Communication from the ASGE Standards of Practice Committee

GUIDELINE

The role of endoscopy in the diagnosis and treatment of cystic pancreatic neoplasms

Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this guideline, a search of the medical literature from January 1990 to September 2015 was performed by using PubMed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When limited or no data existed from well-designed prospective trials, emphasis was given to results from large series and reports from recognized experts. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines were drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence (Table 1).[1]

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines. This guideline supplements and replaces our previous document on the role of endoscopy in the diagnosis and the management of cystic lesions and inflammatory fluid collections of the pancreas.[2]

CYSTIC LESIONS AND FLUID COLLECTIONS OF THE PANCREAS

Cystic lesions and fluid collections of the pancreas often present a diagnostic and therapeutic challenge. Their pathology ranges from pseudocysts and pancreatic necrosis to benign and malignant neoplasms. Pancreatic cystic lesions may be encountered during the evaluation of a patient with pancreatitis or abdominal pain. However, these lesions are found incidentally in 2.5% of patients undergoing abdominal imaging performed for unrelated reasons, and their frequency increases with age to 10% in those aged ≥70 years[3,4] In the absence of characteristic radiographic features and clinical detail, pancreatic cystic neoplasms can be misclassified as pseudocysts, which are inflammatory pancreatic fluid collections that lack a true epithelial lining.[5-7] This guideline will discuss the role of GI endoscopy in the evaluation and treatment of cystic pancreatic neoplasms. The role of endoscopy in the management of inflammatory fluid collections of the pancreas is addressed in another ASGE guideline.[8]

CYSTIC LESIONS OF THE PANCREAS

Cystic lesions of the pancreas consist of nonneoplastic cysts and cystic neoplasms, the latter of which include serous cystic neoplasms, mucinous cystic neoplasms, and intraductal papillary mucinous neoplasms (IPMNs) (Table 2). In addition, certain pancreatic tumors may contain cystic spaces or regions of cystic degeneration, such as solid-pseudopapillary neoplasms, cystic neuroendocrine tumors, and even ductal adenocarcinomas.[9] Recently, several

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TABLE 1. GRADE system for rating the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕O
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕OO
Very low	Any estimate of effect is very uncertain.	⊕OOO

GRADE, Grading of Recommendations Assessment, Development and Evaluation.
Adapted from Guyatt et al.[1]

strategies and guidelines regarding the diagnosis and indications for resection or surveillance of mucinous cystic pancreatic neoplasms have been published elsewhere.[10-14] In a retrospective series of 851 individuals undergoing resection of pancreatic cystic neoplasms over 33 years, the most common pathologic diagnoses were IPMNs (38%), mucinous cystic neoplasms (23%), serous cystic neoplasms (16%), and cystic neuroendocrine neoplasms (7%).[15] Lesions that were identified incidentally accounted for an increasing proportion of resections over time (22% from 1978-1989 to 50% from 2005-2011). Symptomatic cystic neoplasms in this series typically presented with abdominal pain, pancreatitis, jaundice, weight loss, malabsorption, nausea, vomiting, early satiety, or a palpable abdominal mass.

DIAGNOSIS BY EUS

EUS morphology

Several EUS findings have been evaluated as diagnostic criteria for pancreatic cystic lesions.[16-27] When surgical histology is used as a reference standard, the diagnostic accuracy of EUS imaging ranges from 40% to 96%. A single prospective study demonstrated that the sensitivity (56%) and specificity (45%) of EUS morphology alone for differentiating mucinous cysts (mucinous cystic neoplasms and IPMNs) from nonmucinous cysts were low, resulting in poor overall accuracy (51%).[26] In a study among experienced endosonographers, the agreement of whether a cyst was neoplastic versus nonneoplastic by EUS morphologic criteria was fair ($K = 0.24$), with moderate agreement for serous cystic neoplasms ($K = 0.46$) and for solid components ($K = 0.43$).[28]

Small cyst size alone does not exclude malignancy. One series of patients referred to a tertiary-care surgical practice reported that 20% of lesions 2 cm or smaller were malignant, and an additional 45% of lesions had malignant potential.[6] However, only 1 of 28 (3.5%) asymptomatic lesions <2 cm was malignant.[6] Certain EUS features are more predictive of particular types of cystic lesions. Multiple small (<3 mm) compartments within a cystic lesion (also called a microcystic lesion), suggest a serous cystic neoplasm with an accuracy of 92% to 96%,[23] and this feature is not seen in mucinous cystic neoplasms.[29] A cystic lesion without septations or solid components within a pancreas having parenchymal features suggestive of pancreatitis (defined as calcifications, atrophy, or a change in echo texture) indicates a pseudocyst with a sensitivity of 94% and a specificity of 85%.[24]

EUS imaging cannot reliably distinguish benign from malignant IPMNs.[20,24,25,30] Furthermore, it is unclear whether imaging features of mucinous lesions with increased malignant potential are sufficiently predictive to influence clinical management. A meta-analysis of 23 studies with 1373 patients found that a mural nodule, main pancreatic duct dilation, thickened septal walls, and cyst size >3 cm on radiologic or EUS imaging were independent predictors of malignant branch-duct IPMN.[31] Similarly, a recent international consensus guideline identified a main pancreatic duct (MPD) size ≥10 mm or the presence of an enhancing solid component on radiologic imaging as high-risk stigmata.[10] Lower risk findings, categorized as worrisome features, included a cyst size of ≥3 cm, thickened enhancing cyst walls, nonenhancing mural nodules, MPD size of 5 to 9 mm, an abrupt change in the MPD caliber with upstream pancreatic atrophy, or the presence of peripancreatic lymphadenopathy.[10]

Distinguishing cyst wall nodules that are epithelial (neoplastic) from those that are mucinous (nonneoplastic) is critical to properly risk stratify pancreatic cystic neoplasms. A recent blinded interobserver study found that EUS imaging of intracystic mucus appears as a smooth, well-defined hyperechoic rim with a hypoechoic center compared with the surrounding parenchyma. This feature serves to distinguish mucus from true epithelial nodules, which have ill-defined borders and a hyperechoic center.[32] Specific adjuncts to standard EUS may further aid in distinguishing between these 2 entities. Intraductal US may identify malignant IPMN by the presence of protruding lesions ≥4 mm.[33] Contrast-enhanced EUS, which uses a contrast agent to assess the vascularity of lesions, may aid in distinguishing inflammatory cysts from cystic pancreatic neoplasms and vascular epithelial mural nodules from nonvascular mucous in IPMNs.[34-36]