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EUS-guided fine-needle liver biopsy in pediatric patients using a modified technique with one-pass, one-actuation wet suction

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ABSTRACT

Background and aims:

Liver biopsy (LB) can be a valuable tool to determine the etiology of pediatric liver disease. There is limited data of the role of EUS-LB in children. We have evaluated the efficacy and the safety of a modified technique (M)LB in high risk of bleeding or obese children. Additionally, we aimed to compare the tissue yield of EUS-(M)LB and percutaneous (PC) approach.

Methods:

A retrospective analysis comparing EUS-(M)LB and PC-LB in children at a tertiary referral center. All consecutive children referred for PC-LB and EUS-LB who had an unexplained liver test abnormality after exclusion of biliary disorders from march-2017 to August-2018 were included. EUS-(M)LB consists of a one pass wet suction technique using a 19-gauche core needle. Comparison between total specimen length (TSL) and number of complete portal triads (CPTs) were performed.

Results:

There were 28 EUS-(M)LB and 28 PC-LB pediatric cases. The median (IQR) age was 14.5 years (13.4-16). The median TSL was 8.6 (5.8-9.6) in EUS-(M)LB cases and 7 cm (7-9) in PC-LB cases (P =0.788). The maximum intact specimen was 2.8 cm (EUS-(M)LB) and 1.6 cm (PC-LB) (P =0.009). The mean (SD) number of CPTs per sample was 28.2 (7.3) and 11.6 (2.1), respectively (P =0.001). Adverse events included once case of self-limited abdominal pain in the PC-LB group.

Conclusion:

EUS-(M)LB has the potential to be a safe and effective alternative diagnostic modality, at when compared to PC-LB, to evaluate children with unexplained liver test abnormalities who undergo EUS to evaluate biliary disorders.

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INTRODUCTION

Liver biopsy (LB) continues to be the clinical standard for the evaluation, staging and prognosis of hepatic parenchymal disease (1-2). Although the utilization of LB has decreased with the role of noninvasive scores, serological and radiological techniques; they are limited in identifying patients with intermediate fibrosis (2). Traditionally, percutaneous LB (PC-LB) is perceived as the gold standard. However, percutaneous approach has some limitations, such as the presence of ascites, patients at higher risk of bleeding and uncooperative children patients and procedure-related adverse events (0.09-3.1%), particularly in obese patients (3).

Endoscopic ultrasound (EUS)-guided interventions for the liver disease have rapidly evolved, with this new set of interventions branded as "Endo-Hepatology" (4-5). Enabling the endoscopist to new tools in the treatment of gastric fundal varices, performing intrahepatic portosystemic shunts and assessing the liver parenchyma for the degree of fibrosis and detecting occult malignancy (6). Advances in endoscopic doppler ultrasound can now be used to identify blood flow of interposed vessels during the puncture and portal hypertension, preventing unnecessary bleeds. EUS-LB is an attractive alternative to PC-LB with a small risk of post-procedure bleeding and pain (7-10). Moreover, EUS is useful to exclude biliary obstruction in the study of abnormal liver function test (LFT) in children patients.

EUS-modified LB (EUS-(M)LB), has been demonstrated to be a safe method with high histologic yields in adult patients (11). The Franseen needle seems to be more adequate of obtaining liver tissue than a fork-tip needle in adults, however additional studies need to be conducted to assess for this difference to extend to pediatric patient populations (12).

A head-to-head comparison of the histologic yield and safety of EUS-(M)LB with PC-LB in children patients has not been done. The purpose of this study was to determine the specimen adequacy and adverse events of EUS-(M)LB when compared to the tissue yield of PC-LB.

PATIENTS AND METHODS

Study design and study population

This was a single center retrospective study including pediatric patients referred for scheduled EUS-LB or PC-LB at a single tertiary center between March 2017 and August 2018. Patients were retrieved from a prospectively maintained database, identifying high risk of bleeding (defined as platelets <100.000/mL, coagulopathy (international normalized ratio >1.5) or obese subjects, with contraindication for PC-LB, who underwent EUS to evaluate for biliary disease as a cause of abnormal LFTs. Antiplatelets were stopped 5 or 7 days before procedure. No patients had prescribed any anticoagulants. Exclusion criteria were patients whose parents/guardian did not provide informed consent, high risk patients for deep sedation (Comorbidities, respiratory distress or American Society of Anesthesiology class IV-V) and patients with focal hepatic lesions. Both cases involving EUS-(M)LB with PC-LB methods were retrospectively identified. This study was approved by the local Institutional Review Board at Baptist Medical Center.

Data collection

We collected data on patient demographics such as age, gender, clinical indication and date of LB procedure. For all biopsies (EUS-(M)LB and PC-LB), electronic medical records were retrospectively reviewed to include data for the following categories: total specimen length (TSL), maximum specimen length (MSL), complete portal triads (CPTs), pathology result and adverse events. Only patients with exclusion of biliary pathology were included in the study.

Endoscopic Ultrasound modified biopsy technique

All EUS-(M)LB were performed by an experienced endoscopist (J.N). Parents were carefully informed about the procedure of LB including risks, benefits and limitations and signed a written consent. All patients were sedated with propofol administered by an anesthesiologist.

The EUS study was conducted with a linear array echoendoscope (GF-UE160-AL5, Olympus America, Center Valley, Pa). EUS-(M)LB under real-time ultrasound guidance was performed by using a 19-gauge needle (Sharkcore, Medtronic, Sunnyvale, Calif). The needle was primed with saline solution and maximal (20 mL) suction was applied via a syringe after the needle had entered the liver under direct ultrasound guidance. Before the needle puncture of the liver, color doppler imaging was used to ensure no major vascular structures were in the trajectory of the needle. A rapid puncture using a one 7 cm actuation technique was used to obtain the sample. The 19G core needle was passed into the liver and approximately 1 cm, with the three-way stopcock closed (without suction) (Fig 1). The remaining 7 cm of the needle was passed into the liver parenchyma. The liver was accessed utilizing a transgastric (left lobe) or transduodenal route (right lobe) at discretion of the endoscopist. Then, negative suction was applied and opening the threw-way stopcock. The needle was slowly withdrawn about 3 and the tissue acquisition into the bore of the needle, under wet suction, displace the saline solution into the syringe. This maneuver notified to the endoscopist to turn off the suction, by closing the threw-way stopcock

After the procedure, patients were observed for immediate adverse events for at least 30 minutes before being discharged pre and post-procedure antibiotics were not given. All adverse events were documented.

Percutaneous biopsy technique

The PC-LBs were performed by interventional radiologists at Baptist Medical Center with an automatic 19-gauge tru-cut needle (biopsy gun) (CareFusion, McGraw Park, IL) under real-time US guidance. In all patients, the operation site was sterilized with 10% povidone iodine and after waiting for one minute, skin antisepsis was made with 70% alcohol. Local anesthesia (Prilocain, Citanest, AstraZeneca, Germany) was then applied. A small incision was made in entry site of the needle.

Sample processing

Biopsy specimens were place into a 10% formaldehyde solution and blood clots were separated (Fig 2). The specimens were processed by the pathology department. Specimens were then stained with hematoxylin and eosin and immunochemistry (Fig 3). Quantification of TSL, MSL and CPTs was assessed to provide both a histologic diagnosis.

Statistical analysis

Data was collected on a spreadsheet. Descriptive statistics were used to illustrate categorical and continuous variables. Normally distributed values were shown as mean ± standard deviation (SD) or as median and interquartile range (IQR) when appropriate. Student t or nonparametric test were used to compare continuous variable and X^2 test or Fisher´s exact test was used for categorical variables, wherever appropriate. A P value of < 0.05 was considered statistically significant.

RESULTS

A total of 56 pediatric patients underwent LB, after the exclusion biliary disorder, in the setting of abnormal LFTs. There were 28 patients in the EUS-(M)LB (6 high risk of bleeding patients or 22 obese patients) group and 28 patients in the PC-LB groups with a median (IQR) age was 14.5 years (13.4-16), 32 male (57.1%).

The results are described in table 1. EUS-LB of both regions produced significantly more tissue in terms of intact maximum specimen length (ISL) (2.8 *versus* 1.6 cm, *P* = 0.009) and number of CPTs compared with PC-LB (28.2 *versus* 11.6, *P* = 0.001, respectively). EUS-(M)LB did not provide a statistically significant difference in TSL compared with PC-LB (8.6 *versus* 7 cm, *P* = 0.788). Overall, nearly half of patients had a steatosis-related diagnosis (n= 24, 42.9%); Twelve patients presented with hepatic steatosis and twelve patients had nonalcoholic steatohepatitis. The Non-alcoholic fatty liver disease Activity Score (NAS) includes steatosis, lobular inflammation, and

hepatocyte ballooning. The NAS ranged 3-4. Rest of histologic diagnosis included drug induced liver injury (n=8, 14.3%), acute Hepatitis C grade 3 and stage 0 (n= 4, 7.1%), extra/intrahepatic cholestasis (n= 4, 7.1%), autoimmune hepatitis grade 1 and stage 3 (n= 4, 7.1%) and normal LB (n= 12, 21.4%). The comparison of demographics, outcomes and pathological diagnosis between EUS-(M)LB group and PC-LB group are summarized in the table 1.

PC-LB was associated with an episode of abdominal pain controlled with intravenous acetaminophen (1.78%) immediately post-procedure. No patient in the EUS-(M)LB had any reported adverse events.

DISCUSSION

The present case-matched study displays a retrospective analysis including pediatric patients undergoing LB comparing EUS-(M)LB and PC-LB for evaluation of abnormal liver function tests in the absence of biliary pathology.

Traditionally, liver biopsy is done via percutaneous or transjugular approaches. These methods have some disadvantages such as increased risk of bleeding and pain. EUS-guided liver biopsy is an emerging alternative, and may be useful in pediatric patients with contraindications to PC-LB, including ascites, obesity, higher risk of bleeding, lack of cooperation or technical failure (4). The 28 high risk of bleeding or obese pediatric patients who underwent EUS-(M)LB technique yielded adequate specimens for diagnosis of 100% of patients evaluated. Additionally, showcasing the potential of EUS-(M)LB was the statistically significant increase in the median of TSL, ISL and median number of CPTs when compared to conventional techniques such as the (PC-LB) (13-15).

Our study described a similar outcome as a multicenter trial conducted in adult patients assessing the efficacy of EUS-(M)LB over existing techniques for obtaining liver specimens (16). We reported significantly more tissue for ISL (28 versus 16mm), TSL (86 versus 70mm) and for the number of CPTs (28.2 versus 11.6) obtained using EUS-

(M)LB comparing with PC-LB; and meeting the criteria recommended by international liver societies (3, 17, 18).

It has been believed that the diagnostic yield of LB sample is determined by the size and the number of the needle passes. This phenomenon was reported in case series of 22, 10 and 9 patients who underwent EUS-LB guided 19G Tru-cut and non-Tru-cut needles whose median number of passes was 2-3 (15, 19, 20). The median TSL and CPT were smaller at 36.9 mm and 9, 14 mm and 9.2, 12 mm and 7, respectively.

Furthermore, EUS-(M)LB was found to be safe in this analysis. EUS-(M)LB had no complications and increased intact specimen length and CPTs. In this study, there was one reported case of moderate abdominal pain after PC-LB which quickly resolved with analgesic therapy; However, no complications occurred in the EUS-(M)LB group. Similar results were found in the adult patient population in a prior study (7).

There are some limitations that should be mentioned as a retrospective single-center study with a small sample size. Despite screening the database thoroughly, we cannot exclude some degree of underreporting. Secondly, the results may not be generalizable because the yield EUS-(M)LB depends on the endoscopist who performed the procedure; in our study there is an experienced single operator (J.N).

In conclusion, EUS-(M)LB displays much promise as a safe and effective alternative approach compared to PC-LB in the evaluation of high risk of bleeding or obese pediatric patients with unexplained liver test abnormalities. Moreover, EUS-(M)LB can be used to obtain the LB during the endoscopic procedure and exclude biliary disease during the same session.

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FIGURES

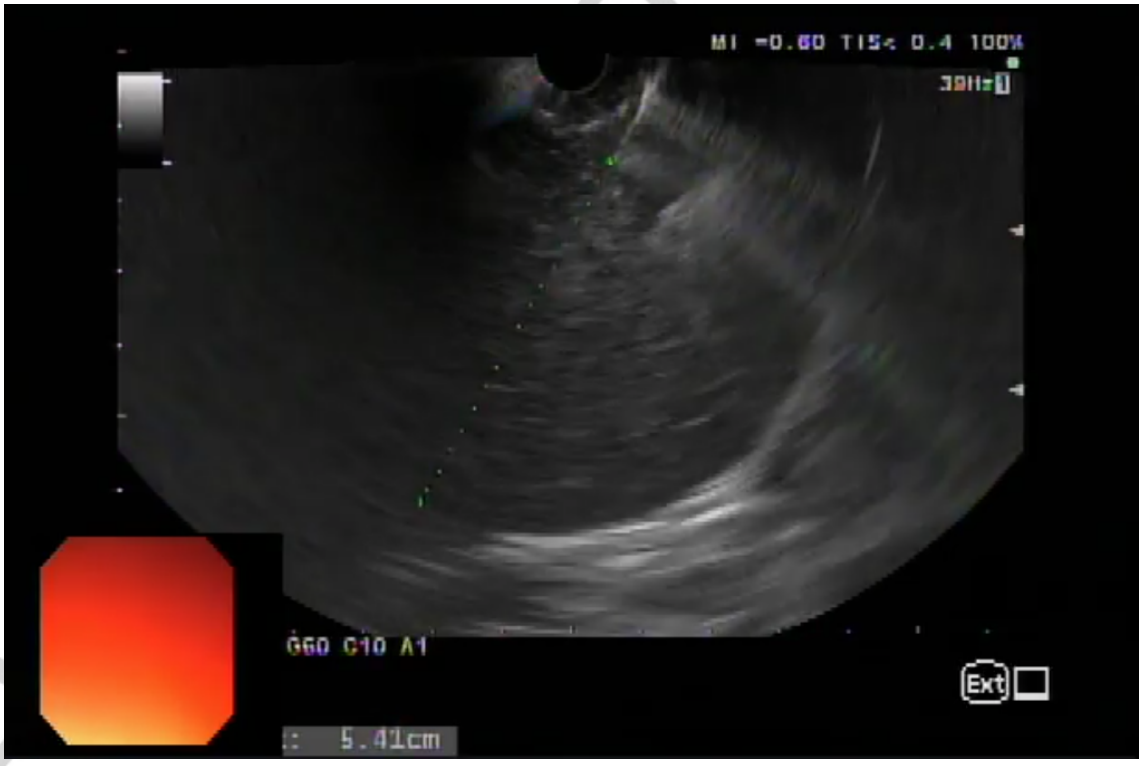

Figure 1: 19-gauge needle advancing through the liver using one pass to obtain optimal viable tissue sample.

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Figure 2: EUS-guided fine needle biopsy specimen of liver using a modified technique with one-pass, one-actuation wet suction

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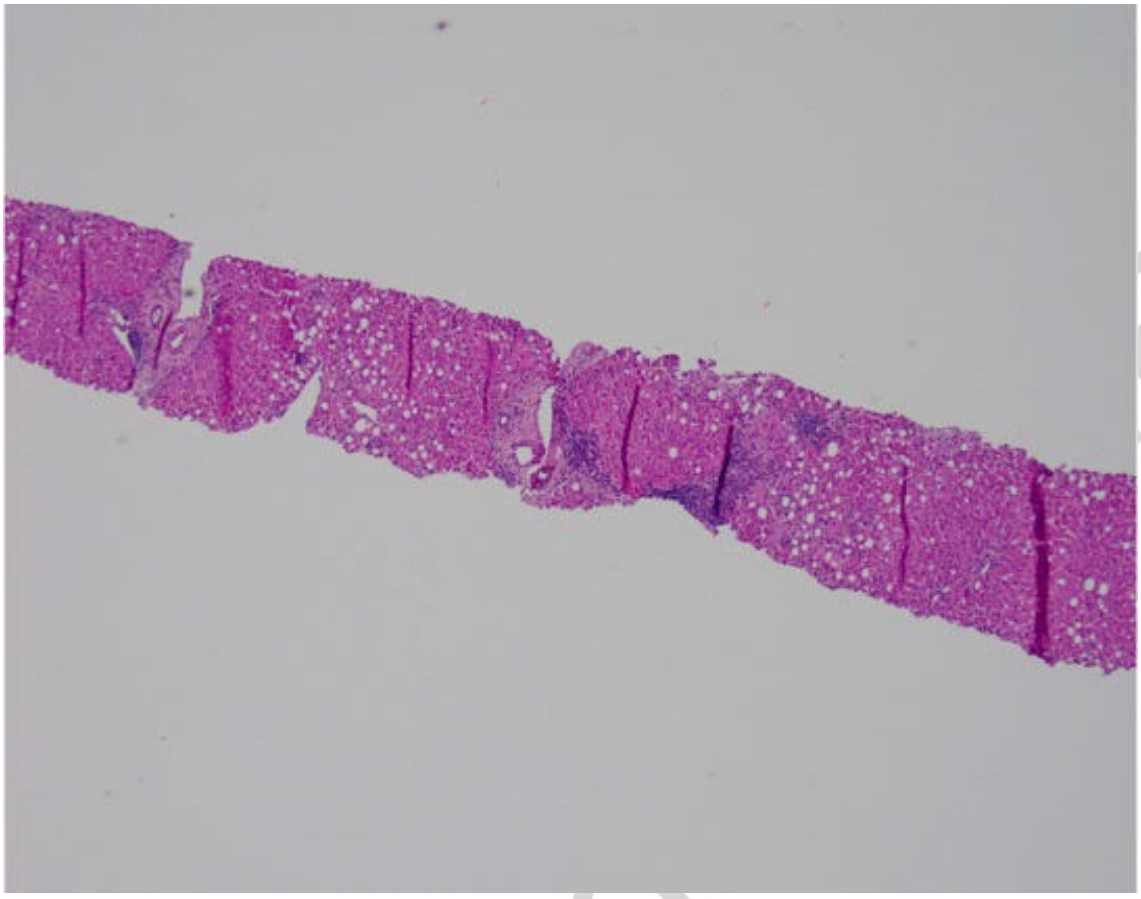

Figure 3: Histologic view of EUS-(M)LB sample.

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TABLE

Table 1. Comparison of patient demographics and outcomes between Endoscopic ultrasound-(M)LB and Percutaneous-LB

Parameters	**Pediatric EUS-(M)LB***	**Pediatric PC-LB †**	***P* value**
Number of patients (N)	28 patients	28 patients	
Age, median, (IQR‡), years	15 (14 – 16)	14 (12 – 16)	0.514
Body mass index (Kg/m^2), mean (SD¶)	33.6 (3.3)	26.8 (2.1)	0.01
Gender, n (%) - Male - Female	 16 (57.1%) 12 (42.9%)	 16 (57.1%) 12 (42.9%)	0.195
American Society of Anesthesiology class (ASA), median (IQR)	2 (1 – 3)	2 (1 – 3)	0.414
Pre-biopsy, labs, median (IQR) INR Platelets (thou/uL) GPT/GOT (mg/dL) Bilirubin (mg/dL)	 1.8 (1.3 – 2.0) 133 (76 – 196) 82/71 1.8	 1 (0.6 – 1.3) 184 (165 – 279) 73/56 1.2	0,094
Indication for liver biopsy, n (%)	Abnormal LFTs§ (100 %)	Abnormal LFTs (100 %)	
Intact maximum specimen length, median (IQR), cm	2.8 cm (2.4 – 5.7)	1.6 cm (1 – 2)	0.009
Total specimen length, median	8.6 cm (5.8 – 9.6)	7 cm (7 – 9)	0.788

(IQR), cm			

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Total specimen length, median (IQR), cm			
Number of CPTs[||], mean (SD[¶])	28.2 (7.3)	11.6 (2.1)	0.001
Risk of adverse event, n (%)	None (0 %)	1 (1.78%)	
Pathological diagnosis			0.316
- Steatosis-related (non-alcoholic, hepatitis)	8 (28.6%)	16 (57.1%)	
- Hepatitis C-related	4 (14.3%)	0 (0%)	
- Drug-induced hepatitis	4 (14.3%)	4 (14.3%)	
- Cholestasis (extra/intrahepatic)	0 (0%)	4 (14.3%)	
- Autoimmune hepatitis	4 (14.3%)	0 (0%)	
- Normal	8 (28.6%)	4 (14.3%)	

* EUS-(M)LB, Endoscopic ultrasound- modified Liver Biopsy; [†] PC-LB, Percutaneous Liver Biopsy; [‡] IQR, Interquartile range; [§] LFTs, liver function test; [||] CPTs, complete portal triads; [¶] SD, Standard desviation.