

Impact of Endoscopic Ultrasound in Evaluation of Upper Abdominal Pain

Bimal Chandra Shil^{*1}, Madhusudan Saha², Md. Royes Uddin³, A N M Saifullah⁴,
Md. Rehan Habib⁵, Imteaz Mahbub⁶, Mamun -Ur Rashid⁷

Abstract

Introduction: Upper abdominal pain is found to be one of the most common presenting symptoms. Endoscopic ultrasound may be a useful tool to yield a specific diagnosis. Aim of our study was to find the etiology of upper abdominal pain with normal endoscopic findings and compare the findings of endoscopic ultrasound with those of trans-abdominal ultrasound. **Materials and Methods:** This was a cross sectional study conducted in the department of gastroenterology, Sir Salimullah Medical College from January 2015 to December 2019. Total 238 patients suffering from upper abdominal pain who previously underwent endoscopy with normal results and trans abdominal ultrasound with doubtful findings were enrolled in this study. All patients were evaluated properly with history, clinical examination and relevant blood investigations. Then the patients underwent endoscopic ultrasound with conscious sedation. Computed tomography, magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography were done in cases where needed and correlated with endoscopic ultrasound results. **Results:** Among the total 238 patients, 137 were male and 101 were female. Most predominant age range was 31-40 years. Pain was moderate in severity in 43.27%, epigastric pain was in 59.66% and pain referred to back was in 37.39% patients. Comparison with trans abdominal ultrasound regarding etiologies of upper abdominal pain was statistically significant ($P=0.000$). Comparative analysis between the two modalities regarding gall bladder, common bile duct, pancreas were also found significant with P values of 0.040, 0.005, 0.000 respectively. Forty two patients were diagnosed as chronic pancreatitis based on Rosemont criteria by endoscopic ultrasound. **Conclusion:** Endoscopic ultrasound is a modern diagnostic tool which can detect hepato-pancreato-biliary pathologies and also mucosal irregularities of stomach and esophagus. So, it can be considered as a first line investigation to diagnose the underlying etiology of upper abdominal pain.

Keywords: Upper abdominal pain, Endoscopic ultrasound, Endoscopy, Trans abdominal ultrasound.

Number of Tables: 07; **Number of References:** 43; **Number of Correspondence:** 06.

*1. Corresponding Author:

Professor Bimal Chandra Shil

Professor & Head, Department of Gastroenterology
Sir Salimullah Medical College, Dhaka.
Email: drbimalshil@gmail.com
Mobile:+8801720038611

2. Professor Madhusudan Saha

Professor, Department of Gastroenterology
Northeast Medical College Hospital, Sylhet.

3. Dr. Md. Royes Uddin

Assistant Professor, Department of Gastroenterology
Sir Salimullah Medical College, Dhaka.

4. Dr. A N M Saifullah

Assistant Professor, Department of Gastroenterology
Sir Salimullah Medical College, Dhaka.

5. Dr. Md. Rehan Habib

Assistant Professor, Department of Gastroenterology
Sir Salimullah Medical College, Dhaka.

6. Dr. Imteaz Mahbub

MD Resident (Phase-B), Department of Gastroenterology
Sir Salimullah Medical College, Dhaka.

7. Dr. Mamun -Ur Rashid

Junior Consultant, Department of Medicine
OSD (DGHS), Dhaka.

Introduction:

In primary health care settings throughout the world, upper abdominal pain is found to be one of the most common presenting symptoms¹. In fact, almost one fourth to one third adults seek medical amenities for upper abdominal pain annually. If reflux symptoms are included then it is about 40% of total adult patients². Moreover, the incidence of unexplained abdominal pain is around 2% to 3%^{3,4,5}. The differential diagnoses seen starting from functional dyspepsia, peptic ulcer disease and cholelithiasis to more unusual diagnoses such as choledocholithiasis, sphincter oddi dysfunction, chronic pancreatitis and upper gastrointestinal malignancies. But many of these conditions are difficult to exclude without invasive procedures and patients may need to undergo esophagogastroduodenoscopy, ultrasound and computed tomography for confirm diagnosis⁶. With all these efforts, many of these cases may yet not be diagnosed⁷. In this context, Endoscopic ultrasound (EUS) may be a useful tool to yield a specific diagnosis.

Endoscopic ultrasound came into light in the early 1980s⁸. It is a specialized endoscope which combines endoscopy and ultrasound to obtain images and information of the digestive tract and its surrounding organs⁶. In this technology, ultrasound transducer is placed within the body so that the distance between transducer and region of interest is reduced by avoiding air filled or bony structures^{9,10,11,12,13,14}. It can successfully obtain clear images and information

regarding the layers of the intestinal wall, lymph nodes, sub mucosal lesions and the blood vessels. Another important aspects of EUS is that it can obtain ultrasound guided tissue samples from suspicious lesions¹⁵.

The established diagnostic indications of endoscopic ultrasound are detection of cholelithiasis, microlithiasis, choledocholithiasis, worm in common bile duct, evaluation of submucosal lesions, pancreatic cysts, diagnosis of acute/chronic pancreatitis, pancreatic calculi, diagnosis and staging of gastrointestinal, pancreaticobiliary and lung cancers¹⁶.

As endoscopic ultrasound has both endoscopy and ultrasound in a single entity, performing this modality in the diagnosis of upper abdominal pain may maximize additional benefits¹⁷. But there are a very few studies regarding utility of endoscopic ultrasound in detecting etiologies of upper abdominal pain with normal upper GI endoscopic findings. This study was designed to find out the etiology of upper abdominal pain with normal endoscopic findings and compare the results of endoscopic ultrasound (EUS) with trans-abdominal ultrasound (TUS) findings of patients with upper abdominal pain.

Materials and Methods:

This was a cross sectional study conducted in the department of gastroenterology, Sir Salimullah Medical College Mitford hospital, Dhaka from January 2015 to December 2019. Total 238 patients suffering from upper abdominal pain who previously underwent endoscopy with normal findings and trans abdominal ultrasound were enrolled in this study. Inclusion criteria for the patients were: Age over 18 years and upper abdominal pain defined as frequent (>6 episodes in previous 12 months) pain or discomfort in the upper abdomen (above the umbilicus). Exclusion criteria included: dysphagia, oesophageal varices, malignancy, bleeding, patients with comorbidities and previous gastric surgery.

Informed consent was taken from all cases; all patients were evaluated properly with history, clinical examination and relevant blood investigations. All the patients underwent Endoscopic ultrasound with conscious sedation. It was carried out by Fujinon echoendoscope (Model EG-530 UR₂ for radial array and E-530 UT₂ for linear array). The findings of endoscopic ultrasound were recorded and compared with those of trans-abdominal ultrasound of respective patients. Computed tomography scan of abdomen, Magnetic resonance imaging/ cholangiopancreatography and endoscopic retrograde cholangiopancreatography were done in cases where needed and correlated with endoscopic ultrasound results to reach the diagnoses. The statistical analysis was done by SPSS 22.0 software (SPSS, Inc. USA). Statistical significance was calculated by Student's t test. Statistical significances of the study was set at <0.05.

Results:

Total 238 patients took part in the study. Of them 137 were male and 101 were females with predominant age range was 31-40 years.

Table I: Demographic characteristics of the 238 patients.

Parameter	Frequency	Percentage
Sex		
Male	137	57.56%
Female	101	42.44%
Age (Years)		
18-30	46	19.33%
31-40	58	24.37%
41-50	54	22.69%
51-60	43	18.07%
61-70	23	9.66%
>70	14	5.88%
Total	238	100%

Clinical characteristics of chronic upper abdominal pain are given in table II. It shows pain was mostly moderate (43.27%), in epigastric region (59.66%) and referred to back (37.39%)

Table II: Clinical Characteristics of pain.

Parameter	Frequency	Percentage
Intensity		
Severe	58	24.37%
Moderate	103	43.27%
Mild	77	32.35%
Location		
Epigastrium	142	59.66%
RUQ	63	26.47%
LUQ	28	11.76%
Central abdomen	05	2.10%
Referred Pain		
Nil	137	57.56%
Back	89	37.39%
Shoulder	12	5.04%

Various etiologies detected by endoscopic ultrasound and along with its comparison with trans abdominal ultrasound is shown in table III which is statistically significant (P=0.000).

Table III: Etiologies of abdominal pain.

Causes	Endoscopic Ultrasound	Trans Abdominal Ultrasound	P Value
Calculous Cholecystitis	48 (20.17%)	45 (18.91%)	0.000
Microlithiasis with Cholecystitis	10 (4.20%)	02 (0.84%)	
GB sludge	24 (10.08%)	19 (9.24%)	
GB Mass	3 (1.26%)	1 (0.42%)	
Worm in GB	1 (0.42%)	0 (0.00%)	
Acalculous Cholecystitis	04 (1.68%)	09 (3.78%)	
Biliary Ascariasis	06 (2.52%)	02 (0.84%)	
Choledocholithiasis	76 (31.93%)	65 (28.15%)	
Acute Pancreatitis	36 (15.13%)	32 (13.45%)	
Chronic Pancreatitis	42 (17.65%)	14 (5.88%)	
Ca Pancreas	06 (2.52%)	1 (0.42%)	
No cause Found	05 (2.10%)	48 (20.17%)	

Table IV shows the gall bladder findings of endoscopic ultrasound and trans abdominal ultrasound and their comparison which is statistically significant (P=0.04).

Table IV: Findings of Gall bladder at Endoscopic ultrasound and Trans abdominal ultrasound.

Parameter	Endoscopic Ultrasound	Trans Abdominal Ultrasound	P Value
Normal	108 (45.38%)	126 (52.94%)	0.04
Calculous Cholecystitis	48 (20.17%)	46 (19.33%)	
Microlithiasis	10 (4.20%)	2 (0.84%)	
GB sludge	24 (10.08%)	22 (9.24%)	
Acalculous Cholecystitis	4 (1.68%)	8 (3.36%)	
Worm	1 (0.42%)	0 (0.00%)	
GB Mass	3 (1.26%)	1 (0.42%)	
Microlithiasis+GB sludge	7 (2.94%)	0 (0.00%)	
Cholelithiasis+GB sludge	3 (1.26%)	3 (1.26%)	
Absent Gall bladder	30 (12.61%)	30 (12.61%)	
Total	238	238	

Table V shows comparative findings of endoscopic and trans abdominal ultrasound in case of bile duct lesions with significance of 0.005.

Table V: Findings of Bile ducts at Endoscopic ultrasound and Trans abdominal ultrasound.

Parameter	Endoscopic Ultrasound	Trans Abdominal Ultrasound	P Value
Normal	65 (27.31%)	98 (41.18%)	0.005
Dilated	54 (22.69%)	38 (15.97%)	
Stone	6 (2.52%)	2 (0.84%)	
Sludge	6 (2.52%)	1 (0.42%)	
SOL suggesting neoplasm	5 (2.10%)	1 (0.42%)	
Worm	6 (2.52%)	2 (0.84%)	
Dilated+Stone	70 (29.41%)	63 (26.47%)	
Dilated+SOL	16 (6.72%)	11 (4.62%)	
Dilated+Sludge	6 (2.52%)	1 (0.42%)	
Dilated+Stricture	4 (1.68%)	2 (0.84%)	
Total	238	238	

Table VI shows comparison of pancreatic findings with endoscopic ultrasound's superiority over abdominal ultrasound with statistical significance $P < 0.0001$.

Table VI: Findings of Pancreas at Endoscopic ultrasound and Trans abdominal ultrasound.

Parameter	Endoscopic Ultrasound	Trans Abdominal Ultrasound	P Value
Pancreatic Size			0.000
Normal	194 (81.51%)	203 (85.29%)	
Swollen	36 (15.13%)	32 (13.45%)	
Smaller Size	8 (3.36%)	3 (1.26%)	
Total	238	238	
Pancreatic Parenchyma			0.000
Normal	204 (85.71%)	216 (90.76%)	
Hyperechoic foci	12 (4.20%)	08 (3.36%)	
Hyperechoic strand	10 (4.20%)	06 (2.52%)	
Hyperechoic foci+strand	12 (5.04%)	08 (3.36%)	
Total	238	238	
Pancreatic duct			0.000
Normal	202 (84.87%)	205 (86.13%)	
Main duct dilatation	13 (5.46%)	15 (6.30%)	
Main duct irregularity	03 (1.26%)	03 (1.26%)	
Calcification	04 (1.68%)	05 (2.10%)	
MPD dilatation	10 (4.20%)	08 (3.36%)	
MPD irregularity	03 (1.26%)	02 (0.84%)	
Worm in MPD	03 (1.26%)	00 (0.00%)	
Total	238	238	

Table VII shows number of chronic pancreatitis patients diagnosed through Rosemont criteria by endoscopic ultrasound.

Table VII: Diagnosis of Chronic Pancreatitis with Endoscopic ultrasound (Rosemont criteria).

Parameter	Endoscopic Ultrasound	Percentage
Consistent with CP	25	10.50%
Suggestive of CP	17	7.14%
Indeterminate	21	8.82%
Normal	175	73.53%
Total	238	100%

Discussion:

Upper abdominal pain is a very common morbidity in day to day practice. Causes may vary from benign to malignant⁶. Yet many patients have no structural diseases which makes the detection of real diagnosis a difficult job^{1,18,19}. For the purpose of yielding definitive diagnosis, patients undergo different invasive and noninvasive procedures like endoscopy,²⁰ trans abdominal ultrasound²¹ and computed tomography⁵. According to American College of Gastroenterology, upper gastrointestinal endoscopy is the first step in the diagnosis of dyspepsia of patients older than 55 years or those having alarm symptoms^{22,23}. In a recently conducted study, it was found that among the patients with

upper abdominal pain referred for further evaluation 40% had undergone previous upper gastrointestinal endoscopy, 65% had a trans abdominal ultrasound, 70% had a computed tomography and 10% had an magnetic resonance imaging²⁴. Endoscopic ultrasound, a specialized instrument which combines both endoscopy and ultrasound may be very effective in diagnosing cases of upper abdominal pain.

Our study was conducted on 238 patients referred to our department for upper abdominal pain. Our demographic data showed, males were 137 (57.56%) and females were 101 (42.44%) in number with slight male predominance. It differs from the studies conducted by Thompson et al⁶ and Chang et al¹⁷. Both the studies showed female predominance with upper abdominal pain symptoms. Possible explanation of this sex difference in our study is that males are more aware of their health problems and also keen to seek physician's advice than women in our country. Most common age groups suffering from upper abdominal pain in our study were 31-40 and 41-50 years group with 58 (24.37%) and 54 (22.69%) in number respectively. This data is almost identical with the data of Chang et al¹⁷ where mean age was 48.6%.

Etiologies of upper abdominal pain was searched and compared with the findings of trans abdominal ultrasound which yielded statistical significance ($P = 0.000$). Most common etiologies were gall bladder disease (37.81%), choledocholithiasis (34.45%), acute pancreatitis (15.13%) and chronic pancreatitis (17.65%). Chang et al¹⁷ showed gall bladder disease as the most common cause of chronic upper abdominal pain with frequency of 32% which is almost similar to our frequency of gall bladder disease of 37.81%.

Different studies have been conducted describing endoscopic ultrasound as adjunctive to trans abdominal ultrasound for detecting gall bladder lesions^{25,26,27}. But our study tried to compare the efficacy of endoscopic ultrasound with trans abdominal ultrasound in detecting gall bladder lesions and we found endoscopic ultrasound to be superior than trans abdominal ultrasound with statistical significance ($P = 0.04$). Sugiyama et al showed the superiority of endoscopic ultrasound over trans abdominal ultrasound for diagnosis of common bile duct pathologies²⁸. Our study showed efficiency of endoscopic ultrasound to detect the common bile duct lesions which were missed in trans abdominal ultrasound. This comparison between the two modalities was found to be significant ($P = 0.005$). Endoscopic ultrasound was proved to be excellent in diagnosing gall bladder and common bile duct microlithiasis and sludge in abdominal ultrasound negative patients in a study conducted in Iran²⁵. It showed 60% patients had common bile duct stones, sludges and microlithiasis in endoscopic ultrasound who did not have any lesions in trans abdominal ultrasound. In comparison, our study found 52% had pathologies of common bile duct in endoscopic ultrasound who had absolutely normal common bile duct in trans abdominal ultrasound. In fact, in a previous study of our centre, gall bladder and common bile duct microlithiasis and sludge are found to be the main reason behind idiopathic acute pancreatitis²⁹.

Endoscopic ultrasound is superior to Trans abdominal ultrasound, Computed tomography, Magnetic resonance imaging in detecting pancreatic pathologies specially solid lesions and neuroendocrine tumors^{15,30,31,32,33,34}. In our study 36 cases have increased pancreatic size (swollen pancreas) by Endoscopic ultrasound and 32 cases have increased pancreatic size by Trans abdominal ultrasound. As the Endoscopic ultrasound see the pancreas from close proximity, it detects pancreatic change better. In fact, important role of Endoscopic ultrasound in acute pancreatitis is to exclude biliary causes to avoid unnecessary Endoscopic retrograde cholangiopancreatography.

Studies suggested that Endoscopic ultrasound is more sensitive for detecting the parenchymal changes of chronic pancreatitis before the development of ductal lesions visible at Endoscopic retrograde cholangiopancreatography. So, it may serve better to diagnose early chronic pancreatitis^{35,36}. Pancreatic parenchymal change detected in our study by endoscopic ultrasound in comparison to trans abdominal ultrasound yielded statistical significance (P= 0.000). In this study main pancreatic duct (MPD) dilatation, duct irregularity and calcification are more detected by Endoscopic ultrasound compared to Trans abdominal ultrasound with statistical significance (P= 0.000). There are different methods for revealing prevalence of chronic pancreatitis in patients with upper abdominal pain. Studies which were based on pancreatic function tests showed prevalence ranging from 22% to 35% in patients with dyspepsia^{37,38,39}. Prevalence of chronic pancreatitis in patients of upper abdominal pain based on Endoscopic ultrasound found in various studies varied from 3% to 39%^{6,17,18,40,41}. Such dissimilarity may be due to differences in inclusion and exclusion criteria, duration of studies, characteristic of abdominal pain, criteria used for diagnosis and hospital settings. We followed Rosemont criteria for diagnosis of chronic pancreatitis. It includes hyperechoic foci with shadowing, main PD calculi and lobularity with honeycombing have been defined as major criteria while the minor criteria for CP include cysts, dilated duct ≥ 3.5 mm, irregular PD contour, dilated side branches ≥ 1 mm, hyperechoic duct wall, hyperechoic strand, non-shadowing hyperechoic foci and lobularity with noncontiguous lobules^{42,43}. We diagnosed 42 cases of chronic pancreatitis where 25 cases were consistent with chronic pancreatitis while 17 cases were suggestive. Prevalence was 17.64% which is almost similar to the prevalence of the study of Atsawarungrangkit et al⁷ of 19.6% while differs from the prevalence recorded by Sahai et al¹⁸ of 39%.

There were some limitations of our study. All the patients included in the study were referred to our center. So, there are chances of confounding factors and referral bias. Moreover, cost effectiveness was not addressed in the study.

Conclusion:

Endoscopic ultrasound is an important diagnostic tool. It

can detect pathologies in liver, pancreas, gallbladder and biliary tree. It can also find out the mucosal irregularities within the stomach and esophagus. It can certainly be used to diagnose the underlying pathology of upper abdominal pain.

Conflict of Interest: None.

Acknowledgement:

The authors are grateful to the referring physicians and surgeons for their referral and also thankful to study subjects for their active, sincere and voluntary participation.

References:

1. Grimpen F, Pavli P. Rational investigation of upper abdominal pain. *Aust Fam Physician*. 2008 Aug; 37(8):602-7.
2. Talley NJ, Silverstein MD, Agréus L, Nyren O, Sonnenberg A, Holtmann G. AGA technical review: evaluation of dyspepsia. *American Gastroenterological Association. Gastroenterology*. 1998 Mar; 114(3):582-95. [https://doi.org/10.1016/S0016-5085\(98\)70542-6](https://doi.org/10.1016/S0016-5085(98)70542-6)
3. Wallander MA, Johansson S, Ruigómez A, García Rodríguez LA. Unspecified abdominal pain in primary care: the role of gastrointestinal morbidity. *Int J Clin Pract*. 2007 Oct; 61(10):1663-70. <https://doi.org/10.1111/j.1742-1241.2007.01529.x> PMID:17681003
4. Ketwaroo GA, Freedman SD, Sheth SG. Approach to patients with suspected chronic pancreatitis: a comprehensive review. *Pancreas*. 2015 Mar; 44(2):173-80. <https://doi.org/10.1097/MPA.0000000000000239> PMID:25675419
5. Nojkov B, Duffy MC, Cappell MS. Utility of repeated abdominal CT scans after prior negative CT scans in patients presenting to ER with nontraumatic abdominal pain. *Dig Dis Sci*. 2013 Apr; 58(4):1074-83. <https://doi.org/10.1007/s10620-012-2473-0> PMID:23179149
6. Thompson MB, Ramirez JC, De La Rosa LM, Wood AS, Desai S, Arjunan A, et al. Endoscopic ultrasound in the evaluation of chronic upper abdominal pain of unknown etiology: a retrospective chart review examining the efficacy of EUS in determining a new diagnosis. *J Clin Gastroenterol*. 2015 Feb; 49(2):e17-20. <https://doi.org/10.1097/MCG.0000000000000174> PMID:25569224
7. Atsawarungrangkit A, Pongprasobchai S, Pausawadi N, Prachayakul V, Leelakusolvong S. Prevalence and Predictors of Chronic Pancreatitis in patients with Chronic Abdominal Pain with Negative Endoscopy and Cross-Sectional imaging. *J Med Assoc Thai*. 2018; 101: 521-7.
8. DiMaggio EP, Buxton JL, Regan PT, Hattery RR, Wilson DA, Suarez JR, et al. Ultrasonic endoscope. *Lancet*. 1980 Mar 22; 1(8169):629-31. [https://doi.org/10.1016/S0140-6736\(80\)91122-8](https://doi.org/10.1016/S0140-6736(80)91122-8)

9. Yanai H, Yoshida T, Harada T, Matsumoto Y, Nishiaki M, Shigemitsu T, et al. Endoscopic ultrasonography of superficial esophageal cancers using a thin ultrasound probe system equipped with switchable radial and linear scanning modes. *Gastrointest Endosc.* 1996 Nov; 44(5):578-82.
[https://doi.org/10.1016/S0016-5107\(96\)70012-3](https://doi.org/10.1016/S0016-5107(96)70012-3)
10. Hasegawa N, Niwa Y, Arisawa T, Hase S, Goto H, Hayakawa T. Preoperative staging of superficial esophageal carcinoma: comparison of an ultrasound probe and standard endoscopic ultrasonography. *Gastrointest Endosc.* 1996 Oct; 44(4):388-93.
[https://doi.org/10.1016/S0016-5107\(96\)70086-X](https://doi.org/10.1016/S0016-5107(96)70086-X)
11. Takemoto T, Yanai H, Tada M, Aibe T, Fujimura H, Murata N, et al. Application of ultrasonic probes prior to endoscopic resection of early gastric cancer. *Endoscopy.* 1992 May; 24 Suppl 1:329-33.
<https://doi.org/10.1055/s-2007-1010493>
PMid:1633775
12. May A, Günter E, Roth F, Gossner L, Stolte M, Vieth M, et al. Accuracy of staging in early oesophageal cancer using high resolution endoscopy and high resolution endosonography: a comparative, prospective, and blinded trial. *Gut.* 2004 May; 53(5):634-40.
<https://doi.org/10.1136/gut.2003.029421>
PMid:15082579 PMCid:PMC1774048
13. Saitoh Y, Obara T, Einami K, Nomura M, Taruishi M, Ayabe T, et al. Efficacy of high-frequency ultrasound probes for the preoperative staging of invasion depth in flat and depressed colorectal tumors. *Gastrointest Endosc.* 1996 Jul; 44(1):34-9.
[https://doi.org/10.1016/S0016-5107\(96\)70226-2](https://doi.org/10.1016/S0016-5107(96)70226-2)
14. Yoshida M, Tsukamoto Y, Niwa Y, Goto H, Hase S, Hayakawa T, et al. Endoscopic assessment of invasion of colorectal tumors with a new high-frequency ultrasound probe. *Gastrointest Endosc.* 1995 Jun; 41(6):587-92.
[https://doi.org/10.1016/S0016-5107\(95\)70196-6](https://doi.org/10.1016/S0016-5107(95)70196-6)
15. Gan SI, Rajan E, Adler DG, Baron TH, Anderson MA, Cash BD, et al. ASGE Standards of Practice Committee, Role of EUS. *Gastrointest Endosc.* 2007 Sep; 66(3):425-34.
<https://doi.org/10.1016/j.gie.2007.05.026>
PMid:17643438
16. Dumonceau JM, Deprez PH, Jenssen C, Iglesias-Garcia J, Larghi A, Vanbiervliet G, et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline - Updated January 2017. *Endoscopy.* 2017; 49(7):695-714.
<https://doi.org/10.1055/s-0043-109021>
PMid:28511234
17. Chang KJ, Erickson RA, Chak A, Lightdale C, Chen YK, Binmoeller KF, et al. EUS compared with endoscopy plus transabdominal US in the initial diagnostic evaluation of patients with upper abdominal pain. *Gastrointest Endosc.* 2010 Nov; 72(5):967-74.
<https://doi.org/10.1016/j.gie.2010.04.007>
PMid:20650452 PMCid:PMC3775486
18. Sahai AV, Mishra G, Penman ID, Williams D, Wallace MB, Hadzijahic N, et al. EUS to detect evidence of pancreatic disease in patients with persistent or nonspecific dyspepsia. *Gastrointest Endosc.* 2000; 52:153-159.
<https://doi.org/10.1067/mge.2000.107910>
PMid:10922084
19. Agréus L, Svärdsudd K, Nyrén O, Tibblin G. Irritable bowel syndrome and dyspepsia in the general population: overlap and lack of stability over time. *Gastroenterology.* 1995 Sep; 109(3):671-80.
[https://doi.org/10.1016/0016-5085\(95\)90373-9](https://doi.org/10.1016/0016-5085(95)90373-9)
20. Lieberman D, Fennerty MB, Morris CD, Holub J, Eisen G, Sonnenberg A. Endoscopic evaluation of patients with dyspepsia: results from the national endoscopic data repository. *Gastroenterology.* 2004 Oct; 127(4):1067-75.
<https://doi.org/10.1053/j.gastro.2004.07.060>
PMid:15480985
21. Heikkinen M, Pikkarainen P, Takala J, Julkunen R. General practitioners' approach to dyspepsia. Survey of consultation frequencies, treatment, and investigations. *Scand J Gastroenterol.* 1996 Jul; 31(7):648-53.
<https://doi.org/10.3109/00365529609009144>
PMid:8819212
22. Krinsky ML. EUS in the initial assessment of upper abdominal pain: time for a paradigm shift? *Gastrointest Endosc.* 2010 Nov; 72(5):975-7.
<https://doi.org/10.1016/j.gie.2010.07.022>
PMid:21034898
23. Talley NJ, Vakil N; Practice Parameters Committee of the American College of Gastroenterology. Guidelines for the management of dyspepsia. *Am J Gastroenterol.* 2005 Oct; 100(10):2324-37.
<https://doi.org/10.1111/j.1572-0241.2005.00225.x>
PMid:16181387
24. Sahai AV, Penman ID, Mishra G, Williams D, Pearson A, Wallace MB, et al. An assessment of the potential value of endoscopic ultrasound as a cost-minimizing tool in dyspeptic patients with persistent symptoms. *Endoscopy.* 2001 Aug; 33(8):662-7.
<https://doi.org/10.1055/s-2001-16223>
PMid:11490381
25. Mirbagheri SA, Mohamadnejad M, Nasiri J, Vahid AA, Ghadimi R, Malekzadeh R. Prospective evaluation of endoscopic ultrasonography in the diagnosis of biliary microlithiasis in patients with normal transabdominal ultrasonography. *J Gastrointest Surg.* 2005 Sep-Oct; 9(7):961-4.
<https://doi.org/10.1016/j.gassur.2005.03.002>
PMid:16137592
26. Dahan P, Andant C, Lévy P, Amouyal P, Amouyal G, Dumont M, et al. Prospective evaluation of endoscopic ultrasonography and microscopic examination of duodenal bile in the diagnosis of cholecystolithiasis in 45 patients with normal conventional ultrasonography. *Gut.* 1996 Feb; 38(2):277-81.
<https://doi.org/10.1136/gut.38.2.277>
PMid:8801211 PMCid:PMC1383037

27. Liu CL, Lo CM, Chan JK, Poon RT, Fan ST. EUS for detection of occult cholelithiasis in patients with idiopathic pancreatitis. *Gastrointest Endosc.* 2000 Jan; 51(1):28-32. [https://doi.org/10.1016/S0016-5107\(00\)70382-8](https://doi.org/10.1016/S0016-5107(00)70382-8)
28. Sugiyama M, Atomi Y. Endoscopic ultrasonography for diagnosing choledocholithiasis: a prospective comparative study with ultrasonography and computed tomography. *Gastrointest Endosc.* 1997 Feb;45(2):143-6. [https://doi.org/10.1016/S0016-5107\(97\)70237-2](https://doi.org/10.1016/S0016-5107(97)70237-2)
29. Shil BC, Saha M, Uddin MR, Saifullah ANM, Mahbub I, Rashid MMU. Idiopathic Acute Pancreatitis (IAP): The Value of Endoscopic Ultrasound. *J Health Med Sci.* 2019; 2: 224-229. <https://doi.org/10.31014/aior.1994.02.02.41>
30. Ardengh JC, Rosenbaum P, Ganc AJ, Goldenberg A, Lobo EJ, Malheiros CA, et al. Role of EUS in the preoperative localization of insulinomas compared with spiral CT. *Gastrointest Endosc.* 2000 May; 51(5):552-5. [https://doi.org/10.1016/S0016-5107\(00\)70288-4](https://doi.org/10.1016/S0016-5107(00)70288-4)
31. Anderson MA, Carpenter S, Thompson NW, Nostrant TT, Elta GH, Scheiman JM. Endoscopic ultrasound is highly accurate and directs management in patients with neuroendocrine tumors of the pancreas. *Am J Gastroenterol.* 2000 Sep; 95(9):2271-7. <https://doi.org/10.1111/j.1572-0241.2000.02480.x>
PMid:11007228
32. Khashab MA, Yong E, Lennon AM, Shin EJ, Amateau S, Hruban RH, et al. EUS is still superior to multidetector computerized tomography for detection of pancreatic neuroendocrine tumors. *Gastrointest Endosc.* 2011 Apr; 73(4):691-6. <https://doi.org/10.1016/j.gie.2010.08.030>
PMid:21067742
33. Sugiyama M, Abe N, Izumisato Y, Yamaguchi Y, Yamato T, Tokuhara M, et al. Differential diagnosis of benign versus malignant nonfunctioning islet cell tumors of the pancreas: the roles of EUS and ERCP. *Gastrointest Endosc.* 2002 Jan; 55(1):115-9. <https://doi.org/10.1067/mge.2002.119604>
PMid:11756931
34. Zimmer T, Ziegler K, Bäder M, Fett U, Hamm B, Riecken EO, et al. Localisation of neuroendocrine tumours of the upper gastrointestinal tract. *Gut.* 1994 Apr; 35(4):471-5. <https://doi.org/10.1136/gut.35.4.471>
PMid:8174983 PMCid:PMC1374794
35. Devière J, Finet L, Dunham F, Cremer M. Endoscopic ultrasonography in chronic pancreatitis. *Endoscopy.* 1994 Nov; 26(9):808-9. <https://doi.org/10.1055/s-2007-1009114>
PMid:7712997
36. Zuccaro G Jr, Sivak MV Jr. Endoscopic ultrasonography in the diagnosis of chronic pancreatitis. *Endoscopy.* 1992 May; 24 Suppl 1:347-9. <https://doi.org/10.1055/s-2007-1010497>
PMid:1633779
37. Andersen BN, Scheel J, Rune SJ, Worning H. Exocrine pancreatic function in patients with dyspepsia. *Hepatogastroenterology.* 1982 Feb; 29(1):35-7.
38. Schulze S, Thorsgaard Pedersen N, Jorgensen MJ, Mollmann KM, Rune SJ. Association between duodenal bulb ulceration and reduced exocrine pancreatic function. *Gut.* 1983 Sep; 24(9):781-3. <https://doi.org/10.1136/gut.24.9.781>
PMid:6884816 PMCid:PMC1420100
39. Smith RC, Talley NJ, Dent OF, Jones M, Waller SL. Exocrine pancreatic function and chronic unexplained dyspepsia. A case-control study. *Int J Pancreatol.* 1991 Apr; 8(3):253-62.
40. Chowdhury R, Bhutani MS, Mishra G, Toskes PP, Forsmark CE. Comparative analysis of direct pancreatic function testing versus morphological assessment by endoscopic ultrasonography for the evaluation of chronic unexplained abdominal pain of presumed pancreatic origin. *Pancreas.* 2005 Jul; 31(1):63-8. <https://doi.org/10.1097/01.mpa.0000164451.69265.80>
PMid:15968249
41. Siddiqui AA, Tholey D, Kedika R, Loren DE, Kowalski TE, Eloubeidi MA. Low but significant yield of endosonography in patients with suspected Sphincter of Oddi Dysfunction Type III with normal imaging studies. *J Gastrointest Liver Dis.* 2012 Sep; 21(3):271-5.
42. Catalano MF, Sahai A, Levy M, Romagnuolo J, Wiersema M, Brugge W, et al. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. *Gastrointest Endosc.* 2009 Jun; 69(7):1251-61. <https://doi.org/10.1016/j.gie.2008.07.043>
PMid:19243769
43. Trikudanathan G, Munigala S, Barlass U, Malli A, Han Y, Sekulic M, et al. Evaluation of Rosemont criteria for non-calcific chronic pancreatitis (NCCP) based on histopathology - A retrospective study. *Pancreatol.* 2017 Jan-Feb; 17(1):63-69. <https://doi.org/10.1016/j.pan.2016.10.010>
PMid:27836330