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Efficacy of Endoscopic Ultrasonography in Evaluation of Undetermined Etiology of Common Bile Duct Dilatation on Abdominal Ultrasonography

Rasoul Sotoudehmanesh [1*], Naimeh Nejati [2], Maryam Farsinejad [3], Shadi Kolahdoozan [3]

1. Professor. Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran,Iran
2. Gastroenterologist. Baghyatallah hospital, Tehran,Iran
3. Research Fellow. Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran,Iran

* **Corresponding Author:**
Rasoul Sotoudehmanesh, MD
Digestive Disease Research Institute, Shariati Hospital, North Kargar Ave., Tehran, Iran
Postal code: 41448-95655
Tel: + 98 21 82415300
Fax: + 98 21 82415400
Email: sotoudehmanesh@tums.ac.ir

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ABSTRACT

BACKGROUND

The cause of common bile duct (CBD) dilatation cannot be determined by imaging modalities in many patients. The aim of this study was to assess the value of endoscopic ultrasonography (EUS) in detecting the cause of CBD dilatation in patients in whom ultrasonography could not demonstrate the cause of dilation.

METHODS

Prospectively, 152 consecutive patients who were referred for evaluation of dilated CBD (diameter ≥7 mm) of undetermined origin by ultrasonography were included in this study. All the patients underwent EUS. Final diagnoses were determined by using endoscopic retrograde cholangiopancreatography (ERCP), EUS-guided fine needle aspiration (FNA), surgical exploration, or follow-up for at least 10 months. Patients with choledocholithiasis were referred for ERCP and sphincterotomy, and patients with operable tumors were referred for surgery. Patients with inoperable tumors underwent biliary stenting with or without chemoradiotherapy.

RESULTS

152 patients (54% female) with dilated CBD were included. Mean (±SD) age of the patients was 60.4 (±17.3) years. The mean CBD diameter for all study group in transabdominal ultrasonography and EUS were 11.7 millimeter and 10.1 millimeter, respectively. Most of the patients with dilated CBD and abnormal liver function test (LFT) had an important finding in EUS and follow-up diagnosis including peri-ampullary tumors. Mean diameter of CBD in patients with and without abnormal LFT were 10.5 IU/L and 12.1 IU/L, respectively. Final diagnoses included choledocholithiasis in 32 (21.1%), passed CBD stone in 35 (23%), opium-induced CBD dilation in 14 (9.2%), post-cholecystectomy states in 20 (13.1%), ampullary adenoma/carcinoma in 15 (15.8%), cholangiocarcinoma in 14 (9.2%), and pancreatic head cancer in 9 (5.9%) patients. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of EUS for patients with abnormal EUS were 89.5%, 100.0%, 100.0%, 91.2%, and 90.9%, respectively.

CONCLUSION

After diagnosis of CBD dilation by transabdominal ultrasonography, EUS may be a reasonable choice for determining the etiology of dilated CBD and tumor staging.

KEYWORDS:Diagnosis, Endosonography, Common bile duct, Ampulla of Vater

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INTRODUCTION

Common bile duct (CBD) dilation on imaging modalities, such as transabdominal ultrasonography (TUS), computed tomography (CT), and magnetic resonance cholangiopancreatography (MRCP) is a common challenging issue in daily practice. TUS should be the first imaging study in evaluation the level of biliary obstruction and gallstones. However, overlying bowel gas and obesity frequently obscure the distal bile duct, ampulla, and pancreas. Thus determining the etiology of CBD dilation by TUS alone is usually impossible.

The diagnostic evaluation of a patient with a bile duct obstruction is designed to differentiate benign lesions such as gallstones from the malignant biliary obstruction and to establish the extent of tumor invasion and spread in cases with malignancy.

Endoscopic retrograde cholangiopancreatography (ERCP) has been the gold standard for evaluation of the pancreatobiliary disorders.[1,2] However, it is associated with complications especially pancreatitis.[3,4] For this reason, less invasive and high accurate diagnostic modalities such as endoscopic ultrasound (EUS) or MRCP are recommended for most suspected periampullary lesions.[5]

In case of isolated dilated CBD on TUS, there is no clear clinical guideline for further evaluation. Therefore we prospectively evaluated the role of EUS in detecting the cause of CBD dilatation in patients in whom TUS could not demonstrate the cause of dilation.

MATERIALS AND METHODS

Between June 2013 and September 2014, we prospectively evaluated individuals who were referred to the endoscopy ward of a referral university-affiliated hospital because of dilated CBD on TUS.

The inclusion criteria were; 1) Internal diameter of CBD $\geq$ 7 mm, 2) no causative lesion in TUS. Exclusion criteria were history of surgery with gastroenteric anastomosis (Roux-en-Y gastrojejunostomy or Whipple's procedure), which made a successful EUS and ERCP unlikely and refusal of giving written informed consent.

Abnormal liver function test (LFT) was defined as AST(aspartate aminotransferase) or ALT(alanine aminotransferase) more than 40 IU/L and or alkaline phosphatase more than 306 IU/L. Weight loss was defined as unintentional loss of weight more than 10% over 10 months.

All EUS procedures were performed with a radial echoendoscope (EG-3630UR, PENTAX Optical Co Ltd, Tokyo-Japan). In case of suspected ampullary mass based on the EUS exam and if it was not adequately visualized by endoscopic view, a duodenoscope (ED-3470TK, Pentax Medical Co.) was used to view the ampulla of Vater and obtain biopsy samples in case of ampullary masses. Whenever we found a lesion in the pancreas requiring tissue diagnosis, we performed EUS-fine needle aspiration (FNA) using a convex array echoendoscope (Pentax EG-3830 UT). All FNAs were performed with a 22-gauge needle (Echotip; Wilson- Cook, Winston Salem, NC). All data regarding the patients' age, sex, complaints, results previous laboratory tests and images, primary indications of EUS, the incidental findings and their locations, size, and origin were recorded in a standard questionnaire. The patients were finally divided in to four major groups: The patients with operable periampullary neoplasms who were referred for surgery, the patients with inoperable periampullary tumors who underwent ERCP and biliary stenting and referred to oncologist, the patients with bile duct stone who were referred for ERCP and sphincterotomy for stone extraction, and the patients with normal pancreatobiliary tract.

Gold standards in this study were ERCP, surgery, a biopsy confirming malignancy, or the clinical course during follow-up (at least 10 months) in cases without evidence of malignancy by clinical visits or phone calls. The study was approved by the Institutional Review Board of the Digestive Diseases Research Institute of Tehran University of Medical Sciences. Written informed consent was obtained according to the guidelines of the institute. Quantitative variables were presented as mean±standard deviation (SD). Sensitivity, specificity, positive and negative predictive values (PPV, and NPV) and accuracy were calculated using the standard formulas. The target conditions considered for statistical analysis were: correct diagnosis of any cause of obstruction, diagnosis of malignancy, or the diagnosis of CBD stone. All calculations were performed using SPSS software, version 20 (SPSS Inc.; Chicago, Illinois, USA).

RESULTS

Table 1: Baseline characteristics of patients with common bile duct dilation in transabdominal ultrasonography

Variables	Total	Normal LFT	Abnormal LFT
Age (year); mean (SD)	60.4 ± 17.7	56.4 ± 18.5	61.34 ± 17.8
Female; N (%)	82 (53.9)	19 (70.4)	53 (49.5)
Opium addiction; N (%)	25 (16.4)	7 (25.9)	15 (14.4)
Previous cholecystectomy; N (%)	34 (22.4)	10 (37.0)	21 (19.6)
Disease duration (month); mean (SD)	4.9 (11.1)	9.7 ± 15.7	3.22 (6.8)
Abdominal pain; N (%)	118 (77.6)	25 (92.6)	78 (72.9)
Weight loss; N (%)	41 (27)	3 (11.1)	34 (31.8)
Jaundice; N (%)	61 (40)	0 (0.0)	56 (52.3)
Abnormal liver tests; N (%)	125 (82.2)	--	--
Bilirubin(mg/dL); mean (SD)	6.1 (7.6)	0.8 ± 0.3	7.3 (7.9)
CBD diameter by ultrasonography(mm); mean (SD)	11.7 (4.1)	10.5 ± 2.9	12.1 (4.4)
GB stone; N (%)	50 (33)	4 (14.8)	42 (39.3)
Performed CT; N (%)	49 (32)	7 (25.9)	36 (33.6)
Performed MRI/MRCP; N (%)	68 (45)	15 (55.6)	46 (43.0)

Common bile duct; mm: Millimeter; SD: Standard deviation; N: Number; GB: Gallbladder; CT: Computerized tomography; MRCP: Magnetic resonance cholangiopancreatography; MRI: Magnetic resonance imaging

During the study period 922 patients underwent EUS. 152 consecutive patients with an enlarged CBD (diameter ≥7 millimeter) of undetermined origin during TUS were included in this study. The patients' characteristics and EUS findings are summarized in table 1. The mean age of the patients was 60.4 year (range=22-90 year). Most of the patients were female (53.9%). EUS exams were done without difficulty or complications. 27 patients (17.8%) had normal LFT (table 2). The mean CBD diameter for all cases in TUS and EUS groups were 11.7 mm and 10.1 mm respectively.13 (8.5%) patients in our study had "normal" findings in EUS. In patients with abnormal LFT, significant findings included: 26 cases of CBD stone, 14 cases of ampullary tumor, 10 with distal CBD tumor, and 8 pancreatic tumors. 68 patients had CBD dilatation in MRCP with unknown etiology. Only 2 of them had a "normal" EUS. Of the remaining 66 patients, 64 had findings consistent with CBD stone/sludge. Five patients (7.8%) underwent ERCP with endoscopic sphincterotomy and stone extraction. 20 patients (31.3%) passed CBD stone with normal LFT and normal clinical findings at follow-up visits. Three patients (4.7%) had pancreatic mass for whom EUS-FNA was done, which showed operable mass in two patients. Seven patients (10.9%) had ampullary tumor for whom biopsy sampling was done by side-view duodenoscope, which showed operable tumor in five patients. Seven patients (11%) had distal CBD tumor, which were operable in all of them. Post cholecystectomy CBD dilation was seen in nine patients (14.1%), opium related CBD dilation was seen in nine patients (14.1%), juxta-ampullary diverticulum in one patient (1.6%), and gallbladder (GB) stone alone was seen in three patients (4.7%).

Table 3 shows the final diagnosis of patients with dilated CBD. For two patients with pancreatic tumor, seven patients with ampullary tumor, six patients with distal CBD tumor, and finally eight patients with CBD stone, MRI/MRCP was performed, which showed no abnormality except for CBD dilation. At the other hand, for four patients with pancreatic tumor, 11 patients with ampullary tumor, five patients with distal CBD tumor, and finally 11 patients with CBD stone, abdominal CT was performed, which showed no abnormality except for CBD dilation.

Overall sensitivity, specificity, PPV, NPV, and accuracy of EUS were 93.8%, 100.0%, 98.1%, 100.0%, and 90.1%, respectively. Sensitivity, specificity, PPV, NPV and accuracy of EUS for patients with abnormal EUS were 89.5%, 100.0%, 100.0%, 91.2%, and 90.9%, respectively.

Table 2: Diagnosis in patients with normal liver function test

Variables	N. (%)
Normal	5 (18.5)
CBD stone/Sludge	2 (7.4)
Passed CBD stone	5 (18.5)
Opium induced CBD dilation	6 (22.2)
Post cholecystectomy state	8 (29.6)
GB stone	1 (3.7)

CBD: common bile duct; GB: gallbladder; N: number.

Table 3: Final diagnosis of patients with dilated CBD

Benign disorders	N. (%)
Choledocholithiasis	32 (21.0)
Post-cholecystectomy	20 (13.1)
Opium addiction	14 (9.2)
Passed CBD stone	35 (23.0)
Malignant disorders	
Ampulla of Vater	15 (9.8)
Distal CBD tumor	14 (9.2)
Pancreas tumor	9 (5.9)
Normal CBD	13 (8.5)
Total	152 (100)

CBD: Common bile duct; N: Number

DISCUSSION

In daily practice there are no clear clinical guidelines regarding further evaluation of patients with a clinical suspicion of periampullary lesions in the absence of an obvious lesion on transabdominal imaging. Our study shows the significant impact of EUS in the diagnosis of benign as well as periampullary tumors when other imaging modalities failed to show the etiology.

Differentiating a primary ampullary carcinoma from the more common periampullary malignancies (arising in the pancreas, duodenum, or bile duct) is challenging. Sometimes it is impossible to determine the exact location and definite diagnosis of periampullary neoplasm until resection and histopathological evaluation of the entire surgical specimen is completed.[6] The most common cause of CBD dilation of our patients was periampullary malignant tumors found in 38 cases (25% of the patients). These included tumor of the papilla of the Vater in 15 patients, cholangiocarcinoma in 14, and pancreas head cancer in 9 cases. This is an important finding that shows relative inability of other imaging modalities for detection of these tumors.

In studies of patients with pancreatic cancer, EUS has been superior to CT for the diagnosis of pancreatic cancer.[7,8] Thus pancreatic masses diagnosed by EUS, can be missed by TUS and CT.

The overall accuracy of TUS for detection of ampullary tumor was 15%, according to one study.[9]

In our study, one-third of the patients performed CT. The cause of CBD dilation could not be determined in four patients who performed abdominal CT. CT is more sensitive than TUS for evaluating the periampullary region. Although helical CT can detect masses obstructing the distal CBD, its sensitivity for detection of small periampullary lesions is low.[10] Moreover, although CT is generally the most useful modality to evaluate the presence of distant metastatic disease, which most frequently involves the regional lymph nodes, liver, peritoneum, lungs, and bone, its overall accuracy was only 20% for detection of periampullary lesions.[9] Especially for the ampullary tumor staging, the accuracy of CT is very low because it cannot determine the depth of the ampullary tumor, definite extension of the lesion toward the adjacent organs like duodenal wall and pancreas tissue or major vascular involvement.[11] MRCP is a non-invasive method of imaging the pancreaticobiliary tree via MRI. Ampullary carcinomas appear as masses (filling defects) protruding into the duodenal lumen, with characteristic delayed enhancement.[12] In one report the overall accuracy of diagnosis with MRCP was 76%.[13]

MRI/MRCP is very poor for imaging the periampullary neoplasms and many MRI/MRCP Reports, which show an unexplained dilated bile duct inevitably read "cannot exclude peri-ampullary pathology/neoplasia".[14] In our study 45% of the patients underwent MRI/MRCP, which only revealed CBD dilation. Of these patients, 17 had periampullary tumors, which showed that in more than one-fourth of the patients MRI/MRCP could not detect the tumors.

The second most common cause of CBD dilation in our study was passed CBD stone, which occurred in 35 patients (23%). These patients presented with colicky abdominal pain relieved at the time of EUS examination. Basis of diagnosis was normalization of LFT after biliary colic, the presence of stone in gall bladder, and lack of symptoms during the 10-month follow up after cholecystectomy and normal LFT.

We found that most of the patients with dilated CBD and abnormal LFT had an important finding in EUS and follow up diagnosis. As shown in table 2 all of the patients with normal LFT had benign conditions. In other word, all of the patients with malignant periampullary lesions had abnormal LFT. This finding has been shown in other studies.[15-17] Choledocholithiasis was found in 32 (21%) of our cases. MRCP and CT were done in 8 (44.4%) and 11 (61.1%) of these patients respectively, which did not reveal the diagnosis. The sensitivity of TUS for CBD stones ranges from 20% to 90%. TUS has poor sensitivity for stones in the distal CBD because the distal CBD is often obscured by bowel gas in the imaging field.[18,19] A review of 13 studies found that MRCP had a sensitivity of 93% and a specificity of 94% for the diagnosis of choledocholithiasis.[20] Abdominal CT and percutaneous cholangiopancreatography are alternative methods for diagnosis of choledocholithiasis.

Both sensitivity and specificity of abdominal CT can be improved from 65% to 93% and from 84% to 100%, respectively by the use of intravenous contrast media combined with a helical cholangiography protocol.[21,22]

Other interesting finding in our study was opium induced CBD dilation found in 14 (9.2%) patients. This finding has been shown by other studies.[23,24] Mechanism of CBD dilatation in opium addicted cases is the effects of morphine on sphincter of Oddi. Morphine causes increase in basic pressure and the range and the frequency of phasic contractions of the sphincter of Oddi.

The combination of these effects leads to CBD dilatation by increasing the CBD internal pressure.[23] In the presence of biliary colic, endoscopic sphincterotomy results in relieving symptoms.[25]

The limitation of our study was that the TUS, MRI/MRCP, and CTs (obtained before EUS) were not standardized with regard to technique and interpretation. It could be possible that the interpretation of some of the images would have changed if another radiologist had reviewed the images.

Other limitation of our study is that CT and MRI/MRCP were not done for all the patients with CBD dilation. This was due to the fact that the patients who were referred to our ward for EUS had already performed their imaging studies and we could not refer them for extra imaging study before EUS.

In conclusion, EUS is a complementary imaging modality after TUS for evaluation of dilated CBD and has an important role in the diagnosis of benign and malignant periampullary tumors with high sensitivity and specificity. Although other studies should confirm our findings, we suggest EUS after detecting CBD dilation by TUS, for diagnosis, staging, and sampling (in cases with neoplastic process) of the lesions. These benefits may not be achieved easily and with high accuracy by other imaging modalities.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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