—Review Article—

EUS-guided *versus* percutaneous liver biopsy: A comprehensive review and meta-analysis of outcomes

Saurabh Chandan[1], Smit Deliwala[2], Shahab R. Khan[3], Babu P. Mohan[4], Banreet S. Dhindsa[5], Jay Bapaye[6], Hemant Goyal[7], Lena L. Kassab[8], Faisal Kamal[9], Harlan R. Sayles[10], Gursimran S. Kochhar[11], Douglas G. Adler[12]

[1]Division of Gastroenterology and Hepatology, CHI Creighton University Medical Center, Omaha, Nebraska, USA; [2]Department of Internal Medicine, Hurley Medical Center, Flint, Michigan, USA; [3]Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; [4]Division of Gastroenterology and Hepatology, University of Utah School of Medicine, Salt Lake City, Utah, USA; [5]Division of Gastroenterology and Hepatology, University of Nebraska Medical Center, Omaha, Nebraska, USA; [6]Department of Internal Medicine, Rochester General Hospital, Rochester, New York, USA; [7]Department of Gastroenterology, The Wright Center for Graduate Medical Education, Scranton, Pennsylvania, USA; [8]Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota, USA; [9]Division of Gastroenterology, University of California-San Francisco, California, USA; [10]Department of Biostatistics, College of Public Health, University of Nebraska Medical Center, Omaha, Nebraska, USA; [11]Division of Gastroenterology, Hepatology and Nutrition, Allegheny Health Network, Pittsburgh, Pennsylvania, USA; [12]Center for Advanced Therapeutic Endoscopy, Centura Health, Porter Adventist Hospital, Denver, Colorado, USA

ABSTRACT

EUS-guided liver biopsy (EUS-LB) has gained momentum in recent years, especially with availability of newer needle designs. Given the emerging comparative data on EUS-LB with second-generation needles and percutaneous LB (PC-LB), we conducted a systematic review and meta-analysis to compare the safety and efficacy of the two techniques. We searched multiple databases from inception through November 2021 to identify studies comparing outcomes of EUS-LB and PC-LB. Pooled estimates were calculated using a random-effects model, and the results were expressed in terms of pooled proportions and odds ratio (OR) along with relevant 95% confidence intervals (CIs). Five studies with 748 patients were included in the final analysis. EUS-LB was performed in 276 patients and PC-LB in 472 patients. Across all studies, PC-LB had an overall higher diagnostic accuracy than EUS-LB, 98.6% confidence interval (CI: 94.7–99.7) *versus* 88.3% (49.6–98.3), OR: 1.65, $P = 0.04$. On assessing data from randomized controlled trials, there was no difference between the two. While pooled diagnostic adequacy and overall adverse events were not significantly different between PC-LB and EUS-LB, the former was superior in terms of the mean number of complete portal tracts (CPT) and total specimen length. PC-LB and EUS-LB produce similar results. PC-LB allows obtaining longer samples and more CPT. Further studies are needed to see if these trends hold up as more providers begin to perform EUS-LB.

Key words: EUS, liver biopsy, meta-analysis

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Address for correspondence

Dr. Douglas G. Adler, Center for Advanced Therapeutic Endoscopy, Centura Health, Porter Adventist Hospital, Denver, Colorado, USA.
E-mail: Douglasadler@centura.org

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INTRODUCTION

Liver biopsy (LB) is often performed to obtain definitive histology for diagnostic and management purposes when information from noninvasive techniques is inadequate.[1] Historically, liver biopsies have been performed through the computed tomography (CT)- or ultrasound (US)-guided percutaneous routes (PC-LB)[2] or a fluoroscopy-guided transjugular route (TJ-LB).[3] A recent analysis showed that the risk of major complications including mortality, major bleeding, and moderate-to-severe pain with PC-LB was 0.01%, 0.5%, and 0.34%, respectively.[4] In addition, compared to other methods, the PC-LB method typically requires more passes to acquire an adequate tissue sample, thus increasing the risk of complications and patient discomfort.[5] TJ-LB is the preferred biopsy method in high-risk patients, such as those with coagulopathy, coagulation disorders, or high-volume ascites and those not clinically stable enough to tolerate PC procedures.[6] Complications following TJ-LB are estimated to range between 2.5% and 7.1%.[7] However, there remains a substantial variation in histologic yield with both PC-LB and TJ-LB routes.[8]

Since the first published description in 2007, EUS-guided LB (EUS-LB) has emerged as an attractive means for obtaining parenchymal LB specimens for the diagnosis and staging of chronic liver diseases.[9] EUS-LB technique allows for high-quality images of both hepatic lobes, which subsequently allows for a safer biopsy technique and improved ability to access focal liver lesions, resulting in an increase in sample adequacy and tissue yield.[10,11] EUS guidance can confirm the presence or absence of bowel, blood vessels, and biliary structures along the needle track in real time, for both lobes, greatly enhancing its safety profile. EUS-LB also minimizes the impact of ascites and body habitus on ability to visualize and obtain liver tissue.[12] In addition, EUS-LB is conducted under sedation, allowing for reduced procedural anxiety and increased patient comfort.[13] The pooled rate of successful histologic diagnoses with EUS-LB is estimated to be 93.9%, while the incidence of adverse events is about 2.3%.[14]

EUS-LB has gained momentum in the recent years, with availability of newer- or second-generation needle designs, which appear to perform better than traditional ones for EUS-LB tissue acquisition, such as the 19G TruCut needle (Quick-Core; Cook Medical Inc., Winston-Salem, NC).[15] Second-generation needles include the EchoTip HD ProCore (Cook Medical Inc., Winston-Salem, NC), SharkCore (Medtronic Inc., Minneapolis, MN), and Acquire (Boston Scientific, Marlborough, MA). A recent *ex vivo* study showed that the specimen adequacy was similar among these three commercially available 19G needles.[16]

Given the emerging comparative data on EUS-LB with second-generation needles and PC-LB, we conducted a systematic review and meta-analysis to compare the safety and efficacy of the two techniques with modern core biopsy needles.

METHODS

Search strategy

The relevant medical literature was searched by a medical librarian for studies reporting on the outcomes of EUS-LB with modern core biopsy needles and PC-LB for liver lesions. The search strategy was created using a combination of keywords and standardized index terms. A systematic and detailed search was run in November 2021 in Ovid EBM Reviews, ClinicalTrials.gov, Ovid Embase (1974+), Ovid Medline (1946+ including epub ahead of print, in-process, and other nonindexed citations), Scopus (1970+), and Web of Science (1975+). Literature search was performed to include studies published in all languages, and in the case of non-English studies, electronic language translation service was used to convert the text to English. The review was not registered, and a protocol was not prepared.

The full-search strategy is available in Supplementary Appendix 1. For observational studies, the MOOSE (Meta-analyses Of Observational Studies in Epidemiology) Checklist was followed[17] and is provided as Supplementary Appendix 2. The PRISMA Flowchart for study selection is provided in Supplementary Figure 1. The quality of evidence presented in the randomized controlled trials (RCTs) and risk of bias in all the included studies was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology [Supplementary Figure 2].[18] Reference lists of the evaluated studies were examined to identify other studies of interest.

Study selection

In this meta-analysis, we only included studies where outcomes of EUS-LB were compared to PC-LB. Studies

included randomized controlled trials, cohort, and case–control studies that reported outcomes of both interventions. Studies were included irrespective of whether they were performed in inpatient or outpatient setting, follow-up time, and country of origin as long as they provided the appropriate data needed for the analysis.

Our exclusion criteria were as follows: (1) studies reporting outcomes of EUS-LB alone, (2) studies reporting outcomes of EUS-LB performed with first-generation biopsy needles, (3) single patient case reports and case series studies, (4) studies with sample size <10 patients, and (5) studies performed in the pediatric population (age <18 years). In cases of multiple publications from a single research group reporting on the same patient cohort and/or overlapping cohorts, data from the most recent and/or most appropriate comprehensive report were retained. The retained studies were determined based on the publication timing (most recent) and/or the sample size of the study (largest). In situations where a consensus could not be reached, overlapping studies were included in the final analysis and any potential effects were assessed by sensitivity analysis of the pooled outcomes by leaving out one study at a time.

Data abstraction and quality assessment

Data on study-related outcomes from the individual studies were abstracted independently onto a standardized form by at least two authors (SC and SRK). The authors (SD, AP, and HG) cross-verified the collected data for possible errors and the two authors (SC and SRK) performed the quality scoring independently.

Outcomes assessed

The following outcomes were assessed:

1. Pooled odds ratio (OR) and proportion of diagnostic adequacy with EUS-LB as compared to PC-LB: Diagnostic adequacy was defined as the specimen's ability to render a diagnosis and accurately stage the disease, independent of the length of biopsy cores or the number of portal tracts present in the specimen
2. Pooled odds ratio (OR) and proportion of diagnostic accuracy with EUS-LB as compared to PC-LB: Diagnostic accuracy was defined as true positive + true negative divided by the total number of patients
3. Pooled OR and proportion of overall adverse events with EUS-LB as compared to PC-LB
4. Mean difference in CPT obtained between EUS-LB and PC-LB
5. Mean difference in total specimen length (TSL) between EUS-LB and PC-LB.

Statistical analysis

We used meta-analysis techniques to calculate the pooled estimates in each case following the methods suggested by DerSimonian and Laird using the random-effects model, and the results were expressed in terms of pooled proportion (PP) and OR along with relevant 95% confidence intervals (CIs).[19] When the incidence of an outcome was zero in a study, a continuity correction of 0.5 was added to the number of incident cases before statistical analysis.[20] We performed pairwise analysis to compare outcomes in patients with cirrhosis and patients without cirrhosis. $P < 0.05$ was used '*a priori*' to define significance between the groups compared and considered descriptive only as they were uncorrected for multiple testing.

We assessed heterogeneity between study-specific estimates using Cochran's Q statistical test for heterogeneity, 95% confidence interval (CI), and the I^2 statistics.[20-22] In this, values of <30%, 30%–60%, 61%–75%, and >75% were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively. We assessed publication bias, qualitatively, by visual inspection of funnel plot, and quantitatively, by the Egger test.[23] When publication bias was present, further statistics using the fail-Safe N test and Duval and Tweedie's "Trim and Fill" test was used to ascertain the impact of the bias.[24]

All analyses were performed using Comprehensive Meta-Analysis software, version 3 (BioStat, Englewood, NJ, USA).

RESULTS

Characteristics and quality of the included studies

We excluded studies prior to 2020 where EUS-LB was performed using first-generation needles.[25-28] Three of the included studies were retrospective in design[29-31] and two were prospective randomized controlled trials.[32,33] PC-LB was performed under US guidance in four studies. Four studies were carried out in the USA, one in Italy and one in Japan. Based on the Newcastle–Ottawa scoring system [Supplementary Table 1], two cohort studies were considered to be of medium quality and one of high quality. There were no low-quality studies. Based on GRADE Methodology for the assessment of randomized controlled trials,

the overall certainty of evidence was graded as high (Grade A).

Search results and population characteristics

All search results were exported to Endnote where 211 obvious duplicates were removed leaving 444 citations. Five studies with a total of 748 patients were included in the final analysis. EUS-LB was performed in 276 patients and PC-LB in 472 patients. The mean age ranged from 51.8 years to 68 years. A schematic diagram demonstrating our study selection is illustrated in Supplementary Figure 1. Further details of indications and etiology, type of needles used for EUS-LB and PC-LB, number of complete portal tracts (CPT), and TSL are described in Tables 1 and 2.

Meta-analysis outcomes

1. Pooled OR and proportion of diagnostic adequacy: Overall diagnostic adequacy was not significantly different between PC-LB and EUS-LB, 96.6% (95% CI: 63.4–99.8; I^2 93%) *versus* 94.9% (95% CI: 40.2–99.8; I^2 93%), OR: 0.81 (95% CI: 1.65–0.03; I^2 0%), $P = 0.06$. The results were similar when the data from observational studies and RCTs were analyzed separately [Figure 1]
2. Pooled OR and proportion of diagnostic accuracy: PC-LB had an overall higher diagnostic accuracy than EUS-LB, 98.6% (95% CI: 94.7–99.7; I^2 0%) *versus* 88.3% (95% CI: 49.6–98.3; I^2 89%), OR: 1.65 (95% CI: 3.21–0.09; I^2 0%), $P = 0.04$. When assessing data only from randomized controlled trials (RCTs), there was no difference between the two techniques [Figure 2]
3. Pooled OR and proportion of overall adverse events: Pooled rate of overall adverse events was not significantly different between PC-LB and EUS-LB techniques, 11.9% (95% CI: 0.0–97.9; I^2 96%) *versus* 13% (95% CI: 0.4–84.9; I^2 95%), OR: 0.39 (95% CI: 1.02–1.79; I^2 0%), $P = 0.6$, including when the data from observational studies and RCTs were analyzed separately [Figure 3]
4. Mean difference in CPT between EUS-LB and PC-LB: The mean number of CPT was higher in the PC-LB cohort compared to EUS-LB; mean difference: 1.18 (95% CI: 2.34–0.02; I^2 95%), $P = 0.05$ [Figure 4]
5. Mean difference in TSL between EUS-LB and PC-LB: The mean TSL was statistically higher in the PC-LB group as compared to EUS-LB; mean difference: 1.25 (95% CI: 2.50–0.00; I^2 96%), $P = 0.05$ [Figure 5].

VALIDATION OF META-ANALYSIS RESULTS

Sensitivity analysis

To assess whether any one study had a dominant effect on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. We found that exclusion of any single study did not significantly affect the primary outcome or influence the heterogeneity.

Heterogeneity

We assessed dispersion of the calculated rates using the I^2 percentage values as reported in the meta-analysis outcomes section. We found low to substantial heterogeneity in our outcomes. This is likely due to variability in the sizes of EUS-LB needles, indications for tissue sampling, operator variability, and location of the lesions.

Publication bias

Publication bias was not assessed, given that the total number of studies was less than 10.

DISCUSSION

Our analysis, based on a limited number of studies, shows that PC-LB has a higher overall diagnostic accuracy when compared to EUS-LB performed with second-generation needles. The two techniques appear to have similar diagnostic adequacy and overall adverse events. When the data exclusively from RCTs are assessed, the two techniques appear to be at par in terms of overall diagnostic accuracy. In addition, PC-LB results in longer specimens and more CPT.

The field of endohepatology continues to evolve with the advent of new-generation EUS-guided biopsy needles, and the growing body of literature suggests that EUS-LB may have fewer contraindications than the traditional PC-LB and TJ-LB techniques.[12] Some of the notable advantages of EUS-LB include the ability to perform several needle passes after a single liver capsule puncture, to assess and treat luminal pathology concurrently, as well as providing faster recovery compared to other approaches. Some of the potential disadvantages of EUS-LB include the additional cost, need for deep sedation, and endoscopist expertise in EUS-guided tissue sampling which often warrants additional training in EUS.[34] A recent study analyzing the complications of tissue acquisition using the PC-LB approach in chronic liver disease patients noted that the

Table 1. Study characteristics

Study, year	Design	Total (*n*)		Sex male/female		Age (range) [SD]		Needle type		Indications/etiology (*n*)	
		EUS-LB	PC-LB	EUS-LB	PC-LB	EUS-LB	PC-LB	EUS-LB	PC-LB	EUS-LB	PC-LB
Ali, 2020	Retrospective, January 2018 to August 2019, Single center, USA	30	60 (US guided)	11/19	22/38	54 (46-63) [median (IQR)]	53 (45-59) [median (IQR)]	19G or 22G Fork-tip SharkCore biopsy needle (Medtronic, Massachusetts, United States)	18G CorVocet needle (Meritmedical, Sought Jordan, Utah, United States) or 15G Jamshidi needle (Care-Fusion, Vernon Hills, Illinois, United States)	5 (fibrosis staging), 17 (elevated liver enzymes), 8 (evaluation of suspected NASH)	43 (fibrosis staging), 10 (elevated liver enzymes), 7 (evaluation of suspected NASH)
Bhogal, 2020	Retrospective, October 2013 to June 2019 (EUS-LB)/June 2016 to June 2019 (PC-LB), Single center, USA	135	287	49/86	145/142	53 [15]	52 [15]	19G needle (Expect FNA 2013 to 2017, Acquire FNB 2017 to 2019 Boston Scientific	NR	120 (abnormal LFT,) 9 (abnormal imaging), 3 (suspected adv fib cirrhosis), 3 (follow-up of chronic condition)	254 (abnormal LFT,) 5 (abnormal Imaging), 4 (suspected adv fib cirrhosis), 22 (follow-up of chronic condition)
Bang, 2021	Prospective, RCT, July 2019 to November 2020, Single Center, USA	21	19	NR	NR	NR	NR	19G Acquire, Boston Scientific	16G Biopince, Argon Medical Devices	NR	NR
Facciorusso, 2021	Retrospective, 2017 to 2021, Multicenter, Italy	54	62 (US guidance)	32/22	38/24	56 (48-69) [median (IQR)]	54 (45-67) [median (IQR)]	22G ProCore® [Cook Medical, Bloomington, IN, US], 22G SharkCore®, or 22G Acquire®) and 19G FNA (EchoTip Ultra®, Cook Medical LLC, Bloomington, IN, USA)	16G biopsy needle (Biopince®, Argon Medical Devices, Frisco, TX, USA)	27 (Focal lesion), 27 (Parenchymal disease)	31 (Focal lesion), 31 (Parenchymal disease)
Nallapeta, 2021 (Abs)	Prospective, RCT, October 2020 to March 2021, Single center, USA	36	44 (US guidance)	10/26	17/27	53.4 [13.7]	51.8 [13.8]	19G Franseen (Acquire™) or 19G Fork-tip (SharkCore™) needle biopsy	18G cutting needles or by suction15G liver biopsy needle	NR	NR

LB: Liver biopsy; PC-LB: Percutaneous LB; IQR: Interquartile range; US: Ultrasound; NR: Not reported; NASH: Nonalcoholic steatohepatitis; LFT: Liver function tests; SD: Standard deviation

Table 2. Study outcomes

	CPT		Outcomes					
			Diagnostic adequacy		Diagnostic accuracy		Adverse events (*n*)	
	EUS-LB	PC-LB	EUS-LB	PC-LB	EUS-LB	PC-LB	EUS-LB	PC-LB
Ali, 2020	5 (5-8) [median (IQR)]/5.75±0.878	13 (8-21) [median (IQR)]/13.75±3.7556	NR	NR	28/30	60/60	0/30	0/60
Bhogal, 2020	19.7 (SD 10) (mean)	17.4 (SD 9) (mean)	134/135	284/287	NR	NR	133/135 (none), 1/135 (severe pain), 0/135 (bleeding), 1/135 (mortality [within 30 days])	285/287 (none), 1/287 (severe pain), 1/287 (bleeding), 0/287 (mortality [WITHIN 30 days])
Bang, 2021	1 (4.8) [0-5], 3 (14.3) [6-9], 17 (81.0) [≥10]	0 [0-5], 1 (5.3) [6-9], 18 (94.7) [≥10]	NR	NR	19/21	19/19	0/21	0/19
Facciorusso, 2021	18.5 (10-23.2) [Median (IQR)]/17.55±3.8	21 (11-24) [median (IQR)]/19.25±3.73	51/52	62/62	24/27	31/31	0/54	0/62
Nallapeta, 2021 (Abs)	Mean 12.5 [SD 10.6]	Mean 18.9 [SD 10.5]	20/36	33/44	36/36	44/44	0/36	0/44

Study, year	TSL		Procedure time (min)	
	EUS-LB	PC-LB	EUS-LB	PC-LB
Ali, 2020	25 mm (21-33) [median (IQR)]/26±3.48	31 mm (20-42) [median (IQR)]/31±6.35	NR	NR
Bhogal, 2020	34.7 mm (SD 10)	29.2 mm (SD 9)	NR	NR
Bang, 2021	19.2 mm (6.9) [mean], 16.5 (IQR 15-21.5, range 9.5-32.5) [median]	25.9 mm (4.3) [mean], 26 mm (IQR 25-30, range 15-32) [median]	NR	NR
Facciorusso, 2021	18.5 mm (10.1-22.4) [median (IQR)]/17.375±3.544	27.4 mm (21-29) [median (IQR)]/26.2±2.3	7 (5-11) min [median (minimum-maximum)]	1 (1-3) min [median (minimum-maximum)]
Nallapeta, 2021 (Abs)	19.5 mm (5.8) [Mean (SD)]	19.6 mm (5.7) [Mean (SD)]	NR	NR

LB: Liver biopsy; PC-LB: Percutaneous LB; IQR: Interquartile range; NR: Not reported; SD: Standard deviation; CPTs: Complete portal tracts; TSL: Total specimen length

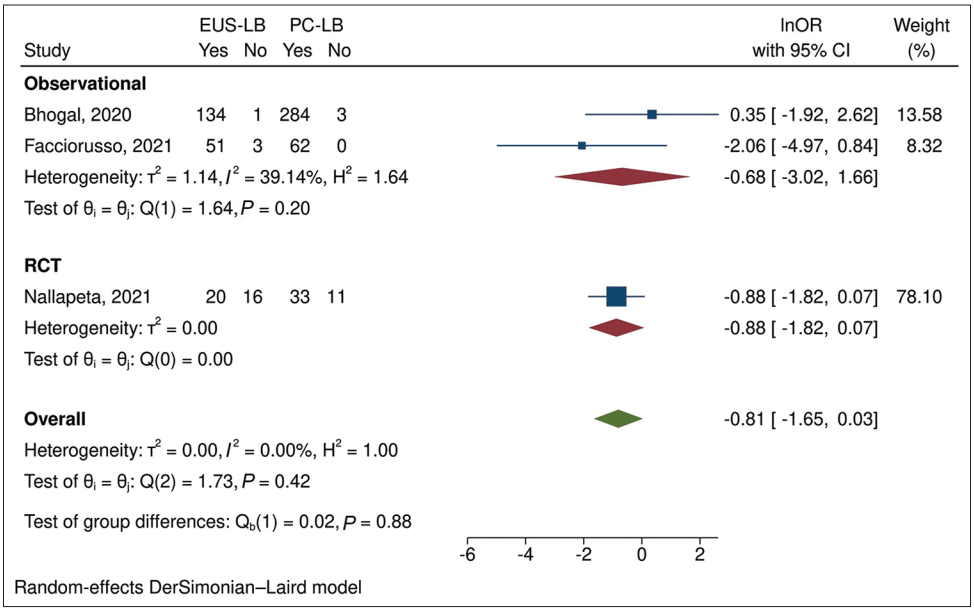

Figure 1. Forest plot, OR, diagnostic adequacy. EUS-LB: EUS-guided liver biopsy; PC-LB: Percutaneous liver biopsy; CI: Confidence interval; OR: Odds ratio; RCT: Randomized controlled trial

incidences of complications such as major and minor bleeding were noted in 0.48% and 0.19% patients, respectively, and postprocedure pain occurred in 0.34% of patients. In addition, technical failure was high at

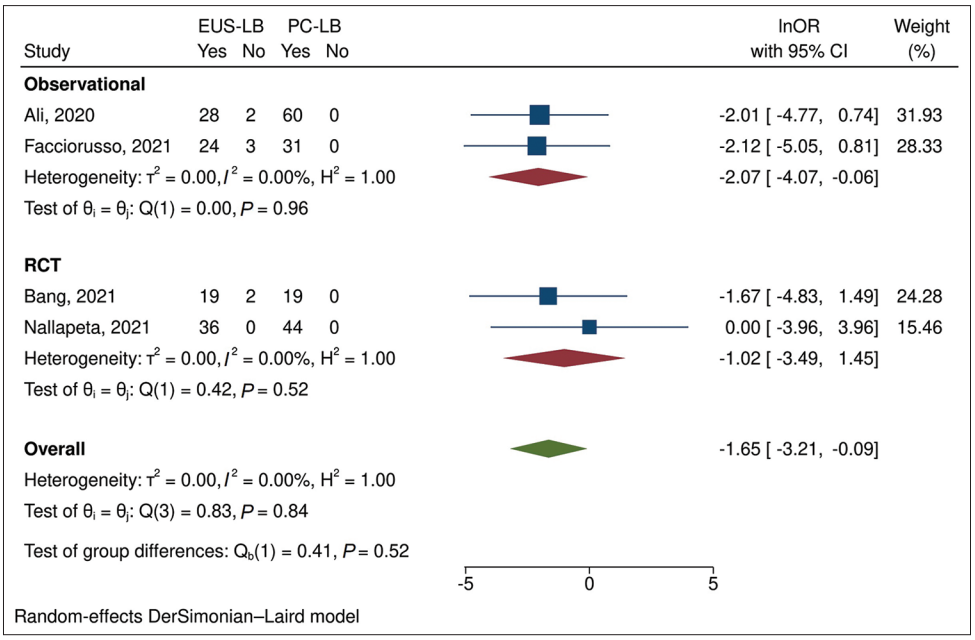

Figure 2. Forest plot, OR, diagnostic accuracy. EUS-LB: EUS-guided liver biopsy; PC-LB: Percutaneous liver biopsy; CI: Confidence interval; OR: Odds ratio; RCT: Randomized controlled trial

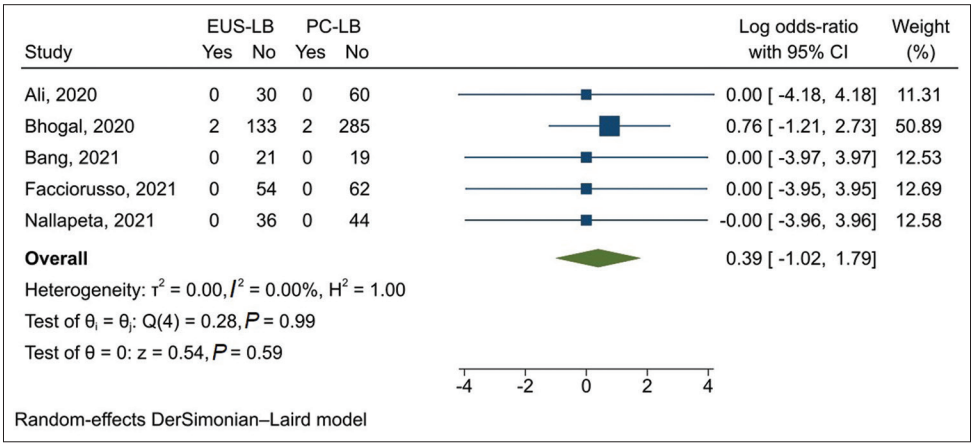

Figure 3. Forest plot, OR, overall adverse events. EUS-LB: EUS-guided liver biopsy; PC-LB: Percutaneous liver biopsy; CI: Confidence interval; OR: Odds ratio

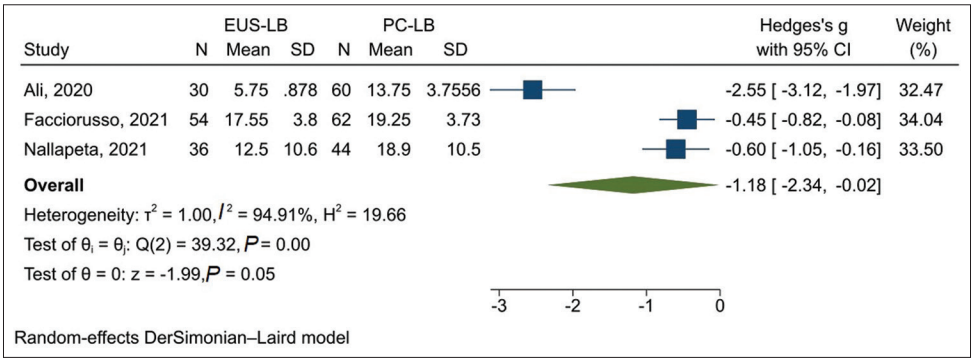

Figure 4. Forest plot, OR, mean complete portal tracts. EUS-LB: EUS-guided liver biopsy; PC-LB: Percutaneous liver biopsy; CI: Confidence interval; OR: Odds ratio

0.94%.[4] In our analysis, we noted that the rate of overall adverse events was similar between EUS-LB and PC-LB, with severe pain occurring in 1 patient in each group, 1 case of postprocedure bleeding in the PC-LB

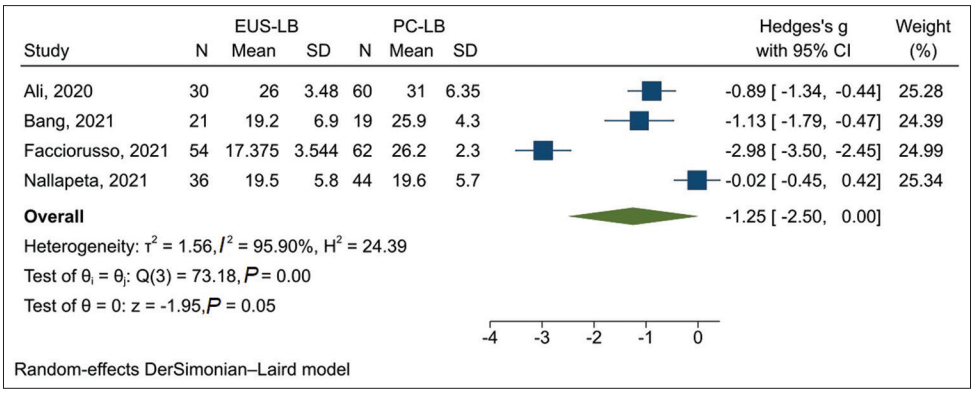

Figure 5. Forest plot, OR, total specimen length. EUS-LB: EUS-guided liver biopsy; PC-LB: Percutaneous liver biopsy; CI: Confidence interval; OR: Odds ratio; RCT: Randomized controlled trial

group, and a single death, unrelated to the procedure, occurring in the EUS-LB group.

Multiple retrospective studies have been previously published comparing the adequacy and clinical safety of EUS-LB with PC-LB. Pineda *et al.* concluded that EUS-guided biopsy yielded a longer total specimen, when both lobes were biopsied and that this technique yields specimens at least comparable to, and in some cases better than, PC or transjugular LB.[26] Another study by Shuja *et al.* reported that while the TSL was longer for EUS-LB, a maximum number of CPT were seen with PC biopsy.[35] However, in these studies, EUS-LB was performed using first-generation fine-needle aspiration needles, and not fine-needle biopsy needles. In a bid to improve the histologic yield of samples with EUS-LB, new-generation of core biopsy needles with specialized tip designs has been developed and been commercially available since 2012. The Procore reversed bevel tip with a tissue trap design (Echo TipHD ProCore; Cook Medical Inc., Winston-Salem, NC) was the first, followed by a fork-tip design (SharkCore, Medtronic Inc., Minneapolis MN) and finally a Franseen tip design (Acquire, Boston Scientific, Marlborough, MA). In our study, 19G or 22G Fork-tip SharkCore™ biopsy needles (Medtronic, Massachusetts, United States) were used in two studies,[29,33] 19G Acquire™ (Boston Scientific) was used in two studies,[30,32] and 22G ProCore® [Cook Medical, Bloomington, IN, US], 22G SharkCore®, or 22G Acquire®) and 19G FNA (EchoTip Ultra®, Cook Medical LLC, Bloomington, IN, USA) were used in another study.[31] We found that the overall pooled diagnostic adequacy of samples was comparable between EUS-LB and PC-LB groups. This trend was also seen when the data from observational studies and RCTs were analyzed separately.

The American Association for the Study of Liver Diseases states that an adequate biopsy sample should be at least 20 mm in length with eleven or more CPT (defined as containing all 3 portal structures: portal vein, hepatic artery, and bile duct).[36] In our analysis, we found that the TSL and the mean number CPTs were both statistically higher in the PC-LB group. This may be due to two possible reasons. First, while two studies in our analysis utilized 18G cutting or 15G suction needles to obtain the biopsy specimen,[29,33] two studies used the 16G biopsy needle (Biopince®, Argon Medical Devices, Frisco, TX, USA), which has shown to be superior to 18G needles in terms of CPTs and TSL.[31,32] Second, in two of the retrospective cohort studies included in our analysis, some EUS-LB procedures were performed using the older-generation 19G FNA needles, which may have resulted in samples with lesser number of CPT and shorter specimen length.[30,31] A recent meta-analysis of five studies comparing outcomes of EUS-LB, PC-LB, and TJ-LB concluded that there was no difference in biopsy adequacy or adverse events for EUS-LB compared to PC-LB and TJ-LB. A comparison of EUS-LB and PC-LB also revealed no difference between specimens regarding CPT; however, a longer TSL was observed with EUS-LB.[37] It is important to note that in all the included studies in the analysis, EUS-LB was carried out using first-generation FNA needles including 19G TruCut needle (Quick-Core; Cook Medical Inc., Winston-Salem, NC) and 19G Expect or ExpectFlexible needles (Boston Scientific, Marlborough, MA). We included only those studies where majority of EUS-LB procedures were performed using the newer second-generation needles to better compare outcomes with PC-LB.

There are several strengths to our analysis. First, we conducted a systematic literature search with

well-defined inclusion criteria, careful exclusion of redundant studies, inclusion of good-quality studies with detailed extraction of data, and rigorous evaluation of study quality. Second, to validate our findings further, we assessed outcomes of observational studies and RCTs separately. There are also several limitations to this study, most of which are inherent to any meta-analysis. First and foremost, our analysis included a limited number of studies as comparative data between EUS-LB with newer-generation needles and PC-LB continues to evolve. Second, only three of the included studies reported the indications for performing LB. In one of the included studies, diagnostic accuracy for both EUS-LB and PC-LB groups was reported only from a sample of focal liver lesions and not parenchymal liver disease.[31] Three of the included studies were retrospective in design which may have resulted in selection bias. Third, one of the included studies in our analysis was only published in abstract format as it is an ongoing randomized controlled trial.[33] Data regarding the number of passes with EUS-LB were not consistently reported in all the studies. In two studies, the authors reported that two passes were performed from either lobe of the liver,[31,32] whereas in patients with focal liver lesions, the number of passes was decided based on the macroscopic appearance of the collected material. In a majority of the included studies, the authors reported that during EUS-guided sampling, the right or left lobe of the liver was punctured either through transduodenal or transgastric approach. Bhogal *et al.* reported that majority of EUS-LB specimens were obtained from the left hepatic lobe via a transgastric approach.[30] Historically, PCLB was performed without image guidance from the right lobe of the liver, which was identified by percussion of the liver, with breath held in inspiration.[38] However, studies suggest that image-guided PC sampling using the subxiphoid approach can be used for targeting the left hepatic lobe.[39] Given anatomical limitations of either method, it remains to be determined whether one approach is better than the other for a particular liver segment. Finally, a majority of the studies in our analysis originated in USA and were carried out in expert centers, making our results not generalizable.

Nevertheless, our analysis is the first in literature to compare outcomes of EUS-LB with second-generation needles and PC-LB. While the two techniques performed at par in terms of diagnostic adequacy and overall adverse events, PC-LB allows obtaining longer specimen samples and more CPT. Further studies are needed to see if these trends hold up as more providers begin to perform EUS-LB.

Acknowledgments

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Nil.

Conflicts of interest

Douglas G. Adler is a Co-Editor-in-Chief of the journal. This article was subject to the journal's standard procedures, with peer review handled independently of the editor and his research group.

Supplementary materials

Supplementary information is linked to the online version of the paper on the *Endoscopic Ultrasound* website.

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Supplementary Appendix 1. Literature search strategy					
Database	**MEDLINE(R) 1946 to Present and Epub Ahead of Print, In-Process and Other Nonindexed Citations and Ovid MEDLINE(R) Daily**	**Embase <1974–2021 November 9>**	**EBM Reviews Cochrane Central Register of Controlled Trials <1991-October 2021>**	**Scopus (1823-present)**	**SCIE ESCI (1900-present)**
Platform/ Vendor	Ovid	Ovid	Ovid	Elsevier	Web of Science
Date Search Run	10 November 2021	10 November 2021	10 November 2021	10 November 2021	10 November 2021
Results Numbers (overall and line by line if used)	156	198	17	207	77
Terms and Field Codes	1 Endosonography/13583 2 (endoscopic adj (ultrasonography or ultrasound)).ab,kf,ti. 13182 3 (EUS or EUS-guided or EUS-LB or endosonograph$ or echo-endoscop$ or ultrasonic-endoscop$ or echoendoscop$).ab,kf,ti. 13224 4 1 or 2 or 3 24899 5 (percutaneous or	1 endoscopic ultrasonography/11837 2 ((endoscopic adj (ultrasonography or ultrasound)) or EUS or EUS-guided or EUS-LB or endosonograph$ or echo-endoscop$ or ultrasonic-endoscop$ or echoendoscop$).ab,kf,ti. 36073 3 1 or 2 39787 4 percutaneous biopsy/ 5497 5 (percutaneous or	1 ((endoscopic adj (ultrasonography or ultrasound)) or EUS or EUS-guided or EUS-LB or endosonograph$ or echo-endoscop$ or ultrasonic-endoscop$ or echoendoscop$).ti,hw,ab. 2210 2 (percutaneous or transcutaneous or PC-LB).ti,hw,ab. 28122 3 (biopsy or biopsies or fine-needle-aspiration$ or FNA or EUS-	((((INDEXTERMS (endosonography OR {endoscopic ultrasonography}) OR TITLE-ABS-KEY ((endoscopic W/1 (ultrasonography OR ultrasound)) OR eus OR eus-guided OR eus-lb OR endosonograph* OR echo-endoscop* OR ultrasonic-endoscop* OR echoendoscop*)) AND (INDEXTERMS ({percutaneous biopsy})	#1 TS=((endoscopic NEAR/1 (ultrasonography OR ultrasound)) OR EUS OR EUS-guided OR EUS-LB OR endosonograph* OR echo-endoscop* OR ultrasonic-endoscop* OR echoendoscop*) #2 TS=(percutaneous OR transcutaneous OR PC-LB) #3 TS=(liver* OR intrahepatic OR “bile

	transcutaneous or PC-LB).ab,kf,ti. 170925 6 exp Biopsy, Needle/68425 7 exp Image-Guided Biopsy/7479 8 pathology.fs. 3,085,151 9 diagnostic imaging.fs. 1315025 10 (biopsy or biopsies or fine-needle-aspiration$ or FNA or EUS-FNA).ab,kf,ti. 433870 11 or/6-10 4296746 12 exp Liver Diseases/586089 13 exp Liver/ 456927 14 (liver$ or intrahepatic or bile-canalicul$ or hepatic or hepatis or hepati).ab,kf,ti. 1026740 15 (alpha-1-antitrypsin adj1 deficien$).ab,kf,ti. 2688 16 (Budd-Chiari or Chiari$-syndrom$ or (hepatic adj (vein or venous) adj (outflow-obstruction or thrombos$))).ab,kf,ti.	transcutaneous or PC-LB).ab,kf,ti. 256098 6 4 or 5 257844 7 liver biopsy/ 62621 8 ((liver and (biopsy or biopsies or fine-needle-aspiration$ or FNA or EUS-FNA)) or LB).ab,kf,ti. 98480 9 7 or 8 122005 10 3 and 6 and 9 211 11 exp animal/ not exp human/4857775 12 10 not 11 204 13 exp infant/ 1045145 14 exp juvenile/ 3676378 15 13 or 14 3676378 16 exp adult/ 9386778 17 15 not 16 2342985 18 12 not 17 201 19 english.lg. 31935015 20 18 and 19 198	FNA).ti,hw,ab. 35153 4 (liver$ or intrahepatic or bile-canalicul$ or hepatic or hepatis or hepati).ti,hw,ab. 66674 5 (alpha-1-antitrypsin adj1 deficien$).ti,hw,ab. 197 6 (Budd-Chiari or Chiari$-syndrom$ or (hepatic adj (vein or venous) adj (outflow-obstruction or thrombos$))).ti,hw,ab. 64 7 (((liver or hepatic) adj3 (injur$ or toxic$ or disease$)) or hepatitis or hepatitides).ti,hw,ab. 37110 8 hepatic-necros?s.ti,hw,ab. 33 9 (yellow adj3 atroph$).ti,hw,ab. 0 10 (intrahepatic adj3 (cholestas?s or biliary-stas?s)).ti,hw,ab. 204 11 (Alagille$ or Watson-Miller or ((cardiovertebral or hepatofacioneurocardiovertebral) adj syndrome) or arteriohepatic-dysplasia or AHD or	OR TITLE-ABS-KEY (percutaneous OR transcutaneous OR pc-lb)) AND ((INDEXTERMS ({liver biopsy}) OR TITLE-ABS-KEY (liver AND (biopsy OR biopsies OR fine-needle-aspiration* OR fna OR eus-fna))) OR ((INDEXTERMS ({Biopsy, Needle} OR {Image-Guided Biopsy}) OR TITLE-ABS-KEY (biopsy OR biopsies OR fine-needle-aspiration* OR fna OR eus-fna)) AND (INDEXTERMS ({Liver Diseases} OR liver OR {liver disease}) OR TITLE-ABS-KEY (liver* OR intrahepatic OR “bile canalicul*” OR hepatic OR hepatis OR hepati OR “Budd-Chiari” OR “Chiari* syndrom*” OR hepatitis OR hepatitides OR “hepatic necrosis” OR “hepatic necroses” OR alagille* OR “Watson-Miller” OR	canalicul*” OR hepatic OR hepatis OR hepati OR “Budd-Chiari” OR “Chiari* syndrom*” OR hepatitis OR hepatitides OR “hepatic necrosis” OR “hepatic necroses” OR Alagille* OR “Watson-Miller” OR “arteriohepatic dysplasia” OR AHD OR cirrhosis OR cholangitis OR cholangitides OR steatohepatitis OR steatohepatitides OR steatosis OR steatoses OR NAFLD OR “fatty liver” OR “focal nodular hyperplasia*” OR ACLF OR PT-NANBH OR ET-NANBH OR “sinusoidal obstruction syndrome” OR pseudosclerosis OR pseudoscleroses OR “wilson* disease*” OR “Westphal-Strumpell” OR “copper storage” OR hepatomegaly OR ZSS OR “portal hypertension*” OR “Cruveilhier-Baumgarten” OR fascioliasis OR

	3603 17 (((liver or hepatic) adj3 (injur$ or toxic$ or disease$)) or hepatitis or hepatitides).ab,kf,ti. 373197 18 hepatic-necros?s.ab,kf,ti. 2568 19 (yellow adj3 atroph$).ab,kf,ti. 214 20 (intrahepatic adj3 (cholestas?s or biliary-stas?s)).ab,kf,ti. 3744 21 (Alagille$ or Watson-Miller or ((cardiovertebral or hepatofacioneurocardiovertebral) adj syndrome) or arteriohepatic-dysplasia or AHD or (cholestasis adj2 pulmonary stenos?s) or (paucity adj3 bile duct$) or (hepatic adj2 hypoplasia)).ab,kf,ti. 2038 22 (cirrhosis or cholangitis or cholangitides).ab,kf,ti. 115034 23 (steatohepatitis or steatohepatitides or steatos?s or		(cholestasis adj2 pulmonary stenos?s) or (paucity adj3 bile duct$) or (hepatic adj2 hypoplasia)).ti,hw,ab. 137 12 (cirrhosis or cholangitis or cholangitides).ti,hw,ab. 11849 13 (steatohepatitis or steatohepatitides or steatos?s or NAFLD).ti,hw,ab. 3901 14 ((Reye$ adj2 syndrome) or fatty-liver).ti,hw,ab. 4353 15 (focal-nodular-hyperplasia$ or ((hepatic or liver or hepatocellular) adj3 (infarct$ or insuffiency or failure$ or abscess$ or am?ebiasis or entam?ebias?s or fibros?s or Echinococcosis or Hydatidosis or Hydatid-Cyst$ or neoplasm$ or cancer$ or adenoma$ or carcinoma$ or tuberculos?s))).ti,hw,ab. 15372 16 ((hepatic or portal-	“arteriohepatic dysplasia” OR ahd OR cirrhosis OR cholangitis OR cholangitides OR steatohepatitis OR steatohepatitides OR steatosis OR steatoses OR NAFLD OR “fatty liver” OR “focal nodular hyperplasia*” OR aclf OR pt-nanbh OR et-nanbh OR “sinusoidal obstruction syndrome” OR pseudosclerosis OR pseudoscleroses OR “wilson* disease*” OR “Westphal-Strumpell” OR “copper storage” OR hepatomegaly OR zss OR “portal hypertension*” OR “Cruveilhier-Baumgarten” OR fascioliasis OR fascioliases OR “fasciola infection*” OR hepatoma* OR “peliosis hepatis” OR porphyria* OR coproporphyria OR coproporphyrinogen OR protoporphyria*) OR TITLE-ABS-KEY (	fascioliases OR “fasciola infection*” OR hepatoma* OR “peliosis hepatis” OR porphyria* OR coproporphyria OR coproporphyrinogen OR Protoporphyria*) OR TS=(“alpha-1-antitrypsin” NEAR/1 deficien*) OR TS=(hepatic NEAR/3 (“outflow obstruction” OR thrombos*)) OR TS=((liver OR hepatic) NEAR/3 (injur* OR toxic* OR disease*)) OR TS=(yellow NEAR/3 atroph*) OR TS=(intrahepatic NEAR/3 (cholestasis OR cholestases OR “biliary stasis” OR “biliary stases”)) OR TS=((cardiovertebral OR hepatofacioneurocardiovertebral) NEAR/1 syndrome) OR TS=(cholestasis NEAR/2 (“pulmonary stenosis” OR “pulmonary stenosis”)) OR TS=(paucity NEAR/3 “bile duct*”)

	NAFLD).ab,kf,ti. 41106 24 ((Reye$ adj2 syndrome) or fatty-liver).ab,kf,ti. 36902 25 (focal-nodular-hyperplasia$ or ((hepatic or liver or hepatocellular) adj3 (infarct$ or insuffiency or failure$ or abscess$ or am?ebiasis or entam?ebias?s or fibros?s or Echinococcosis or Hydatidosis or Hydatid-Cyst$ or neoplasm$ or cancer$ or adenoma$ or carcinoma$ or tuberculos?s))).ab,kf,ti. 208957 26 ((hepatic or portal-systemic or hepatocerebral or portosystemic) adj3 (encephalopath$ or coma$ or stupor$)).ab,kf,ti. 11083 27 (ACLF or PT-NANBH or ET-NANBH).ab,kf,ti. 1279 28 (sinusoidal-obstruction-syndrome		systemic or hepatocerebral or portosystemic) adj3 (encephalopath$ or coma$ or stupor$)).ti,hw,ab. 1862 17 (ACLF or PT-NANBH or ET-NANBH).ti,hw,ab. 219 18 (sinusoidal-obstruction-syndrome or ((hepatolenticular or hepatocerebral or neurohepatic or lenticular) adj1 degeneration$) or pseudoscleros?s or wilson$-disease$ or Westphal-Strumpell or copper-storage).ti,hw,ab. 219 19 (hepatomegaly or ZSS).ti,hw,ab. 325 20 ((hepatopulmonary or hepato-pulmonary or hepatorenal or Zellweger$ or cerebro-hepato-renal) adj2 (syndrome$ or disease or spectrum)).ti,hw,ab. 486 21 (portal-hypertension$ or Cruveilhier-Baumgarten).ti,hw,ab. 1403	“alpha-1-antitrypsin” W/1 deficien*) OR TITLE-ABS-KEY (hepatic W/3 (“outflow obstruction” OR thrombos*)) OR TITLE-ABS-KEY ((liver OR hepatic) W/3 (injur* OR toxic* OR disease*)) OR TITLE-ABS-KEY (yellow W/3 atroph*) OR TITLE-ABS-KEY (intrahepatic W/3 (cholestasis OR cholestases OR “biliary stasis” OR “biliary stases”)) OR TITLE-ABS-KEY ((cardiovertebral OR hepatofacioneurocardiovertebral) W/1 syndrome) OR TITLE-ABS-KEY (cholestasis W/2 (“pulmonary stenosis” OR “pulmonary stenosis”)) OR TITLE-ABS-KEY (paucity W/3 “bile duct*”) OR TITLE-ABS-KEY (hepatic W/2 hypoplasia) OR TITLE-ABS-KEY (reye* W/2 syndrome) OR TITLE-ABS-KEY ((hepatic OR	OR TS=(hepatic NEAR/2 hypoplasia) OR TS=(Reye* NEAR/2 syndrome) OR TS=((hepatic OR liver OR hepatocellular) NEAR/3 (infarct* OR insuffiency OR failure* OR abscess* OR amebiasis OR amoebiasis OR entamebiasis OR entamoebiasis OR entamebiases OR entamoebiases OR fibrosis OR fibroses OR Echinococcosis OR Hydatidosis OR Hydatid-Cyst* OR neoplasm* OR cancer* OR adenoma* OR carcinoma* OR tuberculosis OR tuberculoses)) OR TS=((hepatic OR “portal systemic” OR hepatocerebral OR portosystemic) NEAR/3 (encephalopath* OR coma* OR stupor*)) OR TS=((hepatolenticular OR hepatocerebral OR neurohepatic OR lenticular) NEAR/1

	or ((hepatolenticular or hepatocerebral or neurohepatic or lenticular) adj1 degeneration$) or pseudoscleros?s or wilson$-disease$ or Westphal-Strumpell or copper-storage).ab,kf,ti. 7746 29 (hepatomegaly or ZSS).ab,kf,ti. 8341 30 ((hepatopulmonary or hepato-pulmonary or hepatorenal or Zellweger$ or cerebro-hepato-renal) adj2 (syndrome$ or disease or spectrum)).ab,kf,ti. 4550 31 (portal-hypertension$ or Cruveilhier-Baumgarten).ab,kf,ti. 19898 32 ((esophageal or oesophageal or gastric) adj1 (varix or varices)).ab,kf,ti. 9825 33 (fasciolias?s or fasciola-infection$).ab,kf,ti. 1948 34 (hepatoma$ or		22 ((esophageal or oesophageal or gastric) adj1 (varix or varices)).ti,hw,ab. 1757 23 (fasciolias?s or fasciola-infection$).ti,hw,ab. 27 24 (hepatoma$ or peliosis-hepatis or porphyria$ or coproporphyria or coproporphyrinogen or Protoporphyria$ or ((Hydroxymethylbilane or Uroporphyrinogen or UPS or PBGD or Porphobilinogen or ppox or Protoporphyrinogen or Ferrochelatase or heme-synthetase) adj3 deficien$)).ti,hw,ab. 333 25 or/4-24 84311 26 1 and 2 and 3 and 25 17	liver OR hepatocellular) W/3 (infarct* OR insuffiency OR failure* OR abscess* OR amebiasis OR amoebiasis OR entamebiasis OR entamoebiasis OR entamebiases OR entamoebiases OR fibrosis OR fibroses OR echinococcosis OR hydatidosis OR hydatid-cyst* OR neoplasm* OR cancer* OR adenoma* OR carcinoma* OR tuberculosis OR tuberculoses)) OR TITLE-ABS-KEY ((hepatic OR “portal systemic” OR hepatocerebral OR portosystemic) W/3 (encephalopath* OR coma* OR stupor*)) OR TITLE-ABS-KEY ((hepatolenticular OR hepatocerebral OR neurohepatic OR lenticular) W/1 degeneration*) OR TITLE-ABS-KEY ((hepatopulmonary OR	degeneration*) OR TS=((hepatopulmonary OR hepato-pulmonary OR hepatorenal OR Zellweger* OR “cerebro hepato renal”) NEAR/2 (syndrome* OR disease OR spectrum)) OR TS=((esophageal OR oesophageal OR gastric) NEAR/1 (varix OR varices)) OR TS=((Hydroxymethylbilane OR Uroporphyrinogen OR UPS OR PBGD OR Porphobilinogen OR ppox OR Protoporphyrinogen OR Ferrochelatase OR “heme-synthetase”) NEAR/3 deficien*) #4 TS=(biopsy OR biopsies OR fine-needle-aspiration* OR FNA OR EUS-FNA) #5 (#3) AND #4 #6 TS=(liver AND (biopsy OR biopsies OR fine-needle-aspiration* OR FNA OR EUS-FNA)) #7 (#5) OR #6 #8 ((#7) AND #2) AND

	peliosis-hepatis or porphyria$ or coproporphyria or coproporphyrinogen or Protoporphyria$ or ((Hydroxymethylbilane or Uroporphyrinogen or UPS or PBGD or Porphobilinogen or ppox or Protoporphyrinogen or Ferrochelatase or heme-synthetase) adj3 deficien$)).ab,kf,ti. 39715 35 or/12-34 1445278 36 4 and 5 and 11 and 35 171 37 exp Animals/not exp Humans/4912992 38 36 not 37 169 39 exp Infant/ 1195194 40 exp Child/ 2024760 41 Adolescent/ 2137385 42 or/39-41 3763496 43 exp Adult/ 7642753 44 42 not 43 1995470 45 38 not 44 168 46 english.lg. 28538788 47 45 and 46 156			hepato-pulmonary OR hepatorenal OR zellweger* OR “cerebro hepato renal”) W/2 (syndrome* OR disease OR spectrum)) OR TITLE-ABS-KEY ((esophageal OR oesophageal OR gastric) W/1 (varix OR varices)) OR TITLE-ABS-KEY ((hydroxymethylbilane OR uroporphyrinogen OR ups OR pbgd OR porphobilinogen OR ppox OR protoporphyrinogen OR ferrochelatase OR “heme-synthetase”) W/3 deficien*))))) AND NOT (INDEXTERMS (animal OR animals) AND NOT INDEXTERMS (human OR humans))) AND NOT (INDEXTERMS (infant OR infants OR child OR adolescent OR adolescents OR juvenile OR juveniles) AND NOT INDEXTERMS (adult OR adults))) AND (LANGUAGE (english))	#1 #9 AK=(“population groups” NOT “animal models”) OR (AB=(men OR women OR patient OR female OR male OR subjects OR adult) NOT AK=“animal models”) #10 (#8) AND #9 #11 ((#8) AND #9) AND LA=(English)

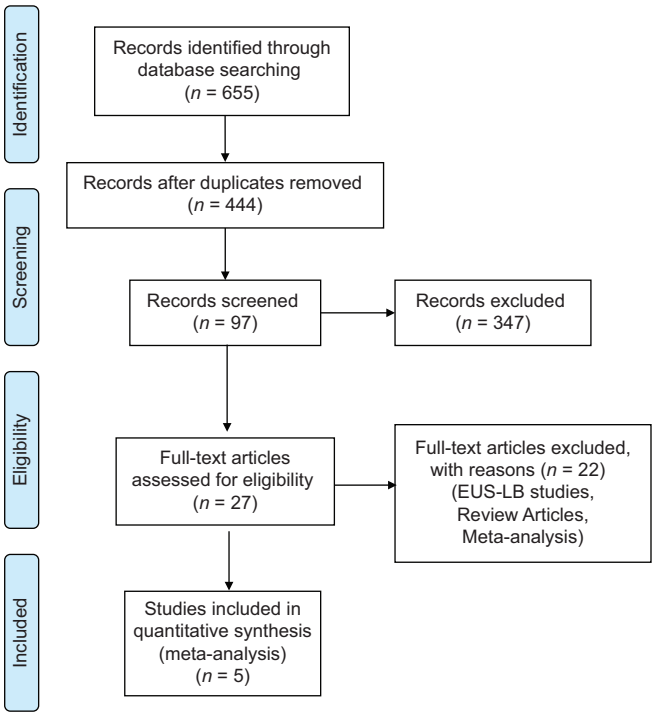
Notes on strategy translatio, date range, citations management software, etc.	All references exported to EndNote. Human and adult study filters applied. Results limited to English language publications Search strategy saved as: "H:\Mayo Clinic Libraries\Systematic Reviews\2021\November\2021-11-9_Kassab SR\Search Strategies\2021-11-10_Kassab SR_Medline search strategy.docx"	All references exported to EndNote Human and adult study filters applied. Results limited to English language publications Search strategy saved as: "H:\Mayo Clinic Libraries\Systematic Reviews\2021\November\2021-11-9_Kassab SR\Search Strategies\2021-11-10_Kassab SR_Embase search strategy.docx"	All references exported to EndNote No limits or filters applied in Central Search strategy saved as: "H:\Mayo Clinic Libraries\Systematic Reviews\2021\November\2021-11-9_Kassab SR\Search Strategies\2021-11-10_Kassab SR_Cochrane Central search strategy.docx"	All references exported to EndNote Human and adult study filters applied. Results limited to English language publications Search strategy saved as: "H:\Mayo Clinic Libraries\Systematic Reviews\2021\November\2021-11-9_Kassab SR\Search Strategies\2021-11-10_Kassab SR_Scopus search strategy.docx"	All references exported to EndNote Human and adult study filters applied. Results limited to English language publications Search strategy saved as: "H:\Mayo Clinic Libraries\Systematic Reviews\2021\November\2021-11-9_Kassab SR\Search Strategies\2021-11-10_Kassab SR_Web of Science search strategy.docx"
SCIE: Science citation index expanded; ESCI: Emerging sources citation index; LB: Liver biopsy; PC-LB: Percutaneous LB					

Supplementary Appendix 2. MOOSE Checklist

Item number	Recommendation	Reported on page number
	Reporting of background should include	
1	Problem definition	4-5
2	Hypothesis statement	5
3	Description of study outcome (s)	5
4	Type of exposure or intervention used	5
5	Type of study designs used	5
6	Study population	6
	Reporting of search strategy should include	
7	Qualifications of searchers (eg, librarians and investigators)	5
8	Search strategy, including time period included in the synthesis and key words	5
9	Effort to include all available studies, including contact with authors	6
10	Databases and registries searched	5
11	Search software used, name and version, including special features used (eg, explosion)	5
12	Use of hand searching (eg, reference lists of obtained articles)	-NA-
13	List of citations located and those excluded, including justification	8-9, Suppl Figure 1
14	Method of addressing articles published in languages other than English	-NA-
15	Method of handling abstracts and unpublished studies	6
16	Description of any contact with authors	-NA-
	Reporting of methods should include	
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	5-6
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	6
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	6
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	6
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	7
22	Assessment of heterogeneity	8
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	8
24	Provision of appropriate tables and graphics	Tables 1-2, Figures 1-5
	Reporting of results should include	
25	Graphic summarizing individual study estimates and overall estimate	Figures 1-5
26	Table giving descriptive information for each study included	Tables 1-2
27	Results of sensitivity testing (eg, subgroup analysis)	12-13
28	Indication of statistical uncertainty of findings	12-13

Supplementary Table 1. Newcastle–Ottawa Scale - Study quality assessment

Study	Selection				Comparability	Outcome			Score	Quality
	Representativeness of the average adult in community	Cohort size	Information on clinical outcomes	Outcome not present at start	Factors comparable between the groups	Adequate clinical assessment	Follow up time	Adequacy of follow-up	Maximum=8	High>6, medium 4 to 6, Low<4
	Population based: 1; multi-center: 0.5; single-center: 0	>40 patients: 1; 39 to 20: 0.5; <20: 0	Information with clarity: 1; information derived from percentage value: 0.5; unclear: 0	Not present: 1; present: 0	Yes: 1; no: 0	Yes: 1; no: 0	Yes: 1; not mentioned: 0	All patients followed up: 1; >50% followed up: 0.5; <50% followed up OR not mentioned: 0		
Ali, 2020	0	1	1	1	1	1	0	1	6	Medium
Bhogal, 2020	0	1	1	1	1	1	0	1	6	Medium
Facciorusso, 2021	0.5	1	1	1	1	1	0	1	6.5	High



Supplementary Figure 1: PRISMA flow chart

Supplementary Figure 2. Risk of bias assessment

	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Blinding of Participants (Performance Bias)	Blinding of Outcome Assessment (Detection Bias)	Incomplete outcome Data (Attrition Bias)	Selective Reporting (Reporting Bias)
Bang, 2021	+	+	+	+	+	+
Nallapeta, 2021	+	+	+	+	+	+

Test	Outcome	Starting grade	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Overall Certainty of evidence	Overall grade
EUS-guided versus percutaneous liver biopsy - A comprehensive review and meta-analysis of outcomes	OR - Diagnostic adequacy	High	NS	NS	NS	NS	None	High (Grade A)	High (Grade A)
	OR - Diagnostic accuracy	High	NS	NS	NS	NS	None	High (Grade A)	
	OR - Overall adverse events	High	NS	NS	NS	NS	None	High (Grade A)	
	OR - Mean complete portal tracts	High	NS	NS	NS	NS	None	High (Grade A)	
	OR - Total specimen length	High	NS	NS	NS	NS	None	High (Grade A)	

S: Serious; NS: Not serious; OR: Odds ratio