

Role of Endoscopic Ultrasound in Detection of Gallbladder Diseases

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Abstract

Background: Diseases of the gallbladder are relatively common, and the most common pathology ischolelithiasis, affecting 10 - 15 % of the population. Aim and objectives: To study the detection rate of gallbladder diseases by Endoscopic Ultrasound (EUS) in comparison to Trans abdominal Ultrasound (TAUS). Patient and methods: This was a prospective cross sectional study conducted on 100 patients fulfilling the inclusion criteria in Maadi Military Hospital. All the data were collected after ethical approval. **Results:** According to indication of EUS there were 19 (19%) patients had pancreatic mass, 55 (55%) patients had abdominal pain, 8 (8%) patients had pancreatitis, 12 (12%) patients had obstructive jaundice, 4 (4%) patients had pancreatic cyst, and 2 (2%) patients had a follow up cancer. Our results showed that there was a significant relationship between EUS and trans-abdominal US findings (P value <0.001). Also, our results showed that there was a significant moderate agreement between EUS and trans-abdominal US findings (k= 0.491, P value <0.001). Conclusion: Endoscopic Ultrasound (EUS) is a valuable tool for detecting gallbladder diseases; it has potential superiority over TAUS in diagnosing gallbladder diseases, especially when a detailed assessment is crucial.

Key words: Gallbladder diseases; EUS; TAUS.

Introduction

Diseases of the gallbladder are relatively common, and the most common pathology ischolelithiasis, affecting 10 - 15 % of the population. Other conditions such as gallbladder polyp are found in around 5% of the world population, while gallbladder cancer has an incidence of approximately 2 per 100,000 populations worldwide. Although not a common gallbladder pathology, the prognosis of gallbladder carcinoma is often dismal as a result of late diagnosis ⁽¹⁾, with only 10% of patients being candidates for curative resection at the initial presentation ⁽²⁾. Trans-abdominal ultrasound (TUS) is the screening modality primary for hepatobiliary diseases. Despite its excellent safety profile and wide availability, TUS has a sensitivity of only 66 % but 100 % specificity in distinguishing between gallbladder polyps and calculi⁽³⁾.

The sensitivity of TUS in the detection of polypoid lesions of the gallbladder ranges from 36 to 99% $^{(4, 5)}$.

EUS is considered superior to TUS for imaging of the biliary system because of its ability to achieve closer proximity and obtain higher resolution images using ultrasound frequencies higher than conventional ultrasonography (5 - 12 versus 2 - 5 MHz). The benefit of EUS was demonstrated in the diagnosis of small (< 2 cm) polypoid lesions ⁽⁶⁾, which increased the diagnostic sensitivity to up to 91.7% and specificity to up to 87.7% when compared with TUS (sensitivity of 54.2% and specificity of 53.8%)⁽⁷⁾.

EUS demonstrated a 92.6 - 100%sensitivity and 55.6 - 91% specificity for the diagnosis of gallbladder microlithiasis ⁽⁸⁾.

In most of these cases, the gallstones were located at the gallbladder infundibulum, which is difficult to effectively visualize with TUS ⁽⁹⁾.

The aim of this work was to study the detection rate of gallbladder diseases by Endoscopic Ultrasound (EUS) in comparison to Trans abdominal Ultrasound.

Patient and methods

This was a prospective cross-sectional study conducted on 100 patients fulfilling the inclusion criteria in Maadi Military Hospital and Department of Hepatology, Gastroenterology, Faculty of Medicine, Benha University, from the May 2022 to May 2023.

Ethical considerations: Informed consent voluntarily to participate in this study according to the approval of permission of the ethical committee of the hospital was obtained. Objectives, purposes of the study, the expected benefits, and types of information to be obtained were explained to the patient. Confidentiality of data was insured ethical approval obtained from hospital ethical committee and Benha, faculty of medicine {M.S.34.7.2022}.

Inclusion criteria: Age: 18 Years and older (Adult, Senior), both Sexes and all patients referred to EUS unit with EUS indication.

Exclusion criteria: Patient unfit for deep sedation by Propofol injection and patient refused to sign consent before doing EUS.

Methods: All the patients were subjected to: History talking, clinical general and local abdominal examination, abdominal US (gallbladder lesion was characterized if mass or stone by its Site, size and number. Other lesions as biliary system, pancreas, lymphadenopathy and ascites were documented), CT abdomen and MRI when indicated, Laboratory investigations and EUS (EUS was done to all patients.

Endoscopic Ultrasound examination:

the gallbladder was examined thoroughly to detect any pathology (microlithiasis, sludge and stone, polypoidal lesions or masses) with possible EUS-FNA when indicated for cytopathological examination. Gall bladder was examined from 3 stations :the duodenal bulb, prepyloric region and the gastric body as well .EUS examination was done as the following All EUS examination was done by EUS linear array Echo endoscope; Pentax EG-3870UTK attached to Hitachi Avius US machine under propofol deep sedation and Fujinon EUS machine, EG-580UT),the images included in this review were The EUS image orientation on screen was as follows: Monitor's right side corresponds to the cranial and left to the caudal end of the patient. Rotation of the echo endoscope is the most crucial aspect to GB imaging. Majority of the movements are performed in a straight position of the echo endoscope, except during EUS imaging from first part of duodenum when the scope is in a J-shaped position. Proper right/left knobs movements along with in/out movement of the echo endoscope are utilized for adequate contact with the gastrointestinal wall for proper EUS imaging.⁽¹⁰⁾

Patient preparations ⁽¹¹⁾

ONE DAY PRIOR

Lower EUS- Only a clear liquid diet for dinner combined with laxatives or enemas prior to the examination.

DAY OF PROCEDURE

Patients should have clear liquids up to 4 hours before your scheduled procedure time.

- Insert each of the enemas one at time 2 - 3 hours before scheduled procedure time and about 20 minutes apart into rectum.

- Continue to take prescribed medications unless otherwise indicated by gastroenterologist. Take medication(s) with a small sip of water.

- Wear loose fitting comfortable clothing and if you wear contact lenses or glasses, please bring a contact lens case or eye glass case with you. - Bring your insurance card and a form of photo identification.

- Please plan to be at the hospital or surgery center for about 2 - 3 hours.

A Clear Liquid Diet Includes:

- Water, apple or white grape juice, soda (No red, purple or blue)

- Clear bouillon / clear broth

- Yellow or green Jell-O (No red, purple or blue)

- Fruit flavored popsicles (No red, purple or blue)

- Hard candies (No red, purple or blue)

- Black coffee or tea (No creamers. No dairy. No non-dairy additives.)

- Clear or lemon-lime Gatorade type products (No red, purple or blue)

Technique

Imaging from duodenal bulb

The GB lies close to the probe between 2 to 4 o'clock positions. The imaging from the antrum is sometimes best done by pushing the echo endoscope from the body of stomach towards the pylorus with a hyper-inflated balloon the imaging from duodenum can be done without a balloon by passing the scope beyond the pylorus and pushing it into the duodenal bulb apex. The contact with the superior and anterior duodenal wall is established after sucking the air out of the lumen of duodenum, by turning in an anticlockwise direction and by moving the up and down knobs generally in a downward direction Home base position is identified with adequate rotation and minor adjustments of both knobs, where the portal vein is seen on the far side of the screen in a long axis Clockwise rotation follows the CBD towards the papilla and anticlockwise rotation makes the scanning towards the liver hilum, the upper part of CBD, the cystic duct and GB The CBD and GB are seen in the area between the probe and portal vein and higher up between the probe and liver ⁽¹²⁾

Imaging through longitudinal Scanning Echoendoscope

The first step is to advance the echoendoscope into the descending part of the duodenum. Having straightened the echoendoscope in the same way as in endoscopic retrograde cholangiopancreatography (ERCP), close contact is established with the duodenal wall at the minor side by suction of the luminal gas and flexion of the tip of the scope. Now the pancreatic head is visualized. Endoscopic visualization of the GB is helpful to position the transducer directly in contact to the papilla. Filling of the water balloon may support acoustic coupling, but is not necessary in most cases. Very slow, cautious, and gentle movements of the scope (predominantly backward and clockwise/counterclockwise torque) will lead to identification of the small triangular or oval hypoechoic structure of the GB. Mostly, the pancreatic duct will appear more distant to the transducer at first. Very gentle counterclockwise rotation will bring a longitudinal section of the distal bile duct into focus. The bile duct runs near the transducer. From this point, the echoendoscope is very slowly withdrawn and slightly rotated counterclockwise along the course of the common bile duct to liver hilum. Conversely, gradual clockwise turning and minimal advancement of the scope shaft will allow the transducer to follow the course of the common bile duct back to papilla again. The liver hilum and gallbladder are imaged best from a position with the duodenal bulb or from the gastral antrum or lower body. The tubular structures of the portal vein, common hepatic artery, and intrahepatic ducts may be very well visualized. Color-coded duplex scanning facilitates correct identification of these anatomical structures^{. (13)}

Transabdominal ultrasound was performed as the following:

It should be performed with a lowfrequency probe, ideally with a large convex footprint. Most common probes utilized are the curvilinear or phased array probes. Disinfectant wipes and cleaning equipment are institution specific and usually determined by the infectious disease department.

Preparation

Ensure that the probe and machine are cleaned before entering a patient room. The correct probes should be connected to the machine. The patient is ideally lying in a supine position on a stretcher with his or her abdomen exposed. Care should be taken to avoid unnecessary exposure with the use of towels tucked around the gown and undergarment edges. This will also aid in keeping unexposed areas clean from ultrasound gel. For dominant right-hand operators, the ultrasound machine should be positioned at the patient's anatomic right near the head of the bed, plugged in (if applicable) and turned on. The lights should be dimmed if possible. For evaluation of the gallbladder, being in a fasting state aid in the engorgement of the gallbladder and better visualization. When evaluating the uterus, informing the patient to maintain a full bladder will aid in visualization secondary to fluid in the bladder providing an acoustic window to deeper structures.⁽¹⁴⁾

Technique or Treatment

A low-frequency convex probe is best for transabdominal а ultrasound. Alternatively, a phased array probe can be used if a convex probe is not available. The settings on the ultrasound machine should be set to the desired exam being performed, for example, abdominal, FAST, vascular. The settings on the machine optimize image quality for the scan being performed. Generally, the probe indicator is always aimed cephalad (toward the patient's head) or to the patient's right side. Specific scanning technique is utilized depending on the organ or pathology being evaluated. For example, when evaluating the gallbladder, the probe is placed in a sagittal plane (with the indicator cephalad) in the right upper quadrant just inferior to the costal margin. The operator then slides the probe medial and lateral along the costal margin while maintaining the sagittal plane (cephalad) evaluating for the optimal sonographic window for image acquisition. Asking the patient to take a deep breath and hold it diaphragm to causes the contract, displacing the liver and gallbladder inferior, and aiding in image acquisition. A coronal scan of the right upper quadrant is another technique that can allow for gallbladder evaluation. With the probe placed on the patient's right in the midaxillary line, indicator cephalad, the operator can then fan the probe anterior and posterior through the liver in an attempt to acquire an optimal window to evaluate the gallbladder. The gallbladder is then evaluated for (1) stones or sludge, (2)wall thickening (normal less than 3 mm), (3) presence of a sonographic Murphy's sign, and (4) pericholecystic fluidThe presence of all four is very sensitive and specific for cholecystitis. This is an example of one specific area of

transabdominal ultrasound. There are specific techniques for most abdominal organs and underlying pathologies that can be evaluated using ultrasound^{.(15)}

Sample size calculation: Gall bladder diseases is found in 20% of the population and in up to 70% of patients with pancreatitis (1,10). With estimation of 40% detection prevalence of GB diseases among patients referred to EUS, to detect this prevalence with 95% CI and 10% margin of error, a sample size of 93 patients is needed.

Statistical analysis: the collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (version 26 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. Descriptive statistics: Mean, Standard deviation $(\pm SD)$ and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data. Frequency and percentage of categorical data. Cohen's Kappa was used for testing the interobserver reliability. The level of significance was set at P value ≤ 0.05 . The agreement was interpreted as being poor (k = 0 - 0.2), fair ($\kappa = 0.21 - 0.40$), moderate $(\kappa = 0.41 - 0.60)$, good ($\kappa = 0.61 - 0.80$), and very good ($\kappa = 0.81 - 1$).

Results:

There were 43 (43%) males and 57 (57%) females. Age ranged from 17 to 75 years with a mean \pm SD of 51.25 \pm 12.98 years (**Table 1**).

18 (18%) patients were smokers, 27 (27%) patients had DM, 29 (29%) patients had HTN, 15 (15%) patients were taking

drugs, all 100 (100%) patients were conscious, 17 (17%) patients had tenderness, and 2 (2%) patients had organomegaly (**Table 2**).

There were 19 (19%) patients had pancreatic mass, 55 (55%) patients had abdominal pain, 8 (8%) patients had pancreatitis, 12 (12%) patients had obstructive jaundice, 4 (4%) patients had pancreatic cyst, and 2 (2%) patients had a follow up cancer (**Table 3**)

There was a significant difference between EUS and trans abdominal US findings (P value <0.001) (**Table 4**).

There was a significant moderate agreement between EUS and trans abdominal US findings (k= 0.491, P value <0.001) (**Table 5**).

Regarding the EUS findings, the studied patients had no abnormality detected (NAD), polys, mud, microlithiasis (biliary gravels 1-2 mm), multiple stones and both multiple stones and polyps by (42,10,11,6,29 and 2) % respectively

Furthermore, the size of the stones and polyps was categorized as small (\leq 2) or large (>2).it was found that patients of the current study had small(3-5mm) and large stones(>5mm) by (56.8% and 43.2%) respectively.as well as patients had small and large polyps by(25% and 75%)respectively

Regarding transabdominal US findings, patients of the study had NAD, polyps, contracted gall bladder, multiple stones, and both multiple stones and polyps by (69%,1%,3% and 1%) respectively.

Table (1): Demographic	data of the	studied patients.
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		N / Mean	% / SD	Median (IQR)	Range	
Sex	Male	43	43.0%	-	-	
	Female	57	57.0%	-	-	
Age (y	years)	51.25	12.98	53.5 (42.5 - 61.5)	(17 - 75)	

SD: Standard deviation

		Ν	%	
Smoking	No	82	82.0%	
-	Yes	18	18.0%	
DM	No	73	73.0%	
	Yes	27	27.0%	
HTN	No	71	71.0%	
	Yes	29	29.0%	
Drugs	No	85	85.0%	
5	Yes	15	15.0%	
Conscious level	No	0	0.0%	
	Yes	100	100%	
Tenderness	No	83	83.0%	
	Yes	17	17.0%	
Organomegaly	No	98	98.0%	
	Yes	2	2.0%	
DM: diabetes mellitus, HTN:	: hypertension			
Table (3): Indication	of EUS of the studi	ed patients.		
		Ν	%	

 Table (2): History of the studied patients

Indication of EUS	Pancreatic mass	19	19.0%	
	Abdominal pain	55	55.0%	
	Pancreatitis	8	8.0%	
	Obstructive jaundice	12	12.0%	
	Pancreatic cyst	4	4.0%	
	Follow up cancer	2	2.0%	

EUS: endoscopic ultrasound

Table (4): Relationship between EUS and transabdominal US findings o	f the studied patients.

		EUS findin	gs				
		NAD	Polyps	Mud	Microlithiasis	Multiple stones	Multiple stones and polyps
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Trans-	NAD	42 (100%)	7 (70%)	10 (90.91%)	5 (83.33%)	5 (17.24%)	0 (0%)
abdominal US findings	Polyps	0 (0%)	1 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Mud	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Microlithiasis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Multiple stones	0 (0%)	0 (0%)	1 (9.09%)	1 (16.67%)	23 (79.31%)	1 (50%)
	Contracted gall bladder	0 (0%)	2 (20%)	0 (0%)	0 (0%)	1 (3.45%)	0 (0%)
	Multiple stones and	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)
P value	polyps	<0.001*					

EUS: endoscopic ultrasound, US: ultrasound, NAD: no abnormality detected, *: significant as P value ≤ 0.05

Table (5): Degree of agreement between EUS and transabdominal US	findings of the studied patients.
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		EUS findings		Sensitivity %	Agreemen	k	P value
		Normal	Abnormal	_	%		
		N (%)	N (%)				
Trans- abdominal US findings	Normal	42 (100%)	27 (46.6%)	53.5%	73%	0.49	<0.001*
	Abnormal	0 (0%)	31 (53.4%)			1	

EUS: endoscopic ultrasound, US: ultrasound, k: kappa analysis, *: significant as P value ≤ 0.05

Discussion

In our study, in terms of demographic data, the study included 100 patients, with 43% males and 57% females. The mean age of the patients was 51.25 years. These findings are consistent with the general distribution of gallbladder diseases, which affect both genders and can occur in various age groups ⁽¹⁶⁾. One of the studies reported that the sex distribution of their sample showed female predominant (66.2%), their ages ranged from 2 - 88 years. They also showed that nearly all ages are at risk for common bile duct stones (CBDS). The mean age of patient was (50.7) years ⁽¹⁶⁾ while, another study found the majority (n = 51; 56.7%) of the patients were aged between 26 years and 30 years, with the minimum and maximum ages being 18 years and 30 years, respectively, and the mean age being 25.84 + 3.3 years. Approximately 34.4% of the patients (n = 31) were in the age group of 21-25 years. (17)

In our study, the most common indications for EUS in the studied patients were abdominal pain (55%) and pancreatic mass (19%). Other indications included pancreatitis (8%), obstructive jaundice (12%), pancreatic cyst (4%), and followup cancer (2%). These results align with previous studies which have reported similar indications for EUS in evaluating gallbladder diseases ^(18, 19).

Our study examined various factors related to the patients' medical history. It was found that 18% of the patients were smokers, 27% had diabetes mellitus (DM), 29% had hypertension (HTN), and 15% were taking drugs. Additionally, 17% had tenderness, and 2% had organomegaly.

In our study, regarding EUS findings, 42% of the patients had no abnormality detected (NAD), 10% had polyps, 11% had mud, 6% had microlithiasis (biliary gravels 1-2

mm), 29% had multiple stones, and 2% had both multiple stones and polyps. Furthermore, the size of stones and polyps was categorized as small (≤ 2) or large (>2). It was found that 56.8% of patients had small stone (3-5 mm), while 43.2% had large stones (>5 mm). Similarly, 25% of patients had small polyps, while 75% had large polyps. This result in similar to another study (15) which illustrated that the main complaint was right abdominal pain in 78.0%; meanwhile, 74.7% had a picture of obstructive jaundice. EUS revealed gallbladder wall thickening in (10%), mud and/or small stones inside the gallbladder (48.7%), positive GB mass and/or in polyp findings in (20%), and biliary lesions such as duct strictures and/or dilatations were detected in (32%) respectively while TAUS findings for the same parameters the current study showed that they were (0%, 9.09%, 16.67%, 79.31%,50%) respectively ⁽¹⁵⁾. another study ⁽²⁰⁾ also, mentioned that Twenty-seven patients (75%) had microlithiasis confirmed by histology and nine did not (25%). EUS findings were positive in twenty-five patients with microlithiasis. Two patients had acute cholecystitis diagnosed at EUS that was confirmed by surgical and histological findings. In two patients, EUS showed cholesterolosis. EUS diagnosed microlithiasis in four cases not confirmed by surgical treatment. The EUS sensitivity, specificity and positive and negative predictive values to identify gallbladder microlithiasis (with 95% confidence interval) were 92.6% (74.2-98.7%), 55.6% (22.7-84.7%), 86.2% (67.4-95.5%) and 71.4% (30.3-94.9%), respectively. Overall EUS accuracy was 83.2%.⁽²⁰⁾

A recent study ⁽²¹⁾ aimed to evaluate the diagnostic role of EUS in common bile

duct stones. They found that EUS as diagnostic tool shows sensitivity, specificity, PPV, NPV and accuracy of 100%, 92.8%, 93.7%, 100% and 96.5% respectively. It can catch 15 true positive cases with only one false positive case and 13 of 14 true negative cases ⁽²¹⁾.

Another study ⁽²²⁾ focused on relatively hypoechoic areas at the cores of the polyps, reporting the presence of such hypoechoic cores on EUS to be a strong predictive factor for neoplastic polyps. The overall accuracy of EUS in differentiating neoplastic from non-neoplastic lesions is 86.5–97%. However, the accuracy of EUS in differentiating neoplastic from nonneoplastic polypoid lesions <10 mm was reported to be low ⁽²²⁾.

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neoplastic polypoid lesions <10 mm was reported to be low ⁽²³⁾.

In our study, regarding transabdominal US findings, 69 (69%) patients had NAD, 1 (1%) patient had polyps, 3 (3%) patients had contracted gall bladder, 26 (26%) patients had multiple stones, and 1 (1%) patient had both multiple stones and polyps. this result is in contradiction with a (15) recent study that found that transabdominal ultrasound was normal in all patients ⁽¹⁵).in this context. Another study ⁽²⁴⁾ estimated that abdominal ultrasound is looked upon as the best available exam for diagnosing gallbladder only because polyps, not of its accessibility and low cost, but also because of its good sensitivity and specificity. The polyps can be located, counted, and measured with ultrasound, and the three layers of the gallbladder wall and any abnormalities can be viewed ⁽²⁴⁾

A different study ⁽¹⁶⁾ reported that, in 71 patients suspected to have CBDS by

TAUS, only 46 patients had stone (65%). sensitivity, specificity, positive predictive value and negative predictive value for TAUS were 80%, 87.5%, 65.5% and 56%, respectively ⁽¹⁶⁾.

Another study ⁽²⁵⁾ reported that, TUS successfully identified patients with cholelithiasis but failed to diagnose 60 patients with dilated CBD. Moreover, most of patients with bulky pancreas on TUS revealed to be definite pancreatic mass on further EUS evaluation ⁽²⁵⁾.

In our study, there was a significant moderate agreement between EUS and transabdominal US findings (k= 0.491, P value <0.001). This result is in the same line of study number ⁽²⁶⁾ that found that the approaches two were statistically equivalent as demonstrated by the McNemar conditional 1-sided test for equivalence of sensitivities (P = .27) in their comparison of Primary upper endoscopy (EGD) and transabdominal US (TUS). (26) Also. study number ⁽²¹⁾.reported that, there are no statistically significant differences were found between EUS and MRCP in the diagnosis of CBD stones, but а trend toward higher sensitivity and specificity for EUS compared to MRCP was evident.⁽²¹⁾.

Study number concluded that, EUS is a very useful technique for the indication of cholecystectomy in patients with microlithiasis sludge typical and symptoms of biliary colic ⁽²⁷⁾ while, study ⁽²⁸⁾.concluded that, EUS seems to be a promising imaging method in the detection of microlithiasis in the gallbladder in patients with clear biliary colic and normal transabdominal US⁽²⁸⁾.

Conclusion

Our study demonstrates that Endoscopic Ultrasound (EUS) is a valuable tool for detecting gallbladder diseases, with a significant relationship and moderate agreement observed between EUS and Transabdominal Ultrasound (TAUS) findings. The high proportion of patients with abnormalities detected by EUS. including polyps, mud, microlithiasis, and multiple stones, underscores its efficacy in comprehensive evaluation. The size categorization of stones and polyps further contributes to the nuanced understanding of the pathology. The most common indications for EUS, such as unexplained abdominal pains, recurrent acute pancreatitis and suspected small pancreatic mass or cysts, align with its recognized utility in assessing abdominal conditions. These findings emphasize the potential superiority of EUS over TAUS in diagnosing gallbladder diseases, especially when a detailed assessment is crucial.

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