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Clinical utility of linear endosonography in patients with unexplained biliary dilatation and negative MRCP, with predictors for detection of neoplastic lesions

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Abstract

Background and study aims: Unexplained biliary dilatation (UBD) frequently represents a diagnostic dilemma. Linear endosonography (EUS), with its close proximity to the pancreaticobiliary system and the ability for tissue acquisition, could have a role in revealing etiologies of UBD particularly in the context of negative other non-invasive modalities. However, in such patients, the decision for this semi-invasive procedure is usually debatable and often needs justification. Thus, we aimed to evaluate the diagnostic utility of linear EUS in patients with UBD after negative magnetic resonance cholangiopancreatography (MRCP) and to delineate predictors for EUS ability to detect neoplastic lesions.

Patients and methods: This was a prospective diagnostic observational study between 2018 and 2021. Included patients with evidence of biliary dilatation on abdominal ultrasound and negative MRCP underwent linear EUS examination. Results were compared to the final diagnosis relied on histopathology after EUS-guided biopsy or surgery for neoplastic lesions, while ERCP, diagnostic EUS criteria plus histopathology for autoimmune pancreatitis, Rosemont criteria for chronic pancreatitis, and/or follow-up for 6 months were the gold standard tests for non-neoplastic etiologies. Logistic regression was conducted to reveal predictors of neoplasm detection by EUS.

Results: Sixty-one patients (mean age 60 years, 32 females) were enrolled; 13.1% of them were asymptomatic. The final diagnosis was categorized into 29 patients with and 32 without neoplasms. Sensitivity, specificity, positive, negative predictive values (PPV, NPV), and accuracy of EUS-positive findings were 98.3%, 100%, 100%, 66.7%, and 98.3%, respectively. Corresponding results for neoplasm identification were 100%, 93.8%, 93.5%, 100%, and 96.7%, respectively. The most common neoplastic etiologies were small pancreatic and ampullary masses. Common bile duct (CBD) diameter > 12.9mm and CA19-9 > 37.1 u/ML were independent predictors for pancreaticobiliary neoplasm at multivariate regression analysis.

Conclusion: Linear EUS appears to have a high accuracy in detecting etiologies of UBD, with higher sensitivity for small pancreatic, ampullary lesions, and CBD stones. CBD diameter > 12.9 mm and elevated CA19-9 > 37.1 u/ML should raise a concern about the presence of occult pancreaticobiliary neoplasm, and then, EUS may be warranted even in asymptomatic patients.

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Keywords: EUS, Unexplained biliary dilatation, MRCP, ERCP, EUS predictors for malignancy

Introduction

Biliary dilatation (BD) of undetermined cause is a frequent indication for extensive work up to exclude occult pancreaticobiliary (PB) malignancies [1] particularly in symptomatic cases. Moreover, the recent increase in the detection rate of incidental BD on various imaging tools necessitates more clarification to define the relation between dilated bile ducts and the presence of an underlying pathology to guide further management plans [2].

Various imaging modalities of the PB system share in evaluating patients with BD; however, the best diagnostic modality remains uncertain [1]. Trans-abdominal ultrasound (US) is the first-line non-invasive imaging option for BD; however, being operator dependent with limited quality images in case of marked gassy bowel or in obese patients are its main limitations [3].

Magnetic resonance cholangiopancreatography (MRCP), as a non-invasive non-contrast imaging tool of the biliary tract, is considered one of the best biliary imaging techniques [4]. It has nearly replaced diagnostic endoscopic retrograde cholangiopancreatography (ERCP) with avoidance of direct-cholangiography-related complications. However, some drawbacks face this modality including the significant decrease in accuracy for small common bile duct (CBD) stones (5mm in diameter or less) [5] and the limited diagnostic role of periampullary lesions [6]. Likewise, the differentiation of biliary strictures either benign or malignant on MRCP could be challenging [4]. Other drawbacks may include the risk of claustrophobia and intolerance for some patients and the relatively longer time for different sequences [7].

In contrast, linear endosonography (EUS) provides, similarly to ERCP, a direct endoscopic view of the periampullary area with an effective capability, more than other imaging tools, to identify small ampullary lesions [8]. Additionally, with its close proximity to the PB system, EUS achieves high-resolution real-time images of the biliary tree, pancreas with the advantage, over radial EUS, to biopsy any suspected lesions [9]. Nonetheless, curvilinear echoendoscopes are less often used for biliary exams, although their accuracy was found to be comparable to radial echoendoscopes with no significant difference regarding the diagnostic performance for patients with suspected obstructive jaundice (OJ) [10]. Thus, we aimed principally in this study to evaluate the diagnostic utility of linear EUS in either symptomatic or non-symptomatic patients of undetermined BD after negative results of MRCP. The secondary objective was to delineate predictors for EUS ability to detect PB neoplasms in these patients.

Methods

This was a prospective clinical study carried out between August 2018 and January 2021. A total of 61 patients with indeterminate BD (cut-off level of dilated CBD > 7 mm by US [11]) were enrolled after excluding cases with obvious cause of BD on US or MRCP. Exclusion criteria also included patients with surgically altered anatomy, patients with severe comorbidities that impede endoscopic procedure, and patients <18 years old. Patients were exposed to thorough history taking and physical examination. Initial laboratory investigations were done including liver and kidney functions and coagulation profile, in addition to virology screen. Tumor markers including carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) were obtained when malignancy was suspected. After initial US and subsequent MRCP were done with non-diagnostic impact, EUS was scheduled, with subsequent ERCP, if needed, in the same session. Results of EUS were compared to the final diagnosis achieved by pathological examination after EUS-guided biopsy or surgery for neoplastic lesions, while ERCP, diagnostic EUS criteria plus histopathology for autoimmune pancreatitis [12] and Rosemont criteria for chronic pancreatitis [13], and/or follow-up for 6 months were the gold standard tests for non-neoplastic etiologies. Further categorization of patients was conducted according to the final diagnosis into "group A" with neoplastic etiologies and "group B" with non-neoplastic etiologies with further analysis of different features among both groups and predictors for neoplastic lesions.

Procedure and equipment for EUS examination

EUS was carried out using a curvilinear echoendoscope (Pentax H121502, Pentax, Tokyo, Japan) equipped with a linear scan transducer attached to the Hitachi sonography machine. EUS examination procedure involved evaluation of the major duodenal papilla, pancreas, visceral vessels, gallbladder, and extrahepatic biliary tract by gradually withdrawing the echoendoscope from the second portion of the duodenum into the stomach. Supplementary EUS-guided fine needle aspiration (FNA) was done when required.

The study protocol was reviewed and approved by the ethical committee at our Faculty of Medicine (MD.18.06.54). The study was conducted in accordance

Table 1 Patient characteristics

	Number	Percentage
Age/years	60 (21–82)	
Sex		
· Male	29	47.5
· Female	32	52.6
Clinical presentation		
· Jaundice	43	70.5
· Upper abdominal pain	10	16.4
· Incidental biliary dilatation	8	13.1
History of cholecystectomy	6	9.8
Laboratory data		
· Bilirubin (total) (mg/dl)	2.8 (0.4–39)	
· ALT (IU/l)	49 (11–293)	
· AST (IU/l)	47 (19–288)	
· Alkaline phosphatase (mg/dl)	223.0 (47–1260)	
· Tumor markers		
CA19-9	39.0 (0.60–1200)	
CEA	2.69 (0.4–15.05)	

Data are expressed as mean ± SD, median (range), or *n* (%)

ALT Alanine transaminase, *AST* Aspartate aminotransferase, *CA19-9* Carbohydrate antigen 19-9, *CEA* Carcinoembryonic antigen

with the Declaration of Helsinki and the consolidated Good Clinical Practice guidelines. Written informed consents were obtained from the patients after assuring confidentiality. All authors had access to the study data, and they all reviewed and approved the final manuscript.

Statistical analysis

All statistical analyses were conducted using IBM SPSS® version 23 (IBM, Armonk, NY, USA) and MedCalc® software version 19.5.3. All *P* values were two-sided, and *P* values of <0.05 were considered significant. Student's *t*-test or Mann-Whitney test was used to assess the relationships involving continuous variables, and the chi-square test was used to evaluate the relationships involving nominal variables. The univariate analyses and multivariate logistic regression analyses were conducted to determine predictors of neoplasm detection by EUS. The receiver operating characteristic (ROC) curve was used for the estimation of cut-off points of these factors with subsequent calculation of validity indices.

Results

Study population and outcome

Sixty-one patients were enrolled (32 female, mean age 60 years) (Table 1). Jaundice was the most common presentation in our cohort ($n=43$, 70.5%) followed by upper abdominal pain ($n=10$, 16.4%) then an incidental finding of BD on imaging ($n=8$, 13.1%) (Table 2). Six patients had a history of prior cholecystectomy.

The final diagnosis (Fig. 1) was subdivided into 29 patients in group A and 32 patients in group B. Group A involved 12 patients with pancreatic head adenocarcinoma (PHC) (41.4%), 11 with ampullary adenocarcinoma (AC) (37.9%), 3 with pancreatic head neuroendocrine tumor (P-NET) (10.3%), and remaining 3 patients (10.3%) with cholangiocarcinoma, metastatic adenomegally, and ampullary adenoma. Group B included 12 patients (37.5%) with missed choledocholithiasis (one of them had co-incidental serous cystic neoplasm), 4 patients with benign distal CBD stenosis (12.5%), 4 with autoimmune pancreatitis (12.5%), 4 with periampullary diverticulum (PAD) (12.5%), 3 patients with a picture of inflammatory process suggesting passed CBD stone (9.4%), 2 with chronic pancreatitis (6.3%), one patient with portal biliopathy (3.1%), and lastly two patients had negative findings on imaging and uneventful follow-up, thus considered normal cases (Figs. 2, 3, and 4). Overall sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of EUS in delineating positive findings were 98.3%, 100%, 100%, 66.7%, and 98.3%, respectively, while sensitivity, specificity, PPV, NPV, and accuracy of EUS in delineating neoplastic lesions were 100%, 93.8%, 93.5%, 100%, and 96.7%, respectively. The median size of neoplastic lesions was 2.3 cm at the largest diameter (range 1.5–4.5cm) and the median size of missed CBD stones was 6.6 mm (3–10.2mm). Fine needle aspiration (FNA) has greatly added to definite diagnosis with pathological confirmation in 28 patients of group A while the remaining patient was referred to Whipple surgery for PHC according to EUS findings only.

Out of the 8 patients with incidental finding of BD, 6 (75%) had positive findings on EUS examination (1 patient was diagnosed with P-NET, 1 with missed CBD stone, 1 with benign biliary stenosis, and 3 with PAD).

Comparison of the features of studied groups

To identify factors associated with EUS ability to detect neoplastic lesions, we analyzed several factors between both studied groups A and B (Table 3). Initially, we compared clinical and demographic data which revealed no significant difference regarding age, sex, and residency, but significantly higher presentation with jaundice in group A versus increased incidental finding of BD in group B. Secondly, we compared laboratory investigations revealing no significant difference between both groups apart from significantly higher bilirubin level, alkaline phosphatase, and tumor marker (CA 19-9) in

Table 2 EUS diagnosis in relation to patient presentation

Presentation		*N* = 61	Percentage
Symptomatic *N* = 53	Pancreatic head adenocarcinoma	12	22.6
	Ampullary adenocarcinoma	11	20.8
	Pancreatic neuroendocrine tumor	2	3.8
	Cholangiocarcinoma	1	1.9
	Metastatic adenomegally	1	1.9
	Ampullary adenoma	1	1.9
	Missed CBD stone	11	20.8
	Autoimmune pancreatitis	4	7.5
	Periampullary diverticulum	1	1.9
	Benign papillary stenosis	3	5.7
	Inflammatory process suggesting passed CBD stone	3	5.7
	Chronic pancreatitis	2	3.8
	Portal biliopathy	1	1.9
Asymptomatic (incidental biliary dilatation) *N* = 8	Pancreatic neuroendocrine tumor	1	12.5
	Missed CBD stone	1	12.5
	Periampullary diverticulum	3	37.5
	Benign papillary stenosis	1	12.5
	Normal	2	25.0

Data are expressed as *n* (%)

CBD Common bile duct

group A. CBD diameter on EUS also was significantly higher in group A.

Univariate and multivariate analyses for identifying factors associating neoplasm detection by EUS

ROC curve was plotted to determine the optimal cut-off level of CA 19-9 to > 37.1 U/ML, EUS-CBD diameter to > 12.9mm, total bilirubin to >2.6 mg/dl, and ALP to >165 mg/dl.

On univariate analysis, these cut-off levels were significant predictors for the presence of neoplastic lesions, while on multivariate analysis, CA 19-9 > 37.1 u/ML (multivariate odds ratio [*OR*] = 0.017, confidence interval [*CI*] = 0.001–0.281, *P* = 0.004) and CBD diameter > 12.9mm (multivariate *OR* = 0.032, *CI* = 0.002–0.470, *P* = 0.012) were independent predictors (Table 4). CA 19-9 > 37.1 u/ML showed 71.4% sensitivity and 96.9% specificity predicting malignancy with AUC as 0.788 while CBD diameter > 12.9mm showed sensitivity and specificity as 69% and 75% with AUC as 0.706.

Discussion

The decision for EUS in patients with BD and negative other imaging modalities usually represents a dilemma for clinicians. Thus, we conducted this prospective diagnostic study to evaluate the role of linear EUS in this category of patients after non-diagnostic MRCP and help in the decision-making through identifying predictors of PB neoplasm on EUS.

In the present study, most patients were symptomatic with a minority of incidental asymptomatic patients. Jaundice (70.5%) was the most common presentation in our cohort of patients, and specifically in group A (89.7%) in contrast to the study by Carriere et al., in which 75% of patients had abdominal pain and only 23% had hyperbilirubinemia, but similarly, 56% of their cases had EUS explanation of CBD dilatation [14]. Chen et al. conducted a similar study on patients with suspected OJ and negative US and also detected pathology in 67.5% of cases [1]. Definitely, many studies revealed a higher incidence of pathological findings in symptomatic patients [1, 2, 14–16] and those with abnormal liver chemistry [17–20] compared to asymptomatic patients [21–23]. This could explain the high rate of positive EUS findings in our study.

EUS has greatly added beneficial steps reaching the definitive diagnosis in the current study. Out of 61 included patients, 59 had a positive finding on EUS examination with diagnostic accuracy as 98.3%. One patient showed negative findings by EUS, but the patient had persistent abdominal pain for which she was further

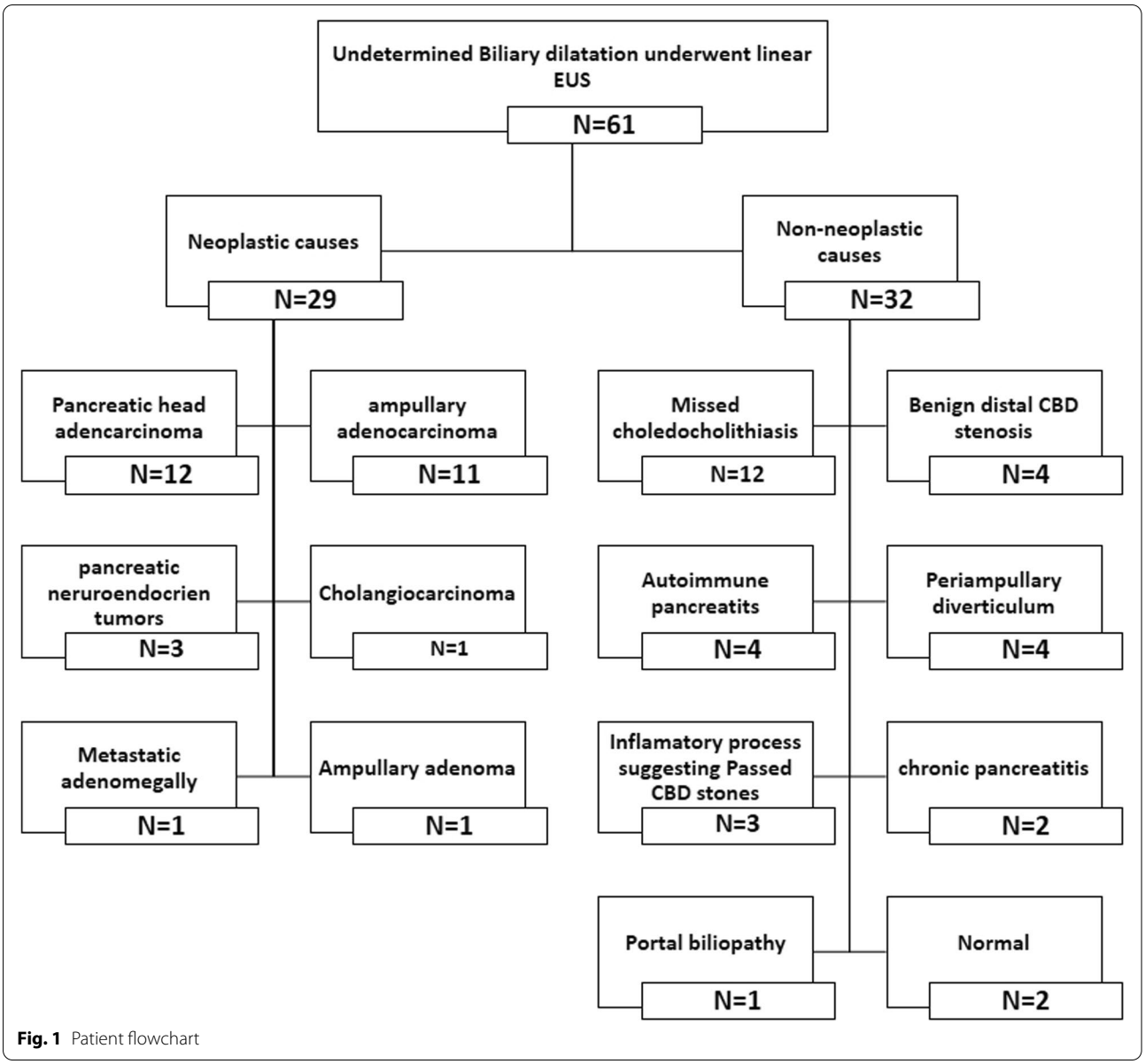

Fig. 1 Patient flowchart

diagnosed as acalcular cholecystitis in another facility and underwent surgical cholecystectomy with biliary exploration revealing a benign distal biliary stenosis. Nonetheless, benign distal stenosis is often difficult to diagnose and actually could be missed during EUS [2]. In the study by Chen and his colleagues, EUS showed 95.9% overall accuracy in detection cause of BD and 100% for no pathological finding [1]. These data demonstrate the vital role of EUS particularly in symptomatic patients even with unrecognizable etiology on other abdominal imaging.

Likewise, the neoplasm detection rate in our cases was 47.5% (29/61) with a diagnostic accuracy of 96.7% and overall sensitivity, specificity, PPV, and NPV as 100%, 93.8%, 93.5%, and 100%, respectively. Similar to our results, malignancy was detected in the study by Chen et al., in 33% of cases with an overall accuracy of 97.6% [1]. One patient in our study had distal CBD inflammatory stenosis which was falsely diagnosed as malignant stricture and another patient with mass-forming AIP was initially diagnosed as malignant pancreatic head mass by EUS and a definite diagnosis for both was achieved after EUS-guided biopsy. Definitely, biliary strictures remain challenging for different diagnostic tools including EUS. A meta-analysis of 36 studies (3532 patients) by Garrow et al. showed a high overall pooled sensitivity (78%) and

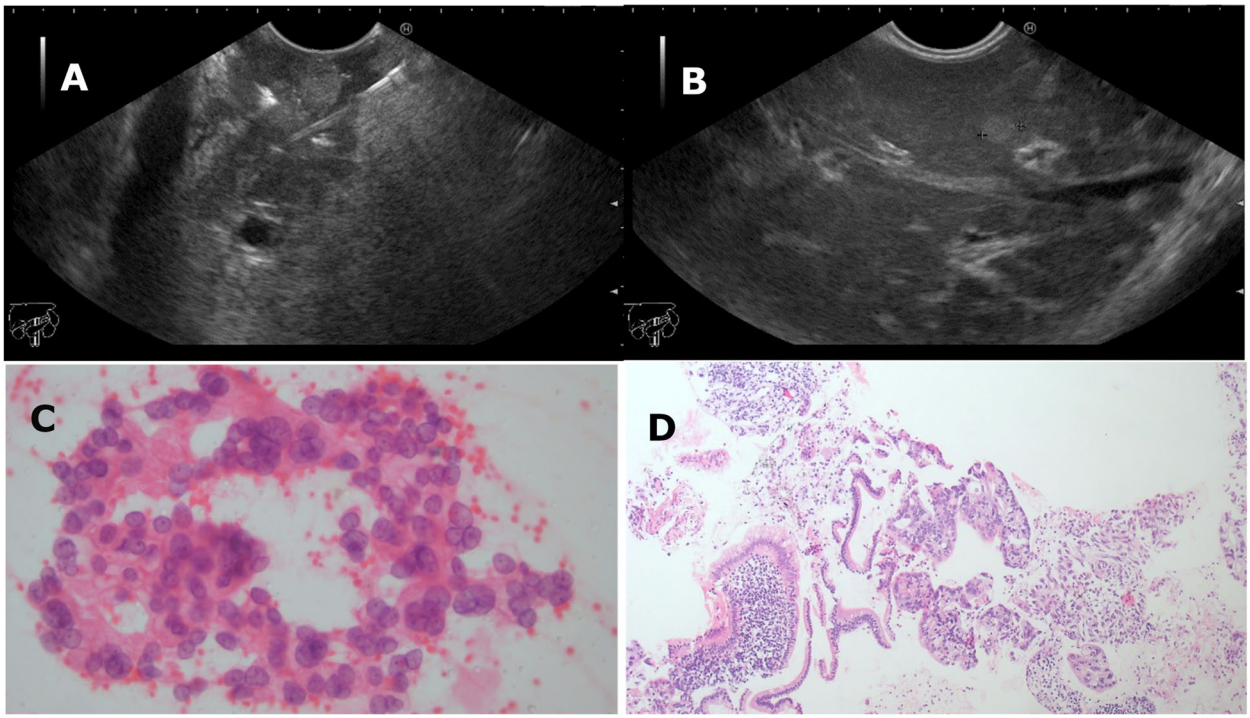

Fig. 2 Endoscopic ultrasound images showing pancreatic head cancer (**A**) and liver metastatic lesions (**B**). Cytopathological examination of EUS-guided fine needle aspiration: smear showing multiple aggregates of atypical polygonal epithelial cells with large hyperchromatic nuclei with irregular nuclear membranes and occasional small distinct nucleoli (**C**), cell block revealing multiple strips of atypical epithelial cells with glandular formations exhibiting moderate atypia and pleomorphism (**D**)

specificity (84%) for malignancy detection by EUS; however, in case of suspected strictures, studies were associated with lower test performance [10].

The most common neoplasm detected by EUS in the current study was PHC 41.3% (12/29) followed by AC 37.9% (11/29) with a median size of 2.3 cm at the largest diameter. Chen and his colleagues found that EUS has accurately detected PHC and AC, 30.9% (13/42) and 54.7% (23/42) respectively with 100% accuracy for each type. Indeed, EUS is well-designed to evaluate the periampullary region due to the close proximity of the transducer to the duodenum. On the other side, in a study by Müller et al., EUS sensitivity for the detection of pancreatic neoplasms < 3 cm in diameter was 93% compared to 53% for CT and 67% for MR imaging [24]. Such small-sized tumors are still amenable to surgical resection [25] while can be easily missed on other abdominal imaging tools.

Contrariwise, missed choledocholithiasis was the most common etiology in group B, 37.5% (12/32). Garrow et al., in their meta-analysis, showed a high overall pooled sensitivity (89%) and specificity (94%) for choledocholithiasis detection by EUS [10]. In addition, a recent meta-analysis showed that EUS had a significantly higher diagnostic accuracy and sensitivity for the detection of CBD stones compared to MRCP, most likely due to a higher detection rate of small choledocholithiasis [26]. The median size of missed CBD stones detected by EUS was 6.6 mm in our cohort. ERCP was performed in the same EUS session after real-time detection of choledocholithiasis. According to an abstract by JS Leeds, EUS and ERCP can be performed safely in the same session with no increase in adverse events [27], and a study by Vila et al. showed that anesthesia dose was significantly reduced when EUS and ERCP are combined versus in two sessions [28]. Cost-effectiveness analyses have shown that EUS is a cost-effective option compared with MRCP, especially if ERCP can be performed during the same session [29, 30]. Interestingly, in the study by Chu and his colleagues, ERCP was canceled in four patients depending on EUS findings [31]. Analogous to their data, ERCP was canceled in two patients in our study with previous suspicion for CBD stones on MRCP and negative EUS (picture of passed stones). Decisively, EUS may be considered as an alternative for MRCP particularly when the therapeutic decision is warranted.

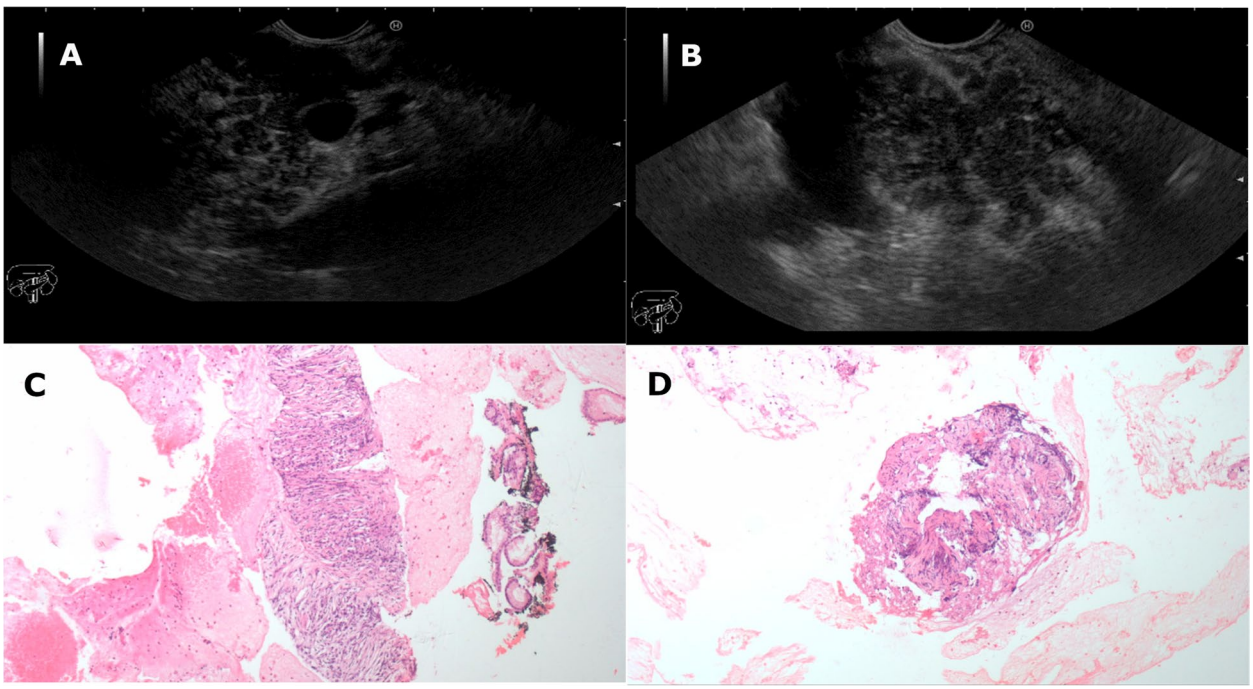

Fig. 3 Endoscopic ultrasound images showing a pancreatic head with a picture of chronic pancreatitis "hyperechoic strands and lobulations" (**A**, **B**). Cytopathological examination of EUS-guided fine needle aspiration revealed a diagnosis of autoimmune pancreatitis (**C**, **D**) with dense fibrosis with scattered mixed chronic inflammatory cells. The inflammatory cells are formed mainly of lymphocytes with scattered plasma cells and some eosinophils

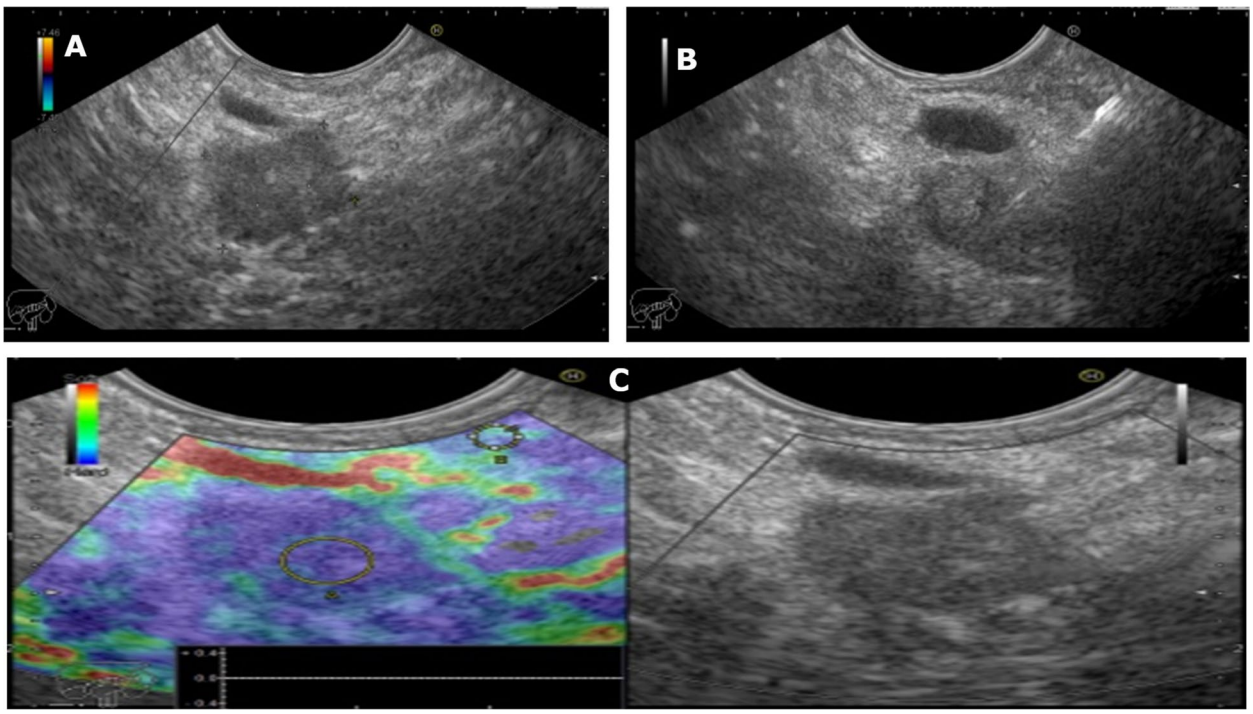

Fig. 4 Endoscopic ultrasound pictures showing ampullary hypoechoic lesion (**A**). EUS-guided fine needle aspiration was done with a final diagnosis of ampullary adenocarcinoma. **C** Heterogenous blue green color by elastography denoting the increased hard stiffness of the lesion

Table 3 Comparison between groups A versus B

	Group A No = 29	Group B No = 32	*P* value
Age	60 (21–82)	59 (33–79)	0.426
Sex			
• Male	13 (44.8%)	16 (50.0%)	0.686
• Female	16 (55.2%)	16 (50.0%)	
Clinical presentation			
• Jaundice	26 (89.7%)	17 (53.1%)	**0.002**
• Abdominal pain	2 (6.9%)	8 (25.0%)	0.056
• Incidental biliary dilatation	2 (3.4%)	7 (21.9%)	**0.033**
Laboratory data			
• Total bilirubin	5.3 (0.4–37.0)	1.4 (0.5–39.0)	**0.002**
• ALT	54.0 (21.0–201.0)	45.5(11.0–239.0)	0.466
• AST	50.0 (23.0–288.0)	44.0(19.0–210.0)	0.355
• Alkaline phosphatase	250 (160–1260)	190 (47–647)	**0.022**
CBD diameter by EUS	13.7 ± 2.92	11.55 ± 3.14	**0.006**

Data are expressed as mean ± *SD*, median (range), or *n* (%)

ALT Alanine transaminase, *AST* Aspartate aminotransferase

sedation-related complications. All these points of costs and expected benefits should be shared with the patient before taking this decision [21].

Regarding post-cholecystectomy state, there has been much debate on its effect on BD, with a suggestion that the upper limit of biliary diameter may be increased to 10 mm after cholecystectomy [4]. In our study, 6 patients had prior cholecystectomy, with a median CBD diameter of 11.25mm (8–13mm), 5 of them were symptomatic. Positive EUS findings were obtained in symptomatic patients including 3 with missed choledocholithiasis, 1 with ampullary adenoma, and 1 with papillary stenosis while the other asymptomatic patient had PAD. This indicates EUS role even in post-cholecystectomy state particularly when symptoms are present.

Factors predicting EUS-positive findings were the main concern of many studies [1, 2, 11, 14, 15, 22, 32]. Our data supported Chen et al. study which showed that abdominal pain, significant weight loss, increased CA19-9, increased ALP, and CBD dilatation were all associated with malignancy and that CBD dilatation

Table 4 Binary logistic regression analysis for prediction of neoplasm detection by EUS

Model	Univariate analysis			Multivariate analysis		
	β	*P*	*OR (95%C.I)*	*β*	*P*	*OR (95%C.I)*
Elevated CA 19-9 > 37.1 u/ML	4.350	**0.001**	77.5 (8.54–702.8)	−4.08	**0.004**	0.017 (0.001–281)
CBD diameter > 12.9 mm	1.897	**0.001**	6.66 (2.17–20.47)	−3.45	**0.012**	0.032 (0.002–0.470)
Elevated bilirubin > 2.6 mg/dl (total)	1.75	**0.002**	5.77 (1.91–17.44)			
Elevated ALP > 165 mg/dl	2.95	**0.006**	19.15 (2.30–158.9)			

OR Odds ratio, *CBD* Common bile duct, *CA19-9* Carbohydrate antigen 19-9, *ALP* Alkaline phosphatase

Indication of EUS examination in symptomatic patients may be logical and easy to decide; however, in asymptomatic subjects with isolated biliary dilatation, this semi-invasive maneuver often needs justification. Many studies [21–23] were conducted to answer this question with a recent meta-analysis [21] which declared that EUS for asymptomatic biliary dilations has a low detection rate of benign findings (9.2%) (including CBD stones, stricture, and PAD) and much lower (0.5%) for biliary neoplasms (mainly ampullary lesions). Although a minority of our patients were asymptomatic, however, EUS succeeded to delineate similar positive findings including P-NET, PAD, and benign biliary stenosis (Table 4). The median CBD diameter in this group of patients was 13.5mm (8–20.8mm). On the other hand, there is an increased concern about risks of the endoscopic procedure in this category of patients including infection risk and other rare events like perforation, hemorrhage, and

was the only independent predictor of malignancy ($P < 0.05$). The optimal cut-off level of CBD diameter in their study was 12.3 mm resulting in 46.3% sensitivity and 76.8% specificity for the presence of malignant obstruction with AUC as 0.702. Similarly, in our data, CA 19-9 to >37.1 U/ML, CBD diameter to > 12.9mm, total bilirubin to >2.6 mg/dl, and ALP to >165 mg/dl, all were significant predictors for the presence of neoplastic lesions at univariate analysis. In addition, both CA 19-9 > 37.1 u/ML and CBD diameter > 12.9mm were independent predictors at multivariate regression analysis with AUC as 0.788 and 0.706, respectively. Although there is published data that nullify the role of CBD diameter in the prediction of malignancy [2, 33], in contrast, our data confirms the vitality of EUS examination once these parameters are present even with non-diagnostic MRCP to exclude any missed lesions.

Limitations

The gold standard test in our study for choledocholithiasis was ERCP which sometimes has fallacies. Owing to resectability terms, surgery could not be performed for all neoplastic lesions in our cohort of patients.

Conclusions

Conceivably, based on our data, EUS may represent a first-line tool for evaluation of occult PB pathology and it makes sense that symptomatic patients who test negative on conventional radiological methods should undergo further EUS evaluation particularly when CBD is > 12.9 with or without elevated CA 19-9. Also, MRCP mainly missed choledocholithiasis and periampullary tumors; thus, EUS may be preferable if these pathologies are suspected.

Abbreviations

AC: Ampullary adenocarcinoma; AUC: Area under the curve; BD: Biliary dilatation; CA19-9: Carbohydrate antigen 19-9; CBD: Common bile duct; CEA: Carcinoembryonic antigen; CI: Confidence interval; ERCP: Endoscopic retrograde cholangiopancreatography; EUS: Endosonography; FNA: Fine needle aspiration; MRCP: Magnetic resonance cholangiopancreatography; NPV: Negative predictive value; OJ: Obstructive jaundice; OR: Odds ratio; PAD: Periampullary diverticulum; PB: Pancreaticobiliary; PHC: Pancreatic head adenocarcinoma; P-NET: Pancreatic neuroendocrine tumor; PPV: Positive predictive value; ROC: Receiver operating characteristic curve; UBD: Unexplained biliary dilatation; US: Ultrasound.

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Authors' contributions

Protocol of the study, conceptualization, and study design: HA, AM, HH, YK, and EG. Follow-up of the patients, data collection, and processing: HA and EG. Data analysis and writing and original draft preparation: HA, AM, EG. Writing and critical review and editing: AM, HH, HS, YK, and EG. Supervision: AM, HH, YK, HS, and EG. Methodology and the procedure: EUS procedures were done by EG and HH. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the ethical committee at Mansoura Faculty of Medicine (MD.18.06.54). The study was conducted in accordance with the Declaration of Helsinki and the consolidated Good Clinical Practice guidelines. Written informed consents were obtained from the patients after assuring confidentiality.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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