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Dilated ducts with or without raised LFTs

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Abstract

Background

Unexplained dilation of CBD and PD, or both, on abdominal imaging are amongst the most common indications for EUS.

Aim

To investigate factors associated with positive EUS findings in patients with dilated ducts and correlate them with LFT results.

Methods

Patients referred for EUS for unexplained dilated CBD and/or PD from 2012 to 2016, for whom LFTs were available, were included in the study. CBD dilatation was defined as a CBD diameter greater than 7mm at any place, while a PD diameter of more than 4 mm in the head and 3 mm in the body and tail was considered dilated.

Results

404 patients met the study criteria.236 (58.4%)were female, and the mean age was 61.72±15.11. 293/404(72.5%) had elevated LFTs, and 111/404(27.5%) had normal LFTs. 299(74%) patients had multiple imaging modalities before the EUS. EUS found a cause of dilated duct in 57% of total cases. Males (65%, p=0.008), patients with dilated CBD and PD (67% p=0.009), elevated bilirubin (72.6% p=0.000) and elevated AKLP (62.3% p=0.049) were associated with positive findings on EUS. The additional common causes seen on EUS for dilated ducts are pancreatic cyst/mass, CBD stone, ampullary tumour/adenoma, papillary stenosis and periampullary diverticulum.

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Discussion
EUS detects previously undiagnosed pathology in 231(57%) of patients with dilated CBD and or PD, especially in males and with raised bilirubin.

Introduction

The pancreaticobiliary ductal system acts as a conduit of bile and pancreatic enzymes to the duodenum.[1] Several radiological tools are available for evaluating pancreaticobiliary (PB) ducts. The size of the common bile duct (CBD) varies slightly depending on the imaging modality used. [2] The upper limit of normal on ultrasound is generally accepted as 7 mm [3] . For the Pancreatic duct (PD), a diameter greater than 4 mm in the head or 2 mm in the body or tail on CT is usually regarded as dilated [4]. An unexplained dilated CBD, PD, or both (double duct sign) is a common reason for referral for Endoscopic Ultrasound (EUS), as the presence of dilated ducts raises concerns about possible occult biliary or pancreatic pathology. EUS is more sensitive than CT for the detection of small pancreatic tumours [5] and more sensitive than MRCP for small CBD stones, especially in the lower CBD and ampulla [6] . Older age and post-cholecystectomy status have been associated with increased CBD diameter [7,8]. Prior cholecystectomy influences CBD diameter as the gallbladder physiologically plays a role in accommodating pressure fluctuation in the biliary system, which, after surgery, could be transmitted to CBD, resulting in dilatation [9].

Aim

The study aimed to assess the yield of EUS in the investigation of patients with unexplained dilatation of the CBD and/or (PD) following non-diagnostic USG/CT and/or MRCP and determine the correlation of positive EUS findings with derangement of LFTs.

Methods

We conducted a retrospective analysis of a prospectively maintained database on consecutive patients who underwent Radial EUS examination of the biliary tree between 2012 and 2016 at our institution. The EUS procedures were performed by two experienced endo sonographers aware of the results of previous biochemical and radiological investigations.

Almost half of the cases were from external institutions. Since it was part of an institutional audit for appropriate patient targeting for EUS, institutional ethical board review was not deemed necessary.

CBD dilatation was defined as a CBD diameter greater than 7mm anywhere. PD diameter, more than 4 mm in the head and 3 mm in the body and tail was considered dilated. The patients included in the study had dilated CBD and /or PD and prior non-diagnostic radiological imaging. Prior imaging included USG, CT or MRCP of the abdomen. Regarding pre-EUS imaging, the maximum recorded duct diameter was used if the patient had undergone more than one radiological test. Patients with no data on LFTs were excluded. Deranged LFTs were defined as any liver enzyme level above the accepted normal laboratory range. In cases where multiple LFT results were available, the one closest to the date of the EUS examination was included. We used IBM SPSS statistics for Windows, version 25.0. Armonk, NY: IBM Corp. Student-test and chi-square test were used where appropriate. The statistical value of $p<0.05$ was considered statistically significant.

Results

A total of 2179 patients underwent EUS during the study period, of which 740 (34%) were performed for dilated ducts. Of these, 404 (55%) LFTs were available, and these patients formed the study cohort. (Figure 1). There were no recorded complications related to the EUS examination.

The average age of participants was 61.72 $\pm$ 15.1, with 58.4% (236) females. The indications for EUS, in addition to ductal dilatation, included abdominal pain 55(13.6%), pancreatitis 38(9.4%), and weight loss 5(1.2%). The imaging modalities included US 138(34.3%), CT 229(57%), and MRI 213 (53%). A large number of patients had more than one radiology imaging with CT&MRI (134), US & MRI (88) and US & CT (76). In total, 298(74%) patients had more than one imaging modality. EUS concurred with dilated ducts on previous imaging in two-thirds (67.1%) of total cases.

The overall mean CBD diameter was 10.75+- 3.84 mm, while in post-cholecystectomy patients, the mean was 10.2+/-3.11mm. There was no difference in the diameter (in mm)

based on gender (male 11.47, females 10.94, p<0.48) and age (< 60 years10.29,> 60 years, 11.15, p<0.106). As regards the PD diameter, the mean was 6.11 mm (+-2.4).

EUS found a cause of dilated duct in 231/404 (57%) of cases. Males (65%, p=0.008), patients with dilated CBD and PD (67% p=0.009), elevated bilirubin (72.6% p=0.000) and elevated AKLP (62.3% p=0.49) were associated with positive findings. Table 2. Patients over 60 years and with only dilated CBD tended to show more positive findings, although without statistical significance.

In patients with CBD dilatation alone, elevated bilirubin as compared to normal bilirubin was associated with a positive finding on EUS (p<0.027) (66% of cases). In those with CBD and PD dilatation, age over 60 years (p=0.000), raised bilirubin (p<0.022), and Alkaline Phosphatase (p<0.018) were associated with positive findings (78.2%, 81.6% and 76.6% respectively). However, increased ALT and GGT were not significantly associated with additional findings.

When comparing patients with or without deranged LFTs (Table 3), EUS added additional positive findings in both groups. 170(58%) in patients with deranged LFTs and 61(55%) in those with normal LFTs. The three common additional findings in the former group were pancreatic mass (33), pancreatic cyst (33) and CBD stone (28). The three commonest findings in the latter group were pancreatic cyst (14), pancreatic mass (10) and papillary stenosis (7). CBD diameter was more dilated in patients with deranged LFTs than in cohorts with normal LFTs but did not achieve statistical significance (p<0.073). Post-cholecystectomy status was more likely to be associated with normal LFTs (p<0.001).

A total of 315/404 patients were symptomatic. There was no difference in positive findings between symptomatic and asymptomatic patients. When the 315/404 symptomatic patients subgroup was analysed, 227 (72%) patients had elevated and 88 (28%) had normal LFTs. There was no difference in positive findings on EUS between these two groups (p<0.584).

In cases of CBD dilatation alone, 153(52.2%) patients had elevated LFTs, and 49(44.1%) had normal LFTs (p<0.147). Compared with isolated PD dilation, LFTs were normal in a significantly higher number of patients (p<0.005). Among patients with dilated CBD, there was no difference in the frequency of additional findings between patients with raised and normal

LFTs ((p=0.673). However, on further analysing this group, those with only raised bilirubin were likely to have an additional positive finding on EUS (p<0.027) as compared to those with deranged ALT, ALKP and GGT (Table) The variables which independently predicted positive findings on EUS in Multivariate analysis were: bilirubin (OR 2.07(CI 1.19-3.59) and male gender (OR 1.7(CI 1.14-2.25).

Discussion

EUS has low complication rates, making it an essential part of the investigative armamentarium of patients referred with a dilated pancreaticobiliary ductal system[10] . EUS is more sensitive for detecting pancreatic neoplasm, especially when the tumour is smaller than 2.0 cm and for CBD stones less than 5 mm[11,12,13,14].

Only a small number of studies to date have addressed the issue of dilated CBD and or PD in the setting of both normal and raised LFTs [15,16] . 293/404 (72.5%) of our patients with dilated ducts referred for EUS had deranged LFTs, while 111 patients (27.5%) had normal LFTs. This result is similar to that of Kaspy et al. [17] where 24% had normal LFTs. In our study, 57% of patients had additional positive findings on EUS that had not been seen on either CT, MRI or US. This included 58% of patients with deranged LFTs and 55% of those with normal LFTs. We were surprised to find pancreatic cysts in 20% of patients, usually well-seen on MRI. This can be explained by the fact that many of these patients had not had an MRI at the time of EUS, and small cysts can be missed on CT and US. Similarly, 5.6% of patients were diagnosed on EUS as having papillary stenosis. We concede that this is a slightly subjective finding and would have been made by the endosonographers based on the endoscopic appearance of a small, tight-looking papilla without any other ampullary abnormalities.

EUS helped identify the cause for dilatation of CBD with or without PD dilatation in both groups of patients, indicating that unexplained dilatation can be a manifestation of significant underlying disease [(18)] Which could be missed in radiological imaging. These results contrast with a much lower finding of pathology in previous studies [17,18] . As discussed above, this may be explained in part by the fact that not all patients had previously undergone MRI assessment, routine access to which can be delayed at times. An older study using abdominal

ultrasound showed that while in patients with CBD dilatation, a significant number of causative biliary tract lesions were identified, laboratory parameters were not helpful for discrimination[19].

We found that the presence or absence of symptoms did not increase the yield of abnormal findings, although most patients were symptomatic in this study. The effects of sex and age on diagnostic yield varied between studies. Previously, a study of 140 patients showed that older patients and males were more likely to have a cause found on EUS [18]. Similarly, we found that males (65%), patients with dilated CBD and PD (67%), elevated bilirubin (72.6%) and elevated AKLP (62.3%) were associated with positive findings. We also found that patients over 60 years old and with CBD dilation only had a trend towards more positive findings, but this did not reach statistical significance. Transaminases and GGT had no association with the presence or absence of positive findings. This may be because these enzymes can be mildly deranged for a multitude of reasons, not least non-alcoholic fatty liver disease, which is endemic in our population and thus had no / low discriminatory value in this study.

Similar to Malik et al. in our study, there was no statistical difference in age and CBD diameter between those with normal and abnormal LFTs. However, there was a trend toward larger ductal diameters in those with raised LFTs (10.99 versus 10.02, $p<0.07$). In patients with CBD dilatation alone and elevated bilirubin, there were significantly more positive findings on EUS (66% of cases). In those with CBD and PD dilatation, age over 60 years, raised bilirubin and Alkaline Phosphatase were associated with positive findings (78.2%, 81.6% and 76.6%, respectively). Isolated PD dilatation was associated with normal LFTs. In contrast to the study of Malik et al., where the additional findings to explain CBD dilatation were related to the elevated LFTs as a whole, we found that raised bilirubin (in the dilated CBD group) and raised bilirubin and ALKP in those with dilated CBD and PD were associated with additional findings. In contrast to the study of Malik et al., we found that statistically, more patients with cholecystectomy had normal LFTs($p<0.001$), suggesting that dilated CBD post-cholecystectomy is more likely to be physiological.

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This is the largest study to date to examine the yield of EUS in all types of dilated duct(s) (CBD, PD, or both) with and without normal LFT and non-diagnostic cross-sectional imaging. All diagnostic EUS examinations in our institution were performed using a radial EUS scope, with additional use of a linear scope where indicated (for FNA). In contrast, a linear EUS endoscope was used in most previous studies. Given its retrospective nature, our study has several limitations. The pre-EUS evaluation was not formalised, and information regarding indications for prior imaging, liver function test results, and medications was sometimes limited, as would be expected from a real-world cohort. The imaging modality used before EUS was not standardised.

EUS adds positive yield in most (over 50%) patients with dilated ducts in both normal and deranged LFTs. In some patients, more than a single cause of ductal dilatation was discovered.

We recommend early access to a diagnostic EUS as a minimally invasive investigation to be incorporated into the diagnostic algorithm of patients with dilated CBD and/or PD regardless of the derangement in LFTs rather than repeating another imaging modality.

Table 1: Characteristics of the study population (n=404)

Gender (Male/Female), n (%)	**168(41.6)/236(58.4)**
Age(years) Mean±SD	61.72±15.11
Age stratification (years), n (%)	
<60	157(39)
≥60	246(61)
CBD dilatation(n%)	202(50%)
PD dilatation(n%)	86(21.3%)
CBD+PD Dilatation(n%)	116(28.7%)
Deranged LFTs(n%)	293(72.5%)
Elevated Bilirubin(n%)	95(23.5%)
Elevated ALT(n%)	155(38.4%)
Elevated ALKP(n%)	191(47.3%)
GGT(n%)	268(66.3%)
USG(n%)	138(34.2%)
CT abdomen(n%)	229(56.7%)

MRCP(n%)	213(52.7%)
Symptomatic(n%)	315(78%)

Figure 1: Flow sheet of patients included in the study

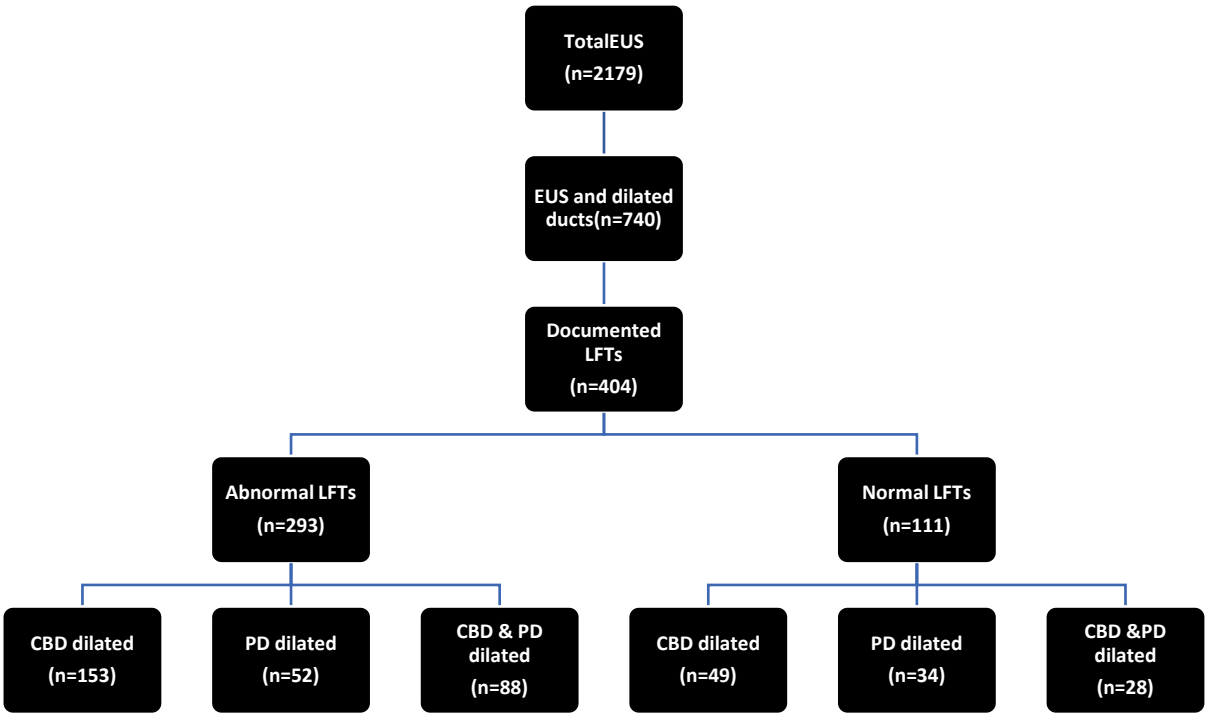

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Figure 2: EUS Findings: In some patients, more than a single cause of ductal dilatation was found on EUS.

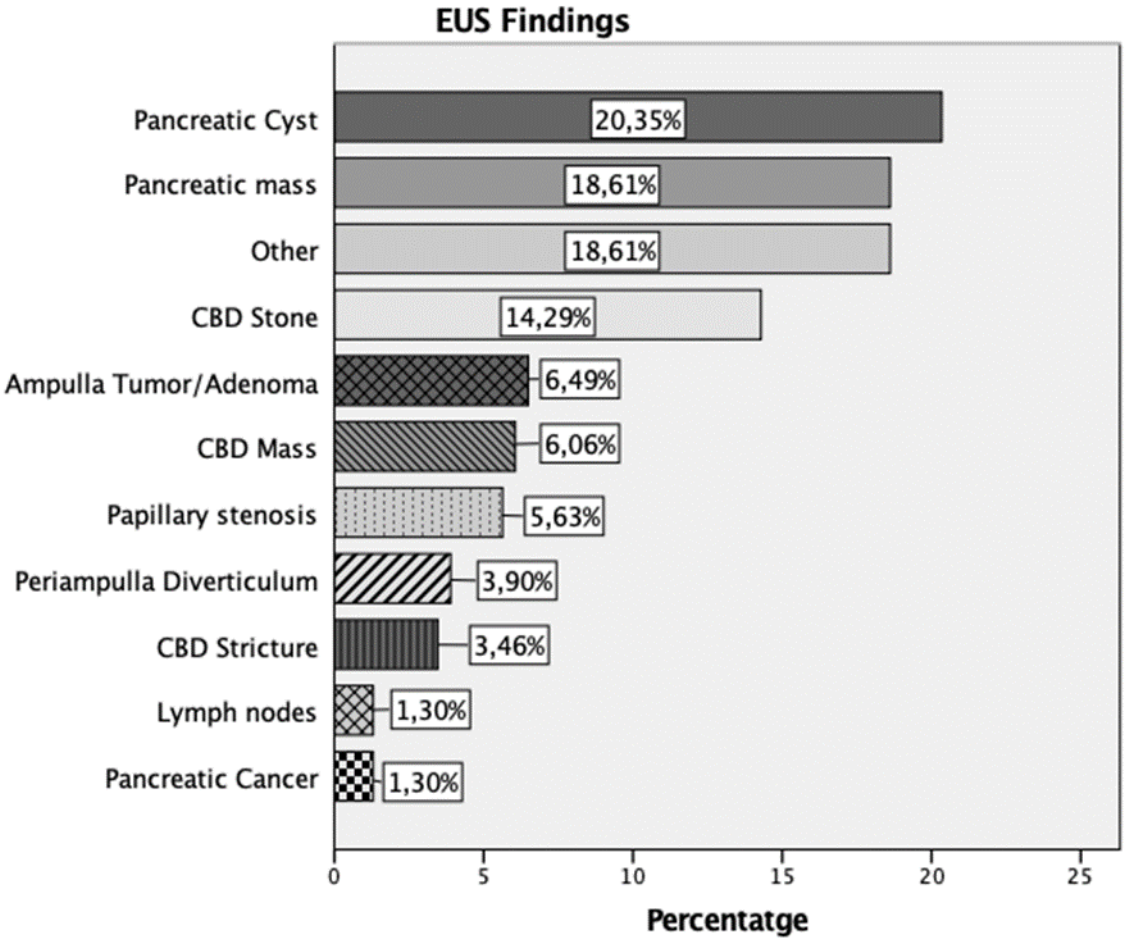

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Table 2. Univariate Analysis. N= 404.

	Positive Findings	Negative Findings	Missing (N)	P Value
Gender (N %)				
Male	109 (64.9)	59 (35.1)		**0.008**
Female	122 (51.7)	114 (48.3)		
Age (N %)				
<60	82 (35.5)	75 (43.6)		0.099
≥ 60	149 (60.6)	97 (39.4)		
Symptoms (N %)				
No	48 (53.9)	41 (46.1)		0.483
Any Symptom	183 (58.1)	132 (41.9)		
Dilated CBD (N %)				
Yes	106 (52.5)	96 (47.5)		0.056
No	125 (61.9)	77 (38.1)		
Dilated PD (N %)				
Yes	47 (54.7)	39 (45.3)		0.593
No	184 (57.9)	134 (42.1)		
Dilated CBD+PD (N %)				
Yes	78 (67.2)	38 (32.8)		**0.009**
No	153 (46.9)	135 (53.1)		
Deranged LFT (N %)				
Yes	170 (58)	123 (42)		0.578
No	61 (55)	50 (45)		
Bilirubin (N %)			1	
Elevated	69 (72.6)	26 (27.4)		**0.000**
Normal	161 (52.3)	147 (47.7		
ALT (N %)				
Elevated	94(60.6)	61(39.4)		0.267
Normal	137 (55)	112 (45)		
ALKP (N %)				
Elevated	119 (62.3)	72 (37.7)		**0.049**
Normal	112 (52.6)	101 (47.4)		
GGT (N %)				
Elevated	155 (57.8)	113 (42.2)	2	0.722
Normal	75 (56)	59 (44)		
Symptoms				
Yes	183 (58.1)	132 (41.9)		0.483

No	48 (53.9)	41 (46.1)		

Table 3: Characteristics of the two Cohorts: patients with and without deranged LFTs.

	Elevated LFTs(n=293)	*Normal LFTs(n=111)*	*p-value*
Age(mean) years	61.28	62.87	0.346**
Gender(females)	165(56.3%)	71(64%)	0.164*
CBD diameter(mm)	10.99	10.02	0.073
CBD dilatation	153(52.2%)	49(44.1%)	0.147*
PD dilatation	52(17.7%)	34(30.6%)	0.005*
CBD&PD dilatation	88(30%)	28(25.2%)	0.340*
Post-Cholecystectomy	26(8.87%)	19(17.1%)	0.001*
Additional Findings (CBD)	79/293(26.9%)	27/111(24.3%)	0.673
Additional Findings (PD)	30/293(10.2%)	17/111(15.3%)	0.484
Additional Findings (CBD+PD)	61/293(20.8%)	17/111(15.3%)	0.398
Symptomatic	227(77.4%)	88(79.2%)	0.696
Positive findings	170(58.02%)	61(54.95%)	0.578
Pancreatic cyst(47)	33/170(19.4%)	14/61(22.9%)	0.706
Pancreatic Mass(43)	33/170(19.4%)	10/61(16.39%)	0.512
CBD stones(33)	27/170(15.8%)	6/61(9.8%)	0.212

**represents Chi-square test*
*** represents student-t-test*

Declarations of Conflicts of Interest:
None declared.

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