Role of EUS-guided FNA in detection , localization &confirmation of focal liver lesions(FLLs)

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ABSTRACT

Background: EUS & EUS-FNA is an important modality for detection , localization & confirmation of many body lesions , including FLLs .Many limitations & restrictions were seen in this study might affect the accuracy of this study , ex. Comparison of different modalities of imaging , which is performed by different medical individuals . This fact definitely can affect the real aim of the study . A brief & simple review to the results gained , emphasized that it's a cost benefit medical procedure , that effectively can change the medical map of the disease(that's called , clinical impact) . Therefore it's not a strange matter to see EUS or EUS-FNA is included in guidelines or diagrams of any abdomino-visceral lesions . **Aim:** Detection of any FLL by EUS either accidently or intendedly , with Localization of these FLL & its relation to other abnormal masses in body & a trail to describe them if possible , with Confirmation of these FLL by FNA . Also , Comparing the accuracy of EUS-FNA findings by other means of imaging , & to reveal if there is any clinical impact of these findings on the clinical map of managements . **Design :** A prospective study . **Location:** gastroenterology & Hepatology Teaching Hospital / Medical City (Baghdad Iraq) . **Patients & Methods:** The data collected include ; age . sex , brief medical history , data of images used (U/S , CT scan & MRI) , EUS findings(location , size , echo texture , margins , numbers , indications , No. of needle passes , needle gauge , elastography .All patients were aged >20 years and had hepatic masses detected by US,CT & MRI. **Results:** The detection rate of FLL in this study of patients was 23 of 701 patients (3.28%). The mean age was significantly higher in this group (65.9±13.4 vs. 55.3±15.9 years) , with (P value 0.000) & with slight non-significant female predominance in gender (P value 0.73) was noticed . A total of 23 patients were registered in this study. Sixteen of twenty three(16/23) patients(69.5%) were diagnosed with malignancy, while benign lesion in 7 of 23 (30.5%).

Tissue acquisition was prospering in 23 of 23 (100 %)patients. Specimens were picked up from the left lobe in 15 patients (65.2%)and from the right lobe in 3 patients (13.1%), while others 5 patients (21.7%) had focal liver lesions(FLL) in both lobes . The average(median) tumor size by EUS was 18 mm .The median number of needle passes was 5 . At pathological level, tissue specimens were determined as adequate in 21 of23patients (91.3%). The pathological diagnosis was negative for malignancy in2 patients (8.69%) . But malignant tissue seen in16 of 23 patients (69.5%),also suspicious for malignancy in 4 patients (17.3%), and atypical in 1 patients (4.3%) .

The final diagnosis was based on Histocytological findings , any means to get a tissue(either biopsy or aspirate) by EUS, trans-cutaneous, endoscopy, surgical) in 20/23 patients (86.9%) and follow-up clinically with(imaging studies ,tumor behavior or marker) in 3 patients (13.1%). Those, who were diagnosed by histocytology , diagnosis was really achieved with EUS-FNA in 17/23 patients (.73.9%), and the surgical specimens in the remaining 6/23 patients(26.1%) showed inconclusive cytological Complications was reported 3 patients(13%), 2 of them(8.6%) were complaining of abdominal pain , dealt with just observation, and simple analgesia . All other complication related to disease association(cholangitis, malignancy, jaundice)& not related to EUS- FNA intervention .

Clinical Impact of the study was widely variable , unfortunately four patients was lost from the study. Different categories were seen depending on the fate of illness . These were discussed in details elsewhere . Overlap between categories occurs intensively & widely affect the clinical course Accuracy of EUS-FNA comparing with other modalities (US ,CT ,MRI ,EUS- FNA)were expressed in terms of percentage were 44% , 62% ,85% , 91% respectively .

Conclusions: EUS-FNA with elastography demonstrates high sensitivity in the differentiation of benign and malignant solid masses. Accuracy and specificity are, ,however, " less favorable " . EUS elastography will therefore never replace tissue acquisition but should be part of the endosonographer's armamentarium to improve its diagnostic performance. EUS-FNA with elastography (although costly with long patient waiting list) is a cost benefit modality regarding detection , localization & confirmation any focal liver lesion .

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Introduction:

EUS uses the properties of endoscopy to introduce HF-US probe in the GIT to imagine the wall and nearby structures. EUS was introduced clinically in the early 1980s but did not receive considerable consideration and was not used widely until the 1990s .Studies reported very high total specificity (100%), sensitivity (96%) ;and for EUS-FNA in both small lesions (less than 2.5 cm) and larger lesions , due to its high resolution , in part, from the closeness of the transducer to the organ examined. EUS can struggle many of the restrictions of trans abdominal ultrasound, such as feeding ,fat and gas .

The practice of EUS-FNA has improved the overall diagnostic yield of EUS, improving the prognosis of patients for better & efficient management . EUS-FNA provides physicians with the cytological diagnosis of such lesions visualized by EUS and has also become a worthy diagnostic tool to deal with liver metastasis .

Echoendoscope: have a transducer positioned in front of the optic lens and are available in two different designs . ***linear-array*** instrument, the preferred choice for FNA, produces an oblique 160 degree range real-time view parallel to the shaft of the echoendoscope, permitting direct ultrasonographic guidance of the fine needle exiting the biopsy channel. Doppler (color) ultrasound allows for visualization of blood flow in vascular structures (Fig. 1).[6]

Radial scanning echoendoscope produces a 360 degree real-time view perpendicular to the shaft of the echoendoscope.

Today, early-stage cancers go undiagnosed mainly because of lack of the screening programs rather than technical limitations.(6-8) .Samples can be obtained effectively from small lesions(<20 mm). Tumors of less than 5 mm in diameter can now be detected by using high-resolution videoendoscopes with precise identification of FLL .

Role of the endosonographer. EUS-FNA sampling accuracy has been shown to increase from 33% to91% following a 2-months formal period of hard training . Accuracy is clearly operator dependent and correlates with experience. EUS-FNA cytology interpretation errors during the initial learning phase are primarily due to inadequate specimens. (15,16,17)

Needle type . The preliminary EUS guided biopsy needle was a 160-cm long, 0.8-mm diameter needle covered within a Teflon catheter. The material obtained with this needle was adequate and diagnosis highly accurate.[9,10] But most of experts , uses 19-, 22-, and 25-gauge (*Wilson-Cook needles)*. 22- and 19-gauge needles are favored for fluid collections and sampling of lymph nodes . A 25-gauge needle is routinely used for the sampling of most lesions and produces minimally bloody specimens ,since specimen adequacy and diagnostic accuracy are augmented by performing immunohistochemical (IHC) stains in cell-block slides. the use of 19-gauge Trucut needle may not increase diagnostic accuracy and specimen adequacy significantly as compared with EUS-FNA ,but instead, it may result in more frequent complications (i.e. infection and bleeding). [11] Although , Trucut needle does appear safe and accurate for the sampling of intestinal wall and abdominal masses .(12-13).Many studies , revealed that *continuous* rather than *intermittent* suction with smaller syringes (510 ml)provides optimal cellularity in EUS-FNA especially for LNs. [14]

Rapid interpretation of the smears increases the diagnostic yield,and allows for increases in sensitivity of near or higher than 90%, and specificity and positive predictive values of near 100%.

Its time-consuming & need special training. [20]

Risks and Complications: Although the risk appears slightly higher than that for standard EUS alone , the overall risk of complications from EUS-FNA is strangely low(1.6%).[21] Complications that may occur include bleeding ,aspiration pneumonia &perforation. [21] Acute extra luminal hemorrhage at the site of the aspiration occurs in 1.3% of patients.[21] Perforation and aspiration pneumonia are rare. Color Doppler assessment almost eliminates the risk of vascular perforation during lesion puncture but the risk of hemorrhage due to decompression of a vascular lesion in the vicinity of a cyst remains. Complications that may occur after the procedure include pancreatitis and infection . Acute portal vein thrombosis and a rare case of severe infection after sampling of a non cystic lesion have also been reported . [21] The antibiotic prophylaxis for patients with cysts and necrotic lesions after EUS-FNA is currently recommended by the **ASGE**. [22]

Tumor Seeding:Since surgical excision removes the needle pathway or the tumor responds to chemotherapy , therefore ,the incidence of needle track tumor seeding in malignancies evaluated by EUS-FNA is difficult to assess. A retrospective review identified that 1 of 46 patients (2.2%) had developed peritoneal carcinomatosis when EUS-FNA diagnostic modalities used for initial diagnosis. Peritoneal implants ,however, have been rarely reported.(23)

Liver:Low frequency EUS (5 MHz)allows for imaging of the majority of the liver; however ,"blind spots" exist near the dome and the outer surface of the right lobe. Right lobe of liver visualized by EUS through the gastric antrum and duodenal bulb/descending duodenum ,while left lobe of the liver is visualized through the proximal

stomach/distal esophagus and. ***EUS has sufficient resolution to detect and sample lesions as small as 5 mm in diameter or smaller***. (24) Smears from aspirates of the liver frequently show gastric contents and hepatocytes.

Regenerative nodules in a cirrhotic liver;. Smears show greater cell variability(polymorphic) than those of HCC (monomorphic) . Focal nodular hyperplasia hyperplasia ,although more common in women, is not related to contraceptive use, while adenoma is seen in women taking oral contraceptives;. A clue for diagnosis, bile ductal epithelial cells and fibrous tissue fragments are seen in nodular hyperplasia and absent in adenoma.

Benign Hepatocytes: Benign hepatocytes are arranged in organized small clusters and sheets of variable size. infrequent capillaries maybe present but peripheral endothelial rimming is absent . Binucleation is common.

Hepatocellular Carcinoma: HCC can present as single or multiple liver masses simulating a metastatic malignancy .Its the most common primary liver malignancy and cirrhosis is the main underlying pathology .EUS-FNA cytology is safe and reliable.. Diagnosis of HCC can generally be made by EUS-FNA without complications .(25)

Early experience suggests that this EUS-FNA may be used in patients with poor liver function and coagulation disorders Poorly differentiated HCC may be difficult to differentiate from metastatic deposits and *immunohistochemistry*, clinical history, and comparison with tissue from other malignancies are helpful for diagnosis ,while Well-differentiated HCC resembling normal liver. *Reticulin stain* is useful to distinguish benign from malignant liver tissue ,

Metastasis: hepatic metastases are the most common liver neoplasms . Most common histological type is by sequence; adenocarcinoma, melanoma, small-cell carcinoma ,and neuroendocrine tumors among others (26).

EUS can effectively identify focal liver lesions as small as 0.3 cm that were not detected at CT, and can identify new or additional lesions (<0.5 cm in size) in 1/4 to 1/2 of patients and may change patient management in 3/4 of cases. Spiral CT and MRI have sensitivities of 93% and 98%, respectively for focal liver lesions greater than 1 cm but have sensitivities about 50% for metastases smaller than 1cm. PET scanning also may fail to detect small lesions.(26)

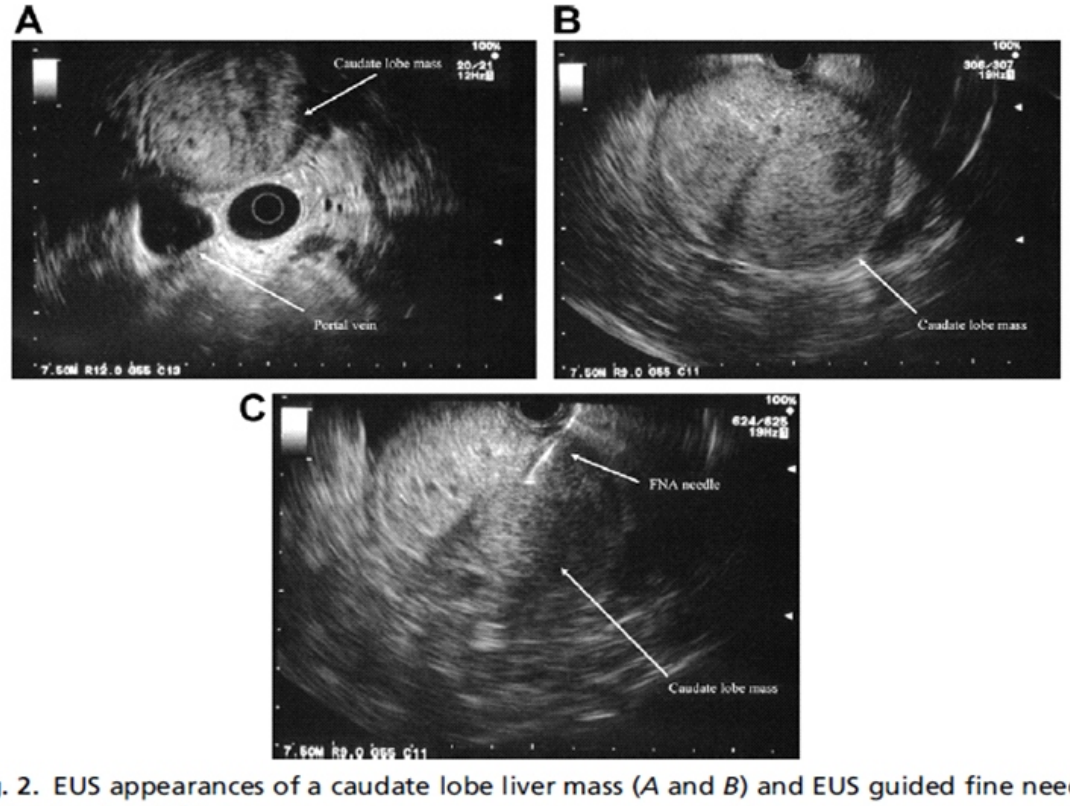

Fig. 2. EUS appearances of a caudate lobe liver mass (*A* and *B*) and EUS guided fine needle aspiration (FNA) (*C*).

EUS Versus CT Scan for Detection of the Metastases to the Liver

The presence of metastasis in the liver can profoundly affect the management and prognosis. therefore, radiologic evaluation of the liver is usually considered essential for the optimal staging of primary tumors of any visceral organ. CT scan imaging is the most frequently performed procedure for evaluating liver metastases (National Comprehensive Cancer (2005)guidelines) . Recent studies have shown many limitations of CT imaging for the detection of metastases of the liver.(30) Endoscopic ultrasound (EUS) is a well-established tool for the diagnosis and/or staging of esophageal, gastric, or pancreatic cancer and has appeared as an alternative tool for imaging the liver .(31)

Impact Of EUS On Clinical State

precise preoperative evaluation remains an essential part of the surgical treatment of Hepatocellular and metastatic liver carcinoma, as the extent of liver involvement may change clinical stage and management. Current preoperative radiologic imaging techniques ,each been limited in their ability to detect small hepatic lesions, (dynamic CT, CT angioportography, MRI, and trans abdominal US). Intraoperative ultrasonography (IOUS) with careful intraoperative palpation is currently the gold standard for the detection of small hepatic lesions. This technique has consistently been shown to be the most accurate method with greater sensitivity and specificity than any preoperative radiologic examination . [33,34] However,IOUS is invasive requiring laparoscopy or formal laparotomy. Recently, EUS-FNA has emerged as an important tool in the diagnosis and staging of malignant gastrointestinal tumors, especially pancreatic cancer .(34)

EUS is A Powerful Tool to Obtain Samples from Small Lesions: EUS, a fairly new modality, is more accurate than CT scan for detecting small lesions (<3.0 cm) and determining their resectability based on vessel invasion.(35) EUS-guided fine-needle aspiration (EUS-FNA) is a useful and accurate modality for characterizing lesions . EUS-FNA can be performed on small lesions, offering an opportunity for early detection, staging of malignancies and helping to avoid unnecessary surgeries. However, size of the lesion ,one of the morefrequently mentioned causes of false-negative results or inadequate sampling . [36] Many studies were undertaken to determine whether the size of a lesion affected the specimen adequacy and diagnostic accuracy for lesions aspirated by EUS-FNA.

EUS elastography: One of the major limitations of EUS, is the limited ability to determine the nature of solid lesions. Therefore , EUS may guide FNA for cytological diagnosis.

EUS-FNA, however ,may provide false-negative results for malignant lesions , may be unfeasible because of technical problems , or associated with a small, but not insignificant, morbidity. As a result , efforts to overcome these drawbacks , most recent US image processors provide elastography, a technique that permits the imaging and quantifying of the hardness of lesions with dedicated software. [37]

EUS elastography principles; based on the hypothesis that the compression of a certain tissue by an echo probe produces a smaller strain (displacement of tissue structure by another) in hard tissue than in soft tissue. Consequently, by calculating the elasticity of tissue, it is possible to discriminate benign (soft) tissue from malignant (hard)tissue.

strain ratio ; The recent introduction of second-generation EUS elastography allows quantitative analysis of tissue toughness(hardness); the simplest of these techniques uses the ratio of the elasticity of a certain mass to that of a nominated reference region within adjacent soft tissue.

The most important benefit of EUS elastography is that it can be done in real time during a diagnostic examination with instant information provided to the endosonographer that can affect the management by demarcation of a lesion and more precise targeting of FNA, ,without need for broad training or costly devices or software.

Multiple diagnostic principles used for EUS elastography in the registered studies to differentiate benign and malignant solid masses ,' color pattern, hue histograms ,and strain ratio.

Color pattern ; as a qualitative pattern analysis is subjected to intraobserver and interobserver variability. ,,When color pattern is used,, there are different scales from red to blue .

hue histogram ; Compared with the strain ratio, hue histogram analysis may provide a more objective method of quantifying tissue stiffness by summing several frames of dynamic elastographic images of a preselected region of interest. This method was shown in a single-center study to have a good sensitivity at 93.8% but suboptimal specificity at 63.6%.

drawback of EUS elastography ; inability to control tissue compression. In external US elastography, it is well known that strong pressure on the target tissue can result in a misdiagnosis; which is almost impossible to avoid during EUS. Usually, no or minimal pressure is required to obtain a good compression from the pulsation of abdominal aorta.

Another trouble is when there is no or minimal soft tissue surrounding the target zone, such as with lymph nodes that are very close to the aorta or spine. In this scenario, artifacts caused by these extremely

rigid tissues could impede the acquisition of good-quality pictures.

Aims of study:

- Detection of any focal liver lesions(FLL) by EUS either accidently or intendedly , with Localization of these FLL & its relation to other abnormal masses in body & a trail to describe them if possible , with Confirmation of these FLL by FNA
- Comparing the accuracy of EUS-FNA findings by other means of imaging , & to reveal if there is any clinical impact of these findings on the clinical map of managements .

Patients & Methods:

Data collection : A prospective study was conducted in Gastroenterology & Hepatology teaching hospital , Medical City , Baghdad , Iraq . This study performed for Iraqi patients who underwent EUS for any indication (details below) from 1st of October 2016 until 1st of April 2018 (18 months). The data collected include ; age . sex , brief medical history , data of images used (U/S , CT scan & MRI) , EUS findings(location , size , echo texture , margins , numbers , indications , No. of needle passes , needle gauge , elastography .

All patients (it's not incidental) were aged >20 years and had hepatic masses detected by US,CT & MRI .No patient used antiplatelet agents within the last 5 days before the procedure. Written informed consent was obtained from all patients before the procedure.

All EUS procedures were done by a well, single expert & professional echoscopist (to lessen the variables abilities from individuals).

Linear array Pentaxendoscopy system (EG-3870UTK) with HitashiAvius echoscope was used for completion of study .

A combination of nil sedation or conscious sedation(benzodiazepine , pethidinei.v injected) on escalating dose according to needs for conscious sedation was administrated for all patients . Supplemental O2 was also given trans nasally sometimes accordingly .

Tissue acquisition was done for any accessible focal liver lesion using echo tip FNA needle , gauge 22 for all patients .

After careful assessment of the target lesion and local vasculature with EUS, including real- time Doppler, FNA was performed from the stomach or duodenum. The needle was advanced in the lesion under EUS guidance. Once the lesion was penetrated, the stylet was removed. Specimen was acquired by moving the needle to-and-fro within the lesion while applying negative pressure by using a 10mL syringe. Suction was released by closing the syringe lock, and the needle was finally detached. The aspiration was repeated until enough specimen was obtained, asdetermined by gross inspection.

Aspiration specimen were ejected onto slides by reinserting the stylet. The material on the slide was carefully inspected by the endosonographer after each pass to determine successful acquisition .Any big blood clot, was removed from the slide. If a specimen obtained by the first needle pass was bloody, EUS-FNA was performed without applying negative pressure. The specimen samples were smeared on slides for cytological examination ,fixed in 95% ethanol, and stained with H&E stain , & another sample is dry sample. Patients were supervised for immediate complications in the recovery room for1 h .

Statistical Analysis :

was conducted by using the available statistical package for social science software (SPSS- 2014) for all calculation , statistical significance were considered when p value less than 0.05 .

Data were expressed in simple measures of frequency , ratio ,percentage , range , mean, sensitivity ,specificity, accuracy, tables for explanation.

Limitation of Study :

Many limitations & restrictions was seen due to:

- Difficult patient follow-up (remote places) and use of phone to communicate with them .
- Delay in referral of patients , many reach beyond beneficial interventions .
- Comparison done with different modality of image which it's not done by single individual or uniform properties version of US , CT & MRI . While EUS done by same individual & system .
- At pathological level , many FNA done out-side our trusted pathological department (which might be not professional in FNA interpretation) .
- Some patients quit from study , & shift to other centers (in & outside Iraq)
- Some patients refuse to intervene .
- Some cases(FLL in Right lobe) were excluded from study, for financial & cost-benefit issues .

Results :

- Study was enrolled on (701) patients, over 78 weeks duration(18months) ,at rate of (8.98 patient/session).

-The detection rate of focal liver lesions(FLL) in this study of patients was 23 of 701 patients (3.28%).

After applying the inclusion criteria for patient selection to the sample , 2 groups of patients were found .

focal liver lesions(FLL) were detected on 23 patients (3.28 %) .

Patients who had no focal liver lesions(FLL) were detected in 678 patients (96.72%), & a selected 120 patients randomly (Double blind control) and matched them as controlled group . The mean age(SD) was (65.9±13.4 vs. 55.3±15.9 years),See table(1)below ;

Table 1 : Age & gender distribution in FLL patients & controlled group .

	Patients with FLL %	*Patients without FLL %*
Gender		
Male	*10 (43.1%)*	*55(45.8%)*
Female	*13 (56.9%)*	*65(54.2%)*
Age(years)		
Mean	*65.9±13.4*	*55± 15.9*
Range	*32 – 95*	*30 -93*
Total	*23*	*120*

A total of 23 patients were registered in this study. The baseline features of patients are briefed in Table (2).

Table (2) : The baseline features of patients who had EUS /FNA

Characteristics	N =23	%
Age (years)	65.9±13.4	
Sex(male /female)	10/13	
Type of FLL		
Benign	7	30.5%
Malignant	16	69.5%
Tumor Location		
Left	15	65.2%
Right	3	13.1%
Both	5	21.7%
Size of FLL (median),mm	18	

Sixteen of twenty three(16/23) patients(69.5%) were diagnosed with malignancy, while benign lesion in 7(30.5%). .Tissue acquisition was prospering in 23 of 23 (100 %)patients. Specimens were picked up from the left lobe in 15 patients (65.2%)and from the right lobe in 3 patients (13.1%),, while others 5 patients (21.7%) had focal liver lesions(FLL) in both lobes . The average(median) tumor size by EUS was 18 mm .The median number of needle passes was 5 .

At pathological level, tissue specimens were determined as adequate in 21 of23patients (91.3%). The pathological diagnosis was *negative* for malignancy in2 patients (8.69%) . But *malignant* tissue seen in16 of 23 patients (69.5%),also *suspicious* for malignancy in 5 patients (21.6%), and *atypical* in 1 patients (4.3%) . Table (3)

Table 3: Clinical properties and cytological Results of EUS /FNA

Characteristics	***N =23***
Site of biopsy	
Left	20
Right	3
Indication; EUS /FNA	
Concurrent FNA for pancreatic and liver lesions	13
Liver mass to assess primary lesion	5
Others	5
Number of needle passes	5
Technical success	23
Needle gauge, 22	22
Sample adequacy	23
Diagnostic categories	
Positive for malignancy	16
Suspicious for malignancy	5
Negative for malignancy	2

The final diagnosis was based on Histocytological finding(any means to get either biopsy or aspirate by EUS, trans-cutaneous, endoscopy, surgical) in 20/23 patients (86.9%) and follow- up clinically with (imaging studies ,tumor behavior or marker) in 3 patients (13.1%) Those, who were diagnosed by histocytology' ,

diagnosis was really achieved with EUS- FNA in 17/23 patients (.73.9%) ,,, and the surgical specimens in the remaining 6/23 patients(26.1%) showed inconclusive cytological findings on EUS-FNA. Table (4) .Category of Suspected maliganancy refers to entity of unproven Final diagnosis that necessate further workup to settle down diagnosis .

Table (4) ; Final diagnosis achieved by endoscopic U/S guided fine needle aspiration (Biobsy, Images, Clinically)

Characteristics	*No.23*	*%*
Final diagnosis		
Pancreatic CA with liver metastasis	7	30.4%
Cholangiocarcinoma	5	21.7%
Hepatocellular CA	1	4.3%
Ampullary CA with liver metastasis	2	8.6%
Gallbladder CA with liver metastasis	1	4.3%
Benign mass	7	30.4%
Procedures of final diagnosis		
Histocytological confirmation	20	86.9%
Cytological confirmation by EUS –FNA	17	73.9%
Histocytological confirmation by surgically resected specimen	3	13.1%
Clinical follow – up	3	13.1%

Complications was reported 3 patients(13%), 2 of them(8.6%) were complaining of abdominal pain , dealt with just observation, and simple analgesia . All other complication related to disease association(cholangitis , malignancy ,jaundice) & not related to EUS FNA intervention . See table (5) below ;

Table (5) ;Complication of EUS FNA

Complications	No.	%
Abdominal pain	2	8.6%
Fever	1	4.3%
Bleeding	Nil	
Perforation	Nil	

Clinical impact of EUS FNA was determined by the following table(6) , which involving the change in medical map according to the new evidences detected by EUS or EUS FNA ,Unfortunately some patient was lost from this study(4) patients . Avoidance to surgery means either it's a benign lesion , or case beyond surgery , while tumor upstage means local metastasis(invasion) or lymphadenopathy since usual previous image doesn't show these evidences . Down staging is vice versa to previous concept . Actually many patient refuse to do surgery for different reasons . Overlap between these categories occurs intensively & widely affect the clinical course .

Table (6) : clinical impact of EUS FNA on patient medical problem .

Clinical impact	No.	%
Avoided surgery	3	13%
Upstage tumor	6	26.1%
Downstage tumor	Nil	
Made Diagnosis	18	78.3%
Made Diagnosis & surgery avoidance	5	21.7%
Made Diagnosis & Upstage tumor	1	4.3%
Made Diagnosis & Upstage tumor & surgery avoidance	3	13%
Avoided surgery & upstage tumor	3	13%
No change	3	13%
Patient loss	4	17.4%

One of the objectives of this study is to compare the accuracy of EUS and other usual images(U/S , CT scan , MRI) for the detection of FLL .The standard for the diagnosis of the FLL was cytological confirmation . As mentioned in the beginning , EUS was done by a single echoscopist ,Abdominal US of the liver was performed with a different US machines, & operators .all CT examination & MRI was done in different centers(this obligate different operators & individuals) .

Regarding statistics used; Sensitivity; specificity; positive predictive value; negative predictive value; and accuracy of CT, MRI, and EUS , EUS-FNA were calculated and compared. High sensitivity test is reliable when its result is negative , since it rarely misdiagnoses those who have the disease so, a test with 100% sensitivity will recognize all patients with the disease by testing positive . A positive result in a test with high specificity is useful for ruling in disease As in table (7) below;

TABLE (7): Comparison of US, CT, MRI, EUS, and EUS-FNA for the detection of the FLL .

	No.	Sensitivity %	specificity %	Positive predictive value %	Negative predictive value %	Accuracy %
US	23	54	33	43	42	44
CT	17	69	61	64	63	62
MRI	20	85	83	86	85	85
EUS- FNA	23	90	92	90	90	91

Discussion :

EUS & EUSFNA is an important modality for detection , localization & confirmation of many body lesions , including FLL . But, it's to some extent is a new modality with an overall world studies isn't so wide , actually many studies is involved to only " tens " of patients . This study, is a humble trail to describe these aims in Gastroenterology & hepatology Teaching hospital (Descriptive study), some features have no comparable data in other centers , although denoted in this research .

Whether the institution of EUS FNA in this medical problem focal liver lesions(FLL) is a cost effective and practical depend largely on its success in detection , localization & confirmation of these focal liver lesions(FLL), as well as its clinical impact .

This current study focused on prevalence of focal liver lesions(FLL) during EUS (for any reason) which found to be low (3.28 %) which is consistent with other studies .Generally many centers have narrow base survey (tens or at most low hundreds of patients)indicating that its new & novel imaging modality (38,39,40,41,42). It might be due to the fact, that the clinical courses of EUS training is much longer & difficult than the usual percutaneous approaches . So a very low No. of echoscopist had these clinical courses , So this affect the total no. of patient involved in studies .

The mean age is elderly patients (65.9±13.4 vs. 55.3±15.9 years) , this might be attributed to disease innate nature & association . Since most of cases is either primary or secondary malignancy , which it is usually related to increased age due to more exposure to environments (40). Slight female predominance is non- significant,(No comparable data found ?).

Sixty nine percent(69.5%) of patients , found to be malignant , while 30.5% were benign . In "NowonEulji center" (38) prevalence was 80.9% & 19.1% respectively, while in "Charleston center" prevalence was 83%& 17% respectively (39). In "Massachusetts General Hospital" prevalence was 77.3% 22.7% respectively (40) . This study "clearly not comparable" Since we exclude many cases that found in right lobe (for financial issues)& emphasized on Lt or both lobe involvement .Also FLL related mainly to pancreatic tumor & HCC which has high prevalence in other countries rather in our society .

Tissue acquisition was prospering 100%, which resembling almost all studies , reflecting a fact that it doesn't depend only on medical personal, but also on techniqualy high quality instrument used, including FNA needle (Cook ,Expect™, Boston Scientific, Natick, Mass…etc.), echoscope system (most centers relay on Olympus in their researches with different versions, as in our center). Needle gauge was variable (19 ,22, 25) , and no study reveal important Significant of needle size , but they accentuate on size relation to complication especially near vascular mass , generally they recommend smaller size near vascular lesion (38) . In this study , we use a single size FNA needle(22 Fr) and we didn't face any overt bleeding complication .

Tumor location(in this study) was unilateral in more than ¾ of cases in a rate of Lt : Rt about 56.2% : 13.1% , while bilateral involvement was seen in 21.7% . NowonEulji Medical Center,(38),shows that Lt lobe : Rt lobe was 51.1% : 27.7% with technical success of tissue acquisition (30/30) 100% in Lt lobe &(16/17)94.1% in Rt lobe , these reflect that distance between echoscope tip and FLL location doesn't affect the result ,presumably due high quality instrument used & high expertise individual operators . Excitingly , our center have the same findings (100%) for both Rt & Lt lobes , also for the same above reasons & to some extent , due to our strategy of selection of FLL from Lt lobe .

However , in NowonEulji Medical Center, (38) , tissue adequacy was higher in Lt lobe (28/30) 93.3% *vs*Rt lobe (14/17)82.4% . while in this study, tissue adequacy was(15/15) 100% in Lt lobe & (1/3) 33.3% of Rt lobe . These may be due small sample size , study strategy of selection ,low frequency for more penetration(depth), therefore , affecting the resolution images (due to increasing depth>5 cm) making tissue sampling inadequate for histopathology . Its important to mention, that bilateral lobes involvement were discarded to obviate the masking results . In EUS ,precise topographic findings of liver(localization in Rt or Lt lobe) is some what difficult to interpret ,but distance can be determined , so we depend on usual images to determine the actual site.

The relation between No. of needle passes & size of FLL , seems to be a positive relationship . Average size of tumor(in this study) is 18 mm , with average needle passes of 5 . the clinical significance of No. of needle passes related to the incremental risk of internal bleeding, which its fortunately , nil in this study , comparing with Jorgen ten Berge et.al(39) which had minor bleeding that treated conservatively in 1/167 (0.6 %) ,providing that all studies don't recommend FNA from any vascular lesion , or even near vascular area to avoid complication . No research founded that had studied this incremental relationship statically .

In this study ,the pathological diagnosis was negative for malignancy in 2 patients (8.69%) . But malignant tissue seen in 16/23 patients (69.5%), suspicious for malignancy in 4 patients (17.3%), and atypical in 1 patients (4.3%) . These are descriptive pathological findings , and many trails to compare them with other researches was failed , since there

are wide variation in findings of other researches (10 researches,(38,…..47) reflecting that type of FLL , whether benign or malignant , primary or secondary had no real or statistical association , and it's not more than a matter of accident of getting a disease .

Final diagnosis that based on histocytology was achieved in 20/23 patient (86.9%) , and clinical follow up(imaging studies, tumor behavior or markers) in 3/23 patients(13.1%), comparing with DongwookOh,et.al (38) that shows 89.4% of cases achieved by histocytology & 10.6% by clinical follow up . Among those(in this study) diagnosed by histocytology(20 patients) , diagnosis really achieved by EUS FNA in 17/23 patient(73.9%),, and by surgical specimen in the remaining 6/23patients (26.1%) showed inconclusive cytological finding on EUSFNA. In DongwookOh,et.al (38) patients who were diagnosed by histocytology, diagnosis was achieved by EUS‑FNA in 38 patients (80.9%). Two patients (4.3%) were diagnosed by US‑guided liver biopsy, and the surgical specimens in the remaining two patients showed inconclusive histological findings on EUS‑FNA. Diagnostic accuracy was statistically significant in both studies (P value in DongwookOh,et.al =0.04 , while in our study P value=0.038) .

Complications were reported in 3/23 patients(13%) ,these were simple & dealt with conservative measures and simple analgesia . These indicate that EUS FNA is safe modality of investigation, that have many advantages(Diagnosis by relatively safe procedure ,no harmful radiation, FNA take once needed in a single session).These are consistent with Jorgen ten Berge et al (38) regarding the level of severity(minor or major complication) but incomparable regarding incidence which is 4% . These may be attributed to technical issues , including no antibiotic use(pre-procedure) especially in obstructive jaundice, that might increase infection . Increasing bleeding tendency on No. of needle passes might lead to bleeding .In Jorgen ten Berge et al, (1)patient(0.6%) died 36 hours after procedure, EUS done for a pancreatic mass, a liver lesion was incidentally identified. The patient was suspected to have an occluded biliary stent at the time of EUS based on a rising bilirubin . So , cholangitis developed and the patient died finally .

Clinical impact of EUS-FNA is a corner stone in instituting it as a crucial modality of investigation . Since it can affect the clinical course of the disease especially if diagnosed much early .These involving the change in medical map according to the new evidences detected by EUS or EUS FNA .

Returning back to table (6) , patients who have making diagnosis is 18/23 (78.3%) which is remarkable percentage and consistent with Jorgen TenBerge et al(71.1%) .Among these 3/23 patients(13%) avoided surgery , while in Jorgen ten Bergeiit was (9.1%) . Tumor upstaging was 26.1% , 5% respectively , may be due to depending on imaging of not well trained operators . Down staging was nil , 0.6% respectively , which is consistent .

EUS can identify a primary & secondary tumor in a large percentage of cases in which US, CT, and MRI fail to do so. A possible cause for this is that the resolution of EUS is higher than CT.(48,…,51) . Higher resolution imaging, better access to lesions in the posterior aspect of the liver, and lack of interposed viscera and vascular structures are possible explanations.

One of the main drawbacks of EUS-FNA of the liver is the inadequate depth of penetration of HF (7.5-12 MHz). Although the resolution is improved at these higher frequencies, the depth of examination is limited to 5 to 6 cm, and thus the remote part of the right lobe of the liver cannot be regularly visualized. Thorough hepatic examination may be promising with newer instruments with lower frequencies.

The demand to localize the primary malignancy in state of liver secondaries is controversial .These will affect the next step in treatment map (especially in primary pancreatic tumor with new modality of treatment) . This applied also on colorectal CA with liver secondaries .

Real diagnostic accuracy of EUS FNA is interpreted in Table (7) , showing that EUS FNA have high sensitivity & specificity comparing with other imaging modality (proposing that these modalities have is optimal conditions) . Pankaj Singh et al (41) shows The diagnostic accuracy of US, CT, MRI, and EUS/EUS-FNA were 38%, 69%, 92%, and 94%, respectively . while the data recorded in this study was 44% , 62% , 85% ,91 % , respectively . These are little bit below the previous data , may be attributed to the wide difference & variability of available imaging tools & individuals . In Pankaj Singh, et al (42), The diagnostic accuracy of EUS/EUS-FNA and CT scan was 98% and 92%, respectively . But , generally these certified that EUS FNA is a crucial diagnostic tool with multi- advantage issues .

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