Received: 28 May 2024 | Accepted: 26 November 2024

DOI: 10.1002/jpn3.70001

JPGN

ORIGINAL ARTICLE

Endoscopy and Procedures

Pediatric endoscopic ultrasound-guided liver biopsy: 3-year experience

Talia S. Schwartz[1] | **Marialena Mouzaki**[1,2] | **Lara Berklite**[3,4] | **Oscar F. Lopez-Nunez**[3,4] | **Alexander Miethke**[1,2] | **Stavra A. Xanthakos**[1,2] | **David S. Vitale**[1,2]

[1]Department of Pediatrics, University of Cincinnati, Cincinnati, Ohio, USA

[2]Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

[3]Division of Pathology and Laboratory Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

[4]Department of Pathology and Laboratory Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA

Correspondence

David S. Vitale, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave., Cincinnati, OH 45229, USA.
Email: david.vitale@cchmc.org

Funding information
None

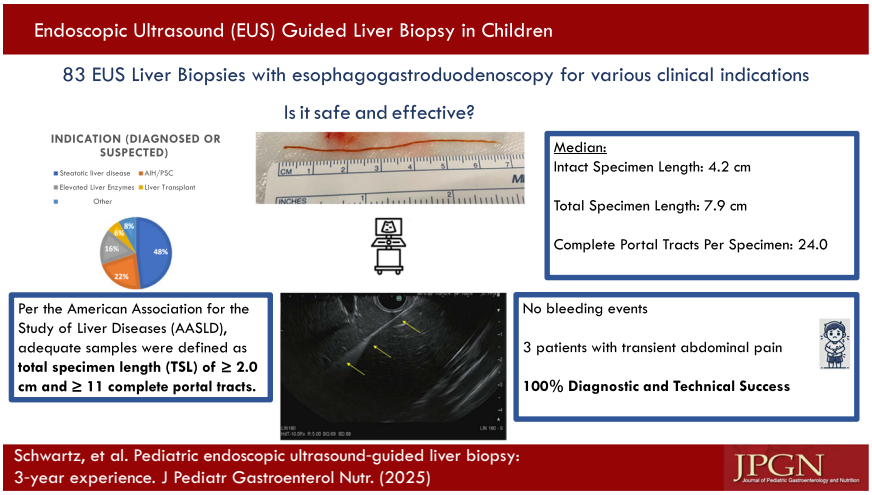
Abstract

Objectives: Liver biopsy is the gold standard for diagnosing and staging liver diseases. Endoscopic ultrasound-guided liver biopsy (EUS-LB) has been reported in adults with equivalent or better safety profiles than percutaneous liver biopsies. The aim of this study was to retrospectively assess the safety and efficacy of EUS-LB in pediatric patients.

Methods: This was a retrospective chart review of consecutive pediatric patients undergoing EUS-LB at Cincinnati Children's Hospital Medical Center from March 2020 to April 2023. Patients ≤21 years old were included. EUS-LB was performed via fine-needle biopsy technique with transduodenal and/or transgastric approach. Histology was independently reviewed by one of two expert pathologists, including length (cm) and complete portal tract (CPT) number per the American Association for the Study of Liver Diseases (AASLD) adequacy criteria. Demographics, clinical data, technical information, diagnostic success, and adverse events were recorded.

Results: Eighty-three patients were included in the analysis, with various indications that required liver biopsy. All biopsies achieved diagnostic and technical success, with 77 (93%) meeting both AASLD criteria for adequacy. Most patients (57, 69%) underwent biopsy of both hepatic lobes, with an overall median of two needle passes. Total specimen length was a median of 7.9 cm (interquartile range [IQR] 5.2–10.3), and the median maximum intact specimen was 4.2 cm (IQR 3.1–5.4). The median CPT number was 24 (IQR 17–32) per patient. Four mild adverse events (5%) occurred; none involved bleeding.

Conclusions: EUS-LB was well tolerated and yielded samples that were technically and diagnostically successful in a pediatric population, with comparable safety to percutaneous liver biopsy.



KEYWORDS

children, endoscopy, liver disease, obesity

1 | INTRODUCTION

While noninvasive techniques to assess liver disease, such as the use of biomarkers, transient elastography, and magnetic resonance imaging, are improving, liver histology remains the gold standard to diagnose and/or stage most liver diseases, particularly in children in whom noninvasive measures are less robust.[1–3] Currently, in large pediatric hospitals, percutaneous ultrasound-guided liver biopsies are typically performed by interventional radiologists.[4–6] However, endoscopic ultrasound-guided liver biopsies (EUS-LB) are increasingly being used in adult practice as an alternative method of obtaining tissue samples.[7,8] With EUS-LB, liver samples are obtained at the time of an upper endoscopy via transgastric or transduodenal needle passes, with the assistance of endoscopic ultrasonography.[9] Studies have shown EUS-LB to be highly technically and diagnostically successful.[10] Furthermore, the endoscopic approach to obtaining liver samples has been associated with low morbidity and mortality, even as compared to conventional percutaneous approaches.[9,10] To date, there is a paucity of pediatric data on the use of EUS-LB, with one small study reporting safe and effective EUS-LB in a limited cohort of 28 patients with obesity or increased bleeding risk.[7]

While percutaneous liver biopsies are considered generally safe, adverse events may include pain, bleeding, and inadequate sample.[6,11] The American Association for the Study of Liver Diseases (AASLD) defines optimal liver biopsy samples as those that have a total specimen length (TSL) of ≥2.0 cm and include ≥11 complete portal tracts (CPTs).[12] With regard to optimal sampling, percutaneous biopsies have been shown to yield adequate samples in 97%–99% of cases; however, they can be limited by sampling error.[4,11] The latter is particularly important for conditions that may have unequal distribution, such as metabolic dysfunction-associated steatotic liver disease (MASLD). EUS-LB offers the ability to biopsy both the right and left hepatic lobes,[13] hence increasing the diagnostic yield. Furthermore, EUS-LB provides the opportunity to concurrently obtain endoscopic evaluations in

What is Known

- Endoscopic ultrasound-guided liver biopsy (EUS-LB) is becoming standard practice in adult gastroenterology.
- Multiple meta-analyses have shown safety and efficacy with adequate samples from EUS-LB in adults.
- Pediatric experience with EUS-LB is lacking.

What is New

- This is the first comprehensive report of a clinically diverse pediatric cohort undergoing EUS-LB.
- EUS-LB was found to be low-risk in children with no bleeding events in this cohort.
- EUS-LB provided adequate specimens per American Association for the Study of Liver Diseases guidelines in 93% of patients and provided a tissue diagnosis in 100%.
- EUS-LB is a potential alternative to percutaneous biopsy in children, particularly when it can avoid a secondary procedure or anesthesia.

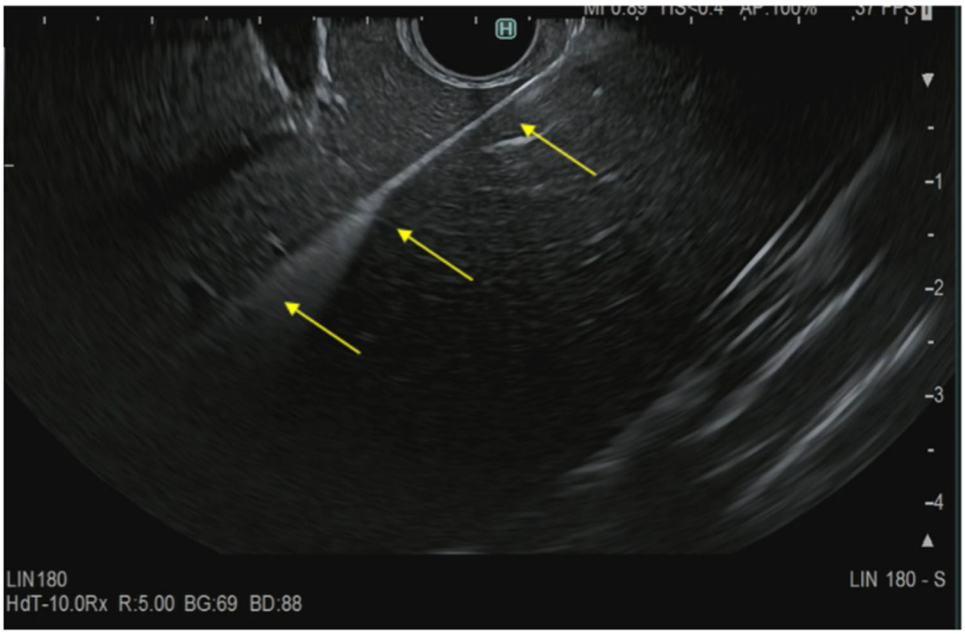


FIGURE 1 Endoscopic ultrasound image of fine needle biopsy of liver.

patients who have symptoms or presentation requiring other endoscopic evaluation.

The objective of this study was to assess the feasibility and safety of EUS-LB obtained for clinical indications in a large pediatric cohort at a quaternary care center.

2 | METHODS

This was a retrospective chart review of consecutive pediatric patients undergoing EUS-LB at Cincinnati Children's Hospital Medical Center from March 2020 to April 2023. All patients ≤21 years old were included. Patients ≥15 kg were considered for EUS biopsy when simultaneous endoscopic evaluation was indicated. Institutional review board approval (IRB# 2021-0343) was obtained to retrospectively collect data with waiver of consent.

Typically, patients selected for EUS-LB at the institution were patients requiring a liver biopsy and a concurrent esophagogastroduodenoscopy (EGD) evaluation, such as those needing assessment or treatment of esophageal varices or evaluation of abdominal pain, eosinophilic esophagitis, or gastroesophageal reflux disease. EUS-LB was performed by a single interventional endoscopist, via fine needle biopsy with a 19-gauge Franseen needle, using a one actuation, wet suction biopsy technique with a transduodenal and/or transgastric approach (Figure 1). Fresh biopsy specimens were collected (Figure 2) and patients were admitted for observation for at least 6 h postbiopsy, per institutional protocol. One or two lobes were biopsied

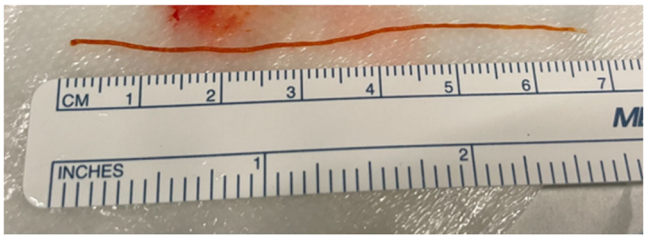


FIGURE 2 Endosopic ultrasound liver biopsy specimen.

based on endoscopist preference and clinical indication. Typically patients with suspected MASLD had both lobes biopsied, as did patients with uncertain diagnoses at the time of the procedure. If a good first pass (typically transduodenal right lobe) specimen was obtained in a patient with an established diagnosis, a second pass (transgastric left lobe) was often avoided.

For the purposes of the study, patient demographics, such as age, sex, ethnicity, anthropomorphic data, and indication for biopsy, were collected from the electronic medical record. Preoperative laboratory values including partial thromboplastin time and international normalized ratio were recorded as well. The number of needle passes and the number of lobes biopsied were retrieved from procedure reports. Liver biopsy histology was independently reviewed by one of two expert pathologists (L. B., O. L. N.) to evaluate specimen length (intact and total) and the number of CPTs per core and per total specimen. Per the aforementioned AASLD criteria, samples were defined as adequate or inadequate. Technical and diagnostic success were defined as obtaining adequate liver

tissue and diagnosing and, therefore, staging a liver condition, respectively. Charts were reviewed, including electronic medical record connecting features (e.g., Care Everywhere) to assess for any adverse events recorded during the procedure, the admission, or within 2 weeks post-EUS-LB.

Statistical analysis was performed to calculate medians and interquartile ranges (IQR) for continuous variables and proportions for categorical variables. The difference in sample adequacy was compared between patients with one versus two liver lobes biopsied using logistic regression.

3 | RESULTS

Eighty-seven patients underwent EUS-LB during the study period; four were excluded due to age >21 years, leading to a study cohort of 83 patients. Thirty-six (43%) patients were female, with a median age of 16 (IQR: 13–18) years (Table 1). Indications for biopsy included MASLD ($n = 40$, 48%), autoimmune hepatitis and/or primary sclerosing cholangitis ($n = 18$, 22%), elevated liver enzymes ($n = 13$, 16%), postliver transplantation indications ($n = 5$, 6%), or other ($n = 7$, 8%). The top indications for concurrent EGD were abdominal pain, evaluation for eosinophilic esophagitis, or gastroesophageal reflux disease. Some patients did also have concurrent colonoscopy or other endoscopic evaluation for various indications.

TABLE 1 Demographics and laboratory results, $n = 83$.

Age (years)	16 (13–18)
Sex, *n* (%female)	36 (43%)
Weight (kg)	77.8 (58.8–100.2)
BMI (kg/m^2)	28.5 (22.9–35.5)
n (%) in overweight/obese BMI range	56 (64%)
BMI z score (range)	–3.1 to 3.1
Percent body fat	43.8 (38.4–49.4)
Indication for liver biopsy, *n* (%)	
Steatotic liver disease	40 (48%)
AIH/PSC	18 (22%)
Elevated liver enzymes	13 (16%)
Postliver transplantation indications	5 (6%)
Other	7 (8%)
INR	1.06 (1.0–1.1)
Platelet count × 1000 cells/μL	267 (209–314)

Note: Data presented as median (interquartile range) or *n* (%).
Abbreviations: AIH, autoimmune hepatitis; BMI, body mass index; INR, international normalized ratio; PSC, primary sclerosing cholangitis.

The youngest patient was 6.9 years old and weighed 34.6 kg, and the smallest patient to undergo EUS-LB was 7.4 years old with a weight of 24.4 kg. BMI z-score (–3.1 to 3.1) spanned a full range of pediatric weight criteria from underweight to class III obesity (>2 standard deviation).[14]

Most patients (57, 69%) underwent biopsy of both hepatic lobes, with an overall median of 2 (IQR: 2–2) needle passes. TSL was a median of 7.9 cm (IQR: 5.2–10.3) and the median maximum intact specimen was 4.2 cm (IQR: 3.1–5.4), with a median of 24 CPTs (IQR 17–32) per patient (Table 2).

All biopsies achieved diagnostic and technical success, with 77 (93%) meeting both AASLD criteria for optimal adequacy. The $n = 6$ inadequate biopsies did not meet AASLD criteria due to CPTs < 11, despite adequate TSL ≥ 2.0 cm in four patients (4.5, 3.9, 3.0, 2.2 cm) and only two with inadequate TSL (1.1 and 1.1 cm). Patients with only one hepatic lobe biopsied more frequently had an inadequate specimen, although this did not reach statistical significance (odds ratio 3.9, 95% CI 0.67–22.8, $p = 0.13$). Three patients who underwent biopsy of both hepatic lobes ($n = 3/57$, 5%) had significant findings present in one lobe, but not the other. These included one patient with fibrosis identified in one lobe only, one patient with discordant level of fibrosis in each lobe, and another with more significant inflammatory changes in one lobe allowing a definitive diagnosis of autoimmune hepatitis in only one of the biopsied lobes.

There were four adverse events (5%). Three patients developed transient abdominal pain in the immediate postoperative period and one patient with splenomegaly, portal hypertension, and prominent gastric collateral vessels had splenic tissue acquired with one needle pass. Of the patients who developed transient abdominal pain, two had both lobes biopsied and one had a single lobe biopsied. There were no bleeding complications. Finally, no other complications were noted in the 2-week period postprocedure.

TABLE 2 Liver biopsy sample data, $n = 83$.

Maximum intact specimen length (cm)	4.2 (3.1–5.4)
Total specimen length (cm)	7.9 (5.2–10.3)
Number of complete portal tracts per specimen	24 (17–32)
Both lobes biopsied	57 (69%)
Adequate specimen (per AASLD guidelines)	77 (93%)
Technical success, *n* (%)	83 (100%)
Diagnostic success, *n* (%)	83 (100%)

Note: Data presented as median (25th–75th percentile) or *n* (%).
Abbreviation: AASLD, American Association for the Study of Liver Diseases.

4 | DISCUSSION

This is the first retrospective, single-center, cohort study of EUS-LB performed in children with varying risk stratifications and clinical indications. Our results highlight that EUS-LB is both diagnostically and technically successful, as well as safe. Almost all samples were of adequate length (81/83, 98%) and a large majority of biopsies (79/83, 95%) yielded samples with adequate CPT counts per AASLD recommendations.[12] No biopsies needed to be repeated. Adverse events were infrequent (5%), mild, and self-limited, without any bleeding complications.

A significant diagnostic benefit of EUS-LB is being able to obtain samples from both lobes of the liver, which is not traditional practice with percutaneous liver biopsies. This approach may increase the diagnostic yield, as shown in three patients in our study with discordant findings between lobes. Most pediatric liver diseases can have heterogeneous parenchymal involvement;[15–17] therefore, sampling from both lobes increases diagnostic accuracy. In terms of sample adequacy (length and CPT number), it is possible that sampling only one lobe also increases the risk of obtaining inadequate specimens. Inadequate samples were obtained in four of 26 (15.4%) patients who underwent a single lobe biopsy and in two of 57 (3.5%) who underwent biopsy of both lobes. Despite these few inadequate samples per AASLD criteria, 100% of samples provided diagnostic success. Image-guided percutaneous biopsies in children have been shown to be insufficient to make diagnoses in between 0% and 19% of biopsies.[18,19]

As seen in the adult literature, we observed a low rate (5%) of complications with pediatric EUS-LB performed in our center with no serious adverse events or bleeding.[9] As per our institutional protocol for percutaneous liver biopsy procedures, patients were observed for at least 6 h after their procedure, which enabled us to comprehensively assess for all immediate postoperative complications. The most reported symptom was abdominal pain ($n = 3$, 4%), the origin of which was not clear. Considering that these patients also underwent endoscopic evaluation, it is not possible to distinguish if the pain was a result of the liver biopsy or the other endoscopy, as even EGDs have a reported 2% frequency of postprocedural pain.[20] In our cohort, there were no bleeding complications in the immediate postprocedural window, which is the most concerning complication of liver biopsies in general.[4,11,21] Typically, bleeding postliver biopsy manifests within 6 h and has been reported to occur in 0.8%–3% of biopsies obtained through the percutaneous approach.[4,6,22] In our study, despite sampling both lobes of the liver in the majority of patients, there were no bleeding complications in any patient within 2 weeks after the procedures. Thus, there were no serious adverse events. While the results of our study are reassuring, it is imperative to perform larger, prospective studies of pediatric EUS-LB to better estimate the safety profile.

A large differentiator between EUS and standard percutaneous biopsy is the need for endoscopy. This may increase the time and the cost of the procedure.[23] In this study, all patients were undergoing an endoscopy for clinical indications and also required a liver biopsy. The speed, safety, and cost-effectiveness of EUS-LB for patients who do not need concurrent luminal exploration need to be compared against percutaneous liver biopsies in future studies.

Our population had a wide range of BMI z-score, spanning a full range from underweight to class III obesity, yet were able to tolerate the procedure with quality samples obtained. Particularly for patients with class III obesity, there can be difficulty in obtaining optimal samples percutaneously due to significant central adiposity, such that a transjugular approach is now widely used in adult patients with class II/III obesity.[24] Furthermore, patients with obesity are more likely to have MASLD, which has a patchy parenchymal distribution and may be more challenging to adequately stage with sampling of only one lobe. Obesity is also associated with gastrointestinal pathology (e.g., GERD, gallstones) that may benefit from sonographic and endoscopic evaluation. As such, EUS-LB may be the ideal procedure to obtain liver samples in patients with obesity but should be investigated further in both adult and pediatric populations.

The strengths of this study include its novelty as the first report of EUS-LB in a large pediatric cohort, with a wide variety of indications for biopsy, rendering the results more generalizable. Further, all samples were systematically reviewed and evaluated for specimen length and CPT number by two expert pediatric pathologists. Limitations include the fact that the study was conducted in a single quaternary referral center, with one pediatric advanced endoscopist performing all the EUS-LB. Due to the retrospective nature of the study, we may have underestimated the number of complications occurring after discharge, since it is possible, though unlikely, that patients may have sought care elsewhere without being captured in our external medical record system. Finally, our sample size of 83 did not permit a more precise estimation of complication risks that might emerge in a larger cohort.

In summary, we found that EUS-LB was well tolerated and yielded samples that were technically and diagnostically successful in a pediatric population. Future directions include larger, prospective studies comparing percutaneous ultrasound-guided versus EUS-LB in terms of safety, effectiveness, tissue quality, and cost. Furthermore, a needs assessment to guide training for the EUS-LB approach should be done to determine the number of endoscopists that will be

needed to be able to obtain these biopsies should the demand and need for pediatric EUS-LB increase. This will help further inform the development and curriculum of pediatric advanced endoscopy fellowship programs.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ORCID

Talia S. Schwartz http://orcid.org/0000-0001-5339-4451
David S. Vitale http://orcid.org/0000-0002-8994-7940

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How to cite this article: Schwartz TS, Mouzaki M, Berklite L, et al. Pediatric endoscopic ultrasound-guided liver biopsy: 3-year experience. *J Pediatr Gastroenterol Nutr*. 2025;80:920-925. doi:10.1002/jpn3.70001