscopic ultrasound in the diagnosis of cystic lesions of the pancreas. *Pancreatology*. 2001;1(6):637–640. doi: 10.1159/000055874
26. Brugge W.R., Lauwers G.Y., Sahani D., Fernandez-del Castillo C., Warshaw A.L. Cystic neoplasms of the pancreas. *The New England journal of medicine*. 2004;351(12):1218–1226. doi: 10.1056/NEJMra031623
27. Katz M.H., Mortenson M.M., Wang H., Hwang R., Tamm E.P., Staerkel G., Lee J.H., Evans D.B., Fleming J.B. Diagnosis and management of cystic neoplasms of the pancreas: an evidence-based approach. *Journal of the American College of Surgeons*. 2008;207(1):106–120. doi: 10.1016/j.jamcollsurg.2007.12.048
28. Pyke C.M., van Heerden J.A., Colby T.V., Sarr M.G., Weaver A.L. The spectrum of serous cystadenoma of the pancreas. Clinical, pathologic, and surgical aspects. *Annals of surgery*. 1992;215(2):132–139. doi: 10.1097/00000658-199202000-00007