Published in final edited form as:

Gastrointest Endosc. 2010 November ; 72(5): 967–974. doi:10.1016/j.gie.2010.04.007.

EUS compared with endoscopy plus transabdominal US in the initial diagnostic evaluation of patients with upper abdominal pain

Kenneth J. Chang, MD, Richard A. Erickson, MD, Amitabh Chak, MD, Charles Lightdale, MD, Yang K. Chen, MD, Kenneth F. Binmoeller, MD, Gregory C. Albers, MD, Wen-Pin Chen, MS, Christine E. McLaren, PhD, Michael V. Sivak, MD, John G. Lee, MD, Gerard A. Isenberg, MD, and Richard C. K. Wong, MD
Orange, California; Temple, Texas; Cleveland, Ohio; New York, New York; Aurora, Colorado; San Francisco, California; Irvine, California, USA

Abstract

Background—Primary upper endoscopy (EGD) and transabdominal US (TUS) are often performed in patients with upper abdominal pain.

Objective—Primary: Determine whether the combination of EGD and EUS was equivalent to EGD plus TUS in the diagnostic evaluation of upper abdominal pain. Secondary: Compare EUS versus TUS in detecting abdominal lesions, and compare EGD by using an oblique-viewing echoendoscope versus the standard, forward-viewing endoscope in detecting mucosal lesions.

Design—Prospective, paired design.

Setting—Six academic endoscopy centers.

Patients—This study involved patients with upper abdominal pain referred for endoscopy.

Intervention—All patients had EGD, EUS, and TUS. The EGD was done using both an oblique-viewing echoendoscope and the standard, forward-viewing endoscope (randomized order) by two separate endoscopists in a blinded fashion, followed by EUS. TUS was performed within 4 weeks of EGD/EUS, also in a blinded fashion. Follow-up: telephone interviews and chart reviews.

Main Outcome Measurements—Diagnose possible etiology of upper abdominal pain and detect clinically significant lesions.

Results—A diagnosis of the etiology of upper abdominal pain was made in 66 of 172 patients (38%). The diagnostic rate was 42 of 66 patients (64%) for EGD plus EUS versus 41 of 66 patients (62%) for EGD plus TUS, which was statistically equivalent (McNemar test; $P = .27$). One hundred ninety-eight lesions were diagnosed with either EUS or TUS. EUS was superior to

Copyright © 2010 by the American Society for Gastrointestinal Endoscopy

Reprint requests: Kenneth J. Chang, MD, Director, Comprehensive Digestive Disease Center, University of California, Irvine Medical Center, 101 The City Drive, Building 22C, First Floor, Room 106, Orange, CA 92868-3298..

Current affiliations: Division of Gastroenterology, Department of Medicine (K.J.C., G.C.A., J.G.L.), H. H. Chao Comprehensive Digestive Disease Center, University of California, Irvine, Orange, California; Scott and White Hospital and Clinic (R.A.E.), Texas A&M University, Temple, Texas; University Hospitals Case Medical Center (A.C., M.V.S., G.A.I., R.C.K.W.), Case Western Reserve University, Cleveland, Ohio; Columbia University Medical Center (C.L.), New York, New York; University of Colorado Health Sciences Center (Y.K.C.), Aurora, Colorado; California Pacific Medical Center (K.F.B.), San Francisco, California; Chao Family Comprehensive Cancer Center (W.-P.C.), Orange, California; Epidemiology Division, Department of Epidemiology (C.E.M.), University of California, Irvine, California, U.S.A.

DISCLOSURE: All authors disclosed no financial relationships relevant to this publication.

TUS for visualizing the pancreas ($P < .0001$) and for diagnosing chronic pancreatitis ($P = .03$). Two biliary stones were detected only by EUS. Two hundred fifty-one mucosal lesions were similarly diagnosed with EGD with either the standard, forward-viewing endoscope or the oblique-viewing echoendoscope ($\kappa = 0.48$ [95% CI, .43-.54]). EGD with the standard, forward-viewing endoscope was preferred for biopsies.

Limitations—No cost analysis.

Conclusion—The combination of EGD with EUS is equivalent to EGD plus TUS for diagnosing a potential etiology of upper abdominal pain. EUS is superior to TUS for detecting chronic pancreatitis. EGD combined with EUS should be considered in the first-line diagnostic evaluation of patients with upper abdominal pain.

Upper endoscopy (EGD) performed early in the work-up of patients with upper abdominal pain (UAP) appears to be cost effective¹⁻³ and accounts for approximately 43% of all upper endoscopies performed nationally.⁴ Transabdominal US (TUS) also is used frequently in patients with UAP. However, EUS has been shown to have equal or higher sensitivity compared with TUS for detecting pancreaticobiliary disease.⁵⁻³² We hypothesized that EGD combined with EUS would be at least equivalent to EGD plus TUS in the initial diagnostic evaluation of patients with UAP. If this proved true, it would support EGD plus EUS becoming a first-line diagnostic approach in lieu of EGD alone in patients with UAP.

METHODS

Study design

This was a prospective, multiple-center, paired design, clinical study conducted among 6 endoscopy centers. Patients who were scheduled for EGD as the initial test for evaluating UAP were recruited. After enrollment, patients were scheduled for EGD with tandem EUS (Fig. 1). TUS was performed within 4 weeks of EGD plus EUS. All patients received a follow-up telephone interview at 6 months or greater.

Study population

The study was carried out in 6 endoscopy centers. Inclusion criteria were patient age over 18 years and UAP, defined as frequent (>6 episodes in previous 12 months) pain or discomfort in the upper abdomen (above the umbilicus). Exclusion criteria included the following indications for EGD: work-up of an abnormal radiologic study result, dysphagia, bleeding; suspicion of Barrett's esophagus, esophageal varices, cancer, or bleeding; previous gastric surgery; imaging studies (endoscopy, upper GI series, US, CT, or magnetic resonance imaging [MRI]) within the previous 12 months. Patients with iron deficiency anemia or weight loss were not excluded.

Study procedures and data capture

The study protocol was approved by the institutional review boards at each institution. Once enrolled, patients were interviewed by a gastroenterologist and a research study coordinator. Data obtained included demographics, duration of UAP, associated symptoms, and previous diagnostic evaluations. All patients then underwent EGD and EUS as tandem procedures. This was accomplished with either of the two types of endoscopes (randomized): (1) the standard, forward-viewing endoscope (fEGD) or (2) the oblique-viewing radial echoendoscope (oEGD) (GFUM 130, GFUM160; Olympus America Inc, Center Valley, PA). EGD and oEGD were performed by two separate, blinded endoscopists during the same sedation period. These two procedures were randomized (in blocks of 4, by using computer randomization [www.tufts.edu/~gdallal/PLAN]), and the assignment of "first" or "second" procedure was concealed in an envelope. Once all findings from both procedures

were recorded, the two endoscopists would confer as to whether there was a need for biopsy (performed by the second endoscopist by using the assigned endoscope). The oEGD endoscope has a smaller working channel, which accommodates only smaller pediatric biopsy forceps.³³ Given this limitation, the second endoscopist could switch to a standard endoscope for taking biopsy specimens if he/she experienced either technical failure or simply preferred the larger biopsy capability. EUS was performed immediately after EGD/oEGD. A diagnosis of chronic pancreatitis was made by using EUS criteria defined in prior publications.^{14,34} The presence of 5 or more EUS criteria was considered diagnostic of chronic pancreatitis. Complete-abdomen TUS was performed by the staff radiologist, who was also blinded to previous imaging results. All patients received a telephone interview at 6 months or greater after the procedure. Captured data included any subsequent surgery, procedures, or imaging tests that were performed for UAP. All data capture forms and source documents were then reviewed by the patient's primary gastroenterologist, who determined, based on these results, the most likely clinical diagnosis. Possible etiologies of UAP that could be diagnosed with EGD, TUS, and/or EUS were classified as peptic ulcer disease, esophagitis/GERD, gallstones/sludge, chronic pancreatitis, pancreatic malignancy, or other conditions. Esophagitis was defined according to the Los Angeles classification.³⁵ Gastritis and duodenitis were defined as the endoscopic appearance of at least one erosion (pale center and surrounding erythema/edema) within the stomach or duodenum, respectively. Other GI etiologies for abdominal pain, such as gastroparesis or other motility disorders cannot be reliably diagnosed with endoscopy or US and were not considered.

Sample size and statistical analysis

The necessary sample size ($N = 172$) to demonstrate equivalence of the two test procedures, EGD plus EUS versus EGD plus TUS, was based on a 1-sided test of equivalence with a significance level of .05, power of 0.90, and a difference in sensitivities for the two procedures of no more than 5%. To test equivalence of the two test procedures for the diagnosis of UAP, the 1-sided test of sensitivity based on the McNemar test was applied.³⁶ Kappa coefficients for concordance were calculated to compare modalities of EGD versus oEGD and EUS versus TUS. The McNemar test of proportions was applied with adjustment for multiple comparisons by the Bonferroni-Holm method. The SAS statistical software was used (V9.13; SAS Institute, Cary, NC).

RESULTS

We enrolled 172 patients. Baseline demographic characteristics are summarized in Table 1. The majority of patients (59%) had UAP for greater than 1 year prior to enrollment.

Cause of UAP

The clinical etiology of UAP was diagnosed during the study period in 66 of 172 patients (38%) (Fig. 2). The highest frequencies of diagnosis were gallbladder disease (32%), esophagitis/GERD (30%), and peptic ulcer disease (21%). This was followed by chronic pancreatitis (11%), pancreatic malignancy (2%), and other diagnoses (5%). One patient had pelvic adhesions found on subsequent surgery. The comparison between EGD plus TUS versus oEGD plus EUS in the diagnostic evaluation of UAP is shown in Table 2. By using a combination of oEGD plus EUS, a diagnosis was achieved in 42 of 66 patients (64%), as compared with 41 of 66 patients (62%) by using a combination of EGD plus TUS. The two approaches were statistically equivalent as demonstrated by the McNemar conditional 1-sided test for equivalence of sensitivities ($P = .27$).

Follow-up data were available in 138 of the 172 patients (80%) (Table 3). The median follow-up period was 6.6 months (mean 9.3 months). The major reason for loss of follow-up

was no current address or telephone number. During the follow-up period, identifiable causes of the UAP were subsequently discovered for 3 patients. All 3 of these UAP causes were missed by the study tests. These included (1) a patient with pelvic adhesions discovered at surgery, (2) a patient with biliary dyskinesia diagnosed by Hepatobiliary Imino-Diacetic Acid (HIDA) scan, and (3) a patient with sphincter of Oddi dysfunction diagnosed by sphincter of Oddi manometry. Among these 138 patients with follow-up data, 85% had no subsequent imaging study. There were 15 patients (11%) who had subsequent surgeries, the majority (11/15) because of positive diagnostic study results from the trial. The follow-up data of patients who had negative diagnostic study results (no identifiable cause of UAP) are also summarized in Table 3. After a negative EGD/EUS/TUS, 8 patients (10%) had subsequent imaging, and 4 patients (5%) had subsequent surgery. The imaging studies conducted included CT (4 patients), MRI (1 patient), HIDA (1 patient), colonoscopy (1 patient), and barium enema (1 patient). The surgeries performed included cholecystectomy (3 patients) and hysterectomy with lysis of adhesions (1 patient). The indications for cholecystectomy were asymptomatic stones in 1 patient, asymptomatic gallbladder polyps in 1 patient, and biliary dyskinesia in 1 patient.

Comparison between EUS and TUS

There were 198 clinically significant lesions diagnosed with either EUS or TUS in 104 patients. The overall concordance between EUS and TUS was fair, with the kappa coefficient (95% confidence interval [CI]) of 0.39 (0.32, 0.47). As judged by kappa coefficients for concordance and the McNemar test of proportions, use of EUS was similar to use of TUS in visualizing most organs/regions, except EUS was superior for visualizing the celiac area and the pancreas (Table 4). The most common lesions detected by TUS and EUS were gallbladder stones or sludge, gallbladder polyps, chronic pancreatitis, and biliary stones (Table 5). The mean time ($\pm$ standard deviation) for EUS examinations was 16.7 ± 8.56 minutes.

Gallbladder—Intact gallbladders were found in 139 patients. There was no difference between TUS and EUS in gallbladder visualization. Cholelithiasis was identified by either TUS or EUS in 26 patients. TUS and EUS were similar in detecting gallbladder stones or sludge. Gallbladder polyps were found in 16 patients: 10 of 16 (63%) were seen with both TUS and EUS, 2 were seen with TUS only, and 4 were seen with EUS only.

Biliary tree—TUS and EUS had similar yields in visualizing the common bile duct (CBD) and assessing dilation. However, 2 patients had CBD stones, and 1 had CBD sludge detected with EUS only. Both patients with CBD stones had endoscopic retrograde cholangiography followed by laparoscopic cholecystectomy. Intrahepatic ductal dilatation was noted in 3 patients with TUS but not with EUS.

Pancreas—Visualization of the entire pancreas was possible with EUS for 99% of patients, compared with 76% for TUS ($P < .0001$). Chronic pancreatitis was diagnosed with EUS in 3% (5 patients) versus 0% of patients with TUS ($P = .03$). The diagnostic impression from TUS in 1 patient stated that the patient had a dilated bile duct and a dilated pancreatic duct suspicious of a pancreatic mass. EUS identified a 2.5×3.0 cm tumor in the pancreas head. EUS-guided FNA was performed, and adenocarcinoma was diagnosed. A subsequent CT scan also showed a dilated CBD and enlargement of the pancreas head, suspicious for a pancreatic head mass. The patient then underwent an uneventful pancreaticoduodenectomy (Whipple resection).

Comparison between oEGD and EGD

There were 251 clinically significant mucosal lesions among 125 patients diagnosed either with oEGD or EGD. The overall agreement between EGD and oEGD was good (kappa coefficient = 0.48 [95% CI, .43 to .54]). The ampulla was visualized by using oEGD in 170 of 172 patients (96%), compared with 144 of 172 patients (81%) with EGD ($P < .0001$; McNemar test). The most common lesions detected are shown in Table 6. There were no differences between oEGD and EGD in detecting mucosal lesions. EGD, however, was preferred for taking biopsies. Fifty-two of 99 biopsies were randomized to oEGD. Twenty-three of 52 biopsies were successfully performed by using the oEGD endoscope. However, in the remaining 29 patients (56%), the endoscopist elected to change to the standard EGD endoscope, because of failed attempts with the oEGD endoscope (31%) or physician preference (69%).

DISCUSSION

UAP is common and can be alarming to both patients and caretakers. These patients will typically undergo multiple diagnostic tests and procedures, including EGD,⁴ TUS,³⁷ and CT scans. A recent study showed that in UAP patients referred for EUS, 40% had undergone previous upper GI series, 65% TUS, 70% CT, and 10% MRI, with most patients having at least two imaging tests.³⁸ The authors postulated that EUS combines the attributes of both EGD and TUS within a single instrument. If EUS is performed early in the diagnostic evaluation of UAP, this may minimize additional testing. Because EUS combines the attributes of both EGD and TUS within a single instrument, it follows that EUS early in the work-up may be as effective as EGD plus TUS for UAP. Therefore, our primary objective was to determine whether the combination of oEGD plus EUS, using a dual function instrument, was diagnostically equivalent to EGD plus TUS in the primary evaluation of UAP patients referred to gastroenterologists.

A recent Hong Kong study³⁹ reported the results of performing EGD, TUS, and EUS all on the same day. Some of these patients, however, had previous imaging tests. The design of this current investigation was a prospective, multiple-center, paired study conducted among different regions of the United States. We enrolled patients who were naïve to previous studies and were referred by their primary physicians for an initial diagnostic evaluation through open-access endoscopy systems.

Our results among 172 patients showed that a diagnosis was made in 38% of the patients. This further supports the notion that the majority of patients with UAP have no identifiable organic etiology. Among identifiable diagnoses, the order of frequency was gallbladder disease, esophagitis/GERD, peptic ulcer disease, chronic pancreatitis, and pancreatic malignancy. About half of the patients had diagnoses from within the lumen of the GI tract, whereas half had extraluminal diagnoses. The two testing strategies (EGD plus TUS versus oEGD plus EUS) proved to be equivalent (64% versus 62%, respectively) for diagnosing the etiology of the UAP. Subsequent diagnosis of the etiology of the UAP during the follow-up period was made in only 3 patients. Those diagnoses (pelvic adhesion and motility disorders) were missed by all our testing strategies. Imaging tests cannot reliably diagnose GI motility disorders, which are part of the differential diagnosis of UAP. Our follow-up data showed that 15 patients (11%) had subsequent surgery. Fourteen of these had surgery as a direct result of the study tests. Only 1 patient had exploratory surgery without a previous diagnosis and was found to have pelvic adhesions (atypical presentation), which were missed with both modalities and responded to surgical intervention. In essence, there were no anatomically identifiable lesions in the upper abdomen that were missed by the study tests.

Equally important to “ruling in” disease, there also was a clinical impact by these tests in “ruling out” disease, specifically the concern for malignancy. It appears that the vast majority of these patients (and their physicians) were sufficiently reassured by these test results, because only 10% of those whose test results were negative had subsequent imaging tests, and only 5% had surgery within the follow-up period.

EUS is currently superior to all other imaging modalities in ruling out pancreatic cancer. Two recent studies showed that the negative predictive value of a normal EUS examination of the pancreas was nearly 100%,^{40,41} which is extremely reassuring and should avoid unnecessary tests. In our current study, there were no malignancies found during the follow-up period. There was one case of pancreatic cancer diagnosed by the study tests. An obvious pancreatic tumor was diagnosed by using EUS, whereas TUS and CT method results were “suspicious” for one. Having the EUS done early in the work-up afforded the patient with a precise diagnosis and probably minimized delay toward definitive therapy.

Our secondary objective was to compare the two testing strategies with regard to diagnosing clinically significant lesions, many of which were incidental to UAP. Overall, EUS was similar to TUS in visualizing pertinent abdominal organs/regions, with the exception of the celiac area and pancreas, which were better visualized by EUS—a distinct advantage of EUS. Although TUS may better visualize the entirety of both kidneys and spleen, these organs are rarely implicated in the differential diagnosis of UAP.

The most common extraluminal lesions detected by TUS and EUS were gallbladder stones or sludge, gallbladder polyps, chronic pancreatitis, and biliary stones. Although there have been studies looking at EUS as adjunctive to TUS,^{7,42,43} to date there have been no prospective paired studies comparing EUS and TUS in gallbladder visualization or stone detection. The current study found them equivalent.

EUS has been compared with TUS in detecting CBD stones and found to be superior,⁴⁴ with a specificity close to 100%. Likewise, EUS has been shown to be equivalent or superior to ERCP and/or MRCP for detecting CBD stones.^{43,45-51} A more recent study showed EUS as useful salvage after a negative TUS, with CBD stones or sludge in 60%.⁷ In the current study, 2 patients had CBD stones, and 1 patient had CBD sludge detected only on EUS. Patients with stones and microlithiasis in the CBD are at higher risk for developing biliary obstruction, cholangitis, and acute pancreatitis. Equally important is the high negative predictive value of EUS in ruling out choledocholithiasis. A negative EUS result would obviate the need for other tests, including ERCP.

In this study, EUS was successfully used to diagnose chronic pancreatitis in 5 patients with UAP, whereas TUS was nondiagnostic. This corroborates an early study showing a sensitivity of EUS of 88% (vs 58% with TUS) and a specificity of 100% (vs 75% with TUS).¹⁵ EUS, when compared with ERCP, has been shown to have similar specificity, yet with a higher sensitivity.^{13,14,52}

Next, we compared oEGD with EGD in diagnosing clinically significant lesions within the GI tract. Although visualization was comparable, the ability to take biopsy specimens with oEGD was inadequate, with a 56% conversion rate. Thus, oEGD cannot replace EGD, especially if biopsies are indicated. Therefore, performing EGD with EUS (by using separate instruments) in tandem during the same procedure appears optimal.

Our study has certain limitations. We have not addressed cost effectiveness. Although the cost of TUS is relatively inexpensive (eg, compared with that of CT or MRI), the incremental additional cost of an EUS in a patient already scheduled for EGD also may be relatively small (the CPT code for EUS includes a diagnostic endoscopy). In addition, there

may be additional costs from the patient's missing another day from work in order to have the subsequent test. The impact of performing EUS as the initial diagnostic test in patients with UAP can be assessed only after such a strategy is implemented in clinical practice. In addition, this study is limited to those patients in which EGD was considered first-line in the diagnostic work-up of UAP. Another limitation is that the study was powered for the primary endpoint regarding the diagnosis of UAP. Thus, some of the subset analysis had too small a sample size. The study cohort included only patients with UAP who were referred by their primary care physicians for diagnostic EGDs. Hence, the results may not be generalizable to all patients with UAP. This study was limited to comparing the diagnostic yield of two strategies for evaluating UAP. The outcome of the diagnostic evaluation was not measured. A long-term, prospective study would be required to determine what subsequent interventions were made as a result of the diagnosis of chronic pancreatitis or cholelithiasis by using EUS and whether the subsequent interventions resolved or improved the UAP.

In summary, this study demonstrates that the combination of EGD with EUS is equivalent to EGD plus TUS in the diagnostic evaluation of UAP and should be considered in the first-line work-up of patients with UAP.

Acknowledgments

The authors would like to acknowledge the contributions of Amy Tan and Chi Lee, MPH.

Abbreviations

CBD	common bile duct
HIDA	Hepatobiliary Imino-Diacetic Acid
MRI	magnetic resonance imaging
oEGD	oblique-viewing radial echoendoscope EGD
TUS	transabdominal US
UAP	upper abdominal pain

REFERENCES

1. Delaney BC, Wilson S, Roalfe A, et al. Cost effectiveness of initial endoscopy for dyspepsia in patients over age 50 years: a randomised controlled trial in primary care. *Lancet*. 2000; 356:1965–9. [PubMed: 11130524]
2. Bytzer P, Hansen JM, Schaffalitzky de Muckadell OB. Empirical H2-blocker therapy or prompt endoscopy in management of dyspepsia. *Lancet*. 1994; 343:811–6. [PubMed: 7980747]
3. Bytzer P. Diagnostic approach to dyspepsia. *Best Pract Res Clin Gastroenterol*. 2004; 18:681–93. [PubMed: 15324707]
4. Lieberman D, Fennerty MB, Morris CD, et al. Endoscopic evaluation of patients with dyspepsia: results from the national endoscopic data repository. *Gastroenterology*. 2004; 127:1067–75. [PubMed: 15480985]
5. Thorboll J, Vilmann P, Jacobsen B, et al. Endoscopic ultrasonography in detection of cholelithiasis in patients with biliary pain and negative transabdominal ultrasonography. *Scand J Gastroenterol*. 2004; 39:267–9. [PubMed: 15074397]
6. Chak A, Hawes RH, Cooper GS, et al. Prospective assessment of the utility of EUS in the evaluation of gallstone pancreatitis. *Gastrointest Endosc*. 1999; 49:599–604. [PubMed: 10228258]

7. Mirbagheri SA, Mohamadnejad M, Nasiri J, et al. Prospective evaluation of endoscopic ultrasonography in the diagnosis of biliary microlithiasis in patients with normal transabdominal ultrasonography. *J Gastrointest Surg.* 2005; 9:961–4. [PubMed: 16137592]
8. Meroni E, Bisagni P, Bona S, et al. Pre-operative endoscopic ultrasonography can optimise the management of patients undergoing laparoscopic cholecystectomy with abnormal liver function tests as the sole risk factor for choledocholithiasis: a prospective study. *Dig Liver Dis.* 2004; 36:73–7. [PubMed: 14971819]
9. Norton SA, Alderson D. Endoscopic ultrasonography in the evaluation of idiopathic acute pancreatitis. *Br J Surg.* 2000; 87:1650–5. [PubMed: 11122178]
10. Canto MI, Chak A, Stellato T, et al. Endoscopic ultrasonography versus cholangiography for the diagnosis of choledocholithiasis. *Gastrointest Endosc.* 1998; 47:439–48. [PubMed: 9647366]
11. Norton SA, Alderson D. Prospective comparison of endoscopic ultra-sonography and endoscopic retrograde cholangiopancreatography in the detection of bile duct stones. *Br J Surg.* 1997; 84:1366–9. [PubMed: 9361590]
12. Sahai AV. EUS and chronic pancreatitis. *Gastrointest Endosc.* 2002; 56(Suppl):S76–81. [PubMed: 12297754]
13. Catalano MF, Lahoti S, Geenen JE, et al. Prospective evaluation of endoscopic ultrasonography, endoscopic retrograde pancreatography, and secretin test in the diagnosis of chronic pancreatitis. *Gastrointest Endosc.* 1998; 48:11–7. [PubMed: 9684658]
14. Sahai AV, Zimmerman M, Aabakken L, et al. Prospective assessment of the ability of endoscopic ultrasound to diagnose, exclude, or establish the severity of chronic pancreatitis found by endoscopic retrograde cholangiopancreatography. *Gastrointest Endosc.* 1998; 48:18–25. [PubMed: 9684659]
15. Buscail L, Escourrou J, Moreau J, et al. Endoscopic ultrasonography in chronic pancreatitis: a comparative prospective study with conventional ultrasonography, computed tomography, and ERCP. *Pancreas.* 1995; 10:251–7. [PubMed: 7624302]
16. Nakaizumi A, Uehara H, Iishi H, et al. Endoscopic ultrasonography in diagnosis and staging of pancreatic cancer. *Dig Dis Sci.* 1995; 40:696–700. [PubMed: 7895567]
17. Yasuda K, Mukai H, Nakajima M. Endoscopic ultrasonography diagnosis of pancreatic cancer. *Gastrointest Endosc Clin N Am.* 1995; 5:699–712. [PubMed: 8535618]
18. Palazzo L, Roseau G, Gayet B, et al. Endoscopic ultrasonography in the diagnosis and staging of pancreatic adenocarcinoma: results of a prospective study with comparison to ultrasonography and CT scan. *Endoscopy.* 1993; 25:143–50. [PubMed: 8491130]
19. Rosch T, Lorenz R, Braig C, et al. Endoscopic ultrasound in pancreatic tumor diagnosis. *Gastrointest Endosc.* 1991; 37:347–52. [PubMed: 2070987]
20. Eloubeidi MA, Chen VK, Jhala NC, et al. Endoscopic ultrasound-guided fine needle aspiration biopsy of suspected cholangiocarcinoma. *Clin Gastroenterol Hepatol.* 2004; 2:209–13. [PubMed: 15017604]
21. Fujita N, Noda Y, Kobayashi G, et al. Staging of bile duct carcinoma by EUS and IDUS. *Endoscopy.* 1998; 30(Suppl 1):A132–4. [PubMed: 9765105]
22. Shoup M, Hodul P, Aranha GV, et al. Defining a role for endoscopic ultrasound in staging periampullary tumors. *Am J Surg.* 2000; 179:453–6. [PubMed: 11004329]
23. Buscail L, Pages P, Berthelemy P, et al. Role of EUS in the management of pancreatic and ampullary carcinoma: a prospective study assessing resectability and prognosis. *Gastrointest Endosc.* 1999; 50:34–40. [PubMed: 10385719]
24. Cannon ME, Carpenter SL, Elta GH, et al. EUS compared with CT, magnetic resonance imaging, and angiography and the influence of biliary stenting on staging accuracy of ampullary neoplasms. *Gastrointest Endosc.* 1999; 50:27–33. [PubMed: 10385718]
25. Palazzo L. Staging of ampullary carcinoma by endoscopic ultrasonography. *Endoscopy.* 1998; 30(Suppl 1):A128–31. [PubMed: 9765104]
26. Gress F, Ciaccia D, Kiel J, et al. Endoscopic ultrasound versus spiral computed tomography for staging pancreatic, biliary and ampullary tumors: a prospective comparison [abstract]. *Gastrointest Endosc.* 1997; 45:A173.

27. Wildi SM, Judson MA, Fraig M, et al. Is endosonography guided fine needle aspiration (EUS-FNA) for sarcoidosis as good as we think? *Thorax*. 2004; 59:794–9. [PubMed: 15333858]
28. Prasad P, Schmulewitz N, Patel A, et al. Detection of occult liver metastases during EUS for staging of malignancies. *Gastrointest Endosc*. 2004; 59:49–53. [PubMed: 14722547]
29. Meenan J, Tibble J, Prasad P, et al. The substitution of endoscopic ultra-sound for endoscopic retrograde cholangio-pancreatography: implications for service development and training. *Eur J Gastroenterol Hepatol*. 2004; 16:299–303. [PubMed: 15195894]
30. DeWitt J, LeBlanc J, McHenry L, et al. Endoscopic ultrasound-guided fine needle aspiration cytology of solid liver lesions: a large single-center experience. *Am J Gastroenterol*. 2003; 98:1976–81. [PubMed: 14499774]
31. tenBerge J, Hoffman BJ, Hawes RH, et al. EUS-guided fine needle aspiration of the liver: indications, yield, and safety based on an international survey of 167 cases. *Gastrointest Endosc*. 2002; 55:859–62. [PubMed: 12024141]
32. Nguyen P, Chang K. Endoscopic ultrasound (EUS) and EUS-guided fine needle aspiration (FNA) of liver lesions in patients with gastrointestinal malignancies. *Gastrointest Endosc*. 1999; 50:357–61. [PubMed: 10462656]
33. Yusuf TE, Tsutaki S, Wagh MS, et al. The EUS hardware store: state of the art technical review of instruments and equipment (with videos). *Gastrointest Endosc*. 2007; 66:131–43. [PubMed: 17591487]
34. Chowdhury R, Bhutani MS, Mishra G, et al. Comparative analysis of direct pancreatic function testing versus morphological assessment by endoscopic ultrasonography for the evaluation of chronic unexplained abdominal pain of presumed pancreatic origin. *Pancreas*. 2005; 31:63–8. [PubMed: 15968249]
35. Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut*. 1999; 45:172–80. [PubMed: 10403727]
36. Lu Y, Bean JA. On the sample size for one-sided equivalence of sensitivities based upon McNemar's test. *Stat Med*. 1995; 14:1831–9. [PubMed: 7481214]
37. Heikkinen M, Pikkarainen P, Takala J, et al. General practitioners' approach to dyspepsia: survey of consultation frequencies, treatment, and investigations. *Scand J Gastroenterol*. 1996; 31:648–53. [PubMed: 8819212]
38. Sahai AV, Penman ID, Mishra G, et al. An assessment of the potential value of endoscopic ultrasound as a cost-minimizing tool in dyspeptic patients with persistent symptoms. *Endoscopy*. 2001; 33:662–7. [PubMed: 11490381]
39. Lee YT, Lai AC, Hui Y, et al. EUS in the management of uninvestigated dyspepsia. *Gastrointest Endosc*. 2002; 56:842–8. [PubMed: 12447295]
40. Catanzaro A, Richardson S, Veloso H, et al. Long-term follow-up of patients with clinically indeterminate suspicion of pancreatic cancer and normal EUS. *Gastrointest Endosc*. 2003; 58:836–40. [PubMed: 14652549]
41. Klapman JB, Chang KJ, Lee JG, et al. Negative predictive value of endoscopic ultrasound in a large series of patients with a clinical suspicion of pancreatic cancer. *Am J Gastroenterol*. 2005; 100:2658–61. [PubMed: 16393216]
42. Dahan P, Andant C, Levy P, et al. Prospective evaluation of endoscopic ultrasonography and microscopic examination of duodenal bile in the diagnosis of cholecystolithiasis in 45 patients with normal conventional ultrasonography. *Gut*. 1996; 38:277–81. [PubMed: 8801211]
43. Liu CL, Lo CM, Chan JK, et al. EUS for detection of occult cholelithiasis in patients with idiopathic pancreatitis. *Gastrointest Endosc*. 2000; 51:28–32. [PubMed: 10625791]
44. Sugiyama M, Atomi Y. Endoscopic ultrasonography for diagnosing choledocholithiasis: a prospective comparative study with ultrasonography and computed tomography. *Gastrointest Endosc*. 1997; 45:143–6. [PubMed: 9040999]
45. Verma D, Kapadia A, Eisen GM, et al. EUS vs MRCP for detection of choledocholithiasis. *Gastrointest Endosc*. 2006; 64:248–54. [PubMed: 16860077]
46. Liu CL, Fan ST, Lo CM, et al. Comparison of early endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in the management of acute biliary pancreatitis: a

- prospective randomized study. *Clin Gastroenterol Hepatol*. 2005; 3:1238–44. [PubMed: 16361050]
47. Dittrick G, Lamont JP, Kuhn JA, et al. Usefulness of endoscopic ultra-sound in patients at high risk of choledocholithiasis. *Proc (Bayl Univ Med Cent)*. 2005; 18:211–3. [PubMed: 16200174]
48. Kondo S, Isayama H, Akahane M, et al. Detection of common bile duct stones: comparison between endoscopic ultrasonography, magnetic resonance cholangiography, and helical-computed-tomographic cholangiography. *Eur J Radiol*. 2005; 54:271–5. [PubMed: 15837409]
49. Chotiprasidhi P, Scheiman JM. Suspected choledocholithiasis: EUS, magnetic resonance cholangiopancreatography, or intraoperative cholecystectomy? *Gastrointest Endosc*. 2002; 56:951–5. [PubMed: 12501865]
50. Liu CL, Lo CM, Chan JK, et al. Detection of choledocholithiasis by EUS in acute pancreatitis: a prospective evaluation in 100 consecutive patients. *Gastrointest Endosc*. 2001; 54:325–30. [PubMed: 11522972]
51. de Ledinghen V, Lecesne R, Raymond JM, et al. Diagnosis of choledocholithiasis: EUS or magnetic resonance cholangiography? A prospective controlled study. *Gastrointest Endosc*. 1999; 49:26–31. [PubMed: 9869719]
52. Kahl S, Glasbrenner B, Leodolter A, et al. EUS in the diagnosis of early chronic pancreatitis: a prospective follow-up study. *Gastrointest Endosc*. 2002; 55:507–11. [PubMed: 11923762]

Take-home Message

- If an EGD and transabdominal US are indicated for the initial work-up of upper abdominal pain, one should consider the alternative of combining an EGD with EUS during the initial procedure.

Figure 1.

Algorithm of patient procedures. *UAP*, upper abdominal pain; *oEGD*, EGD with oblique-viewing echoendoscope; *TUS*, transabdominal US.

Figure 2. Number and percentage of patients with upper abdominal pain with identifiable diagnoses (N = 66). *Panc CA*, pancreatic cancer; *PUD*, peptic ulcer disease.

TABLE 1

Demographics for 172 enrolled patients

Patient characteristic	
Age, years, mean ($\pm$ SD)	48.6 ($\pm$ 14.37)
Median	48.0
Minimum	20
Maximum	81
Sex, no. (%)	
Female	127 (74)
Male	45 (26)
Race, no (%)	
White	65 (38)
African American	36 (21)
Asian	22 (13)
Hispanic	44 (26)
Other	5 (3)

SD, Standard deviation.

TABLE 2

Number and percentage of patients with upper abdominal pain with identifiable diagnoses as determined by standard, forward-viewing endoscope EGD plus transabdominal US versus oblique-viewing echoendoscope EGD plus EUS

Diagnosis [*]	No. of patients (%)		Total no. of patients with identifiable causes of upper abdominal pain (N = 63)
	EGD + TUS	oEGD + EUS	
Gallstones/sludge	18 (86)	14 (67)	21
Esophagitis/GERD	9 (45)	12 (60)	20
Peptic ulcer disease	13 (93)	10 (71)	14
Chronic pancreatitis	0	5 (71)	7
Pancreatic malignancy	1 (100)	1 (100)	1

TUS, Transabdominal US; fEGD, standard, forward-viewing endoscope EGD; oEGD, oblique-viewing echoendoscope EGD.

^{*}The diagnoses for 3 patients with upper abdominal pain were classified as *other*.

TABLE 3

Six-month follow-up data

	No.	Mean (months)	Median (months)	Imaging studies	Surgery
All patients with follow-up data	138	9.3	6.6	21 (15%)	15 (11%)
Patients with no identifiable cause of upper abdominal pain after EGD/EUS/TUS	109	9.6	7.0	8 (10%)	4 (5%)

TUS, Transabdominal US.

TABLE 4

Visualization of abdominal organs by EUS versus TUS

	Gallbladder	Spleen	Liver	Biliary tree	Celiac area	Pancreas
EUS, %	99	99	100	99	100	99
TUS, %	100	95	99	98	NA	77
McNemar <i>P</i> value	NS	NS	NS	NS	NA	< .0001

TUS, Transabdominal US; *NA*, not applicable; *NS*, not significant.

TABLE 5

Most common lesions detected by TUS and EUS

	Chronic pancreatitis	Gallbladder stones	Gallbladder sludge	Gallbladder polyps	Biliary stones/sludge
Either (+)	5	26	13	16	3
TUS missed	5	4	7	4	3
EUS missed	0*	8	5	2	0

TUS, Transabdominal US.*P* < .05 with the McNemar test with Bonferroni-Holm adjustment for multiple comparisons.

TABLE 6

Most common lesions detected by EGD and oEGD

	Erosive esophagitis	Barrett's esophagus	Schatzki's ring	Erosive gastritis	Gastric ulcer	Pyloric stenosis	Submucosal gastric lesion	Duodenal ulcer
Either (+)	23	5	15	28	5	3	6	5
EGD missed	9	0	12	14	1	2	0	3
oEGD missed	8	3	2	6	4	1	4	2

EGD, Standard, forward-viewing endoscope EGD; oEGD, oblique-viewing echoendoscope EGD.

Statistical significance was not reached for any of these comparisons by using the McNemar test with Bonferroni-Holm adjustment for multiple comparisons.