ORIGINAL RESEARCH

Dilated common bile duct unexplained on transabdominal ultrasonography; the role of endoscopic ultrasonography and predictors of malignancy

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Abstract

Background: The aim of the this prospective study was to evaluate the endoscopic ultrasonography (EUS) in detecting the cause of common bile duct (CBD) dilatation in patients in whom ultrasonography(US) could not indicate the cause of dilation.

Methods: Seventy patients with the search criteria of unexplained dilated CBD (diameter > 7 mm) were examined by EUS. All patients (except 4 patients with pancreatic mass) were further evaluated by ERCP.

Results: The following diagnoses were made by EUS and ERCP: choledocholithiasis in 45, pancreato-biliary malignancy (PBM) in 17, papillary stenosis in 5, and no finding in 3 cases. We found that the majority of patients (95.7%) had findings on EUS to explain the etiology of their dilated CBD. The prevalence of pathology is lower (76.9%) in patients with normal liver function tests (LFTs).The yield of EUS is higher (100%) when elevated liver enzymes. Lower hemoglobin levels, larger diameter of CBD and pancreatic duct (PD) and ESR greater than 30 mm/h were independent risk factors for PBM, whereas, patients with previous cholecystectomy, normal LFTs and abdominal pain were less likely to have this diagnosis.

Conclusion: the majority of patients referred for EUS for dilated CBD will have an etiology discovered
Therefore, EUS should be the first diagnostic strategy for dilated CBD of unexplained origin, even in patients with normal LFTs. In patients with dilated CBD accompanied by anemia, abnormal LFTs and ESR or dilated PD, malignancy should be considered.

Key Words: Endoscopic ultrasonography, ERCP, Dilated CBD, Pancreato-biliary malignancy.

Introduction

By increasing the use of abdominal ultrasonography (US) with nonspecific symptoms (such as abdominal pain) *patients* are being *diagnosed more often* with a dilated CBD.[1]The top normal value for CBD diameter is controversial , which *generally accepted* to be 7mm. [2-3]A diameter more than 7mm defines as a CBD dilatation, which may indicate the presence of *biliary* pathology

Precise evaluation of dilated CBD is extremely important. Abdominal US is as the *imaging procedure of choice to evaluate these* patients with a dilated CBD[4-6]. Dilated bile ducts can be reliably demonstrated with *US*, however, the cause can be determined in only two thirds of patients.[4-6]Especially, the distal part of the CBD and the papillary region may not be clearly visualized on abdominal US.

ERCP has the highest accuracy for the *diagnosis* of different *imaging techniques* and is currently considered as a the "gold standard" in evaluation of dilated CBD.[7]In patients with biliary dilatation, clinical index is based on presenting symptoms , and liver enzyme profile of serum. Indeed, due to the inherent risk associated with ERCP, recent guidelines have suggested using ERCP as a solely diagnostic tool in cases with high probability for therapeutic intervention but in a review by Godfrey et al is showed that the literature does not clearly suggest the best approach to patients with asymptomatic or unexplained CBD dilatation where MRCP has not been able to determine the etiology of CBD dilatation and this challenge is the cornerstone of this study while apparently cost effectiveness studies should also be taken into consideration. When a low or moderate clinical suspicion on pathological diagnosis is exist, magnetic resonance cholangiopancreatography (MRCP) and EUS are acceptable as imaging alternatives of safety profile for the biliary tract given.[7]

EUS is an excellent procedure for *visualizing* the biliary tract given its proximity when imaging from the duodenum.[8,9] Unlike trans-abdominal US, EUS provides excellent sonographic visualization of the extra-hepatic biliary tree without interference of bowel gas, because of its ability to place the transducer in close proximity to the extrahepatic bile duct. Additionally, EUS permits accurate and systematic visualization of the duodenal wall, including the papillary region.[8,9]EUS is superior to computed tomography (CT) and abdominal US for detection of choledocholithiasis and ampullary tumors And its accuracy is vividly expressed in approaching patients with unexplained CBD dilatation which is up to 90%. [10,11]

Based on the cause, biliary dilatation can be divided into two general categories: obstructive and non-obstructive.[12]Biliary obstruction may be secondary to any process that impairs the passage of bile through the biliary tract and into the duodenum. Such processes include choledocholithiasis, extrinsic compression (e.g. caused by Mirizzi's syndrome or a tumor), sphincter of oddi dysfunction (SOD) or papillary stenosis, cholangiocarcinoma, pancreatic head mass or papillary tumor and parasitic infection. Choledocholithiasis is the most common cause of obstructive dilatation. The acuity in symptom onset can be helpful in narrowing the differential diagnosis, because sudden onset and pain would be typically associated with choledocholithiasis, whereas painless jaundice, insidious onset, and weight loss suggest a malignant process. Non-obstructive etiologies of biliary dilatation include aging, post-cholecystectomy state and bile duct cysts.[12] The aim of this prospective study was to determine the role of EUS in evaluation of patients with biliary dilatation and non-diagnostic sonography findings.

Subjects and Methods

Seventy four patients were identified from November 2013 to September 2014 with the search criteria of unexplained dilated CBD. Once the patients were identified, their electronic records were reviewed for demographics, pertinent medical history and laboratory data. Patients were considered for inclusion in the study if they had CBD dilation shown on abdominal US (diameter > 7 mm) with unexplained origin. Patients who had a clear etiology for their dilated duct(s) (i.e. choledolithiasis, pancreatic cancer etc.) and patients who underwent therapeutic ERCP

(sphincterotomy or stenting) were excluded from the study.

All patients were examined first with a forward-oblique viewing echoendoscope (Olympus GF-UM2000, Tokyo, Japan) with a radial scan transducer at the tip (5 and 10 MHz frequencies). All procedures were performed by an expert endosonographist(B.S.) without knowledge of the patient's clinical history, laboratory data, or radiologic imaging results.

70 patients (Except the 4 patients with pancreatic mass) was investigated by EUS-FNA and ERCP using standard duodenoscopes (Olympus TGF-150; Olympus Co.).The time interval between EUS and ERCP examinations was low than 7 days. The endoscopists (T.R.) were blinded to the results of the EUS. Four patients were excluded from the study due to unsuccessful cannulation of CBD. This brought the total number of patient's to70 (43 women and 27 men). Overall, the success rate was 100% for EUS and 95.7% for ERCP. Two patients had mild post-ERCP pancreatitis, and self-limited post-sphinctrectomy bleeding occurred in 3 patients. There were no serious complications after ERCP and EUS.

66 cases of a*ll* patients *initially* underwent *EUS* followed by *ERCP* (with or without sphincterotomy) as well as 4 cases with pancreatic mass on the final diagnosis were confirmed by EUS-FNA. The diagnosis of papillary stenosis was based on the typical biliary pain with or without abnormal enzymes suggested on EUS as probable papillary stenosis because of dilated CBD with distal tapering without any other findings and confirmed by ERCP when symptoms were relieved completely after sphincterotomy. The diagnosis of cholangiocarcinoma was confirmed by pathologic examination of brushing specimens that were obtained during ERCP in one patient. In the second patient, ERCP showed a distal stricture and pathologic examination revealed no malignancy whileCA19-9 was above2000 U/mL (without any clinical evidence of cholangitis and with normal serum IgG4 level). The diagnosis of ampullary cancer was confirmed by pathologic examination of the biopsy specimens obtained by duodenoscope.

Data were analyzed with a statistical software program (SPSS version 18.0, SPSS Inc., Chicago, IL). Continuous variables are presented as means ± standard deviation (SD) and are compared across groups using the one-way and t-test. Categorical variables are expressed as percentages and compared among groups using the chi-squared test. Multivariate analysis was performed. A *p-value* of less than 0.05 was considered significant. The institutional review board of our medical center approved this study.

Results

Main characteristics of patients are summarize -d in table 1.Our study group was composed of 70 patients in whom US failed to demonstrate the cause of dilated CBD. The average age in the study was 61.8 years of age (range = 25–83 years), which the majority were female (61.4%). The major presenting symptoms were abdominal pain (78.6%), jaundice (35.7%) and weight loss (20%).

EUS and ERCP findings were choledocholithiasis in 45 cases, papillary stenosis in 5 cases and in 3 cases there are no examination findings of symptoms. In 17 cases, the underlying malignant disease was identified by EUS which including, ampullary tumor (11 cases), pancreatic tumor (4 cases) and distal cholangiocarcinoma (2 cases).

Furthermore, in 13 patients with normal LFTs findings consist of choledocholithiasis (9 cases), papillary stenosis (1 case) and also, in 3 cases any finding were no observable. All patients had abdominal pain except for 2 patients, which were asymptomatic with normal LFTs and there was no finding. The final diagnosis in 57 cases with abnormal LFTs included choledolithiasis in 36 cases, ampullary cancer in 11 cases, papillary stenosis in 4 cases, pancreatic cancer in 4 cases and cholangiocarcinoma in 2 cases .All of the patients with abnormal LFTs were symptomatic.

Four out of five patients with diagnosis of papillary stenosis had abnormal LFTs beside dilated CBD and considered type 1 SOD. One out of five patients had normal LFTs beside dilated CBD and underwent ERCP sphinctrectomy without previous manometric study (because there was no access to this study) and this case considered type 2 SOD due to significant relief of biliary pain after sphinctrectomy.

Indices of diagnostic abdominal ultrasonography on 29 patients with cholelithiasis demonstrated that the findings for dilated CBD were choledocholithiasis in 24 cases, ampullary cancer in 4 cases, and pancreatic cancer in one patient. Our findings in 8 cases with previous cholecystectomy included choledocholithiasis in 4, papillary stenosis in 3, and no pathology in one patient. In three patients with cholecystectomy, gallbladder remnant containing's sludge was found, which was missed on abdominal ultrasonography.The findings in 3 cases with opioid addiction (for more than 5 years) included ampullary cancer in 2 and pancreatic cancer in one patient.

A bivariate analysis was performed with two groups based on those who had benign etiology on EUS and patients withpancreato-biliary malignant (PBM) etiology for their ductal dilatation. There was a statistically significant difference in the mean level of hemoglobin (Hb), alanine transferase (ALT) and bilirubin and mean diameter of pancreatic duct (PD) and CBD of patients with a PBM compared to those without a PBM(table 2).

Male gender, presence of jaundice, weight loss and ESR greater than 30 mm/h were all predictors of PBM on univariate analysis. Normal LFTs and presence of abdominal pain were negative predictors for PBM on univariate analysis. When multivariate analysis was performed, the presence of ESR greater than 30 mm/h (OR 0.004, 95% CI 0-0.13), lower levels of Hb (OR 3.04, 95% CI 1.2-7.7) and larger diameter of CBD (OR 0.67, 95% CI 0.47-0.96) and PD (OR 0.3, 95% CI 0.01-0.56) were independent risk factors for PBM.

Discussion

Endoscopic ultrasonography as an imaging technique is a highly accurate and very sensitive modality of imaging the biliary system and detecting the cause of CBD dilatation. Isolated dilation of CBD is unexplained by US is a dilemma for clinicians and it is a challenge to decide when further evaluation is necessary.

In the majority of cases, the etiology of dilated CBD is benign, however, clinicians are always concerned about an underlying neoplasm or malignancy.[13]Vernon et al.[14] reported that older patients, males and those presenting with concurrent elevations in the AST/ALT were more likely to have an underlying etiology discovered on EUS. Moreover, Savio et al.[15]reported that male gender, presence of jaundice, abnormal LFTs, weight loss, and nonspecific trans abdominal imaging results, such as abnormal appearing pancreas, predicted the presence of PBM, whereas patients with previous cholecystectomy and abdominal pain were less likely to have this diagnosis. In parallel, in agreement with study above we observed that lower hemoglobin levels, larger diameter of CBD, PD and ESR more than 30 mm/h were independent risk factors for PBM, whereas patients with previous cholecystectomy, normal LFTs and abdominal pain were less likely to have this diagnosis. These findings are comparable to those obtained in the a mentioned study.[15]In patients with dilated CBD accompany with anemia, abnormal LFT and ESR or dilated PD, malignancy should be considered and additional imaging is recommended if EUS is not diagnostic.

Furthermore, Yildiran et al.[16] have revealed that EUS provides an accurate explanation for CBD dilatation in 70 of the 76 patients (92%). In addition, such as report above we also have found that the majority of patients (95.7%) had findings on EUS to explain the etiology of their dilated CBD. Moreover, in this study, choledocholithiasis (48 cases) and malignancy (17 cases) were the most common findings that were comparable to those obtained in previous reports.[13,14,16]

Kim[17] noted in patients with incidentally discovered biliary dilatation, absence of clinical signs or symptoms, and normal hepatic chemistries, the yields from further investigation with EUS and ERCP was low. Adrian et al.[12]also proposed that data are limited regarding the yield of further investigations in patients with incidentally identified modest ductal dilatation without symptoms or laboratory abnormalities and additional investigations are more likely to identify clinically relevant findings in patients with more pronounced dilatation. Similar to previous studies,[13,14] it was found that patients with a dilated CBD and abnormal LFTs were more likely to have findings on EUS to explain the dilated common bile duct, the yield of EUS was 100% in this group. The prevalence of pathology was lower (76.9%) in patients with normal LFTs.

On the other hand, the present study indicated the yield of EUS in evaluating biliary dilatation is significantly more than previous studies, especially in patients with normal enzymes. Therefore, it may be logical to consider EUS when abdominal US does not reveal a cause for CBD dilatation, regardless of laboratory findings especially in the presence of abdominal pain. We argue against the previous concept that further evaluation may not be necessary in patients with modest CBD dilatation without laboratory abnormalities, given the significant prevalence of pathology in our findings. However, we agree that further evaluation may not be necessary in asymptomatic patients with normal LFTs.

Limitations of this study

Our study demonstrated the presence of gallstone and opioid addiction can be incidental findings and other etiologies (such as malignancy) should be considered for their ductal dilatation. **Although our sample size was too small for this conclusion,** other studies with focus on dilated CBD in the presence of gallstone or opioid addiction will be helpful.

In conclusion, we recommend further studies with larger sample sizes, especially with a focus on asymptomatic patients with unexplained dilated CBD and normal enzymes.

Conflict of interests

Authors declare no conflict of interests.

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Table 1. Patient characteristics

Characteristicsn(%)	
Cholecystectomy	8 (11.4%)
Opioid addiction	3 (4.3%)
Age (years) mean(SD)	61.8 (± 15.2)
Sex	
male	27(38.6%)
female	43 (61.4%)
Abdominal pain	55 (78.6%)
Jaundice	25 (35.7%)
Weight loss	14 (20%)

Table 2. Comparison between patients with and without pancreato-biliary malignancy (PBM)

Characteristics	**with PBM (n=١٧)**	**without PBM (n=٥٣)**	**P- value**
Age (years (SD))	65.6 (± 11.5)	60.5 (±16.1)	0.253
Male/female	10/7	17/36	0.049
Cholecystectomy	0/8	8/8	0.185
Abdominal pain	9 (52.9%)	46 (86.8%)	0.003
Jaundice	12 (70.6%)	13 (24.5%)	0.001
CBD diameter (mm)	12.2 (± 3.4)	10.1 (± 2.8)	0.012
PD diameter (mm)	4.4 (± 1.4)	3.2 (± 0.5)	0.002
Hb (mg/dL)	11.4 (± 1.1)	12.4 (±1.8)	0.015
ESR > 30 mm/h	13 (76.5%)	4 (7.5%)	0.024
Normal LFTs	0	13 (24.5%)	0.024
AST (IU/L)	92.4 (36-161)	134.1 (10-804)	0.103
ALT (IU/L)	85.1 (27-190)	172.4 (7-1353)	0.015
Alkaline phos. (IU/L)	880.5 (157-2104)	593.5 (19-2826)	0.051
Bilirubin (mg/dL)	9.6 (0.6-31)	3.9 (0.2-33)	0.004