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TOPIC HIGHLIGHT

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Utility of endoscopic ultrasound in pancreatitis: A review

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Abstract

The close proximity of the endoscopic ultrasound probe to the pancreas results in superior spatial resolution compared to CT scan and MRI. In addition, endoscopic ultrasound (EUS) is a minimally invasive procedure that does not share the relatively high complication rate of ERCP. Due to these advantages, EUS has evolved into an important technique to assess pancreatobiliary disease. This review will discuss the role of EUS in patients with pancreatitis. The indications can be divided into acute pancreatitis and chronic pancreatitis. In acute pancreatitis, EUS is used to determine the etiology; in suspected chronic pancreatitis it is helpful to establish the diagnosis. Lastly, this review will discuss biliary pancreatitis with suspicion for persistent choledocholithiasis.

Key words: Idiopathic pancreatitis; Acute pancreatitis; Chronic pancreatitis; Endoscopic ultrasound; Endosonography; Pancreas divisum; Cholelithiasis; Microlithiasis; Choledocholithiasis; Biliary pancreatitis

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INTRODUCTION

Overlying intestinal gas and the retroperitoneal location of the pancreas distant from the abdominal wall can impair the visualization of this organ with trans-abdominal ultrasound. This problem has been overcome by integrating the ultrasound probe into an endoscope in order to place it directly into the gastric and duodenal lumen. The close proximity of the endoscopic ultrasound probe to the pancreas results in high spatial resolution that is superior to that of Computer Tomography (CT) and magnetic resonance imaging (MRI). In addition, endoscopic ultrasound (EUS) is a minimally invasive procedure that does not share the relatively high complication rate of endoscopic retrograde cholangiopancreatography (ERCP). Due to these advantages, EUS has evolved into an important technique to assess pancreatobiliary disease.

This review will discuss the role of EUS in patients with pancreatitis. The indications can be divided into acute pancreatitis and chronic pancreatitis. In acute pancreatitis, EUS is used to determine the etiology; in suspected chronic pancreatitis it is helpful to establish the diagnosis. Another indication that will be discussed is biliary pancreatitis with suspicion for persistent choledocholithiasis.

ACUTE IDIOPHATHIC PANCREATITIS

The diagnosis of acute idiopathic pancreatitis (AIP) is applied when an etiology cannot be determined after the initial evaluation that includes a thorough history and physical exam, laboratory evaluation and abdominal ultrasound or CT[1-4]. In-depth evaluation of AIP using EUS often yields the diagnosis of microlithiasis, pancreatic divisum, chronic pancreatitis[1,5-7] or even neoplasm[1,4].

Occult gallstones and microlithiasis

A substantial number of patients with AIP and unexplained biliary pain turn out to have biliary sludge or small gallstones that have gone undetected by abdominal ultrasound (US) or CT. The term 'biliary microlithiasis' was coined to describe gallstones of < 3 mm in diameter[8-10]. Although sonographic characteristics of cholelithiasis do not differ between EUS and trans-abdominal ultrasound, EUS is more sensitive in detecting gallstones[11] due to the proximity of the endoscope tip to the gallbladder. Small gallbladder stones present as bright floating foci. Larger stones have posterior shadowing. Sludge presents as hyperechoic content within the gallbladder or bile duct (Figures 1 and 2).

The reported incidence of occult gallstones in patients with AIP varies widely. It ranges from 10%-73%[12-15]. Gallstones remain the most common cause of pancreatitis in patients with intact gallbladder. Therefore, it is

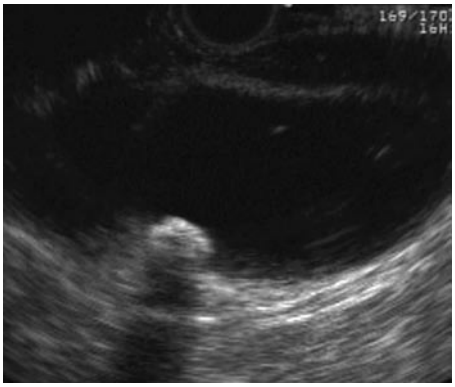

Figure 1 Linear EUS of gallbladder with shadowing stone.

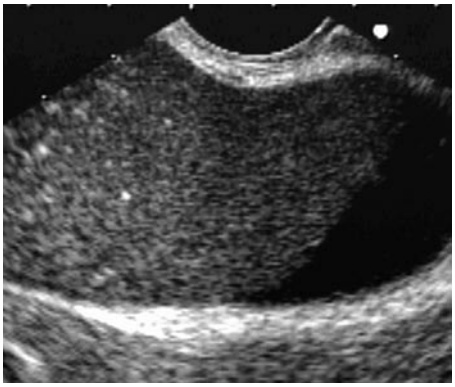

Figure 2 Linear EUS of gallbladder with sludge, and bright shadowing foci representing small stones.

commonly believed that the finding of microlithiasis explains the etiology of the pancreatitis. This has recently been challenged. In a study by Garg *et al*. Seventy-five patients with AIP were studied with duodenal bile microscopy and EUS. Initially, the cause of the recurrent pancreatitis was attributed to biliary microlithiasis in 10 of 75 patients. Eight of these 10 patients underwent cholecystectomy or endoscopic sphincterotomy yet continued to have recurrent pancreatitis flares[16] which implies that gallstones or biliary crystals were innocent bystanders in these patients. In contrast, other studies have demonstrated response to cholecystectomy[5,17], sphincterotomy[11] or ursodeoxycholic acid (UDCA)[10] in patients with microlithiasis suggesting a causal relationship.

Liu *et al* prospectively evaluated 89 consecutive patients who presented with symptoms of acute pancreatitis with trans-abdominal ultrasound, CT, or both. ERCP was performed in all patients with confirmed or suspected biliary pancreatitis. EUS was performed in patients suspected of having idiopathic pancreatitis. Of the 18 patients classified as idiopathic pancreatitis who underwent EUS, 14 had stones that were between 1 and 9 mm in size which was confirmed by cholecystectomy. Three had concomitant choledocholithiasis confirmed by ERCP[17].

Another study retrospectively evaluated 31 patients with AIP who underwent EUS 2-3 wk after resolution of symptoms[5]. Five of 31 patients had microlithiasis diagnosed by EUS (n = 3), or by bile microscopy after EUS (n = 2). All 5 patients underwent cholecystectomy and remained asymptomatic during the follow-up period. Sludge was found on pathology examination in all 5 gallbladders. Gallstones or sludge were not diagnosed in any of the other 26 subjects during the follow-up period.

In summary, EUS is an effective modality in diagnosing microlithiasis and may strengthen the indication for a subsequent intervention. Treatment with cholecystectomy, endoscopic sphincterotomy or ursodeoxycholic acid may reduce recurrent attacks of pancreatitis[10,11]. However, it remains debatable how intensively we have to search for occult gallstones. Statistically, gallstones remain by far the likeliest cause of unexplained recurrent pancreatitis in patients with intact gallbladders. The morbidity of laparoscopic cholecystectomy is very low, and one could argue that this procedure is justified regardless of the findings of cross sectional imaging.

Pancreas divisum

Pancreas divisum is a common congenital malformation. The prevalence is estimated at 5%-10% in a Western population[18]. This abnormality is characterized by lack of connection between the dorsal and ventral pancreatic ducts due to incomplete fusion of the pancreatic buds during embryologic development. As a result, the ventral duct drains only a small portion of the pancreas *via* the major papilla, whereas the dorsal pancreatic duct drains the majority of the pancreas *via* the minor papilla. The small size of the minor papilla in relation to the drainage volume may lead to relative outflow obstruction. Since only a minority of patients with pancreas divisum becomes symptomatic, it has been suggested that symptomatic disease requires additional factors leading to minor papilla stenosis. Symptomatic patients present with recurrent acute pancreatitis, chronic pancreatitis, or chronic abdominal pain without evidence of pancreatitis. Pancreas divisum has been implicated in as much as 20% of patients with AIP[12]. Patients with discrete episodes of acute pancreatitis commonly improve after ERCP with minor papillotomy, whereas the results are less favorable for those with chronic pancreatitis or chronic abdominal pain[19] .

ERCP is the gold standard for the diagnosis of pancreas divisum but poses a risk of post procedure pancreatitis. Small series suggest that EUS enables a fairly reliable diagnosis of pancreas divisum and may therefore present an alternative to ERCP with minimal complication rate[5,7,20,21]. Different EUS-criteria have been used: Bhutani *et al* suggest that the absence of a "stack sign" may be useful in determining the diagnosis. The stack sign is obtained by positioning a radial echoendoscope in the long position with the transducer in the duodenal bulb. The balloon is then inflated and advanced snugly into the apex of the bulb. From this position, the bile duct and the pancreatic duct can be seen running parallel through the pancreatic head. In six patients with known pancreas divisum that underwent EUS, the stack sign was found in only two patients. Of the two patients with presence of a stack sign, one had a ventral duct that was markedly dilated, and the other patient had an unusually large ventral pancreas[20]. Tandon *et al* used different sonographic criteria. The authors required direct visualization of the dorsal duct coursing to the duodenal wall, and excluded patients with a sonographically visible ventral pancreatic duct. The authors feel that their criteria will exclude some

cases of pancreas divisum and many cases of "incomplete pancreas divisum," but may be more specific as compared to the absence of a stack sign[5]. Lai *et al* suggests that evaluation using a linear-array echoendoscope is possible. The main pancreatic duct can be followed continuously from the major papilla into the pancreatic body. The duct can be seen crossing a sonographic border between the ventral and dorsal pancreas. Absence of this feature suggests pancreas divisum. In the retrospective study, of the 78% who had adequate visualization of the pancreatic duct, sensitivity, specificity, positive and negative predictive values for EUS were 95%, 97%, 86%, and 99%, respectively[21].

Occult neoplasm

It has been estimated that pancreatic neoplasms cause pancreatitis at some point in the disease course in up to 7 percent of patients[22]; however, they are a rare differential diagnosis in patients with AIP.

Mujica *et al* surveyed 19 physicians regarding 45 patients who presented with acute pancreatitis prior to a diagnosis of a neoplasm. The patients had a mean number of 2 episodes of acute pancreatitis prior to the diagnosis of neoplasm. The mean time to diagnosis of the neoplasm after the initial episode was 34 wk. The majority of patients were diagnosed using conventional cross-sectional imaging, whereas only 3 patients in the series were diagnosed using EUS[22].

Albeit rare, it has been suggested that pancreatic malignancy should be suspected in patients with unexplained pancreatitis who are older than 40 years of age[23]. EUS is superior to CT in detecting small pancreatic neoplasms[24,25], however, inflammatory changes during a pancreatitis flare may decrease the image quality. Therefore, cross-sectional imaging and/or EUS should be repeated after the resolution of the acute attack.

Single episode of idiopathic pancreatitis

The utility of an evaluation with EUS after a single episode of unexplained pancreatitis is not well studied and remains unclear[4]. In a small series by Tandon *et al*, EUS found an etiology in 7 of 14 patients with a single episode of idiopathic pancreatitis (3 microlithiasis, 1 pancreas divisum, 3 alcoholic chronic pancreatitis). The diagnosis changed in only 1 patient[23] during the follow-up period. A series reported by Yusoff *et al* included 201 patients with a single episode of acute pancreatitis. A presumptive diagnosis was made after EUS in 31%; chronic pancreatitis and sludge were the most common diagnoses in those with a gallbladder, whereas chronic pancreatitis and pancreatic divisum were the most prevalent diagnoses in patients who had a prior cholecystectomy[6].

Although these studies suggest a high yield of EUS in patients with a single episode of unexplained pancreatitis, some skepticism remains. Only 20%-50% of patients will have recurrent symptoms[26] following the initial attack. Furthermore, it is difficult to be sure about the causal relationship of an abnormal EUS finding after a single episode of pancreatitis. Pancreas divisum, for example, is common in the general population, and may be a coincidental finding rather than the cause of the pancreatitis. Even microlithiasis may be a harmless bystander[16]. As discussed in detail in a later paragraph, the diagnosis of chronic pancreatitis with EUS is problematic due to lack of specificity in early stages. In our opinion, further studies are necessary before advocating EUS for every patient after a single episode of idiopathic pancreatitis.

Table 1 EUS criteria of chronic pancreatitis

Parenchymal criteria	Pancreatic ductal criteria
Hyperechoic foci	Dilation (4 mm in head, 3 mm in body, 2 mm in tail)
Hyperechoic strands	Irregularity
Lobularity	Hyperechoic duct margins
Heterogeneity	Visible branch ducts
Shadowing calcifications	Intraductal stones
Cysts	

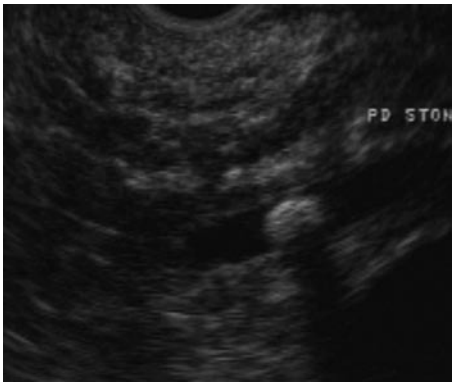

Figure 3 Linear EUS showing a shadowing stone within the pancreatic duct (PD STONE).

CHRONIC PANCREATITIS

The diagnosis of chronic pancreatitis (CP) can be challenging. The normal pancreas has a homogeneous fine granular echo-pattern (salt and pepper appearance), with a thin and regular main pancreatic duct. Certain sonographic changes can be observed in patients with CP. In an attempt to develop diagnostic scores for the EUS-diagnosis of chronic pancreatitis, "EUS criteria" have been developed. These were first described by Jones *et al*[27], and later refined by Wiersema *et al*[28]. The criteria can be divided into pancreatic duct findings and parenchymal findings. Parenchymal findings include hyperechoic foci, hyperechoic strands, lobularity, heterogeneity, shadowing calcifications, and cysts. Pancreatic duct findings include dilation (> 4 mm in the head, > 3 mm in the body, > 2 mm in the tail), irregularity, hyperechoic duct margins, and visible side-branches (Table 1, Figures 3-6). Multiple studies have evaluated the ability of EUS to diagnose CP using the above criteria. In a prospective, blinded study by Sahai *et al*, 126 patients who were admitted for abdominal pain underwent ERCP followed by EUS performed by a blinded operator. ERCP diagnosis of CP was based on Cambridge Criteria. EUS sensitivity was uniformly greater than 85% when the diagnosis of CP was based on the

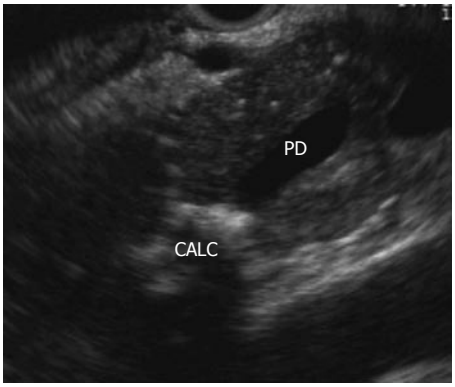

Figure 4 Linear trans-gastric EUS of the pancreas showing parenchymal calcifications (CALC) causing dilatation of the upstream pancreatic duct (PD).

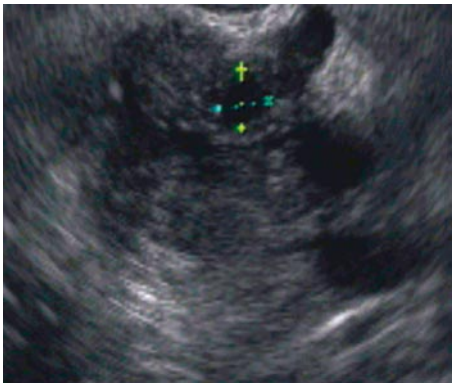

Figure 5 Linear trans-gastric EUS showing a small pancreatic cyst (labeled with measurement markers).

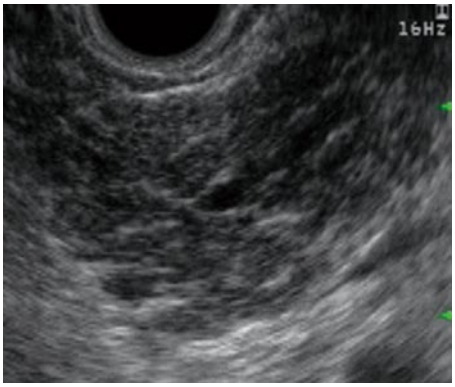

Figure 6 Linear EUS of pancreatic body with echogenic strands and lobularity.

presence of fewer than three criteria, but the specificity was less than 60%. Specificity increased as the number of criteria increased and was greater than 85% when more than five criteria were used. "Moderate to severe chronic pancreatitis" was unlikely (NPV > 85%) when fewer than three criteria were present[29]. When criteria that can easily be detected by other imaging methods (ductal dilation, calcification, and cysts) were excluded, the number of parenchymal EUS criteria remained an independent predictor of CP[29].

There are nuances that need to be considered when using the above score. Firstly, the role of ERCP as a diagnostic "gold-standard" is debatable[30]. Thus, it is difficult to determine whether EUS is over-diagnosing pancreatic disease based on minimal changes or whether ERCP is a false negative in those with abnormal EUS findings but normal ERCP. In a study by Kahl *et al*[31], 32 patients with abnormal EUS but normal initial pancreatogram developed findings of CP on repeat ERCP after a median follow-up of 18 mo suggesting that EUS findings may precede ERCP findings. The sensitivity to diagnose chronic pancreatitis was 100% for EUS, but only 81% for ERCP.

Another concern when using an EUS scoring system to diagnose CP is that not all criteria may be equally important. For example, the presence of intraductal calcifications or parenchymal calcifications alone may be diagnostic of CP even in the absence of other criteria[30]. Age related changes in the pancreas may also affect the diagnostic threshold. The pancreatic duct becomes progressively wider with a hyperechoic wall with increased age. Another aspect to consider is interobserver variability of different criteria. Wiersema *et al*[28] found excellent interobserver agreement among 3 experienced endosonographers reading individual criteria of CP. There was 88% interobserver agreement on presence of echogenic foci, 94% agreement on focally reduced echogenicity, 94% agreement on lobular gland pattern, 83% agreement on the main pancreatic duct echogenicity, and 94% agreement on main pancreatic duct irregularity. On the contrary, Wallace *et al*[32] could not confirm these optimistic results. EUS-exams on 33 patients with suspected CP and 12 controls without suspected CP were videotaped by 3 experienced endosonographers. Eleven expert endosonographers, who were blinded to clinical information, independently evaluated the examinations for the presence of CP and were asked to rank the importance of individual EUS features. There was moderately good interobserver agreement in the final diagnosis of CP (Kappa = 0.45).

Interobserver agreement was good for the individual criteria "ductal dilation" and "lobularity" but was poor for the other 7 criteria. The presence of stones was regarded as the most predictive feature of CP by all endosonographers, followed by visible side branches, cysts, lobularity, irregular main pancreatic duct, hyperechoic strands, main pancreatic duct dilation and main duct hyperechoic margins[32].

In our opinion, the early diagnosis of CP remains problematic due to lack of specificity and the presence of interobserver variability. The overall interpretation of the experienced endosonographer may be more valuable than a diagnosis based on a scoring system.

Only a few studies have evaluated the utility of biopsy in addition to EUS for the diagnosis of CP. One small study suggested that fine needle aspiration may improve the negative predictive value but not the specificity of EUS[33], however this study was limited by the small number of patients without chronic pancreatitis. Out of 37 patients, 31 had chronic pancreatitis. Only 4 patients had normal EUS findings, 3 without and one with chronic pancreatitis (negative predictive value of 75%). The negative predictive value was improved to 100% by FNA-cytology. In our opinion, it is difficult to draw conclusions based on such small numbers. Another study found that EUS-guided core biopsies with a Trucut needle was poor at diagnosing CP[34].

In conclusion, current data do not support a role of EUS-guided biopsies in the diagnosis of CP. In addition

to their questionable diagnostic value, pancreatic biopsies carry a potential risk of post-procedure pancreatitis.

CP makes the detection of pancreatic cancer more difficult. In a series of 282 patients with pancreatic mass (210 with adenocarcinoma), a lower sensitivity for EUS-FNA was observed in patients with CP (more than 4 EUS-criteria) than in those without CP (73.9% *vs* 91.3%). Patients with CP required more EUS-FNA passes to establish a diagnosis versus those without CP (5 *vs* 2)[35].

In summary, the diagnosis of CP remains challenging. EUS criteria have been established. Although these criteria are highly sensitive, they lack specificity in early stages. EUS is accurate in ruling out CP if no pancreatic abnormalities are found and in diagnosing CP if multiple criteria are present. However, a wide grey zone remains for patients with minimal to moderate findings.

CP decreases the sensitivity of EUS-FNA in the evaluation of pancreatic masses.

BILIARY PANCREATITIS AND CHOLEDOCHOLITHIASIS

In most patients with biliary pancreatitis, the causal gallstone has already passed. This makes it difficult to identify those patients in whom ERCP with sphincterotomy may be beneficial. In this context, EUS may provide a minimally invasive modality to diagnose or exclude choledocholithiasis. A review of five studies by Verma *et al* evaluating the efficacy of different modalities in diagnosing choledocholithiasis found an aggregated sensitivity of EUS of 0.93, a specificity of 0.96, a positive predictive value of 0.93, and a negative predictive value of 0.96. There was no statistical difference between MRCP and EUS[36]. In a study by Lui *et al*[37], 100 patients admitted for acute pancreatitis were evaluated with trans-abdominal ultrasound, EUS, and ERCP. EUS was found to be as sensitive as ERCP in the detection of choledocholithiasis, but with a lower complication rate.

Arguedas *et al* proposed a decision analysis model in evaluating biliary pancreatitis. Cost-effectiveness of strategies involving observation, intraoperative cholangiography, EUS, MRCP, and ERCP was evaluated. The results demonstrated that the choice of strategy is strongly influenced by the pretest probability of choledocholithiasis. If cost-minimization is the goal, observation with intraoperative cholangiography at the time of cholecystectomy is preferred in patients considered at "low risk" for choledocholithiasis. EUS is cost effective in patients at "intermediate risk" and ERCP is the preferable strategy in patients at "high-risk". There was no utility for MRCP in this model, as EUS was less costly[38]. Scheiman *et al*[39], also suggested that there is no role for MRCP for biliary pancreatitis in centers where EUS is available.

Sugiyama *et al* prospectively evaluated 35 patients with suspected acute biliary pancreatitis. All patients underwent trans-abdominal ultrasound, CT, EUS, and ERCP. The severity of pancreatitis was graded using APACHE Ⅱ scores. EUS and ERCP were significantly more sensitive in the detection of CBD stones than trans-abdominal ultrasound and CT. ERCP and EUS were equivalent in CBD stone detection. Based on the severity of the pancreatitis, 20 of 35 ERCP were determined to be potentially avoidable[38].

In summary, EUS is both sensitive and specific in the detection of common bile duct stones and has a considerably lower complication rate than ERCP. While patients with high likelihood of cholelithiasis should undergo ERCP directly, EUS may enable selective use of ERCP in those with intermediate likelihood[1,3,7,10,38,39].

CONCLUSION

EUS is helpful in the evaluating patients with AIP and in diagnosing CP. In patients with AIP, EUS enables the diagnosis of occult cholelithiasis, pancreas divisum, chronic pancreatitis or an occult neoplasm. While EUS may be more sensitive than ERCP in diagnosing CP, the specificity is limited in early stages. In biliary pancreatitis, EUS allows accurate detection of common bile duct stones and can be used to select patients who will benefit from ERCP.

REFERENCES

1 **Norton SA**, Alderson D. Endoscopic ultrasonography in the evaluation of idiopathic acute pancreatitis. *Br J Surg* 2000; **87**: 1650-1655
2 **Frossard JL**, Sosa-Valencia L, Amouyal G, Marty O, Hadengue A, Amouyal P. Usefulness of endoscopic ultrasonography in patients with "idiopathic" acute pancreatitis. *Am J Med* 2000; **109**: 196-200
3 **Draganov P**, Forsmark CE. "Idiopathic" pancreatitis. *Gastroenterology* 2005; **128**: 756-763
4 **Levy MJ**, Geenen JE. Idiopathic acute recurrent pancreatitis. *Am J Gastroenterol* 2001; **96**: 2540-2555
5 **Tandon M**, Topazian M. Endoscopic ultrasound in idiopathic acute pancreatitis. *Am J Gastroenterol* 2001; **96**: 705-709
6 **Yusoff IF**, Raymond G, Sahai AV. A prospective comparison of the yield of EUS in primary vs. recurrent idiopathic acute pancreatitis. *Gastrointest Endosc* 2004; **60**: 673-678
7 **Coyle WJ**, Pineau BC, Tarnasky PR, Knapple WL, Aabakken L, Hoffman BJ, Cunningham JT, Hawes RH, Cotton PB. Evaluation of unexplained acute and acute recurrent pancreatitis using endoscopic retrograde cholangiopancreatography, sphincter of Oddi manometry and endoscopic ultrasound. *Endoscopy* 2002; **34**: 617-623
8 **Levy MJ**. The hunt for microlithiasis in idiopathic acute recurrent pancreatitis: should we abandon the search or intensify our efforts? *Gastrointest Endosc* 2002; **55**: 286-293
9 **Rashdan A**, Fogel E, McHenry L, Lehman G, Sherman S. Frequency of biliary crystals in patients with suspected sphincter of Oddi dysfunction. *Gastrointest Endosc* 2003; **58**: 875-878
10 **Saraswat VA**, Sharma BC, Agarwal DK, Kumar R, Negi TS, Tandon RK. Biliary microlithiasis in patients with idiopathic acute pancreatitis and unexplained biliary pain: response to therapy. *J Gastroenterol Hepatol* 2004; **19**: 1206-1211
11 **Mirbagheri SA**, Mohamadnejad M, Nasiri J, Vahid AA, Ghadimi R, Malekzadeh R. Prospective evaluation of endoscopic ultrasonography in the diagnosis of biliary microlithiasis in patients with normal transabdominal ultrasonography. *J Gastrointest Surg* 2005; **9**: 961-964
12 **Kaw M**, Brodmerkel GJ. ERCP, biliary crystal analysis, and sphincter of Oddi manometry in idiopathic recurrent pancreatitis. *Gastrointest Endosc* 2002; **55**: 157-162
13 **Lee SP**, Hayashi A, Kim YS. Biliary sludge: curiosity or

culprit? *Hepatology* 1994; **20**: 523-525
14 **Ros E**, Navarro S, Bru C, Garcia-Pugés A, Valderrama R. Occult microlithiasis in 'idiopathic' acute pancreatitis: prevention of relapses by cholecystectomy or ursodeoxycholic acid therapy. *Gastroenterology* 1991; **101**: 1701-1709
15 **Venu RP**, Geenen JE, Hogan W, Stone J, Johnson GK, Soergel K. Idiopathic recurrent pancreatitis. An approach to diagnosis and treatment. *Dig Dis Sci* 1989; **34**: 56-60
16 **Garg PK**, Tandon RK, Madan K. Is biliary microlithiasis a significant cause of idiopathic recurrent acute pancreatitis? A long-term follow-up study. *Clin Gastroenterol Hepatol* 2007; **5**: 75-79
17 **Liu CL**, Lo CM, Chan JK, Poon RT, Fan ST. EUS for detection of occult cholelithiasis in patients with idiopathic pancreatitis. *Gastrointest Endosc* 2000; **51**: 28-32
18 **Dhar A**, Goenka MK, Kochhar R, Nagi B, Bhasin DK, Singh K. Pancrease divisum: five years' experience in a teaching hospital. *Indian J Gastroenterol* 1996; **15**: 7-9
19 **Gerke H**, Byrne MF, Stiffler HL, Obando JV, Mitchell RM, Jowell PS, Branch MS, Baillie J. Outcome of endoscopic minor papillotomy in patients with symptomatic pancreas divisum. *JOP* 2004; **5**: 122-131
20 **Bhutani MS**, Hoffman BJ, Hawes RH. Diagnosis of pancreas divisum by endoscopic ultrasonography. *Endoscopy* 1999; **31**: 167-169
21 **Lai R**, Freeman ML, Cass OW, Mallery S. Accurate diagnosis of pancreas divisum by linear-array endoscopic ultrasonography. *Endoscopy* 2004; **36**: 705-709
22 **Mujica VR**, Barkin JS, Go VL. Acute pancreatitis secondary to pancreatic carcinoma. Study Group Participants. *Pancreas* 2000; **21**: 329-332
23 **Wilcox CM**, Varadarajulu S, Eloubeidi M. Role of endoscopic evaluation in idiopathic pancreatitis: a systematic review. *Gastrointest Endosc* 2006; **63**: 1037-1045
24 **Rösch T**, Lorenz R, Braig C, Feuerbach S, Siewert JR, Schusdziarra V, Classen M. Endoscopic ultrasound in pancreatic tumor diagnosis. *Gastrointest Endosc* 1991; **37**: 347-352
25 **Hunt GC**, Faigel DO. Assessment of EUS for diagnosing, staging, and determining resectability of pancreatic cancer: a review. *Gastrointest Endosc* 2002; **55**: 232-237
26 **Gullo L**, Migliori M, Pezzilli R, Oláh A, Farkas G, Levy P, Arvanitakis C, Lankisch P, Beger H. An update on recurrent acute pancreatitis: data from five European countries. *Am J Gastroenterol* 2002; **97**: 1959-1962
27 **Jones SN**, Lees WR, Frost RA. Diagnosis and grading of chronic pancreatitis by morphological criteria derived by ultrasound and pancreatography. *Clin Radiol* 1988; **39**: 43-48
28 **Wiersema MJ**, Hawes RH, Lehman GA, Kochman ML, Sherman S, Kopecky KK. Prospective evaluation of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in patients with chronic abdominal pain of suspected pancreatic origin. *Endoscopy* 1993; **25**: 555-564
29 **Sahai AV**, Zimmerman M, Aabakken L, Tarnasky PR, Cunningham JT, van Velse A, Hawes RH, Hoffman BJ. Prospective assessment of the ability of endoscopic ultrasound to diagnose, exclude, or establish the severity of chronic pancreatitis found by endoscopic retrograde cholangiopancrea tography. *Gastrointest Endosc* 1998; **48**: 18-25
30 **Raimondo M**, Wallace MB. Diagnosis of early chronic pancreatitis by endoscopic ultrasound. Are we there yet? *JOP* 2004; **5**: 1-7
31 **Kahl S**, Glasbrenner B, Zimmermann S, Malfertheiner P. Endoscopic ultrasound in pancreatic diseases. *Dig Dis* 2002; **20**: 120-126
32 **Wallace MB**, Hawes RH, Durkalski V, Chak A, Mallery S, Catalano MF, Wiersema MJ, Bhutani MS, Ciaccia D, Kochman ML, Gress FG, Van Velse A, Hoffman BJ. The reliability of EUS for the diagnosis of chronic pancreatitis: interobserver agreement among experienced endosonographers. *Gastrointest Endosc* 2001; **53**: 294-299
33 **Hollerbach S**, Klamann A, Topalidis T, Schmiegel WH. Endoscopic ultrasonography (EUS) and fine-needle aspiration (FNA) cytology for diagnosis of chronic pancreatitis. *Endoscopy* 2001; **33**: 824-831
34 **DeWitt J**, McGreevy K, LeBlanc J, McHenry L, Cummings O, Sherman S. EUS-guided Trucut biopsy of suspected nonfocal chronic pancreatitis. *Gastrointest Endosc* 2005; **62**: 76-84
35 **Varadarajulu S**, Tamhane A, Eloubeidi MA. Yield of EUS-guided FNA of pancreatic masses in the presence or the absence of chronic pancreatitis. *Gastrointest Endosc* 2005; **62**: 728-736; quiz 751, 753
36 **Verma D**, Kapadia A, Eisen GM, Adler DG. EUS vs MRCP for detection of choledocholithiasis. *Gastrointest Endosc* 2006; **64**: 248-254
37 **Liu CL**, Lo CM, Chan JK, Poon RT, Lam CM, Fan ST, Wong J. Detection of choledocholithiasis by EUS in acute pancreatitis: a prospective evaluation in 100 consecutive patients. *Gastrointest Endosc* 2001; **54**: 325-330
38 **Arguedas MR**, Dupont AW, Wilcox CM. Where do ERCP, endoscopic ultrasound, magnetic resonance cholangiopanc reatography, and intraoperative cholangiography fit in the management of acute biliary pancreatitis? A decision analysis model. *Am J Gastroenterol* 2001; **96**: 2892-2899
39 **Scheiman JM**, Carlos RC, Barnett JL, Elta GH, Nostrant TT, Chey WD, Francis IR, Nandi PS. Can endoscopic ultrasound or magnetic resonance cholangiopancreatography replace ERCP in patients with suspected biliary disease? A prospective trial and cost analysis. *Am J Gastroenterol* 2001; **96**: 2900-2904

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