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ORIGINAL ARTICLE

The role of endoscopic ultrasonography in detection of gall bladder microlithiasis, sludge and stone in patients with biliary pain

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ABSTRACT

Aim: To evaluate the role of endoscopic ultrasonography (EUS) in the diagnosis of gallbladder microlithiasis, sludge, and stone in patients with clinical suspicion of cholecystitis, but with normal transabdominal ultrasonography (TUS) during six months follow-up after laparosopic cholecystectomy (LCT).

Background: Endosonography has been shown to be highly sensitive in the detection of choledocholithiasis, especially in patients with small stones and nondilated bile ducts, and gallbladder microlithiasis.

Patients and methods: A prospective study was performed on patients with biliary pain and normal transabdominal ultrasonography, for presence of microlithiasis, sludge, and stone in gallbladder at Arad hospital, Tehran, Iran from January 2004 to January 2007. EUS examination was performed with a mechanical radial scanning UM-20 echo-endoscope (Olympus Optical, Tokyo, Japan). Patients in whom EUS demonstrated gallbladder sludge, microlithisis, and stone were offered laparoscopic cholecystectomy within one week.

Results: A total of 245 patients (176 female and 69 male) were included in this study from January 2005 to January 2007. 88 out of 245 (36%) patients had gallbladder abnormalities which were diagnosed by EUS including: 43 gallbladder microlithiasis (48.3%), 23 gallbladder sludge (26%), 22 gallbladder stone (24.7%). Surgery performed for all these cases. Episodes of biliary pain during six months after LC reported in eight cases with gallbladder stone, but in no cases of microlithiasis or sludge.

Conclusion: EUS seems to be a choice imaging method for detection of microlithiasis, sludge and stone of gallbladder in patients with biliary colic but normal transabdominal ultrasonography. In subjects with biliary pain and negative EUS, it is not reasonable to offer cholecystectomy.

Keywords: *Gallbladder microlithiasis, Sludge, Stone, Radial endoscopic ultrasonography.*

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INTRODUCTION

The widespread availability of endoscopic ultrasound has facilitated the evaluation of the pancreas and extrahepatic biliary system. Endosonography has been shown to be highly sensitive in the detection of choledocholithiasis (especially in patients with small stones and nondilated bile ducts) and gallbladder microlithiasis (1). 'Sludge' is the solid material which results from the slow settling of particles dispersed in a liquid medium. Biliary sludge in the gallbladder can be detected by transabdominal ultrasonography, and the typical echoes derive mainly from pigment precipitates mixed with cholesterol crystals. A portion of biliary sludge

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contains comparatively large particles (1-3 mm) called microliths, the formation of which is an obligatory intermediate step in the development of all types of gallstone. Microlithiasis and sludge in bile may cause colicky pain, cholecystitis, cholangitis, and acute pancreatitis, and are thus of clinical relevance (2). Endoscopic ultrasonography (EUS) has the advantages over endoscopic retrograde cholangipancreatography (ERCP) to be less invasive (complication rate similar to diagnostic upper GI endoscopy) and to be able to detect small stones and sludge that can easily be masked by contrast medium during ERCP. In comparison with magnetic resonance imaging (MRI), EUS has the advantage to be close to the investigated areas and to allow the detection of very small stones or sludge, even in non dilated bile ducts. Main indications of EUS include the detection of choledocholithiasis in patients with a low and intermediate probability of the presence of stones, in idiopathic acute pancreatitis, in mild and moderate pancreatitis after normal transabdominal ultrasonography, in pregnant women, in intensive care patients, in the diagnosis of gallbladder lithiasis or sludge, and also when MRI is contraindicated (claustrophobia and metallic implants) or fails to provide a diagnosis or when it is not available. Screening of choledocholithiasis with EUS has also been proposed in patients scheduled for laparoscopic cholecystectomy, but this is not common practice in Belgium (3). A study provides firm evidence showing that in most patients with idiopathic acute pancreatitis, the disease is related to microscopic gallstones, as evidenced by the follow-up development of macroscopic stones or sludge and by the prevention of relapses with either cholecystectomy or a cholelitholytic bile acid. Occult gallstones should be strongly suspected when acute pancreatitis of unknown cause occurs in a relapsing manner and in aged patients and when it is associated with altered liver function test results. Biliary microscopy and/or follow-up ultrasonography of the gallbladder provide a simple mean of uncovering them to institute appropriate therapy and prevent further attacks (4).

This manuscript aims to evaluate the role of endoscopic ultrasonography (EUS) in the diagnosis of gallbladder microlithiasis, sludge, and stone in patients with clinical suspicion of cholecystitis, but normal AUS during six months follow-up after laparosopic cholecystectomy at Arad hospital, Tehran, Iran.

PATIENTS and METHODS

This prospective study was performed on patients with biliary pain and normal AUS for presence of gallbladder microlithiasis, sludge, and stone from January 2004 to January 2007. The terms microlithiasis, biliary sludge, and biliary crystals are often used interchangeably.In our study; microlithiasis refers to stones of < 3 mm, and biliary sludge is a suspension of crystals without posterior shadow with various size. All patients had normal AUS examination performed by an experienced radiologist. Patients then examined by EUS with a mechanical radial scanning UM-20 echo-endoscope (Olympus Optical, Tokyo, Japan) at Arad hospital, Tehran, Iran. Patients in whom EUS demonstrated gallbladder sludge, microlithisis, and stone were offered laparoscopic cholecystectomy within one week. Surgery was done by an experienced surgeon at the same hospital. After discharge from hospital, clinical data were obtained by phone during at least six months and patients visited monthly. Patients with negative EUS were followed for six months.

RESULTS

A total of 245 patients (176 female and 69 male) were included in this study from January 2005 to January 2007. In 88 out of 245 (36%) patients (67 female and 21 male), 22 subjects had

Table 1- Age, abnormal EUS and months of follow-up in patients underwent endoscopic ultrasonography

	Patients with gallbladder microlithiasis	Patients with gallbladder sludge	Patients with gallbladder stone
Age (years)	47.7 (21-81)*	54.0 (34–71)	43.6 (17–79)
Abnormal EUS†	43 (48.3)‡	23 (26)	22 (24.7)
Months of follow-up	8	8	8

*Mean (range); †Endoscopic ultrasonography; ‡Number (%)

gallbladder stone (24.7%), 23 subjects had gallbladder sludge (26%), 43 subjects had gallbladder microlithiasis (48.3%) by EUS. Mean (range) of age was 47.7 (21–81) years in microlithiasis group, 54 (34–71) years in patients with sludge and 43.6 (17–79) years in gall bladder stone group (table 1).

The size of stones was: 4-5mm in 15 cases; and 5-6 mm in 7 cases. The number of stones was single in 19 cases and 3 patients had two ones (2-3 mm). Biliary tree was normal in all the patients. Regarding pain in 88 patients: it was isolated biliary-type pain (group 1: 59 cases, 67%), biliary-type pain and elevated transaminases (group 2: 19 cases, 22%), and biliary-type pain plus previous history of acute pancreatitis (group 3: 10 cases, 11%). EUS found nothing in remaining cases. Surgery performed with no complications. In 21 out of 22 patients (95%) with gallbladder stone, and in 23 out of 23 gallbladder sludge (100%) the EUS diagnosis was verified by surgery, but it was not so in any of the cases of microlithiasis group. Eighty-six of the patients (97%) had abnormal gallbladder histopathology. After discharge, 8 cases with gallbladder stone (36%) had persistent and unchanged abdominal pain, but it was not so in any of the cases of gallbladder microlithiasis and sludge. 8 cases with pain were treated conservatively without manometric evaluation for sphincter of Oddi dysfunction (SOD).Patients with microlithiasis and sludge had no biliary pain after LC, although, epigastric fullness and flatulence were reported by some of them.

Patients with negative EUS (66% of remaining patients) were followed for six months; there were recurrent symptoms in 65 patients (41%; 65/157 cases). These symptomatic patients were reevaluated by second EUS and TUS at the end of six months. EUS was negative in all these cases, but TUS was positive in 28 patients (43%). The findings in TUS included: one gallbladder stone in 11 patients and gallbladder sludge in 17 cases. The size of stone was less than 1 cm in 9 patients and between 1-1.5 cm in 2 cases. LC was done for these patients (28%) with no complications. In 9 out of 11 patients (80%) with gallbladder stone and in 15 out of gallbladder sludge (88%), the TUS diagnosis was verified by surgery. 26 patients (90%) had abnormal gallbladder histopathology. After discharge, 3 cases with gallbladder stone (27%) had persistent and unchanged abdominal pain, but it was not seen in any cases of gallbladder microlithiasis and sludge.

DISCUSSION

Cholecystitis is the differential diagnosis of many patients admitted to hospitals for abdominal pain. Physicians need more detailed findings by imaging modalities besides frequent physical examinations. There are some debate about the safety and sensitivity of imaging modalities.

In a prospective study of 20 patients with extrahepatic obstructive jaundice (n= 15) or common bile duct dilatation (CBD) without cholestasis (n= 5) who underwent negative transabdominal ultrasonography (US) (n= 20) and computed tomography (CT) (n= 16): The definitive diagnosis of a tumor (n= 8), choledocholithiasis (n= 7), stone migration (n= 1),

choledochocele (n= 2) or slight dilatation of the CBD without obstruction (n= 2) was confirmed by endoscopic retrograde cholangiopancreatography (ERCP) (n= 13), percutaneous transhepatic cholangiography (PTC) (n= 2), intraoperative cholangiography (n= 1). Dilatation of the CBD could be demonstrated in all cases by EUS. Common bile duct stones (2-15 mm) were demonstrated by EUS in every case. CBD dilatation without underlying obstruction was correctly identified by EUS in all patients. EUS correctly described the localization of a malignant obstruction, all tumors (3 pancreatic head carcinomas, 5 periampullary tumors) (5).

Sixty-six patients with biliary-type pain and a negative transabdominal ultrasound examination underwent combined endoscopic ultrasound and stimulated biliary drainage (EUS/SBD). Stimulated biliary drainage was obtained following intraduodenal infusion of magnesium sulfate or intravenous sincalide, a CCK analogue. EUS was considered positive if sludge or small stones were seen in the gallbladder. Stimulated biliary drainage was considered positive if calcium bilirubinate granules or cholesterol crystals were seen on microscopic examination of aspirated bile. Combined endoscopic ultrasound and stimulated biliary drainage (EUS/SBD) had a high sensitivity of 92.4% and a positive predictive value of 100% in the diagnosis of cholecystitis when transabdominal ultrasound was negative. A significant majority (90.5%) of patients with positive EUS/SBD who underwent cholecystectomy had resolution of their biliary pain (6).

One hundred thirty-two patients with symptomatic cholelithiasis were evaluated prospectively using standard abdominal ultrasonography (US), US plus EUS, and US plus endoscopic retrograde cholangiography (ERC) for the detection of choledocholithiasis prior to laparoscopic cholecystectomy.

Twenty-eight patients (21.2%) had choledocholithiasis, and six patients with common bile duct stones had normal-sized ducts on US. The common bile duct was successfully examined in all patients using EUS, but only in 65.9% of patients when US was used and 94.7% of patients when ERC was used, were successfully examined. US plus EUS detected choledocholithiasis in 25 of 28 patients (89.3%), US in 19 of 28 patients (67.9%), and US plus ERC in 26 of 28 patients (92.9%). While no complications as a result of EUS were encountered, while complications resulting from ERC occurred in seven patients (5.3%), including cholecystitis in two patients, cholangitis in three patients, and pancreatitis in two patients. In view of the complication and failure rates, EUS appears to offer significant advantages over ERC. These results suggest that EUS is more sensitive than standard abdominal ultrasonography, and appears to be as sensitive, and safer than ERC in the detection of choledocholithiasis prior to laparoscopic cholecystectomy (7).

Cholelithiasis is detected by EUS in a large number of patients classified as having idiopathic pancreatitis by conventional radiologic examinations. With identification of a biliary cause of acute pancreatitis, treatment can be initiated early, thereby reducing the risk of recurrent pancreatitis with its associated morbidity and mortality. EUS is a valuable diagnostic modality in the management of patients with acute pancreatitis (8).

Radial scanning endoscopic ultrasonography (EUS) has been shown to be a safe and accurate means of detecting bile duct stones. The results of EUS with those of endoscopic retrograde cholangiopancreatography (ERCP) were compared. EUS compared with ERCP had 97% sensitivity, 77% specificity, and 90% accuracy. In 14% of patients EUS provided an additional or alternative diagnosis: chronic pancreatitis (n= 3), duodenitis (n= 2), bile duct stricture (n= 1),

chronic gastritis (n= 1). We found in this early experience that linear array EUS is a reasonably safe and accurate means of detecting choledocholithiasis. Linear array EUS, despite the learning curve, seems to be about equivalent to radial EUS in accuracy. Appropriate use of this less invasive technique may possibly replace the use of diagnostic ERCP (9).

. In a study the diagnostic efficiency of linear EUS in a large group of patients suspected to have bile duct stones, using endoscopic retrograde cholangiopancreatography (ERCP) with endoscopic sphincterotomy and exploration of the CBD using a Dormia basket, or surgical choledochotomy with choledochoscopy, as diagnostic "gold standards." was evaluated.

134 patients with clinical suspicion of CBD stones were included in the study and prospectively evaluated, using EUS, and ERCP with endoscopic sphincterotomy (127 patients), or choledochotomy with choledochoscopy where ERCP was unsuccessful (seven patients). CBD stones were found in 91 (68%) patients at ERCP with ES or at surgery. The correct diagnosis was established by EUS in 85 patients. The remaining 43 patients without CBD stones were correctly diagnosed in 41 cases by means of EUS, giving an accuracy of 94%, sensitivity of 93%, specificity of 93 %, a positive predictive value of 98 %, a negative predictive value of 87%, and a Youden's index of 89%. Linear EUS is a fairly reliable method for the evaluation of patients with high suspicion for CBD stones (10).

Twenty patients with symptomatic cholelithiasis and suspected choledocholithiasis were evaluated in an ongoing prospective trial using endoscopic ultrasonography (EUS), standard abdominal ultrasonography (US) and ERCP for the detection of choledocholithiasis prior to laparoscopic cholecystectomy. EUS was used successfully to image the extrahepatic bile duct in all patients. EUS detected three of four proven bile duct stones and correctly identified 16 bile ducts as stone free, thus being more accurate than standard abdominal US. The preliminary results of this ongoing prospective trial and the experience reported by other authors suggest that EUS may be as sensitive as ERCP in the detection of choledocholithiasis (11).

Combined endoscopic ultrasound and stimulated biliary drainage (EUS/SBD) has been shown to have better sensitivity than transabdominal ultrasonography (AUS) in the diagnosis of subtle gallbladder disease.

Eighty-one patients underwent cholecystectomy for biliary pain after negative AUS findings (except for gallbladder sludge in three cases), but with positive EUS/SBD findings. EUS/SBD was performed as previously reported, with a positive result defined as gallbladder sludge or small stones noted on EUS or a positive biliary drainage. Clinical outcome data were obtained by phone over an average of 15.4 months postoperatively. All 81 patients had a positive EUS/SBD, and all underwent cholecystectomy. Seventy-six of the patients (93.8%) had abnormal gallbladder histopathology. When EUS/SBD results are positive, this correlates strongly with long-term symptom resolution or relief (96.3%) after cholecystectomy. EUS/SBD demonstrated better sensitivity (93.8%) than AUS in diagnosing subtle gallbladder disease (12).

In a study, EUS was compared to direct cholangiography in the evaluation of 422 patients for common duct stones. Ductal stones were imaged by EUS in 168 patients (43.4%). No complications were encountered. EUS failed in 2.3% of cases, ERCP failed in 8.3%, and surgical exploration failed in 0.5%. Comparison of EUS with surgical exploration in 185 patients showed a sensitivity of 94.9%, a specificity of 97.8%, and an accuracy of 95.9%. EUS was compared to ERCP in 219 patients. All common duct stones found by ERCP were evident by EUS. Concordance was obtained in 91.3% of cases. Review of videotapes disclosed 3 false-positives

and 16 unequivocal true-positives. The study concluded that EUS is a safe and highly accurate mean of detecting common duct stones and should be proposed before laparoscopic cholecystectomy in patients at risk of choledocholithiasis (13).

In a prospective 1-year follow-up study, 238 patients referred for biliary EUS because of suspicion of CBD stone, in whom EUS findings were normal: 59 (25%) patients underwent cholecystectomy, with (n= 31) or without (n= 28) cholangiography, and 30 patients underwent ERC (13%). CBD stone was found in 14 (6%) patients. Of these 30 patients, ERC was done in 15 cases in the first week after EUS, because of persistent suspicion of a CBD stone which was found in 10 patients. The 15 late ERC procedures (carried out more than 1 week after EUS) revealed only one CBD stone. The negative predictive value of EUS for the diagnosis of CBD stones was 95.4 %. Patients with suspicion of CBD stones but normal EUS findings have a low risk of needing ERC in a 1-year period (14).

In a study to investigate the role of endoscopic ultrasonography (EUS) in the diagnosis of microlithiasis in patients with upper abdominal pain and normal AUS, thirty-five patients with biliary-type abdominal pain and normal AUS results were prospectively studied. Of 35 patients, 33 were revealed to have gallbladder sludge or small stones, and 21 had CBD sludge or microlithiasis. 13 underwent combined endoscopic biliary sphincterotomy and cholecystectomy, 10 underwent cholecystectomy, and 3 underwent biliary sphincterotomy alone. In a postoperative follow-up at 9.2 months, 25 patients (96.2%) were symptom free. EUS is an important diagnostic tool in patients with unexplained biliary colic (15).

According to our study, EUS seems to be an appropriate imaging method for detection of microlithiasis, sludge and stone of gallbladder in patients with biliary colic and normal transabdominal US. In subjects with biliary pain and positive EUS, we can recommend LC. Follow-up after LC is optimistic for these patients. EUS is a good modality in approach to evaluate of unrecognized RUQ pain.

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