HHS Public Access

Author manuscript

Clin Gastroenterol Hepatol. Author manuscript; available in PMC 2023 October 04.

Published in final edited form as:

Clin Gastroenterol Hepatol. 2022 August ; 20(8): 1663–1667.e1. doi:10.1016/j.cgh.2022.03.002.

Pancreatic Cyst Surveillance

Anne Marie Lennon[*], **Santhi Swaroop Vege**[‡]

[*]Division of Gastroenterology and Hepatology, The Johns Hopkins Medical Institutions, Baltimore, Maryland

[‡]Division of Gastroenterology & Hepatology, Mayo Clinic, Rochester, Minnesota

Abstract

Pancreatic cysts (PC) are an increasingly common problem facing general gastroenterologists and generalists. They can be divided into 3 groups. First, those that have no risk of developing into pancreatic cancer, such as a pseudocyst or serous cystadenomas (SCAs). Second, mucinous cystic neoplasms (MCNs) and intraductal papillary mucinous neoplasms (IPMNs), which are precursor lesions to high-grade dysplasia and pancreatic cancer. Third, solid cancers of the pancreas, such as neuroendocrine tumors and pancreatic adenocarcinomas, which have undergone cystic degeneration.

Pancreatic Cyst Types

The key questions when seeing a patient with PC are first, what type of cyst do they have, and second, is there evidence of high-grade dysplasia or pancreatic cancer. Patients with a pseudocyst typically have a prior history of pancreatitis and have a low cyst fluid carcino-embryonic antigen (CEA) (<5 ng/mL) and high amylase (Supplementary Table 1). SCAs present as single cysts, with no communication with the main pancreatic duct. Half have a classic microcystic appearance with multiple tiny cysts, with a scar in the center occurring in less than 30%. Cyst fluid analysis shows a low cyst fluid CEA. A *VHL* mutation, in the absence of other mutations, confirms the diagnosis of an SCA with 46% sensitivity and 100% specificity.[1] Cystic degeneration of a neuroendocrine or pancreatic cancer may present with high-risk or worrisome features (Table 1). They typically have a solid component or enhancement on imaging, a low cyst fluid CEA, with the diagnosis confirmed with cytology. IPMNs can present with a dilated (>5 mm) pancreatic duct (main duct type IPMN), a PC (branch duct type IPMN), or both (mixed type IPMN). Othere rarer forms like solid papillary neoplams and others are not dicussed.

Address requests for reprints to: Santhi Swaroop Vege, MD, Division of Gastroenterology & Hepatology, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905. vege.santhi@mayo.edu; fax: (507) 266-0350.

Conflicts of interest

The authors disclose no conflicts.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of Clinical Gastroenterology and Hepatology at www.cghjournal.org, and at http://doi.org/10.1016/j.cgh.2022.03.002.

MCNs are single cysts that occur almost exclusively in women in the body or tail of the pancreas. MCNs are differentiated from IPMNs by the lack of communication between the cyst and the main pancreatic duct. IPMNs and MCNs can have a *KRAS* mutation. IPMNs may also have a *GNAS* mutation.

Guidelines

The American College of Gastroenterology (ACG),[2] the American Gastrointestinal Association (AGA),[3] European,[4] American College of Radiology (ACR),[5,6] and International Association of Pancreatology[7] (IAP) group (also known as the Fukuoka) have developed PC guidelines. The ACG, AGA, ACR, and European guidelines provide guidance for a broad range of cysts, whereas the International Association of Pancreatology relate to IPMNs only.[7] The guidelines are very similar (Table 2) in the majority of their recommendations; however, they differ in a small number of important areas. One of the major reasons for these differences is the relatively low quality of the supporting evidence, meaning that several recommendations are based mostly on expert opinion.[3] In the following section, we provide a step-by-step practical approach to manage PCs, and highlight areas where there is and is not agreement among the guidelines.

Management

Important Things to Think About Before Starting Surveillance

It is important to discuss the pros and cons of surveillance with a patient before commencing. In addition, patients who have a limited life expectancy or are not medically fit for surgery should not undergo surveillance.[2,3]

Which Cysts Should Undergo Surveillance?

Pseudocysts and serous cysts require no surveillance.[2,4] Cyst caused by cystic degeneration of a pancreatic adenocarcinoma or neuroendocrine tumor should be referred for consideration of surgical resection.[2–4,7] Only patients with an IPMN or MCN require surveillance.[2–4,7]

What Type of Imaging Should You Use for Surveillance?

Magnetic resonance imaging is noninvasive, lacks radiation, and has the greatest accuracy for evaluating communication between a cyst and the main pancreatic duct and is recommended by most guidelines[2–5] as the primary tool to evaluate patients with PC.

One area of controversy is when to perform endoscopic ultrasound (EUS) and EUS fine-needle aspiration (FNA). Most groups recommend EUS ± FNA when there are worrisome features (Table 1).[2,4] In addition, EUS can be considered in large PCs, which most groups define as size of >2 cm,[2,4,7] with the most recent ACR guideline using >2.5 cm.[5] One group that has a different approach is the AGA, who recommended EUS if 2 or more high-risk features (size ≥3 cm, dilated pancreatic duct, solid component) are identified.[3] The difference in opinion between the groups is caused by the fact that EUS is more invasive than magnetic resonance imaging, but is the most sensitive test to identify a solid component

and allows one to sample the cyst fluid. In our practice we use EUS when it is likely to alter patient management.

When Should You do Fine-Needle Aspiration and What Should You Send it for?

EUS-FNA and cyst fluid analysis should be considered in PCs when the diagnosis is unclear and the results are likely to alter management.[2,4] Cyst fluid is typically sent for CEA and cytology.[2,4] Molecular markers (eg, *GNAS, KRAS, VHL*) may be considered in cases in which the diagnosis is unclear, and the results are likely to change management.[2,4]

When Should You Bring a Patient Back for Surveillance Imaging?

The guidelines vary on their recommendations (Table 2) with recommended surveillance intervals of between 6 and 24 months for patients with PCs with no concerning features. Patients who develop either worrisome features[2,4,5,7] or new-onset diabetes[2,4] should have a shortened surveillance interval with repeat imaging in 6 months.[2] In the authors' practice, such features as pancreatitis, or new enhancing mural nodule, main duct dilation, or increased serum CA19–9, are concerning and we perform an urgent EUS for these indications. One recurring debate is what is a rapid increase in cyst size with guidelines varying in their definition from 2.5 mm,[2] 3 mm,[7] and 5 mm[4] per year.

Is There a Role for Ablating Pancreatic Cysts?

The ACG, European, and IAP guidelines state that there is insufficient evidence to support the routine use of cyst ablation.[2,4,7] It may be considered in patients who refuse, or are not a candidate for, surgery as part of a clinical trial.

When Should You Refer to a Group for Consideration of Surgical Resection?

All the guidelines recommend that patients are referred to a multidisciplinary group for further evaluation[2,5] or undergo surgical resection if there is a significant concern for pancreatic cancer.[3,4,7] The AGA has a unique approach and requires there to be a solid component and a dilated and/or concerning features on EUS-FNA to undergo surgery.[3] The rationale for this approach was to decrease unnecessary surgery. In contrast, the ACG, IAP, and European guidelines recommend consideration of surgery if any high-risk feature (Table 1) is present.[2,4,7] Most guidelines recommend further evaluation of patients with worrisome features with EUS,[2,7] with surgical resection if a concerning lesion is found. The cyst size used for surgery is debated. The IC and ACG recommend consideration of surgery for cysts >3 cm,[2,7] with the European guidelines using a cutoff of 4 cm.[4] In our practice we refer patients with cysts >3 cm for consultation with a surgeon, but typically do not operate if there are no other concerning features and the cyst is <4 cm.

What Cysts Need Follow-Up After Surgical Resection?

Patients with SCA, pseudocysts, or MCNs without invasive cancer require no surveillance after resection.[2] The ACG, AGA, IAP, and European guidelines recommend surveillance of the remnant pancreas in patients with IPMNs.[2–4,7] The rationale for this is that IPMNs are a field defect and affect the entire pancreas with recurrence rates of up to 31% reported for patients with an IPMN with high-grade dysplasia. The surveillance interval varies

with different guidelines because of a lack of high-quality data, with most recommending surveillance every 6 months[2,7] for 2 years followed by yearly[7] for patients with high-grade dysplasia. The ACG, European, and IAP recommend surveillance every 24 months for low-grade dysplasia,[2,4,7] whereas the AGA recommends no surveillance for this group.[3]

Is There a Time When You Should Stop Surveillance?

The ACG and ACR guidelines address whether surveillance should stop at a certain age.[2,6] The ACG recommends reviewing the utility of ongoing surveillance at age >75, with an individualized approach for those aged 76–85 including an informed discussion about surgery,[2] whereas the ACR recommends against continuing ongoing surveillance in individuals aged 80.[6] The authors approach is to discuss the pros and cons of ongoing surveillance with patients at age 75 or older. Patients with multiple comorbidities have an 11-fold higher risk of non-IPMN-related death within 3 years. In our practice use the presence of multiple comorbidities at any age support stopping surveillance.

An area of significant controversy is whether to stop surveillance. The AGA and ACR recommend stopping surveillance if there is no change in the cysts after 5^3 or 10^6 years, respectively. In contrast the ACG, European, and ICC recommend ongoing surveillance.[2,4,7] There is no doubt that most patients with IPMNs and MCNs will not develop pancreatic cancer. Given the large number of patients with PCs it is not feasible to follow patients indefinitely. The approach of stopping surveillance after 5 years is supported by a retrospective study of 7211 patients with PCs in which 79 (1.1%) developed pancreatic cancer.[8] Most of the patients developed cancer within the first 5 years, with 14% developing cancer after 5 years. The argument for continuing surveillance past 5 years is that studies show that it takes 20 years from an initiating mutation to develop pancreatic cancer. Therefore, from a biologic perspective, the risk of developing pancreatic cancer likely increases, rather than decreases, with time. In addition, using an arbitrary time point, rather than other features to stop surveillance, caused significant concern. A recent multicenter prospective Japanese study evaluated 1404 patients with IPMNs, rather than all PCs, and found a cumulative incidence of pancreatic cancer of 3.3% at 5 years, 6.6% at 10 years, and 15% at 15 years.[9] The risk of pancreatic cancer was 10-fold higher in this group when compared with age-matched control subjects. In the authors' opinion the key question is, what is the best way to identify that small group of patients, who are at highest risk of developing pancreatic cancer, and will benefit from surveillance, from the larger group with a much lower risk of cancer, who require minimal or no long-term surveillance. This is an area that is being extensively researched.

Take Home Message

PCs are an extremely common finding on abdominal imaging, and rarely lead to pancreatic cancer. CT, magnetic resonance imaging, and EUS are useful to identify the type of PC, and detecting high-grade dysplasia or cancer in IPMN and MCNs. Similarities and differences in the multiple existing guidelines highlight the need for better quality data to guide management of these patients. Significant progress has been made in the management of PCs over the last 10 years. Although IPMNs and MCNs offer the opportunity for early

cancer detection, it is important to also realize the potential harms to the patient by invasive investigations and treatments, and the enormous cost to the health care system. As the number of patients with cysts increases, alternative strategies are needed to identify those individuals at highest risk of pancreatic cancer who will benefit from surveillance or surgery, while minimizing unnecessary resections or surveillance in the remaining patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

Supported by SPORE NIH (5P50CA062924) and IPMN Global Foundation grant.

References

1. Springer S, Masica DL, Dal Molin M, et al. A multimodality test to guide the management of patients with a pancreatic cyst. Sci Transl Med 2019;11:eaav4772. [PubMed: 31316009]
2. Elta GH, Enestvedt BK, Sauer BG, et al. ACG clinical guideline: diagnosis and management of pancreatic cysts. Am J Gastroenterol 2018;113:464–479. [PubMed: 29485131]
3. Vege SS, Ziring B, Jain R, et al. American Gastroenterological Association Institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology 2015;148:819–822. [PubMed: 25805375]
4. European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. Gut 2018;67:789–804. [PubMed: 29574408]
5. Expert Panel on Gastrointestinal I, Fabrega-Foster K, Kamel IR, et al. ACR appropriateness criteria(R) pancreatic cyst. J Am Coll Radiol 2020;17:S198–S206. [PubMed: 32370963]
6. Megibow AJ, Baker ME, Morgan DE, et al. Management of incidental pancreatic cysts: a white paper of the ACR Incidental Findings Committee. J Am Coll Radiol 2017;14:911–923. [PubMed: 28533111]
7. Tanaka M, Fernandez-Del Castillo C, Kamisawa T, et al. Revisions of International Consensus Fukuoka Guidelines for the management of IPMN of the pancreas. Pancreatology 2017;17:738–753. [PubMed: 28735806]
8. Anand GS, Youssef F, Liu L, et al. Pancreas cancer incidence and pancreas cancer-associated mortality are low in national cohort of 7211 pancreas cyst patients. Dig Dis Sci 2021 Mar 30. 10.1007/s10620-021-06923-5.
9. Oyama H, Tada M, Takagi K, et al. Long-term risk of malignancy in branch-duct intraductal papillary mucinous neoplasms. Gastroenterology 2020;158:226–237. [PubMed: 31473224]

Table 1.

High-Risk and Worrisome Features in Pancreatic Cysts

High-risk	Worrisome
Jaundice secondary to the cyst	Acute pancreatitis
Cytology with high-grade dysplasia or cancer	Mural nodule <5 mm, thickened/enhancing cyst walls
Pancreatic duct of ≥10 mm	Main duct size 5–9 mm
5-mm mural nodule or solid mass	Abrupt change in caliber of pancreatic duct
	Increased serum level of CA19–9
	Rapid cyst growth
	Cyst size >3[7] or 4 cm[4]

Modified from Tanaka M, Fernandez-Del Castillo C, Kamisawa T, et al. Revisions of International Consensus Fukuoka Guidelines for the management of IPMN of the pancreas. Pancreatology 2017;17:738–753.

NOTE. The International Association of Pancreatology, American Gastrointestinal Association, American College of Gastroenterology, American College of Radiology, and European guidelines use different size cutoffs.

Table 2.

Comparison of Different Guidelines

	2015 AGA guidelines	2017 IAP	2018 European guidelines	2018 ACG guidelines	2017 ACR guidelines
Target cyst types	Asymptomatic neoplastic pancreatic cysts	IPMNs	Neoplastic pancreatic cysts	Pancreatic cysts	Incidental pancreatic cysts
Target lesion	PDAC	High-grade dysplasia or PDAC	High-grade dysplasia or PDAC	High-grade dysplasia or PDAC	High-grade dysplasia or PDAC
Methodology	Systematic review, GRADE methodology	Scientific review, expert consensus	Systematic review, GRADE methodology	Systematic review, GRADE methodology	Scientific review, expert consensus
Indications for EUS	At least 2 high-risk features	Worrisome features	Clinical or radiologic features of concern AND results are expected to change clinical management	When the diagnosis is unclear, and results are likely to alter management	Worrisome or high-risk features
Indications for surgery	Both dilated pancreatic duct and solid component and/or concerning features on EUS-FNA	High-risk features strong consideration for surgery in young with cyst >3 cm	Absolute indications vs relative indications	N/A	N/A
Surveillance end point	5 y with no interval change	Lifelong	Lifelong	Review at 75	Stability over 9–10 y
Growth rate	N/A	≥5 mm/2 y	≥5 mm/y	≥3 mm/y	Based on % increase depending on cyst size
Symptoms Jaundice	HR	HR	Absolute indication for surgery	HR	HR
Acute pancreatitis	—	Worrisome factor	Relative indication for surgery	HR	—
Surveillance intervals					
<1 cm	MRIAt 1 y, then every 2 y	CT/MRI 6 mo then every 2 y if no change	EUS/MRI, CA 19–9 6 mo for 1 y, then annually	MRI every 2 y, lengthen if stable	MRI or CT 1 y for <1.5 cm
1–2 cm	“	CT/MRI 6 mo, 1 y, and annually for 2 y, and lengthen if stable	“	MRI yearly for 2 y then every 2 y	MRI or CT 6 mo for 1.5–2.5 cm × 4 then lengthen if stable
2–3 cm	“	EUS 3–6 mo, then every year alternating MRI with EUS as appropriate	“	EUS or MRI every 6 mo for 3 y then yearly	MRI or CT >2.5 cm every year for 10 y For those >80 y, CT/MRI every 2 y
>3 cm	“	Alternate MRI/EUS 3–6 mo	“	“	“
Stopping surveillance	Stop after 5 y if no change	Lifelong	Lifelong	Lifelong	Stop after 10 y if no change

Modified from Hasan A, Visrodia K, Farrell JJ, et al. Overview and comparison of guidelines for management of pancreatic cystic neoplasms. World J Gastroenterol 2019;25:4405–4413CJ

ACG, American College of Gastroenterology; AGA, American Gastrointestinal Association; ACR, American College of Radiology; CT, computed tomography; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; HR; IAP, International Association of Pancreatology; IPMN, intraductal papillary mucinous neoplasm; MRI, magnetic resonance imaging; HR, high risk; N/A, not available; PDAC, pancreatic ductal adenocarcinoma.