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Safety and diagnostic accuracy of ultrasound-assisted percutaneous liver biopsy in pediatric patients: a retrospective single-center study

Maria Rogalidou[a]*, Aglaia Zellos[b], Kalliopi Stefanaki[c], Amalia Patereli[c], Konstantina Dimakou[d], Paraskevi Galina[e], David Oikonomopoulos[f], Alexandra Papadopoulou[a,d]

National and Kapodistrian, University of Athens, "Agia Sofia" Children's Hospital, Athens, Greece; National and Kapodistrian, University of Athens, Panagiotis & Aglaia Kyriakou Children's Hospital, Athens, Greece

Abstract

Background Liver biopsy remains essential for diagnosing and managing pediatric liver diseases, despite advances in noninvasive techniques. However, data on the current indications, diagnostic yield, and safety of ultrasound-assisted percutaneous liver biopsy in children are limited.

Methods We retrospectively analyzed 60 pediatric patients who underwent ultrasound-assisted percutaneous liver biopsy at Agia Sofia Children's Hospital between January 2018 and September 2025. Data collected included demographics, laboratory values, biopsy indications, histopathology and complications. Biopsies were performed under anesthesia using an 18-G Tru-Cut needle with real-time ultrasound guidance. Hemoglobin and hematocrit were measured pre-procedure and at 4 and 24 h post-procedure. Specimen adequacy was assessed by core length and number of complete portal tracts (CPTs).

Results The mean patient age was 8.6 years (range 1 month to 17 years), with weights from 2.9-65 kg. Indications included persistent hypertransaminasemia, cholestasis, autoimmune and metabolic liver disease, and post-transplant evaluation. Mean biopsy length was 1.12 cm (range 0.5-2 cm), with a mean of 11 CPTs (range 4-17). Histopathology revealed autoimmune hepatitis (AIH) in 38.3%, AIH with primary sclerosing cholangitis in 13.3% of patients with inflammatory bowel disease, and other diagnoses in the remainder. No major complications or postprocedural bleeding occurred. Hemoglobin and hematocrit remained stable, and all specimens were adequate for histologic assessment.

Conclusions Ultrasound-assisted percutaneous liver biopsy with an 18-G needle is safe, and yields sufficient tissue for diagnosis in pediatric patients. It continues to be indispensable for the definitive diagnosis, staging, and management of diverse liver diseases in children.

Keywords Pediatric liver disease, ultrasound-assisted percutaneous liver biopsy, diagnostic accuracy, complications, histopathology

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Conflict of Interest: None

Correspondence to: Maria Rogalidou, Division of Pediatric Gastroenterology, Hepatology and Nutrition, First Pediatrics Department, National & Kapodistrian University of Athens, "Agia Sofia" Children's Hospital, Papadiamantopoulou & Thivon St., Goudis, 11527, Athens, Greece, e-mail: rogalidoum@yahoo.com

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Introduction

Liver disease in childhood encompasses a wide range of conditions, including metabolic and genetic disorders, autoimmune liver disease, chronic cholestasis, infectious hepatitis, and complications following liver transplantation. Although noninvasive diagnostic modalities such as elastography, serum fibrosis markers, genetic testing and advanced cross-sectional imaging have greatly improved the evaluation of pediatric liver disorders, liver biopsy remains an essential tool in clinical practice [1,2].

In many pediatric patients, clinical presentation and laboratory findings are nonspecific, while several hepatobiliary diseases share overlapping phenotypes. Therefore,

histopathological, assessment continues to play a crucial role in establishing a definitive diagnosis, determining disease severity and guiding therapeutic decisions. Liver biopsy enables direct evaluation of architectural distortion, inflammatory activity, cholestasis, bile duct injury, steatosis and metal deposition, as well as accurate staging of fibrosis [1,2]. Certain conditions, such as autoimmune hepatitis, often require histologic confirmation to support the diagnosis and to grade inflammatory activity [3].

Despite ongoing advances in noninvasive biomarkers, none provide the comprehensive information needed to replace histology, particularly in early fibrosis, complex metabolic disease, or situations in which treatment decisions—such as initiation of immunosuppression or chelation—depend on precise tissue assessment. The widespread use of real-time ultrasound guidance has further improved the safety profile of percutaneous liver biopsy, with recent reports confirming its safety even in higher-risk groups, including post-hematopoietic stem cell transplantation patients [4].

Given its continued clinical significance, up-to-date data on the safety, indications, and diagnostic performance of liver biopsy in children remain essential. The present study aimed to contribute to this evidence base by assessing the indications, diagnostic yield and complication rates associated with ultrasound-assisted percutaneous liver biopsy in children.

Materials and methods

Data collection

Institutional Review Board and Ethics Committee approval was obtained for this retrospective study (20688/2.9.2025/ Approval 10/9/2025). A continuous 7-year period, from January 1, 2018, to September 10, 2025, was included. For each procedure, patient age, liver condition, blood parameters, histopathological findings and final diagnosis were recorded. Procedural complications early and late were assessed through retrospective patient's chart review.

Inclusion and exclusion criteria

All liver biopsies performed using a Tru-Cut needle with a semi-automatic biopsy system during the study period at Agia Sofia Children's Hospital were included. Biopsies performed using other needle types (e.g., Menghini needle), computed tomography-guided biopsies for focal lesions, or surgical or laparoscopic liver biopsies were excluded from the present study.

[a]Division of Pediatric Gastroenterology, Hepatology and Nutrition, 1st Pediatrics Department, National and Kapodistrian, University of Athens, "Agia Sofia" Children's Hospital, Athens, Greece (Maria Rogalidou, Alexandra Papadopoulou); [b]Second Department of Pediatrics, National and Kapodistrian, University of Athens, Panagiotis & Aglaia Kyriakou Children's Hospital, Athens, Greece (Aglaia Zellos); [c]Pathology Department, "Agia Sofia" Children's Hospital, Athens, Greece (Kalliopi Stefanaki, Amalia Patereli); [d]Gastroenterology Department, "Agia Sofia" Children's Hospital, Athens, Greece (Konstantina Dimakou, Alexandra Papadopoulou); [e]Radiology Department, "Agia Sofia" Children's Hospital, Athens, Greece (Paraskevi Galina); [f]Anesthesiology Department, "Agia Sofia" Children's Hospital, Athens, Greece (David Oikonomopoulos)

Procedure protocol

Biopsies were performed according to ESPGHAN guidelines [1] for pediatric patients, following the indications, contraindications and procedural approach established in our department. For all patients, the international normalized ratio (INR) was ≤1.5, and the platelet count was ≥60,000. Periprocedural antibiotics were not routinely given after biopsy.

Pre-biopsy workup

Before each liver biopsy, an initial laboratory assessment was carried out to evaluate the risk of bleeding. This evaluation included a complete blood count, prothrombin time, fibrinogen with INR, partial thromboplastin time and bleeding time. The patient's blood group was determined and packed red blood cells were reserved according to the patient's weight. Patients did not receive antiplatelet or anticoagulant medications.

Anesthesia

Biopsies were obtained under anesthesia according to the patient's age; the age-specific anesthesia protocols used were as follows:

Patients <10 years of age

Inhalational anesthesia was induced with sevoflurane at concentrations of 8%, then reduced to 6%, 4% and finally 2%, while maintaining spontaneous respiration and establishing intravenous access. Fentanyl was administered at a dose of 2 μg/kg. Spontaneous breathing was maintained, and the biopsy was performed at the end of inspiration. Sevoflurane was then discontinued, and patients were returned to their parents within approximately 20 min.

Patients ≥10 years of age

A 50% O_2/N_2O gas mixture was administered to facilitate intravenous access, followed by 50% oxygen. Fentanyl was administered at a dose of 2 μg/kg, followed by propofol at 2-3 mg/kg, while maintaining spontaneous respiration. The biopsy was performed at the end of inspiration. Anesthetic agents were discontinued, and patients were returned to their parents within approximately 20 min.

Liver biopsy procedure

Patients were positioned supine on the surgical table with the right arm placed above the head to allow optimal expansion of the intercostal spaces. Once the patient was in a stable position, and all parameters were confirmed to be stable after palpation, ultrasound marking of the site of the biopsy was conducted under guidance from a radiologist who, jointly with the gastroenterologist, confirmed the appropriateness of the biopsy site and needle tract. This included measurement of the distance from the skin to the liver capsule, identification of vessels or other anatomical structures to be avoided, and determination of the maximum safe needle insertion depth. The optimal biopsy entry point was marked on the skin using an indelible marker.

The skin was prepared and draped in a sterile fashion. Local anesthesia, typically 1% lidocaine, was administered along the upper border of the rib to minimize the risk of intercostal arterial injury, as these vessels typically course along the inferior border of the rib. Prior to injection of the anesthetic, aspiration was performed to ensure that the needle was not within a blood vessel.

Local anesthesia was delivered using a fine 23- or 25-G "finding" needle. After adequate anesthesia was achieved, a small skin incision was made using a No. 11 surgical blade. Biopsies were then performed using a Tru-Cut needle with a semi-automatic biopsy system and an 18-G outer coaxial cannula needle. The entire procedure is illustrated in Fig. 1.

After needle removal, manual pressure was applied to the biopsy site for several minutes, followed by application of a sterile bandage. Patients were then positioned in the right lateral decubitus position. Vital signs, including blood pressure and heart rate, as well as pain levels, were monitored every 15 min during the first h, every 30 min during the second h, and hourly thereafter until the hemoglobin measurement was obtained 4 h after the procedure.

All patients were admitted for a 24-h observation period to monitor for potential complications. Hemoglobin and hematocrit levels were measured at 4 and 24 h post-biopsy.

Histological specimens were reviewed by experienced pathologists. Specimen adequacy was assessed based on core length (cm) and the number of complete portal tracts (CPTs). The final diagnosis and any notable histopathological findings were recorded.

Results

During the 7½-year study period, 60 ultrasound-assisted percutaneous liver biopsies were performed in 60 patients. The main indications for liver biopsy in our cohort were persistent hypertransaminasemia, cholestasis, positive immunological work-up, metabolic associated liver disease, elevated liver stiffness on elastography, and reevaluation of clinically stable patients with autoimmune hepatitis to assess eligibility for treatment discontinuation; in addition, 1 patient with bone marrow transplantation was evaluated in order to exclude graft-vs.-host disease.

Patient ages ranged from 1 month to 208 months (median 64 months), with weights ranging from 2.9-65 kg. Fifty percent of the patients were male. A radiologist performed the ultrasound with a pediatric gastroenterologist–hepatologist performing the liver biopsy. Approximately 70% of the biopsies were performed by a single operator.

None of the patients experienced major adverse events or bleeding, as evidenced by normal pre- and postprocedural hemoglobin/hematocrit levels. The hematocrit and hemoglobin values 4 h before and 24 h after biopsy are shown in Table 1.

All biopsy specimens were evaluated at our institution by 2 experienced pathologists. In selected cases, the samples were independently reviewed by both pathologists to ensure

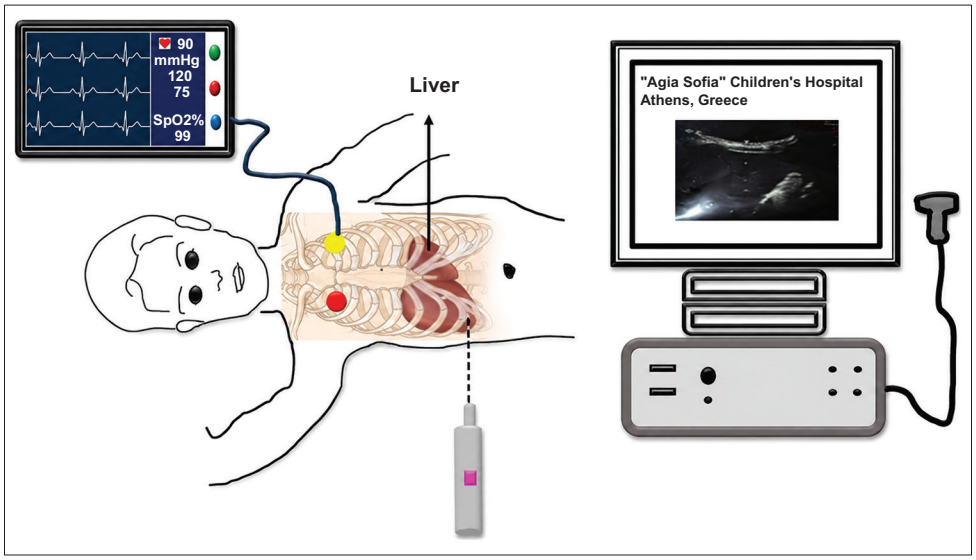

Figure 1 The liver biopsy procedure

Table 1 Hemoglobin and hematocrit values

Parameter	Before procedure	4 h after biopsy	24 h after biopsy
Hemoglobin	11.8 (8.8-15.5)	11.2 (8.8-15)	11.6 (9.4-15.7)
Hematocrit	36.9 (27.8-47.6)	35.2 (26.8-47)	35.8 (28.8-47.7)

Data are given as mean value with 95% confidence interval

diagnostic accuracy. No specimens were referred to a central laboratory or to an external institution abroad. Histology revealed liver sample tissue with a length of 1.12 cm (0.5-2 cm) and containing a mean of 11 CPTs (range 4-5 to 15-17 CPTs). The main histological findings are given in Table 2. Images from liver biopsies are shown in Fig. 2.

Table 2 Main histological findings from liver biopsy

Biopsy results	N	%
Non-pathognomonic	11	18.3
Acute hepatitis	2	3.3
Autoimmune hepatitis	23	38.3
Cholestatic/pharmaceutical-DILI	2	3.3
AIH+PSC+IBD	8	13.3
Patients with malignancies/BMT (for exclusion of GVHD) No specific findings	3	5
Neonatal hepatitis	3	5
Repetition of biopsy in AIH patients for treatment discontinuation	5	8.3
Resolving hepatitis	3	5

DILI, drug-induced liver injury; AIH, autoimmune hepatitis; PSC, primary sclerosing cholangitis; IBD, inflammatory bowel disease; BMT, bone marrow transplantation; GVHD, graft-vs.-host disease

Discussion

Liver biopsy in children is performed when histological evaluation is necessary to diagnose, stage, or guide the management of liver disease that cannot be clarified by less invasive tests. Such conditions include unexplained liver test abnormalities, chronic hepatitis, metabolic or storage disorders, autoimmune liver disease, cholestasis, hepatosplenomegaly of unknown cause, focal lesions, or evaluation of liver transplant complications or rejection. These indications are consistent with general biopsy guidelines, although specific pediatric series also highlight viral hepatitis, autoimmune disease and neoplasms as common reasons for biopsy in children [1,5-6].

Contraindications include significant coagulopathy, bleeding disorders, vascular lesions, uncorrectable ascites or extreme patient instability. Transjugular biopsy may be preferred when risks are elevated [5,6].

Over the past decade, ultrasound-assisted percutaneous liver biopsy has become the preferred technique in children, given its better safety and higher diagnostic adequacy. Recent studies demonstrate low rates of major complications and a high diagnostic yield.

Adequate liver biopsy specimens are generally evaluated by the number of portal tracts present. The American Association for the Study of Liver Diseases (AASLD) recommends at least 11 portal tracts to ensure accurate diagnosis and minimize sampling error [7]. In pediatric patients, obtaining larger cores can be technically challenging, so a pragmatic minimum of about 6 portal tracts is often considered sufficient for diagnostic purposes. Although smaller samples may still provide useful information, diagnostic accuracy improves with higher portal tract counts, emphasizing the importance of tissue integrity and careful handling [8]. In our study, the mean number of CPTs was 11, and although a few patients had fewer than 6, all biopsies were considered diagnostic by our pathologists.

Although liver biopsy specimens containing fewer than 11 CPTs may still yield valuable information, establishing a definitive diagnosis becomes more challenging in such cases. A small number of portal tracts increases the risk of sampling error and may limit the pathologist's ability to adequately evaluate liver architecture and detect subtle histologic changes. Careful handling and meticulous evaluation of smaller specimens are therefore essential to maximize diagnostic yield, particularly in pediatric patients, in whom obtaining larger biopsy cores can be technically difficult.

Notably, many liver biopsies fail to meet adequacy standards, despite adherence to recommended tissue length and portal tract criteria. While biopsy technique plays an important role, evidence suggests that tissue fragmentation during laboratory processing is a major and underrecognized contributor to inadequacy. A prospective quality improvement study demonstrated that targeted interventions—including staff education, reduced heat exposure during processing, optimized formalin fixation, and gentler tissue chilling—significantly decreased fragmentation rates. These measures increased the number of evaluable portal tracts per specimen without increasing tissue length, thereby improving overall biopsy adequacy. The findings underscore laboratory processing as a modifiable factor that can enhance liver biopsy quality and diagnostic yield [9].

A randomized study compared 16- and 18-G ultrasound-guided liver core biopsies to assess their effects on specimen adequacy and complications [10]. No significant differences were found in bleeding or postprocedural pain between the 2 groups. Although 16-G biopsies yielded slightly more portal tracts and 18-G biopsies produced slightly longer cores, overall specimen adequacy based on AASLD criteria did not differ significantly. The results indicate that both needle sizes are similarly safe and that biopsy gauge alone does not meaningfully improve liver biopsy adequacy.

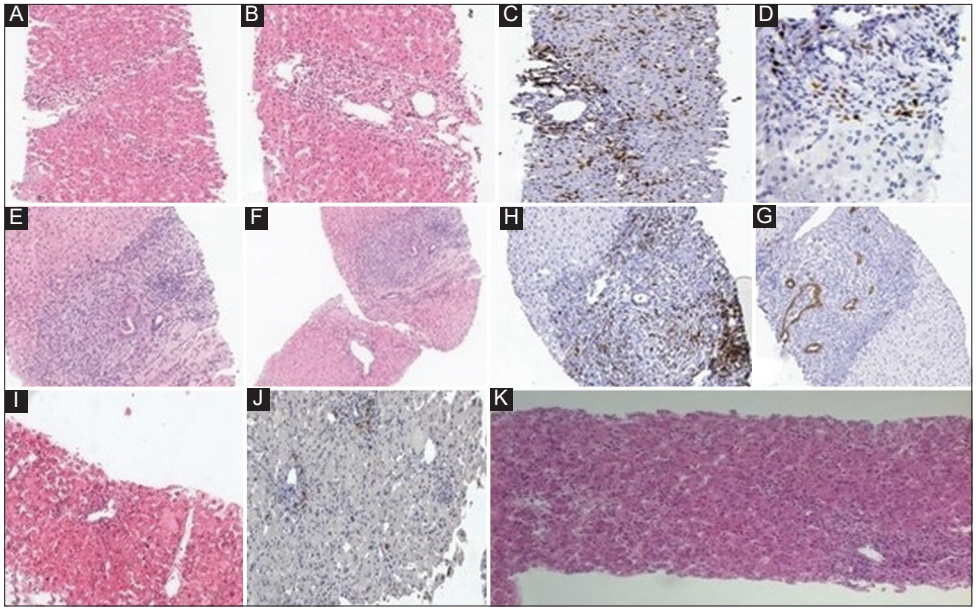

Figure 2 Autoimmune hepatitis (A, B C, D). (A) Expansion and infiltration of the portal tracts by lymphocytes, plasma cells, macrophages and eosinophils with focal piecemeal necrosis [hepatitis]. (B) Higher magnification. (C) CD3+ lymphocytes infiltrating a portal tract and parenchyma. (D) Immunohistochemical expression of MUM-1 in plasma cells infiltrating the portal tract. Overlap syndrome (E, F, H, G). (E) Expansion and moderate fibrosis of the portal, with brisk infiltration of the portal tract by lymphocytes, plasma cells and macrophages, eroding the bile duct. (F) Higher magnification. (H) CD3 immunohistochemical expression in portal lymphocytic infiltrate. (G) Cytokeratin 7 immunohistochemical expression in bile ducts. Neonatal hepatitis (I, J). (I) Expansion of the portal tract by chronic inflammatory cells, obvious bile ducts. Giant cell transformation of hepatocytes and foci of extramedullary hemopoiesis. (J) Cytokeratin 7 immunohistochemical expression in bile ducts. (K) Drug-induced liver injury. Lymphocytic infiltration of the portal tract and lobules. Necrotic hepatocytes and rare bile plugs

The consistent use of the 18-G needle in our cohort supports its suitability for pediatric patients of varying sizes and suggests that, when performed with proper technique, larger needles can be safely employed without increasing procedural risk. All biopsy specimens obtained were adequate for histopathologic evaluation, enabling reliable assessment of liver architecture and portal tracts. Importantly, no patients experienced adverse events, including significant bleeding, more than mild transient pain, or other procedure-related complications. These findings are consistent with prior comparative studies of 16- and 18-G needles, which demonstrate that both sizes are generally safe and that needle gauge alone does not significantly influence biopsy adequacy [10].

Additional evidence further supports the safety of pediatric liver biopsy in the modern era. A 2023 study, including 867 ultrasound-guided biopsies in pediatric and young adult patients, reported no hemorrhagic complications, and all reviewed specimens were diagnostically adequate [11]. Similarly, a pediatric cohort study conducted between 2014 and 2019 (n=102) found a complication rate of only 3.9%, reinforcing the view that contemporary ultrasound guidance substantially reduces procedure-related risk [12].

In a 6-year retrospective review of 223 liver biopsies performed at a tertiary pediatric center, 179 were percutaneous or transjugular procedures. No deaths or major complications were reported, and minor complications—most commonly pain—were infrequent, with most identified within 8 h of the procedure. These findings further support the safety of pediatric liver biopsy and suggest that, in the absence of early complications, discharge within 8-12 h post-procedure is appropriate [13].

In another study of 275 ultrasound-guided liver biopsies performed in 190 children, 3 major and 28 minor bleeding events were reported, with no procedure-related mortality. Administration of low-dose acetylsalicylic acid within 5 days prior to biopsy was not associated with an increased risk of bleeding, whereas use of low-molecular-weight heparin and biopsies targeting focal lesions were linked to a higher bleeding risk. Acute liver failure significantly increased the likelihood of major complications [14].

In our cohort, approximately 70% of the biopsies were performed by a single experienced operator, which may have contributed to procedural consistency and the low complication rate observed. This concentration of procedures, however, may limit the generalizability of our findings to centers with less operator experience or greater procedural variability.

A systematic review and meta-analysis of 30 cohort studies (2010-2020; n=64,356) reported major complications in 2.4% of cases (mortality 0.01%, hospitalization 0.65%, major bleeding 0.48%) and minor complications in 9.5%, mainly mild pain (12.9%). Technical failure occurred in 0.91% of procedures. Younger patients and those with severe liver disease had higher risks of hospitalization and major bleeding. These results confirm that, while percutaneous liver biopsy is generally safe, patient age and disease severity influence the risk of complications [15].

In children undergoing outpatient percutaneous liver biopsy, same-day observation (≤8 h) appears safe and well-

tolerated. In a retrospective review of 112 patients, no major complications or acute hospitalizations were observed, and minor interventions such as analgesia or fluid boluses occurred within the initial observation period [16]. Compared with overnight monitoring, same-day observation was associated with significantly lower healthcare costs. These findings suggest that, with appropriate risk assessment, brief postprocedural monitoring may be a feasible and cost-effective strategy for low-risk pediatric patients. Although our study followed patients for 24 h, the absence of adverse events indicates that alternative, shorter observation policies could be considered.

In a review of 626 liver biopsies in 497 children, complications occurred in 4.8%, mostly subcapsular hematomas, all detected within 8 h. Risk factors such as needle size or number of passes did not affect outcomes. With an 8-h observation period, outpatient pediatric liver biopsy is safe and could reduce hospital costs [17].

Compared to liver biopsies performed by interventional radiologists, ultrasound-assisted percutaneous biopsy performed within the pediatric hepatology team offers practical advantages. Conducting the procedure in-house allows seamless coordination with clinical and anesthesia teams, optimizing workflow and reducing potential delays. Ultrasound-guided liver biopsy is safe and effective in pediatric patients, providing a high diagnostic yield with low rates of major complications. Outcomes are similar whether performed by interventional radiologists or pediatric gastroenterologists, highlighting the value of real-time ultrasound guidance, regardless of the operator's specialty [18].

In conclusion, ultrasound-assisted percutaneous liver biopsy appears to be a safe and effective diagnostic tool in pediatric patients. In our 7½-year experience, all 60 biopsies yielded adequate tissue for histopathological evaluation, enabling reliable assessment of liver architecture, portal tracts, and disease-specific features. No major complications, including bleeding or other significant adverse events, were observed. These findings support the safety of the procedure when performed under real-time ultrasound guidance with appropriate preprocedural assessment and anesthesia.

Our results support the continued role of liver biopsy in children, particularly in the diagnosis and management of autoimmune liver diseases, metabolic disorders, cholestatic conditions, and post-transplant evaluation, where noninvasive methods may be insufficient. The use of an 18-G Tru-Cut needle consistently provided adequate specimens across a broad pediatric age and weight range, suggesting that standardized technique and careful procedural handling are important for optimizing diagnostic yield and patient safety.

In summary, within the limitations of this retrospective single-center study with a relatively small sample size, percutaneous liver biopsy remains a valuable tool in pediatric hepatology, offering clinically meaningful information that guides decision-making, while maintaining a low observed complication rate. Larger, prospective multicenter studies are warranted to further validate these findings.

Summary Box

What is already known:

- Liver biopsy remains an essential diagnostic tool in pediatric hepatology, particularly when noninvasive tests are inconclusive
- Ultrasound-assisted percutaneous liver biopsy in children is associated with a low rate of major complications
- Biopsy adequacy depends on sufficient tissue length and an adequate number of portal tracts, with sampling error remaining a concern in pediatric patients
- Needle gauge alone does not reliably predict biopsy adequacy or complication risk

What the new findings are:

- Consistent use of an 18-G Tru-Cut needle produced adequate liver biopsy specimens across a wide pediatric age and weight range
- All biopsies in this cohort were diagnostically adequate, with a mean of 11 complete portal tracts
- No major complications, including bleeding or clinically significant adverse events, were observed
- Standardized biopsy technique and careful tissue handling can optimize diagnostic yield while maintaining patient safety in children

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