Pancreatic cystic lesions

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Purpose of review

Pancreatic cystic neoplasms are increasingly identified and their management remains uncertain. Recent studies demonstrate an evolving clinical approach.

Recent findings

The vast majority of asymptomatic pancreatic cysts without concerning clinical or imaging features can be observed without surgery. Clinical predictors for malignancy at surgery include male sex, age above 50 years, weight loss, and high cyst fluid carcinoembryonic antigen (CEA), but these factors are insufficient for patient selection. Endoscopic ultrasound (EUS)-guided fine needle aspiration with cyst fluid analysis for risk stratification and selective resection appears the most cost-effective approach. In addition to CEA, DNA analysis, differential protein expression, and proteomic studies of cyst fluid may be helpful in differentiating cystic lesions in selected patients. EUS-guided ethanol lavage of cysts resulted in regression; this method may have a role in treatment in the future. More future research investigating the safety of this procedure, technique modifications, and choice of agent is needed.

Summary

The approach to incidentally discover pancreatic cystic lesions is challenging due to the difficulty in preoperative definitive lesion characterization. Recently developed diagnostic and treatment strategies show promise for improved patient outcomes.

Keywords

carcinoembryonic antigen, cyst fluid DNA analysis, endoscopic ultrasound, endoscopic ultrasound-guided ethanol lavage, intraductal papillary mucinous neoplasm, mucinous cystadenoma, pancreatic cystic neoplasm, serous cystadenoma

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Introduction

Pancreatic cystic lesions (PCLs) are commonly identified due to increased use of cross-sectional imaging in patients with nonspecific abdominal complaints. The majority of PCLs are inflammatory pseudocysts. Although cystic neoplasms account for approximately 10% of PCLs, management remains difficult because of the challenges in unequivocal cyst characterization as well as the uncertain natural history of neoplastic cysts. Among neoplasms, serous cystadenomas (SCAs), mucinous cystadenomas (MCAs), and intraductal papillary mucinous neoplasms (IPMNs) account for 90%; the mucinous types are the key lesions with risk of malignancy [1,2]. Therefore, diagnostic methods to improve the differentiation between benign from (pre)-malignant as well as neoplastic from nonneoplastic lesions remain a source of active investigation.

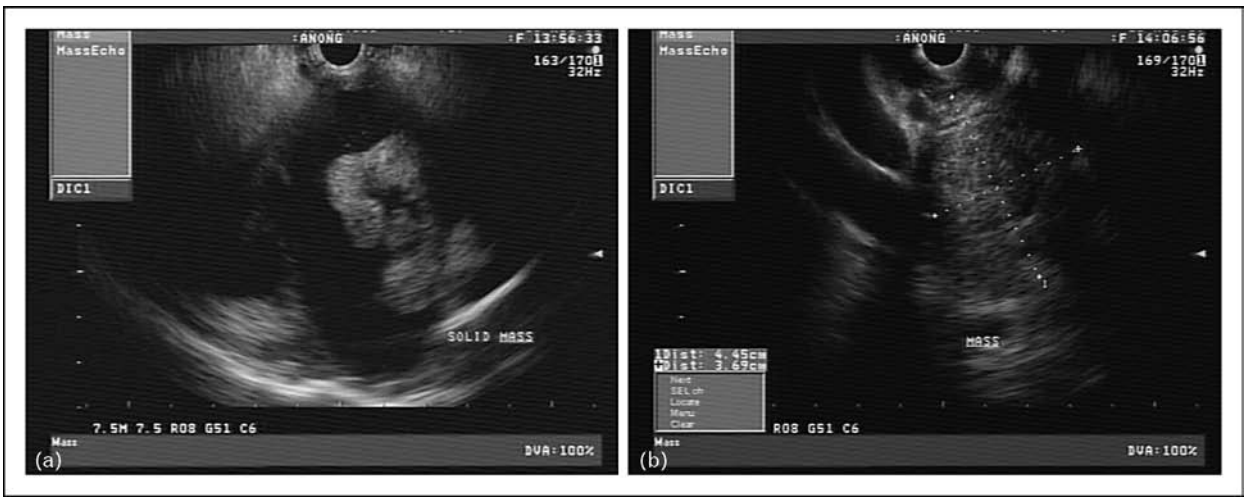
Epidemiology

A report found that the prevalence of incidental pancreatic cysts seen on multidetector computed tomography (MDCT) was 2.6%. Cysts were strongly associated with increasing age and Asian race [3]. Ishikawa *et al.* [4] found that the prevalence of PCLs including IPMNs among patients on hemodialysis was higher than normal population.

PCLs may occasionally cause abdominal pain, pancreatitis, or obstructive jaundice, but most are asymptomatic. Recent studies, evaluating the natural history of incidental PCLs, demonstrated that the vast majority of asymptomatic pancreatic cysts without concerning clinical or imaging features could be followed safely without surgery [5•,6].

Buscaglia *et al.* [7•] developed a predictive model for cyst malignancy to improve selection for surgical resection. White patients above 50 years old presenting with weight loss and cyst size of more than 1.5 cm had 6-fold higher likelihood of having malignancy than patients without these factors. They confirmed the value of a very high cyst carcinoembryonic antigen (CEA) as a predictor of malignancy. The results of this study were in agreement with the findings that older age, male gender, and

Figure 1 EUS images of a large cystic lesion with a solid component



(a) EUS images of large cystic lesion with a solid component. Solid mass associated with cyst. Pathology confirmed mucinous cystadenocarcinoma. (b) Another solid view of the mass associated with the cystic neoplasm.

malignant cytology from endoscopic ultrasound (EUS) predict malignancy at surgical resection in another series [8]. Cadili *et al.* [9] demonstrated that overall survival in patients with neoplastic pancreatic cysts is determined by patient factors (i.e. age and sex) rather than factors descriptive of the cyst such as size and morphology.

Cross-sectional imaging

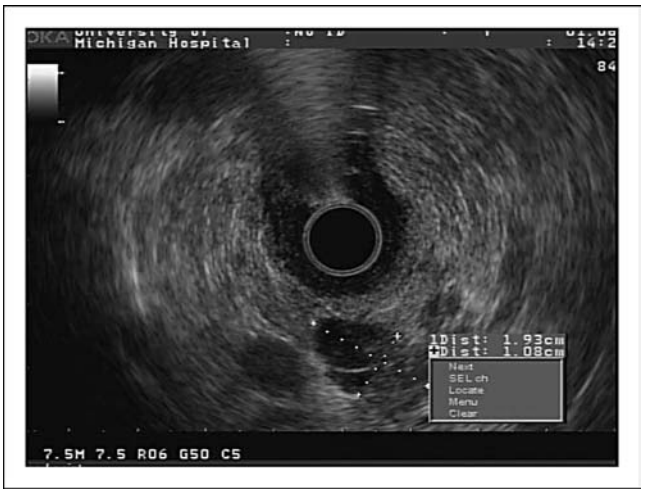
There is significant variability in the appearance of serous and mucinous neoplasms. Several authors have reported the limited value of transabdominal ultrasound, CT, and MRI for differentiating SCAs (especially its macrocystic variant) from mucinous lesions [1]. More recently, Kim *et al.* [10] assessed CT features to distinguish benign from premalignant and malignant lesions in macrocystic pancreatic cysts. They report that lobulated shape, thin wall, and smooth internal surface were more frequent in benign cysts, whereas round or oval shape or complex cystic shape with tubular cyst, thick wall, and an irregular internal surface were more frequent in premalignant and malignant cysts. When MDCT was compared with MRI–magnetic resonance cholangiopancreatography (MRCP) in characterizing small pancreatic cysts ($\leq$3 cm), the accuracy was higher in classifying cysts as mucinous or nonmucinous than determining a specific diagnosis (71–84.2% vs. 39.5–44.7%, respectively). The accuracy of the two techniques in characterizing cysts into nonaggressive and aggressive categories was similar (MDCT vs. MRI, 75–78% vs. 78–86%, respectively, $P > 0.05$). A different report suggests MRI may be slightly better for the assessment of the morphology of small cysts than MDCT [11]. These recent data continue to confirm the limitations of imaging alone for PCL characterization.

Endoscopic ultrasound

EUS provides high-resolution images of cyst morphology and can obtain cyst fluid by fine needle aspiration (FNA). The diagnostic accuracy of EUS morphology alone for PCLs varies between 51 and 73% in different studies [1,2].

Endosonographic features like the presence of a solid component associated with the cyst (Fig. 1), mural nodule, associated mass (Fig. 2), cyst size of more than 3 cm, dilated pancreatic duct, and lymphadenopathy usually suggest premalignant or malignant lesions. However, interobserver agreement among experienced

Figure 2 Mural nodule in side branch intraductal papillary mucinous neoplasm



endosonographers is moderately good in the presence or absence of solid component only but not for other EUS features. EUS alone, like other imaging tests, is inadequate in characterizing PCLs [12]. Therefore, EUS-guided FNA (EUS-FNA) for cyst fluid analysis remains an important addition to further characterize PCLs. Antillon *et al.* [13] recently reported a case of EUS-assisted biopsy of the wall of a large cyst that confirmed a pseudocyst ; however, this approach would not be useful for most of the small indeterminate cystic lesions.

Cyst fluid cytology

Cytologic examination of cyst fluid is insensitive due to the few cells present. In an attempt to improve diagnostic accuracy of cytology, the EchoBrush, a disposable cytologic brush for FNA was developed. Bruno *et al.* [14] recently reported their experience in 39 patients (12 with solid pancreatic masses, 12 with pancreatic cysts, seven with enlarged lymph nodes, and eight with submucosal masses). The material collected with the EchoBrush and with a standard FNA needle was evaluated by two blinded cytopathologists. Adequate material for cytologic analysis was collected in 17 of 39 patients (43.6%) with a single pass of the EchoBrush. Results were better for pancreatic lesions (for solid and cystic lesions, the adequacy was 58.3 and 50%, respectively); adequacy was low (28.6 and 25%, respectively) for lymph nodes and submucosal masses. The overall sensitivity and specificity was poor; there were no adverse events with the procedure.

Cyst fluid amylase, lipase, carcinoembryonic antigen and other tumor markers

Elevated lipase (>6000 U/l) in the cyst fluid indicates communication of the cyst with the ductal system that is found in most pseudocysts and many IPMNs.

A low concentration of lipase is seen in SCAs and in the majority of mucinous cystic neoplasms (MCNs). However, there seems to be an overlap of cyst fluid amylase and lipase levels between the different types of PCLs [1]. Therefore, the use of fluid amylase and lipase can be misleading.

Several studies have attempted to differentiate mucinous from nonmucinous lesions by measuring levels of different glycoprotein markers, such as CEA, carbohydrate antigen (CA) 19-9, CA 72-4, and CA 15-3 from aspirated cyst fluid. Although reviews suggest that cyst fluid CEA, CA 72-4, CA 19-9, and cytology are useful tools in distinguishing SCAs, MCNs, and nontumorous cysts [15], CEA appears be the most useful marker in differentiating mucin from non-mucin producing tumors [16]. A CEA level of more than 192 ng/ml had an accuracy of 79% for accurate mucinous lesion characterization and was superior to cytology, EUS morphology, and all combined together in a large multicenter study. Walsh *et al.* [17] confirmed that asymptomatic patients with cyst fluid lacking mucin and CEA of more than 200 ng/ml do not harbor a mucinous neoplasm requiring resection within 2 years of follow-up. Leung *et al.* [18] confirmed the value of a thick cyst wall or intracystic growth, elevated cyst fluid CEA, in their retrospective review of EUS at a cancer referral center. They propose assessing cyst fluid viscosity with a 'string sign' that associated with premalignant or malignant cysts. This surrogate, like CEA, was imperfect in characterization of PCLs and alone cannot be used to diagnose the nature of the lesion with certainty.

Molecular analysis of cyst fluid

A recently published multicenter study, called the PANDA (pancreatic cyst fluid DNA analysis) study, demonstrated a strong association of mucinous cystic neoplasms with K-ras mutations occurring with other loss of heterozygosity (LOH) mutations [19•]. Shen *et al.* [20] assessed the correlation between this commercially available molecular diagnosis with a clinical consensus diagnosis for malignant, benign mucinous, and benign nonmucinous pancreatic cysts. The consensus diagnosis was defined by histology, malignant cytology, or two concordant tests (such as EUS, cytology, or CEA $\geq$192 ng/ml for mucinous cysts). The molecular diagnosis included analysis of K-ras mutation, LOH, and quantity/quality of DNA. The study showed that the two diagnostic methods correlated well and molecular analysis of pancreatic cyst fluid added diagnostic value to the preoperative diagnosis with high sensitivity, specificity, and positive predictive value for the diagnosis of malignant and benign mucinous pancreatic cysts.

In contrast, comparative analysis of pancreatic cyst fluid CEA and DNA mutational analysis in the detection of mucinous or malignant cysts in two other studies showed poor agreement between CEA levels and molecular analysis for diagnosis of mucinous cysts [21,22]. Diagnostic sensitivity, however, was improved when results of CEA levels and molecular analysis were combined. In the detection of malignant cysts, elevated CEA levels were more predictive of histology in comparison to K-ras-2 or LOH mutations. Additionally, false positivity of LOH mutations was noted to be considerably higher than K-ras-2 mutations or even fluid CEA levels. These findings suggest that DNA mutation analysis should not be used routinely, but rather very selectively in the evaluation of pancreatic cysts [22]. Cyst fluid DNA analysis can provide us additional clinically meaningful information to justify the effort and cost of the test in only highly selected circumstances and should not be used routinely [23•].

Cyst fluid biomarkers

In an attempt to differentiate serous from premalignant mucinous cysts, researchers have investigated the pattern

of biomarker expression. Using a commercially available custom-designed multiplex assay and studying aspirates of lesions at the time of surgery, they found the majority of proteins were downregulated in IPMN and MCN compared with SCA. The only proteins significantly overexpressed in mucinous cysts were CEA and CA 72-4. They report that using multimarker sample classification, they could accurately discriminate between SCAs and IPMNs in 92% of patients [24]; further studies in nonselected patient populations are awaited.

In addition, preliminary work on biomarkers using proteomic analysis in order to improve diagnostic accuracy was reported. A panel of potential biomarker proteins that correlated with CEA including two homologs of amylase, solubilized molecules of four mucins, four solubilized CEA-related cell adhesion molecules (CEACAMs), and four S100 homologs. This approach required less than 40 μl of cyst fluid per sample, offering the possibility to analyze cysts smaller than 1 cm in diameter [25]. These preliminary reports appear worthy of further study.

Endoscopic retrograde pancreatography

With the advent of EUS and MRCP, the role of endoscopic retrograde pancreatography (ERP) in the evaluation of PCLs has become limited to evaluation of suspected IPMNs. Communication between the main pancreatic duct and a cyst, an important characteristic of IPMNs, may not be apparent on EUS. MRCP is a noninvasive method to evaluate ductal communication of a cyst when EUS is inconclusive. ERP is not useful in evaluation of SCAs and MCNs because these lesions do not communicate with the main pancreatic duct. In IPMN, a side-viewing duodenoscope may show the pathognomonic finding of mucus extruding from a patulous pancreatic orifice. In addition, pancreatoscopy with or without biopsy can be helpful for main duct disease [1].

Management of pancreatic cystic lesions

Despite improvements in imaging and evaluation of cyst contents with biochemical as well as molecular profiling, accurate preoperative diagnosis remains elusive. This leads to uncertainty for patients and clinicians and the advocacy for surgical resection in all patients fit for surgery.

In 2004, a set of expert consensus guidelines was published for the management of mucinous cystic lesions of the pancreas [26]. It recommends that all patients, even if asymptomatic, be considered for surgical resection. It outlines an approach to evaluation and surveillance based on lesion type and size. The Johns Hopkins group sought to assess physician awareness of these guidelines and characterized practice habits [27•]. Although the low rate of survey response is a major limitation, the results provide insight into the limited impact of these guidelines and current clinical variability in practice. The majority of the general gastrointestinal specialists (64.1%) were unaware of any published practice guidelines, compared with 33.3% of EUS specialists ($P < 0.001$). Management based upon clinical vignettes demonstrated moderate consistency with guidelines, appropriately answering 66.7% of the questions. For 9-mm cysts, only 25% of the questions were answered consistent with guidelines. Interestingly, EUS specialists were less likely to refer main-duct IPMNs for surgery and more likely to opt for EUS-FNA for branch-duct IPMNs ($P < 0.001$). The authors speculate EUS specialists favor EUS for evaluation and management because this is the skill they possess. Reliance on FNA results, or the ability to detect certain 'concerning features' by EUS (e.g. mural nodule), may afford an endosonographer confidence in the decision to delay surgical referral or continue with surveillance. Conversely, for those physicians who are less familiar with the capabilities of EUS or who practice in an area in which EUS is less accessible, they may be more likely to rely upon other imaging modalities or their local surgical expertise to manage such lesions of the pancreas. The International Association of Pancreatology (IAP) guidelines are currently being revised; this paper stresses that better dissemination of such 'expert' consensus documents is critically needed.

Despite concern of progression to malignancy in presumed neoplastic cysts, the increasing prevalence of incidental, asymptomatic lesions, many in elderly patients with comorbid diseases, calls into question the risk benefit of prophylactic surgery. As there are no controlled trials (and likely never to be) on the optimal management of patients with asymptomatic, incidental cystic lesions, investigators from the Mayo Clinic, Scottsdate turned to decision to compare different hypothetical management strategies to determine the most appropriate and cost-effective management of these patients [28••]. Their goal was also to identify factors important in influencing clinical decisions, guiding future clinical investigation.

Three strategies were examined using a Markov model: natural history without intervention, resection, and EUS-FNA with cyst fluid analysis for risk stratification and mucinous cysts considered for resection. An operability risk score based on patient age, comorbidity, and size and location of the cyst was developed to estimate the probability of surgical resection. The model results suggested that the EUS-FNA strategy yielded the highest quality-adjusted life years with an acceptable incremental cost-effectiveness ratio. Not surprisingly, the operability risk score was the critical determinant of the optimal management strategy. This analysis supports the evolving approach advocating careful selection

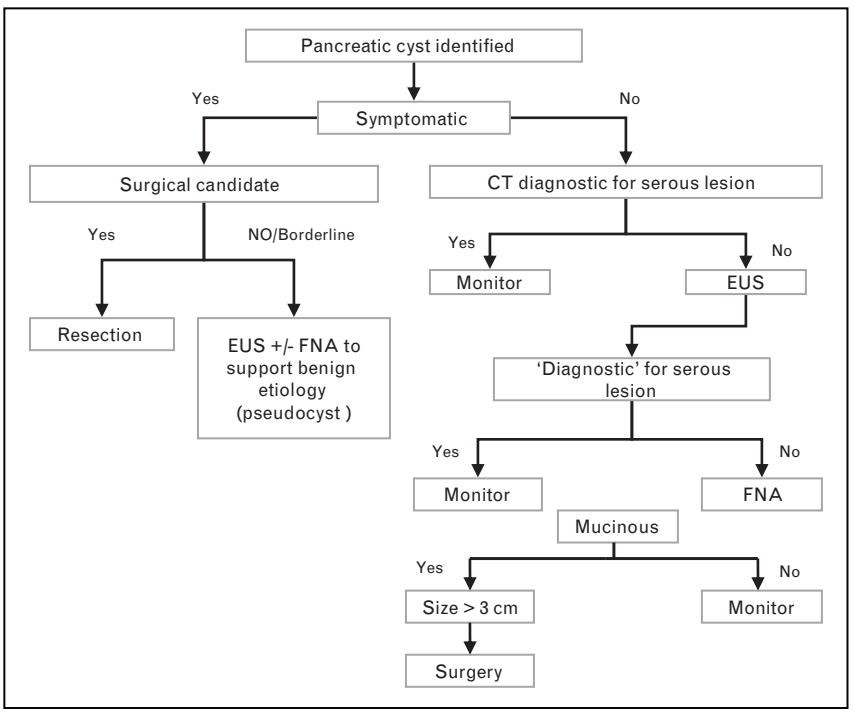
of asymptomatic patients with incidental pancreatic cystic neoplasms for surgery. Their results strongly challenge a blanket policy for surgical resection and advocate risk stratification for malignant potential by EUS-FNA and cyst fluid analysis.

Given the uncertainty of preoperative diagnosis and the morbidity and mortality of surgery, investigators have explored the safety and potential utility for ablation of the cysts with nonsurgical means. In a pilot study, 25 patients underwent EUS-guided pancreatic cyst lavage with ethanol concentrations as high as 80% with varying degrees of histologic epithelial ablation with cyst resolution in eight (35%) patients [29]. To further explore the utility and safety of this approach, EUS-guided ethanol lavage was compared with saline lavage in a prospective trial [30••]. Patients referred for EUS with a 1–5-cm unilocular pancreatic cyst were randomized to blinded ethanol or saline solution lavage. Cysts with possible main pancreatic duct communication were excluded. Three months later, a second unblinded ethanol lavage was performed. Ethanol lavage resulted in a greater decrease in cyst surface area (−42.9%) compared with saline solution (−11.4%, $P < 0.009$). Nineteen (76.0%) of 25 and 14 (82.3%) of 17 patients randomized to ethanol and saline solution, respectively, underwent a second ethanol lavage. A follow-up CT scan demonstrated resolution in 12 (33.3%) of 36 cysts. Histology of four resected cysts demonstrated epithelial ablation ranging from 0% (saline solution alone) to 50–100%. Complication rates were noted as similar by the investigators (20% abdominal pain in ethanol and 11.8% in saline groups. However, acute pancreatitis occurred in one patient treated with ethanol lavage after treatment of a 1.1-cm cyst in the pancreatic head requiring a 10-day hospitalization. Major limitations of this study include the inclusion of presumed SCAs as well as pseudocysts. The authors' conclusion, that a single EUS-guided lavage of 80% ethanol resulted in a statistically greater mean decrease in pancreatic cyst size compared with a single saline solution injection, was clearly demonstrated. However, the clinical utility of short-term evidence of cyst ablation in 33% and variable histopathologic degrees of cyst epithelial ablation remains of dubious value. We agree that future research investigating the safety of this procedure, modifications of the technique, choice, and number of the lavage agents used (other studies have used paclitaxel for example), is needed. Most importantly, criteria to optimize selection of the appropriate pancreatic cysts for such treatment is essential, given the viability of surveillance and the evolving data supporting EUS with or without FNA for risk stratification.

A proposed management approach

Given the explosion in cystic lesion identification, a selective approach to detailed testing and surgical intervention is essential to improve outcomes as well as

Figure 3 A rational approach



contain costs. A multidisciplinary approach to such patients is important; we have emphasized close collaboration between surgeons and gastroenterologists [31].

Our approach is summarized in Fig. 3 and summarized as follows. The approach to the patient begins with a detailed history looking for symptoms related to the lesion itself or a related condition such as pancreatitis. Fit patients with symptomatic lesions (not characterized as pseudocysts) usually proceed to surgery. Most asymptomatic patients have lesions too small to cause symptoms. Typical symptoms of malignancy are usually absent. Clinical decision-making is driven by an understanding of the differential diagnosis of the cyst and, in the case of the asymptomatic patient, its likelihood of causing harm with intervention.

Conclusion

The fundamental issue to be addressed is whether the cyst is neoplastic or not, and if so, what is its risk for malignant degeneration. In the absence of a history of pancreatitis, pseudocyst is quite unlikely (but not impossible), and the concern of a cystic neoplasm is paramount. If preoperative characterization of the lesion will change management, EUS with or without FNA for cytology and fluid analysis may provide information of diagnostic and prognostic value. For those patients with benign-appearing lesions, such as those with a classic appearance of a SCA, a decision regarding the patient's willingness to observe the lesion should be developed in collaboration with a pancreatic surgeon. In many circumstances, selected use of EUS with or without FNA with cytology and fluid measurement can further provide evidence to support the approach of watchful waiting. Patients can then be carefully monitored with serial examinations (EUS or less invasive cross-sectional imaging) to exclude change in size. Watchful waiting clearly represents a carefully considered trade-off between delayed surgery for unresectable disease and unnecessary surgical morbidity and mortality.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 536–537).

1 Vignesh S, Brugge WR. Endoscopic diagnosis and treatment of pancreatic cysts. J Clin Gastroenterol 2008; 42:493–506.

2 Friedel DM, Abraham B, Georgiou N, *et al.* Pancreatic cystic neoplasms. South Med J 2010; 103:51–57.

3 Laffan TA, Horton KM, Klein AP, *et al.* Prevalence of unsuspected pancreatic cysts on MDCT. AJR Am J Roentgenol 2008; 191:802–807.

4 Ishikawa T, Takeda K, Itoh M, *et al.* Prevalence of pancreatic cystic lesions including intraductal papillary mucinous neoplasms in patients with end-stage renal disease on hemodialysis. Pancreas 2009; 38:175–179.

5 • Pausawasdi N, Heidt D, Kwon R, *et al.* J. Long-term follow-up of patients with incidentally discovered pancreatic cystic neoplasms evaluated by endoscopic ultrasound. Surgery 2010; 147:13–20.
This study highlights the benign clinical outcomes in patients with incidentally discovered pancreatic cysts without concerning EUS features. It emphasizes the usefulness of EUS to select patients at low risk for progression.

6 Brounts LR, Lehmann RK, Causey MW, *et al.* Natural course and outcome of cystic lesions in the pancreas. Am J Surg 2009; 197:619–622; discussion 622–623.

7 • Buscaglia JM, Giday SA, Kantsevoy SV, *et al.* Patient- and cyst-related factors for improved prediction of malignancy within cystic lesions of the pancreas. Pancreatology 2009; 9:631–638.
This paper identified that age of >50, weight loss, cyst size >1.5 cm, and high CEA were clinical predictors of malignancy.

8 Huang ES, Turner BG, Fernandez-Del-Castillo C, *et al.* Pancreatic cystic lesions: clinical predictors of malignancy in patients undergoing surgery. Aliment Pharmacol Ther 2010; 31:285–294.

9 Cadili A, Bazarrelli A, Garg S, Bailey R. Survival in cystic neoplasms of the pancreas. Can J Gastroenterol 2009; 23:537–542.

10 Kim SH, Lim JH, Lee WJ, Lim HK. Macrocystic pancreatic lesions: differentiation of benign from premalignant and malignant cysts by CT. Eur J Radiol 2009; 71:122–128.

11 Sainani NI, Saokar A, Deshpande V, *et al.* Comparative performance of MDCT and MRI with MR cholangiopancreatography in characterizing small pancreatic cysts. AJR Am J Roentgenol 2009; 193:722–731.

12 Ahmad NA, Kochman ML, Brensinger C, *et al.* Interobserver agreement among endosonographers for the diagnosis of neoplastic versus nonneoplastic pancreatic cystic lesions. Gastrointest Endosc 2003; 58:59–64.

13 Antillon MR, Tiwari P, Bartalos CR, Marshall JB. Taking SpyGlass outside the GI tract lumen in conjunction with EUS to assist in the diagnosis of a pancreatic cystic lesion (with video). Gastrointest Endosc 2009; 69:591–593.

14 Bruno M, Bosco M, Carucci P, *et al.* Preliminary experience with a new cytology brush in EUS-guided FNA. Gastrointest Endosc 2009; 70:1220–1224.

15 Repak R, Rejchrt S, Bartova J, *et al.* Endoscopic ultrasonography (EUS) and EUS-guided fine-needle aspiration with cyst fluid analysis in pancreatic cystic neoplasms. Hepatogastroenterology 2009; 56:629–635.

16 Brugge WR, Lewandrowski K, Lee-Lewandrowski E, *et al.* Diagnosis of pancreatic cystic neoplasms: a report of the cooperative pancreatic cyst study. Gastroenterology 2004; 126:1330–1336.

17 Walsh RM, Vogt DP, Henderson JM, *et al.* Natural history of indeterminate pancreatic cysts. Surgery 2005; 138:665–671.

18 Leung KK, Ross WA, Evans D, *et al.* Pancreatic cystic neoplasm: the role of cyst morphology, cyst fluid analysis, and expectant management. Ann Surg Oncol 2009; 16:2818–2824.

19 • Khalid A, Zahid M, Finkelstein SD, *et al.* Pancreatic cyst fluid DNA analysis in evaluating pancreatic cysts: a report of the PANDA study. Gastrointest Endosc 2009; 69:1095–1102.
This prospective trial examined the value of cyst fluid DNA analysis in selected patient populations with pancreatic cystic lesions.

20 Shen J, Brugge WR, Dimaio CJ, Pitman MB. Molecular analysis of pancreatic cyst fluid: a comparative analysis with current practice of diagnosis. Cancer Cytopathol 2009; 117:217–227.

21 Sawhney MS, Devarajan S, O'Farrel P, *et al.* Comparison of carcinoembryonic antigen and molecular analysis in pancreatic cyst fluid. Gastrointest Endosc 2009; 69:1106–1110.

22 Sreenarasimhaiah J, Lara LF, Jazrawi SF, *et al.* A comparative analysis of pancreas cyst fluid CEA and histology with DNA mutational analysis in the detection of mucin producing or malignant cysts. JOP 2009; 10:163–168.

23 • Anderson MA, Kwon RS, Scheiman JM. PANDA cyst-fluid analysis: eats, shoots and leaves? Gastrointest Endosc 2009; 69:1103–1105.
This editorial critically evaluated the strengths and limitations of the study and emphasizes the selective use of cyst fluid DNA analysis.

24 Allen PJ, Qin LX, Tang L, *et al.* Pancreatic cyst fluid protein expression profiling for discriminating between serous cystadenoma and intraductal papillary mucinous neoplasm. Ann Surg 2009; 250:754–760.

25 Ke E, Patel BB, Liu T, *et al.* Proteomic analyses of pancreatic cyst fluids. Pancreas 2009; 38:e33–e42.

26 Tanaka M, Chari S, Adsay V, *et al.* International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006; 6:17–32.

27 Buscaglia JM, Shin EJ, Giday SA, *et al.* Awareness of guidelines and trends in
• the management of suspected pancreatic cystic neoplasms: survey results among general gastroenterologists and EUS specialists. Gastrointest Endosc 2009; 69:813–820.

This study shows the current limited impact of guidelines and current clinical variability in practice for pancreatic cyst managment.

28 Das A, Ngamruengphong S, Nagendra S, Chak A. Asymptomatic pancreatic
•• cystic neoplasm: a cost-effectiveness analysis of different strategies of management. Gastrointest Endosc 2009; 70:690–699.

This study emphasizes the cost-effectiveness of various treatments and advocates careful selection of asymptomatic patients with incidental pancreatic cystic neoplasms for surgery. It affirms risk stratification for malignant potential by EUS-guided FNA and cyst fluid analysis.

29 Gan SI, Thompson CC, Lauwers GY, *et al.* Ethanol lavage of pancreatic cystic lesions: initial pilot study. Gastrointest Endosc 2005; 61:746–752.

30 DeWitt J, McGreevy K, Schmidt CM, Brugge WR. EUS-guided ethanol versus
•• saline solution lavage for pancreatic cysts: a randomized, double-blind study. Gastrointest Endosc 2009; 70:710–723.

This prospective study shows that EUS-guided ethanol lavage may lead to regression of pancreatic cystic lesions after a short-term follow-up. Further study of nonsurgical treatments in highly selected patients is warranted.

31 Scheiman JM. Management of Cystic Lesions of the Pancreas. J Gastrointest Surg 2008; 12:405–407.