Low but Significant Yield of Endosonography in Patients with Suspected Sphincter of Oddi Dysfunction Type III with Normal Imaging Studies

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Abstract

Aim: To determine the yield of endosonography (EUS) in patients with suspected Sphincter of Oddi Dysfunction (SOD) Type III in detecting abdominal abnormalities in those with normal upper endoscopy and imaging studies. **Methods**: A retrospective review of patients with suspected SOD who underwent EUS prior to undergoing an ERCP was performed. The inclusion criteria were: 1. patients with right upper quadrant abdominal pain for ≥3 months; 2. no evidence of abnormalities on upper endoscopy, imaging studies and laboratory tests. Exclusion criteria were: history of acute or chronic pancreatitis, pancreas divisum, jaundice or any significant abnormality detected on prior studies. The main outcome measurements were to determine the diagnostic yield of EUS to diagnose the etiology of abdominal pain and detect clinically significant lesions. **Results**: We identified 143 patients with suspected SOD type III who had undergone EUS. A diagnosis of the etiology of abdominal pain by EUS was made in 12 of 143 patients (8%) with previously normal endoscopy and imaging studies. EUS identified the following: changes consistent with chronic pancreatitis (n=5), biliary stone (n=1), side-branch intraductal papillary mucinous neoplasms of the pancreas (n=3), benign bile duct stricture (n=1). Papillary stenosis was diagnosed in two patients with common bile duct dilation detected by EUS. **Conclusions**: EUS may detect significant abnormalities in a small subset of patients with suspected SOD with previous normal endoscopies and imaging studies. Although the yield of EUS is low, it should be considered in patients with persistent pain and those with a high clinical suspicion for pancreatic pathology.

Received: 06.04.2012 Accepted: 25.05.2012
J Gastrointestin Liver Dis
September 2012 Vol. 21 No 3, 271-275
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Key words

Endosonography – sphincter of Oddi – sphincter of Oddi dysfunction.

Introduction

Sphincter of Oddi dysfunction (SOD) is a benign, non-calculous obstructive disorder which occurs at the sphincter of Oddi. The most common presentation of SOD is chronic upper abdominal pain, cholestasis and/or pancreatitis. Dysfunction of the sphincter may lead to epigastric or right upper quadrant abdominal pain as a result of increased pressure in the biliary or pancreatic ducts [1]. These pains are usually intermittent, have symptom free intervals and are outlined by the Rome III consensus [2]. Patients with objective findings on laboratory tests or imaging studies (i.e. elevated liver function tests or dilated biliary tree) have been classified by Hogan et al as having SOD type I or II [3]. Patients with similar symptoms but no evidence of abnormalities on imaging studies and laboratory tests are classified as SOD type III. The diagnostic evaluation of these patients is challenging given the fact that there is no objective marker for their abdominal pain, and undergoing an ERCP carries the highest risk of complications particularly pancreatitis.

In patients presenting with suspected SOD type III, diagnostic evaluation begins by ruling out structural causes for pain. Laboratory tests including liver biochemistry and pancreatic enzymes are evaluated. The type of radiologic imaging is site dependent but may usually include an abdominal computed tomography (CT) scan and/or magnetic resonance cholangiopancreatography (MRCP). In addition, upper endoscopy (EGD) is often performed early in these patients to check for mucosal lesions in the proximal gastrointestinal tract. Many centers also advocate the use of endosonography (EUS) in this subset of patients to detect subtle abnormalities of the pancreatico-biliary tract not detected on prior imaging. Chang et al have previously demonstrated that EGD combined with EUS may detect

significant abnormalities in a small subset of patients with chronic, unexplained abdominal pain [4]. There is currently limited data on the utilization of EUS prior to undergoing an ERCP in patients with suspected SOD type III. The aim of our study was to determine the yield of EUS in detecting abdominal lesions in patients with suspected SOD having normal EGD and imaging studies prior to undergoing an ERCP.

Patients and methods

We conducted a retrospective analysis by reviewing the electronic record database at Thomas Jefferson University for patients who were seen at the pancreatico-biliary clinic for suspected SOD type III from 2006 to 2011. The inclusion criteria for the study were: 1. patients with right upper quadrant or epigastric abdominal pain thought to be of pancreatico-biliary origin for a duration of three months or greater; 2. no evidence of abnormalities on upper endoscopy, transabdominal imaging studies (CT scan and/or MRI) and laboratory tests. Exclusion criteria were: history of acute or chronic pancreatitis, pancreas divisum, jaundice, gallstones, inflammatory bowel disease, cancer or any significant abnormality detected on prior imaging studies within the previous 12 months. This study was approved by the institutional review board of our university.

Study procedures and data collection

The following baseline data were collected: patient demographics (i.e. age, gender, and race), duration of abdominal pain, any associated symptoms, and previous diagnostic evaluations. All patients underwent an EUS within four weeks of an upper endoscopy and imaging studies. EUS examinations were performed by experienced faculty endoscopists who had each performed more than 500 EUS procedures. Endosonography was performed using either a radial scanning echoendoscope (Olympus GF-UE160, Melville, NY) or a curvilinear echoendoscope (Olympus GF UCT 140 or UCT 160).

Outcome measurements

The main outcome measurements were the determination of the diagnostic yield of EUS to diagnose the possible etiology of right upper or epigastric abdominal pain and detect clinically significant lesions. Possible etiologies of upper abdominal pain that were diagnosed with EUS were classified as chronic pancreatitis, biliary stones, pancreatic cystic lesions, biliary strictures, pancreatic malignancies or other conditions. A diagnosis of chronic pancreatitis was made by using EUS criteria, i.e. hyperechoic foci, hyperechoic strands, lobularity, hyperechoic duct, irregular duct, visible side-branches, ductal dilation, calcification, and cysts [5].

Complications from EUS were defined as any divergence from the routine course after EUS as reported by the endoscopists, recovery room nurses, or in the medical records. Complications during the procedure such as perforation, bleeding, hypotension or respiratory distress were carefully documented. The electronic medical records were also evaluated for any patient admissions required after the procedure.

Results

We identified 143 patients with suspected SOD type III [86% females, mean age 43 ± 1.7 (SE) years] who had undergone an EUS. The patient demographics are summarized in Table I. All patients had unexplained right upper quadrant or epigastric abdominal pain for greater than 12 months prior to the procedure. The clinical etiology of pain by EUS was found in 12 of 143 patients (8%) with previously normal upper endoscopy and imaging studies. EUS identified the following: changes consistent with chronic pancreatitis (n=5), common bile duct stones, pancreatic cystic lesions of compatible with sidebranch intraductal papillary mucinous neoplasms (IPMN), benign appearing common bile duct stricture, and bile duct dilation from presumed papillary stenosis. These findings are summarized in Table II.

Table I. Demographic characteristics of the 143 enrolled patients.

Mean age, years ± SD (range)	43 ± 12.5 (18-68)
Sex, number (%)	
Male	20 (14)
Female	123 (86)
Race, number (%)	
White	96 (67)
African American	17 (12)
Asian	14 (10)
Other	16 (11)

Table II. Identifiable causes of unexplained right upper quadrant or epigastric abdominal pain by EUS in patients with normal cross-sectional imaging

Diagnosis	Number of patients (%)
Normal EUS	131 (92.2)
Chronic pancreatitis	5 (3.5)
Common bile duct stone	1 (0.7)
Side branch IPMN	3 (2.1)
Common bile duct stricture	1 (0.7)
Papillary stenosis with biliary dilation	2 (1.4)

Identification of the above mentioned etiology of abdominal pain led to changes in patient management. The patients with chronic pancreatitis were treated supportively and did not undergo an ERCP with manometry. The two patients with papillary stenosis and biliary dilation underwent a biliary sphincterotomy. The patient with the biliary stricture underwent an ERCP with biliary brushing and placement of a biliary stent; biliary brushings confirmed that the stricture was benign. The patient with bile duct stone was treated appropriately with an ERCP with the removal of a 5mm common bile duct stone. One of the three patients

with side branch IPMN was referred for surgical treatment due to the presence of a mural nodule visualized on EUS; the other two were followed by serial imaging studies.

The 131 patients with a normal EUS subsequently underwent an ERCP with manometry; mean basal sphincter pressures of ≥40 mm Hg indicating SOD were found in 73/131 (56%) patients. Overall, etiology of the upper abdominal pain was not identified in 58/143 (41%) patients by initial testing. Follow-up data were available in 42 of 58 patients (72%) in whom no discrete etiology of upper abdominal pain was identified. The median follow-up period was 7.2 months. Loss of follow-up was primarily due to no current telephone number. During follow-up of the 42 patients, cause of the right upper or epigastric abdominal pain missed on prior studies was identified in four patients: two patients were diagnosed with biliary dyskinesia by an abnormal hepatobiliary iminodiacetic acid (HIDA) scan with cholecystokinin and underwent a cholecystectomy; one patient with prior abdominal surgery was found to have an intermittent small bowel obstruction as a result of adhesions and underwent surgery with lysis of adhesions, and one patient was found to have a nodule in the right lower lung on a chest x-ray which on further evaluation was diagnosed as a primary lung malignancy. In patients in whom no discrete etiology was found, the pain was presumed to be from visceral hyperalgesia. These patients were treated symptomatically by their primary care providers and/or referred to pain management specialists.

Discussion

Epigastric or right upper quadrant abdominal pain is a common symptom which can be of significant concern to both the patient and physician. These patients will usually undergo a multitude of tests and procedures including laboratory tests, cross-sectional imaging studies and upper endoscopies. Patients with chronic, unexplained epigastric or right upper quadrant abdominal pain are often referred to tertiary care centers for evaluation of SOD type III. The utility of performing an EUS for diagnosing a potential etiology of the upper abdominal pain in this subset of patients is unknown. The current study demonstrates EUS may detect significant abnormalities in a small subset of patients with suspected SOD type III with previously normal endoscopies and imaging studies. Although the yield of EUS is low, it should be considered in patients with persistent pain and those with a high clinical suspicion for pancreatic pathology.

SOD type III is thought to cause upper abdominal pain as a result of high sphincteric pressures (basal sphincter of Oddi pressures of >40 mm Hg) and is diagnosed by performing an ERCP with manometry. However, patients who undergo manometry are at a substantially higher risk for developing post-ERCP pancreatitis (20-30%) [6-8]. Hence, it is essential that prior to being referred for an ERCP with manometry, this group of patients undergo diagnostic tests to evaluate for any organic etiology of the abdominal pain so as not to subject them to a test with the above mentioned complication. Endoscopic ultrasound is very sensitive at detecting extrahepatic biliary tract disease and small pancreatic lesions that may be missed by conventional cross-sectional imaging, and therefore is valuable in assessing patients with upper abdominal pain of uncertain etiology.

Chang et al showed that the combination of EGD with EUS was equal to EGD plus transabdominal ultrasound for the diagnosis of an etiology of upper abdominal pain [4]. A diagnosis of the etiology of upper abdominal pain was made in 38% of cases. This study recommended that EGD combined with EUS should be considered the first-line diagnostic tests for patients with upper abdominal pain. However, this study did not specially address those patients with suspected SOD type III. In addition, the majority of these patients had not undergone cross-sectional imaging prior to undergoing EGD and EUS.

In the present study, the etiology of abdominal pain by EUS was found in only 12 of 143 patients, 8% of patients. This study supports the notion that the majority of patients with suspected SOD type III have no recognizable organic disease. Among the diseases that were identified on EUS, the order of frequency was chronic pancreatitis, pancreatic IPMN, common bile duct dilation from presumed papillary stenosis, bile duct stone and benign biliary stricture. These diseases had not been recognized on previous cross-sectional imaging of the abdomen by CT scan and/or MRI. Identification of the above mentioned etiology of abdominal pain led to changes in patient management.

Of the 131 with normal EUS, 73 patients were found to have SOD type III as confirmed by elevated mean basal sphincter pressures by manometry. Subsequent diagnosis of the etiology of the abdominal pain during the clinical follow-up period was found in only 4 patients. Those diagnoses (biliary dyskinesia, abdominal adhesion and lung cancer) were missed by initial testing strategies.

The current study also confirms the utility of EUS in diagnosing chronic pancreatitis which has not been visualized previously on either abdominal CT scan or MRI imaging. Buscail et al have demonstrated that EUS allows for early diagnosis of chronic pancreatitis in symptomatic patients [9]. EUS allows for the recognition of several features of chronic pancreatitis that are not available using other imaging modalities. These include hyperechoic walls of the pancreatic duct, discrete lobularity of the parenchyma, and small cystic changes in the parenchyma. EUS has also been found to be a useful test in the detection of chronic pancreatitis in symptomatic patients with inconclusive findings on other imaging tests [10, 11].

Similarly, EUS is a useful and safe procedure for diagnosing patients with biliary disease [12, 13]. De Ledinghen et al confirmed that EUS is an accurate and noninvasive procedure for the diagnosis of common bile duct stones [14]. Another study evaluating the operating characteristics of EUS for the diagnosis of extrabiliary stones showed a sensitivity of 91% and specificity of 100% [15]. EUS is particularly sensitive for stones smaller than 5 mm [16]. The sensitivity of MRI and CT scan seems to

diminish in the setting of small (<6mm) stones and it is this scenario where EUS is a particularly useful test [17, 18]. Recent studies have also demonstrated that EUS is equivalent or superior to ERCP and/or MRCP for detection of biliary stones [16, 19]. This confers with the present study where the bile duct stone removed was small (5mm in size) and therefore not visualized by conventional imaging studies. Similarly, EUS can diagnose biliary strictures that are undetectable on CT, especially in malignant lesions [20].

In our trial, we diagnosed three patients with side branch IPMN that were not detected by CT scan. This led to a significant change in the medical management of the aforementioned patients. One was referred for surgical therapy and two were followed by annual surveillance by MRI.

Performing an EUS is also important in "ruling out" disease, especially in older patients where there is a concern of malignancy. EUS is superior to all modalities for the detection of solid pancreatic cancer, especially smaller lesions [21, 22]. In addition, clinical trials have revealed that the negative predictive value of a normal EUS examination of the pancreas is 100% [23, 24]. In the current study, no pancreatic malignancies were detected by EUS or during the follow-up period. Therefore, performing an EUS allows for the reassurance of both the patient and clinician, in addition to avoidance of further unnecessary tests.

Certain limitations of the present study should be acknowledged. First, it was a retrospective study. We did not address the cost effectiveness of performing an EUS on every patient who is referred for suspected SOD type III. While the number of patients with significant abnormalities found by EUS was small, it did result in important changes in their management. Due to the size of the study cohort, subset analysis could not be done. A prospective clinical trial with long-term follow up would be required to determine which subset of patients with suspected SOD type III and normal imaging studies would specially benefit from an EUS prior to undergoing an ERCP with manometry.

Conclusion

Endosonography may detect significant abnormalities in a small subset of patients with suspected SOD in whom previously normal endoscopies and imaging studies were evidenced. Although the yield of EUS is low, it should be considered in patients with persistent pain and those with a high clinical suspicion for pancreatic pathology. Our data indicates the need for further studies to redefine the role of EUS in patients with suspected SOD.

Conflicts of interest

None to declare.

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