

## Diagnostic and therapeutic role of endoscopic ultrasound in liver diseases: A systematic review and meta-analysis

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### Abstract

#### BACKGROUND

In hepatology, the clinical use of endoscopic ultrasound (EUS) has experienced a notable increase in recent times. These applications range from the diagnosis to the treatment of various liver diseases. Therefore, this systematic review summarizes the evidence for the diagnostic and therapeutic roles of EUS in liver diseases.

**AIM**

To examine and summarize the current available evidence of the possible roles of the EUS in making a suitable diagnosis in liver diseases as well as the therapeutic accuracy and efficacy.

**METHODS**

PubMed, Medline, Cochrane Library, Web of Science, and Google Scholar databases were extensively searched until October 2023. The methodological quality of the eligible articles was assessed using the Newcastle-Ottawa scale or Cochrane Risk of Bias tool. In addition, statistical analyses were performed using the Comprehensive Meta-Analysis software.

**RESULTS**

Overall, 45 articles on EUS were included (28 on diagnostic role and 17 on therapeutic role). Pooled analysis demonstrated that EUS diagnostic tests had an accuracy of 92.4% for focal liver lesions (FLL) and 96.6% for parenchymal liver diseases. EUS-guided liver biopsies with either fine needle aspiration or fine needle biopsy had low complication rates when sampling FLL and parenchymal liver diseases (3.1% and 8.7%, respectively). Analysis of data from four studies showed that EUS-guided liver abscess had high clinical (90.7%) and technical success (90.7%) without significant complications. Similarly, EUS-guided interventions for the treatment of gastric varices (GV) have high technical success (98%) and GV obliteration rate (84%) with few complications (15%) and rebleeding events (17%).

**CONCLUSION**

EUS in liver diseases is a promising technique with the potential to be considered a first-line therapeutic and diagnostic option in selected cases.

**Key Words:** Focal liver lesion; Liver abscess drainage; Fine needle aspiration; Gastric varices; Endoscopic ultrasound

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**Core Tip:** This is an extensive systematic review to assess the efficacy and accuracy of the endoscopic ultrasound (EUS) in dealing with different liver pathologies. The EUS guided liver abscess drainage (EUS-AD) was highly accurate (90.7%) and very safe, with more than 90% of patients experienced no complications post EUS-AD. The safety profiles of the EUS guided aspiration and EUS guided biopsy was very promising with very low complication rate. EUS guided interventions is a safe and accurate procedure and this was demonstrated in different interventions such as EUS guided gastric varices obliteration which was successful in 84% with only 15% rebleeding risk.

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**INTRODUCTION**

Since its introduction in the 1980s, endoscopic ultrasonography (EUS) has emerged as a pivotal diagnostic and therapeutic tool, particularly for assessing a wide range of gastrointestinal (GI) and hepatobiliary disorders[1,2]. Traditionally, EUS has not been commonly used to assess liver conditions. However, since its first publication in 1999 demonstrating the efficacy of EUS and fine-needle aspiration (EUS-FNA) in diagnosing focal liver lesions (FLL), the clinical utilization of EUS for evaluating the liver has gained interest[3]. Research has shown that owing to its ability to provide high-resolution images, EUS is valuable for detecting small liver lesions that often go unnoticed after transabdominal ultrasound (US) and computed tomography (CT)[4]. However, research on EUS for liver tumors often fails to provide details on the location of tumors within the liver segments. This may be because EUS anatomical segmentation of the liver is considered less significant.

EUS offers advantages that distinguish it from other diagnostic tools. EUS is performed by inserting the probe into the GI tract; therefore, it can provide close proximity to the target tissues[5]. This close proximity is particularly valuable for evaluating lesions within the GI wall, adjacent lymph nodes, and surrounding vasculature. It is also valuable in guiding FNA and fine-needle biopsy (FNB) for the collection of tissue samples from lesions and suspicious areas identified during the course of examination[6]. Furthermore, EUS can provide real-time imaging, which allows for dynamic assessment and precise localization of lesions[7].

Despite its advantages, evidence of the role of EUS in liver disease is limited. Therefore, this systematic review aimed to evaluate the diagnostic and therapeutic roles of EUS in liver disease.

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## MATERIALS AND METHODS

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### Information sources and searches

PubMed, Medline, Cochrane Library, Web of Science, and Google Scholar databases were comprehensively searched for all randomized and nonrandomized studies published from inception to October 2023. The bibliographies of potential articles were also scrutinized for additional studies. Studies with the following MeSH terms and keywords were retrieved from the electronic databases: (Endoscopic ultrasound OR endosonography OR EUS OR endoscopic ultrasound-guided fine needle aspiration OR EUS-FNA OR endoscopic ultrasound-guided fine needle biopsy OR EUS-FNB) AND (diagnosis OR diagnostic OR detection OR treatment OR interventional OR therapeutic) AND (hepatic OR liver). The gray literature and duplicates were not retrieved, as they would have interfered with the scientific purpose of the current study.

### Eligibility criteria

Two independent reviewers scrutinized potential studies using predefined inclusion and exclusion criteria. Studies were eligible for review and analysis if they were full articles published in English, included human participants, or reported on the role of EUS in the diagnosis or treatment of liver diseases, including portal hypertension. On the other hand, articles that went against these criteria or were designed as case reports, systematic reviews, conference abstracts, and letters to the editors or reported the therapeutic and diagnostic role of EUS in extrahepatic structures such as bile duct and gall bladder were excluded. In the event of differences between the reviewers, a third reviewer was consulted to harmonize discrepancies.

### Data extraction

Two impartial reviewers examined all included records and abstracted the data required for review and analysis into separate Excel files. Discrepancies in the extracted data were resolved through constructive discussions or by consulting a third reviewer. The extracted data included the Author ID (surname of the primary author and publication date), study design, study location (country), characteristics of the enrolled patients (sample size, sex distribution, mean/median age, and indication for conducting EUS/EUS-guided diagnostic tests), diagnostic tests used, intervention, treated liver disorder, and outcomes.

The outcomes of our study were divided into the therapeutic and diagnostic groups. The diagnostic endpoints included diagnostic accuracy and yield. Diagnostic accuracy was defined as the ratio of true positives to true negatives for an accurate cytological or histological diagnosis in the total number of patients. Therapeutic outcomes included procedure-related complications, technical and clinical success, gastric varices (GV) obliteration, and rebleeding.

### Quality appraisal

Randomized and nonrandomized studies were included in the current review; therefore, quality assessment was performed using two different tools. The Newcastle-Ottawa scale was used to assess the methodological quality of non-randomized studies. This tool evaluates studies according to the selection, comparability, and outcome domains. For every domain, a maximum of one star was assigned for a fully answered criterion; otherwise, no stars were assigned. In the selection domain, a maximum of 4 stars could be attained, whereas a maximum of two and three stars could be achieved for the comparability and outcome domains, respectively.

On the other hand, bias assessment of randomized trials was performed using Cochrane's risk of bias (RoB) tool embedded within the Review Manager software. RoB was assessed based on selection, attrition, performance, reporting, and other biases. A low RoB was assigned to a domain that was sufficiently addressed within the study, whereas a high and unclear risk was assigned to domains that were not entirely addressed or had insufficient information to make a judgment.

### Data synthesis

The comprehensive meta-analysis software (CMA V3) was used to conduct all statistical analyses in the present study. The random-effects model was used to pool the estimated weighted effect size and counter-anticipated heterogeneity. The inter-study heterogeneity was calculated using the  $I^2$  statistics, of which values > 50% were regarded as significant [8]. Moreover, the effect sizes were calculated together with their 95% confidence intervals, and when possible, subgroup analyses were performed according to diagnostic tests or EUS-guided interventions.

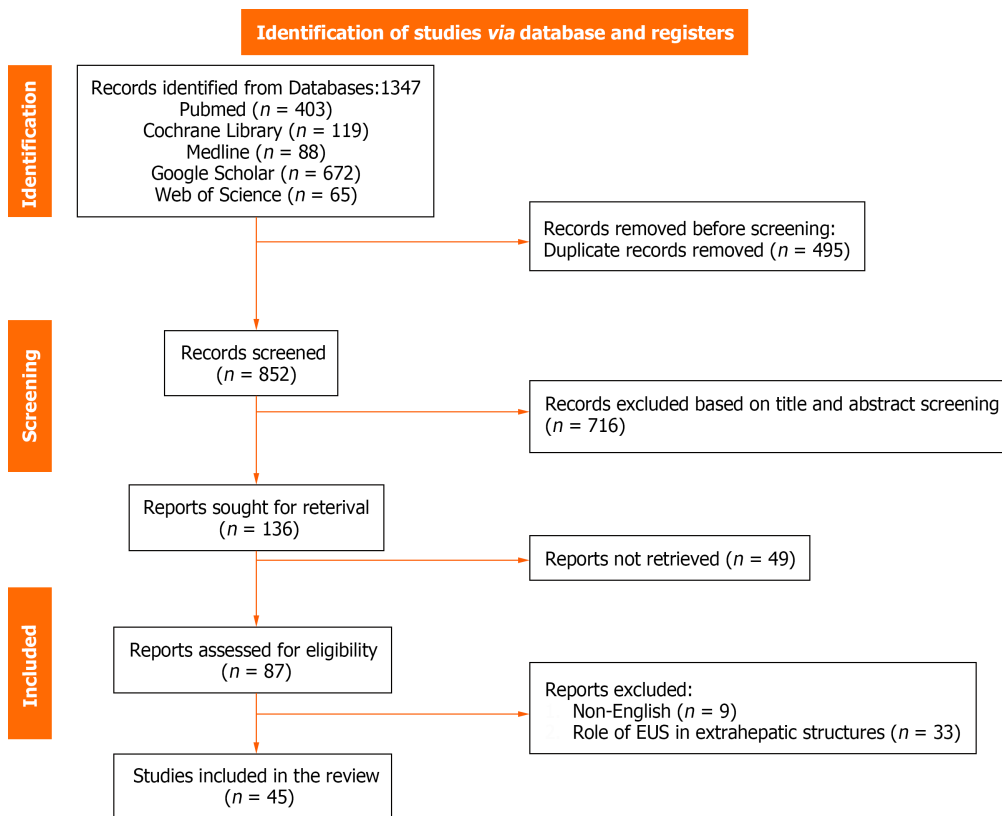
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## RESULTS

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### Study selection

An extensive database search identified 1347 potential articles. Duplicate screening resulted in the exclusion of 495 duplicate studies. Subsequently, 716 records were eliminated based on title, abstract, and title screening, and 49 were not retrieved as they were either case reports, reviews, conference abstracts, or letters to the editor. Finally, 45 records were included and the remaining 42 were excluded for the following reasons: nine were published in different languages and 33 evaluated the diagnostic or therapeutic role of EUS in extrahepatic structures and other parts of the body (Figure 1).



**Figure 1** The preferred reporting items for systematic reviews and meta-analyses flow diagram for study selection. EUS: Endoscopic ultrasound.

### Methodological quality and RoB assessment

Using the Newcastle-Ottawa scale and Cochrane RoB, we found that most studies were of good or fair quality. [Table 1](#) presents the Newcastle-Ottawa scale results and [Figure 2](#) summarizes the RoB.

### Diagnostic role of EUS in the diagnosis of liver diseases

Twenty-eight studies reported the diagnostic role of EUS, of which 16 evaluated its value in detecting FLL, 10 in detecting parenchymal liver diseases (PLD), and two in detecting portal hypertension. Furthermore, all the studies were conducted in individual countries (11 in the United States, 2 in Japan, 3 in Romania, 2 in Turkey, 3 in Korea, 1 in Italy, 1 in Germany, 1 in India, 2 in China, and 1 in Egypt; [Table 2](#)).

### Role of EUS in the detection of FLL

The cumulative analyses on the role of EUS in detecting FLL have shown an overall diagnostic accuracy rate of 92.4% (95%CI: 89.2 – 0.95). A subgroup analysis of the EUS diagnostic tests has shown that EUS alone had a diagnostic accuracy of 90.1%, whereas EUS-FNA and EUS-FNB had diagnostic accuracies of 93.4% and 98%, respectively. Furthermore, analysis of data from two studies has shown that Contrast-enhanced EUS (CEH-EUS) had a diagnostic accuracy of 94% for detecting FLL ([Figure 3A](#)).

Additionally, a safety analysis was performed to determine the safety of EUS-FNA and EUS-FNB in diagnosing FLL. Our subgroup analysis suggested that EUS-FNA had a complication rate of 2.9%, whereas the rate of complications when using EUS-FNA was 3.8% ([Figure 3B](#)).

### Role of EUS in the detection of PLD

Seventeen studies assessing the value of EUS in detecting parenchymal liver disease reported an overall diagnostic accuracy of 96.6%. A subgroup analysis of data from these studies showed that EUS-FNA had a diagnostic accuracy of 96.6%, whereas EUS-FNB had a diagnostic accuracy of 97.6% for the detection of PLD ([Figure 4A](#)). Furthermore, a safety evaluation of these diagnostic tests has shown complication rates of 6.2% and 9.6% for EUS-FNA and EUS-FNB, respectively ([Figure 4B](#)).

### Role of EUS in the detection of portal hypertension

Although studies on the role of EUS in portal hypertension are limited, we to identify two human studies evaluating the efficacy of EUS-guided portal pressure gradient (PPG) measurements. A meta-analysis of data from these studies revealed that 40 patients underwent EUS-PPG, with a technical success rate of 95.1% ([Figure 5A](#)). No complications related to this procedure have been previously reported.

**Table 1** Methodological quality using the Newcastle-Ottawa scale

Ref.	Selection (/4)	Comparability (/2)	Outcome (/3)	Overall methodological quality
Ichim <i>et al</i> [9], 2022	3	1	2	Good
Minaga <i>et al</i> [10], 2021	2	1	1	Poor
Takano <i>et al</i> [11], 2021	3	1	2	Good
Ichim <i>et al</i> [12], 2020	3	1	2	Good
Facciorusso <i>et al</i> [13], 2021	3	1	3	Good
Chon <i>et al</i> [14], 2019	3	1	2	Good
Akay <i>et al</i> [15], 2021	3	1	3	Good
Chen <i>et al</i> [16], 2020	3	1	3	Good
Hollerbach <i>et al</i> [17], 2003	3	1	2	Good
Singh <i>et al</i> [18], 2007	2	1	2	Fair
tenBerge <i>et al</i> [19], 2002	2	1	2	Fair
Lee <i>et al</i> [20], 2015	3	2	1	Poor
Oh <i>et al</i> [21], 2018	3	2	2	Good
Singh <i>et al</i> [22], 2009	3	1	2	Good
Okasha <i>et al</i> [23], 2023	3	1	2	Good
Hasan <i>et al</i> [24], 2019	2	1	3	Good
Bhogal <i>et al</i> [25], 2020	3	1	3	Good
Diehl <i>et al</i> [26], 2015	2	1	2	Fair
Sundaram <i>et al</i> [27], 2023	4	1	2	Good
Saab <i>et al</i> [28], 2017	2	1	1	Poor
Sey <i>et al</i> [29], 2016	3	2	1	Poor
Shah <i>et al</i> [30], 2017	2	1	1	Poor
Sisman <i>et al</i> [31], 2020	2	1	2	Fair
Stavropoulos <i>et al</i> [32], 2012	3	2	1	Poor
Zhang <i>et al</i> [33], 2021	3	1	2	Good
Huang <i>et al</i> [34], 2017	3	1	2	Good
Ogura <i>et al</i> [35], 2016	3	1	2	Good
Tanikawa <i>et al</i> [36], 2023	3	1	2	Good
Tonozuka <i>et al</i> [37], 2015	2	1	2	Fair
Carbajo <i>et al</i> [38], 2019	3	1	2	Good
Nakaji <i>et al</i> [39], 2016	3	1	2	Good
Frost <i>et al</i> [40], 2018	2	1	2	Fair
Bhat <i>et al</i> [41], 2016	3	1	2	Good
Bick <i>et al</i> [42], 2019	3	1	2	Good
Binmoeller <i>et al</i> [43], 2011	3	1	2	Good
Bazarbashi <i>et al</i> [44], 2020	3	2	1	Poor
Mukkada <i>et al</i> [45], 2018	3	1	2	Good
Lee <i>et al</i> [46], 2000	2	2	2	Fair
Gubler <i>et al</i> [47], 2014	2	1	2	Fair
Koziel <i>et al</i> [48], 2019	3	1	2	Good
Romero-Castro <i>et al</i> [49], 2013	4	2	2	Good

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Allocation Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ching-Companiononi <i>et al</i> <sup>[51]</sup> 2019	+	-	+	+	+	+	
Gheorghiu <i>et al</i> <sup>[50]</sup> 2022	+		-	+	+	+	+
Lôbo <i>et al</i> <sup>[53]</sup> 2019	+	+		+	+	+	+

Figure 2 Risk of bias summary.

### Therapeutic role of EUS in liver diseases

In the current review, the role of EUS in the treatment of liver diseases was reported in 17 studies. Four of these studies reported the efficacy of EUS-guided liver abscess drainage (EUS-AD), whereas two reported the value of EUS-guided interventions for the treatment of liver lesions. Additionally, 11 studies reported the therapeutic efficacy of various EUS-guided treatments of GV (Table 3).

### Role of EUS in drainage of liver abscess

The efficacy of EUS-AD was reported in four studies[35-38]. A pooled analysis of data from these studies has shown that EUS-AD had a high technical (90.7%) and clinical success (90.7%; Figure 5B and C). Furthermore, two studies that included patients with hepatic abscesses reported that EUS-AD did not have any immediate or delayed complications.

### Role of EUS in the treatment of solid liver lesions

The use of EUS to guide the treatment of FLL is a new and evolving field that has mostly been reported in case reports and animal studies. However, we identified two human studies[39,52] reporting the efficacy of EUS-guided interventions for solid liver lesions. Jiang *et al*[52] reported that EUS-guided therapy (ethanol injection,  $n = 10$ ; iodine-125 seed brachytherapy,  $n = 13$ ) was successful in most cases of left-sided liver tumors (23/25) without any procedure-related complications. Furthermore, complete tumor response was achieved in 65.2% of the patients, whereas partial response was achieved in 34.8%[52].

Nakaji *et al*[39] studied the efficacy of EUS-guided ethanol injections in the treatment of hepatocellular carcinoma (HCC). They found that the overall survival at 1, 2, and 3 years after the EUS-guided intervention was 91.7%, 75%, and 53.3%, respectively. Moreover, they reported two episodes of fever related to the procedure. However, no serious complications, such as intra-abdominal hemorrhage, abscesses, or bilomas were recorded[39].

### Role of EUS in the management of GV

The role of EUS in GV treatment has not yet been fully established and remains an area of investigation. Therefore, we evaluated the efficacy and safety of EUS-guided interventions [cyanoacrylate (CYA), coil embolization, thrombin, and a combination of CYA and coil embolization] for GV. The pooled analyses revealed that EUS-guided interventions had a technical success rate of 98%. In addition, the rate of complication, GV obliteration, and rebleeding events were 15%, 84%, and 17%, respectively. Subgroup analyses of individual EUS-guided interventions are presented in Table 4.

## DISCUSSION

This systematic review and meta-analysis summarizes the evidence for the therapeutic and diagnostic roles of EUS in hepatic diseases. The pooled analysis showed that EUS is an effective and safe tool for the diagnosis of FLL, PLD, and portal hypertension. We found that EUS-guided interventions were effective and safe for the treatment of liver diseases.

### Diagnostic role of EUS

Despite the establishment of transabdominal US, CT, and magnetic resonance imaging as diagnostic tools for liver diseases, the use of EUS as a diagnostic and therapeutic modality has increased considerably in recent years. In our analysis, we found that EUS-guided liver biopsy (FNA and FNB) for parenchymal liver disease had high diagnostic accuracy (96.6%) and low complication rates (8.7%). This finding is consistent with that reported in the first meta-analysis

**Table 2 Characteristics of studies on the role of endoscopic ultrasound in the diagnosis of liver diseases**

Ref.	Study design	Study location	Participants characteristics				Diagnostic test	Outcomes
			Sample (n)	M/F	Age (yr)	Indication		
Ichim <i>et al</i> [9], 2022	Single-arm observational study	Romania	30	17/13	64.3	FLL	EUS-FNA	Diagnostic accuracy: 97% Complications: 1 patient
Minaga <i>et al</i> [10], 2021	Retrospective study	Japan	426	248/178	69 (63–75)	FLL	CEH-EUS	Diagnostic accuracy: 98.4%
Takano <i>et al</i> [11], 2021	Retrospective study	Japan	106	60/46	68 (32–87)	FLL	EUS-FNA	Diagnostic accuracy: 96% Complications: 1 patient
Ichim <i>et al</i> [12], 2020	Prospective study	Romania	48	27/21	66.3 (40–83)	FLL	EUS-FNA	Diagnostic accuracy: 98% Complications: None
Facciorusso <i>et al</i> [13], 2021	Retrospective study	Italy	116	70/46	NR	FLL	EUS-FNB	Diagnostic accuracy: 88.8% Complications: None
Chon <i>et al</i> [14], 2019	Retrospective study	Korea	58	35/23	68.1 (42–86)	FLL	EUS-FNB	Diagnostic accuracy: 89.7% Complications: 1 patient
Akay <i>et al</i> [15], 2021	Retrospective study	Turkey	25	15/10	62.73 ± 15.24	FLL	EUS-FNA	Diagnostic accuracy: 86.3% Complications: None
Gheorghiu <i>et al</i> [50], 2022	Prospective RCT	Romania	30	21/9	60 (37–84)	FLL	EUS-FNA and EUS-FNB	Diagnostic accuracy: 100% and 86.7% for EUS-FNB and EUS-FNA, respectively Complications: None
Chen <i>et al</i> [16], 2020	Retrospective study	China	38	35/3	55.7 ± 11.8	FLL	EUS-FNB	Diagnostic accuracy: 90% Complications: 3 patients
Hollerbach <i>et al</i> [17], 2003	Prospective study	Germany	41	NR	66 ± 7	FLL	EUS-FNA	Diagnostic accuracy: 94% Complications: 2 patients
Singh <i>et al</i> [18], 2007	Prospective study	United States	17	NR	56 (43–85)	FLL	EUS and EUS-FNA	Diagnostic accuracy: 65% and 94% for EUS and EUS-FNA, respectively Complications: None
tenBerge <i>et al</i> [19], 2002	Retrospective study		26	NR	NR	FLL	EUS-FNA	Diagnostic accuracy: 89% Complications: 6 patients
Lee <i>et al</i> [20], 2015	Retrospective study	Korea	21	9/12	63 (37–81)	FLL	EUS-FNB	Diagnostic accuracy: 90.5% Complications: None
Oh <i>et al</i> [21], 2018	Prospective study	Korea	30	19/11	66.5 (55.5–74)	FLL	CEH-EUS and CEH-EUS-FNA	Diagnostic accuracy: 80% and 86.7% for CEH-EUS and CEH-EUS-FNA, respectively Complications: None
Singh <i>et al</i> [22], 2009	Prospective study	United States	131	128/3	67 (45–86)	FLL	EUS and EUS-FNA	Diagnostic accuracy: 97% and 98% for EUS and EUS-FNA, respectively Complications: None
Okasha <i>et al</i> [23], 2023	Cross-sectional study	Egypt	43	32/11	56	FLL	EUS and EUS-FNA/FNB	Diagnostic accuracy: 94%, and 100% for EUS and EUS-FNA/FNB

Ching-Companiononi <i>et al</i> [51], 2019	Prospective RCT	United States	40	NR	NR	PLD	EUS-FNA and EUS-FNB	Complications: None Diagnostic accuracy: 100%
Hasan <i>et al</i> [24], 2019	Prospective study	United States	40	14/26	61 (46.7–68.2)	PLD	EUS-FNB	Complications: 13 patients Diagnostic accuracy: 100%
Bhagal <i>et al</i> [25], 2020	Retrospective study	United States	513	244/269	NR	PLD	EUS-FNA and EUS-FNB	Complications: 9 patients Diagnostic accuracy: 99%
Diehl <i>et al</i> [26], 2015	Prospective study	United States	110	48/62	53 (9–87)	PLD	EUS-FNA	Complications: 1 patient Diagnostic accuracy: 98%
Sundaram <i>et al</i> [27], 2023	Retrospective study	India	74	37/37	44.5 (18–79)	PLD	EUS-FNA	Complications: 5 patients Diagnostic accuracy: 97.3%
Saab <i>et al</i> [28], 2017	Retrospective study	United States	47	16/31	54	PLD	EUS-FNB	Complications: 2 patients Diagnostic accuracy: 100%
Sey <i>et al</i> [29], 2016	Cross-sectional study	United States	75	24/51	51	PLD	EUS-FNB	Complications: 2 patients Diagnostic accuracy: 82.7%
Shah <i>et al</i> [30], 2017	Retrospective study	United States	24	NR	NR	PLD	EUS-FNB	Complications: 2 patients Diagnostic accuracy: 96%
Sisman <i>et al</i> [31], 2020	Retrospective study	Turkey	40	24/16	44 (22–72)	PLD	EUS-FNB	Complications: 2 patients Diagnostic accuracy: 100%
Stavropoulos <i>et al</i> [32], 2012	Prospective case series	United States	22	6/16	61 (32–79)	PLD	EUS-FNA	Complications: None Diagnostic accuracy: 91%
Zhang <i>et al</i> [33], 2021	Prospective study	China	12	9/3	NR	PH	EUS-PPG	Complications: None Technical success rate: 91.7% EUS-PPG correlates well with HVPG ( $r = 0.923$ )
Huang <i>et al</i> [34], 2017	Prospective study	United States	28	18/10	63 (30–80)	PH	EUS-PPG	Complications: None Technical success rate: 100% EUS-PPG correlates well with clinical parameters of PH

EUS: Endoscopic ultrasound; FLL: Focal liver lesions; CEH-EUS: Contrast-enhanced endoscopic ultrasound; FNA: Fine-needle aspiration; FNB: Fine-needle biopsy; NR: Not report; RCT: Randomized clinical trial; PLD: Parenchymal liver diseases; EUS-PPG: Endoscopic ultrasound-guided portal pressure gradient; PH: Portal hypertension; HVPG: Hepatic venous pressure gradient; M/F: Male/female.

of nine studies published between 2009 and 2016 [54]. According to that meta-analysis, EUS-liver biopsy (EUS-LB) had an overall diagnostic yield of 93.9% and a complication rate of 2.3%. Similarly, a more recent meta-analysis evaluating the efficacy and safety of EUS-LB in patients with parenchymal liver disease and FLL revealed that EUS-LB had a high diagnostic yield (95%) and low adverse event rate (3%) [55]. The evidence from these studies and our analysis suggests that EUS-LB may be a safer diagnostic alternative for PLD. However, our subgroup analysis has shown that adverse events were more prevalent when using FNB needles than FNA needles (9.6% *vs* 6.2%). Therefore, high-quality randomized trials are needed to evaluate the safety of EUS-FNA compared with EUS-FNB in the diagnosis of PLD.

EUS is also a valuable diagnostic tool for FLL. EUS can provide high-resolution images of the liver anatomy, enabling the identification and characterization of focal lesions. In our analyses, we found that EUS-guided biopsy had an overall diagnostic accuracy of 92.4% and a low complication rate (3.1%). This finding is consistent with a previous review article reporting that the diagnostic yield of EUS-guided biopsy of FLL ranges from 89.7% to 100% [7]. Furthermore, our



**Table 3 Characteristics of studies on the therapeutic role of endoscopic ultrasound**

Ref.	Study design	Study location	Participant characteristics		Condition	Intervention	Outcomes
			Sample (n)	M/F			
Ogura <i>et al</i> [35], 2016	Retrospective study	Japan	27	20/7	Liver abscess	EUS-AD	Clinical success: 100% Technical success: 100% Complications: None
Tanikawa <i>et al</i> [36], 2023	Retrospective study	Japan	8	4/4	Liver abscess	EUS-AD	Clinical success: 87.5% Technical success: 87.5%
Tonozuka <i>et al</i> [37], 2015	Retrospective case series	Japan		NR	Liver abscess	EUS-AD	Clinical success: 100% Technical success: 100% Complications: None
Carbajo <i>et al</i> [38], 2019	Retrospective study	Spain	9	NR	Liver abscess	EUS-AD	Clinical success: 88.9% Technical success: 88.9%
Nakaji <i>et al</i> [39], 2016	Retrospective study	Japan	12	10/2	Solid liver lesions	EUS-guided ethanol injection	Complications: 2 Overall survival: 91.7%, 75%, and 53.3% at 1, 2, and 3 years
Jiang <i>et al</i> [52], 2016	Case series	China	26	17/9	Solid liver lesions	EUS-guided ethanol injection and iodine-125 brachytherapy	Complications: None
Frost <i>et al</i> [40], 2018	Case series	Ireland	8	7/1	GV	EUS-guided thrombin injection	Complications: None Obliteration: 75% Rebleeding: 1 patient
Bhat <i>et al</i> [41], 2016	Retrospective study	United States	152	97/55	GV	EUS-guided CYA and coil embolization	Technical success: 99% Obliteration: 93% Rebleeding: 20 patients Complications: 9 patients
Bick <i>et al</i> [42], 2019	Retrospective study	United States	104	62/42	GV	EUS-guided CYA	Obliteration: 79% Rebleeding: 12 patients Complications: 13 patients
Binmoeller <i>et al</i> [43], 2011	Retrospective study	United States	30	19/11	GV	EUS-guided CYA and coil embolization	Technical success: 100% Obliteration: 95.8% Rebleeding: 4 patients Complications: None
Bazarbashi <i>et al</i> [44], 2020	Prospective study	United States	40	27/13	GV	EUS-Guided coil embolization	Technical success: 100% Obliteration: 100% Complications: 1 patient
Lôbo <i>et al</i> [53], 2019	RCT	Brazil	32	13/19	GV	EUS-guided CYA and coil embolization	Complications: 13 patients Obliteration: 93.3%
Mukkada <i>et al</i> [45], 2018	Retrospective study	India	30	NR	GV	EUS-Guided coil embolization	Rebleeding: 6 patients
Lee <i>et al</i> [46], 2000	Prospective study	China	101	69/32	GV	EUS-guided CYA	Obliteration: 79.6% Complications: 22 patients Rebleeding: 19 patients

Gubler <i>et al</i> [47], 2014	Retrospective study	Switzerland	40	25/15	GV	EUS-guided CYA	Complications: 2 patients
Koziel <i>et al</i> [48], 2019	Retrospective study	Poland	16	9/7	GV	EUS-guided CYA and coil embolization	Technical success: 94% Complications: 6 patients
Romero-Castro <i>et al</i> [49], 2013	Retrospective study	Germany	30	22/8	GV	EUS-guided coil embolization	Obliteration: 90.9% Complications: 1 patient Rebleeding: None

M/F: Male/female; NR: Not report; RCT: Randomized clinical trial; EUS-AD: Endoscopic ultrasound guided liver abscess drainage; GV: Gastric varices; CYA: Cyanoacrylate.

**Table 4 Outcomes of endoscopic ultrasound-guided interventions in the management of gastric varices**

Outcome	Cumulative analyses (95%CI)	Subgroup analyses (95%CI)			
		EUS-CYA	EUS-Coil	EUS-CYA + Coil	EUS-thrombin
Technical success	0.98 (0.92–0.99)	NR	0.96 (0.55–0.99)	0.98 (0.92–0.99)	NR
Obliteration	0.84 (0.79–0.88)	0.78 (0.70–0.85)	0.93 (0.71–0.99)	0.93 (0.88–0.97)	0.75 (0.38–0.94)
Complications	0.15 (0.07–0.28)	0.20 (0.07–0.44)	0.10 (0.02–0.31)	0.22 (0.04–0.69)	0.06 (0.003–0.51)
Rebleeding	0.17 (0.13–0.23)	0.26 (0.13–0.49)	0.08 (0.02–0.34)	0.16 (0.11–0.23)	0.13 (0.02–0.54)

EUS-CYA: Endoscopic ultrasound-cyanoacrylate; NR: Not report.

subgroup analysis has shown that both EUS-FNA and EUS-FNB used in sampling FLL had excellent diagnostic accuracy (93.4% and 98%, respectively). However, a recent prospective trial found that a 22G EUS-FNB had significantly better diagnostic accuracy than a 22G EUS-FNA for FLL (100% *vs* 83.3%)[50]. However, these findings cannot be used independently to guide the clinical diagnosis of FLL owing to various limitations. First, the trial was carried out in a single center and had a limited number of patients, indicating that it is not representative of all FLL cases worldwide. Second, cytology was not performed on the EUS-FNA samples; thus, the diagnostic accuracy of EUS-FNA may have decreased. Finally, rapid on-site or macroscopic on-site evaluation was not conducted; hence, it is possible that the diagnostic accuracy decreased.

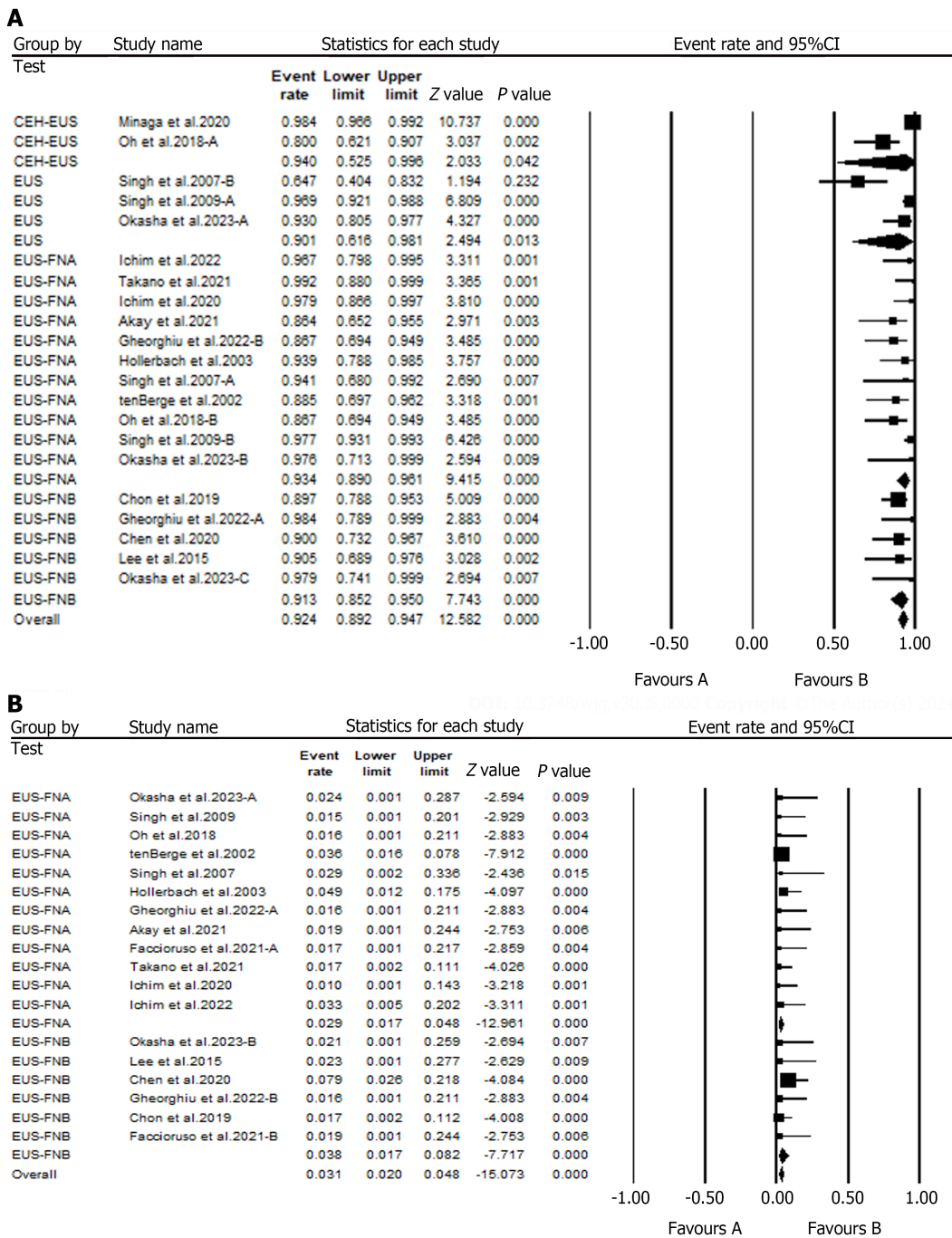
In addition, the use of CEH-EUS for FLL examination has gained interest. Owing to the dual blood supply to the liver, US contrast agents help examine the FLL in the arterial, portal, and venous phases. A pooled analysis of data from two studies in our review has shown that CEH-EUS achieved a diagnostic accuracy of 94% without any reported complications. Therefore, CEH-EUS has the potential to be integrated into daily clinical practice for the detection of suspected FLLs and for maximizing the management of these patients. However, further studies are required to confirm these findings.

EUS has several clinical applications in portal hypertension, including assessment of GV, assessment of collateral veins, and measurement of hemodynamic changes. It is also valuable for direct measurement of the PPG, which reflects the severity of portal hypertension and is an excellent prognostic factor in hepatic disease[56]. The two human studies[33,34] in the current review have shown that EUS can be used to guide the measurement of PPG, with a technical success rate of 95.1% and minimal complications. Zhang *et al*[33] observed a strong correlation between EUS-PPG using a 22G FNA needle and the hepatic venous pressure gradient (Pearson correlation,  $r = 0.93$ ). Therefore, EUS is safe and has a potential significance in the management and understanding of portal hypertension. However, larger clinical trials are needed to confirm these findings.

### Therapeutic role of EUS

In addition to its use as a diagnostic tool, EUS plays an important role in the treatment of liver diseases. Percutaneous drainage (PCD) is considered the first-line therapy for liver abscess drainage because it is minimally invasive and has a considerably high technical success[57,58]. However, this is disadvantageous because external drainage and self-tube removal may cause patient discomfort. Therefore, EUS-AD was developed to address these challenges. Although the efficacy of EUS-AD has largely been examined in case reports[59–65], we identified four small case series. The pooled analysis of data from these studies has shown that it has a high clinical (90.7%) and technical success rate (90.7%), and no major complications. This finding has been supported by a previous review that found that EUS-AD has a technical success rate of 97.5% for draining liver abscesses that are difficult to access[64]. Therefore, EUS-AD is a safe and viable intervention, especially for abscesses inaccessible by PCD.

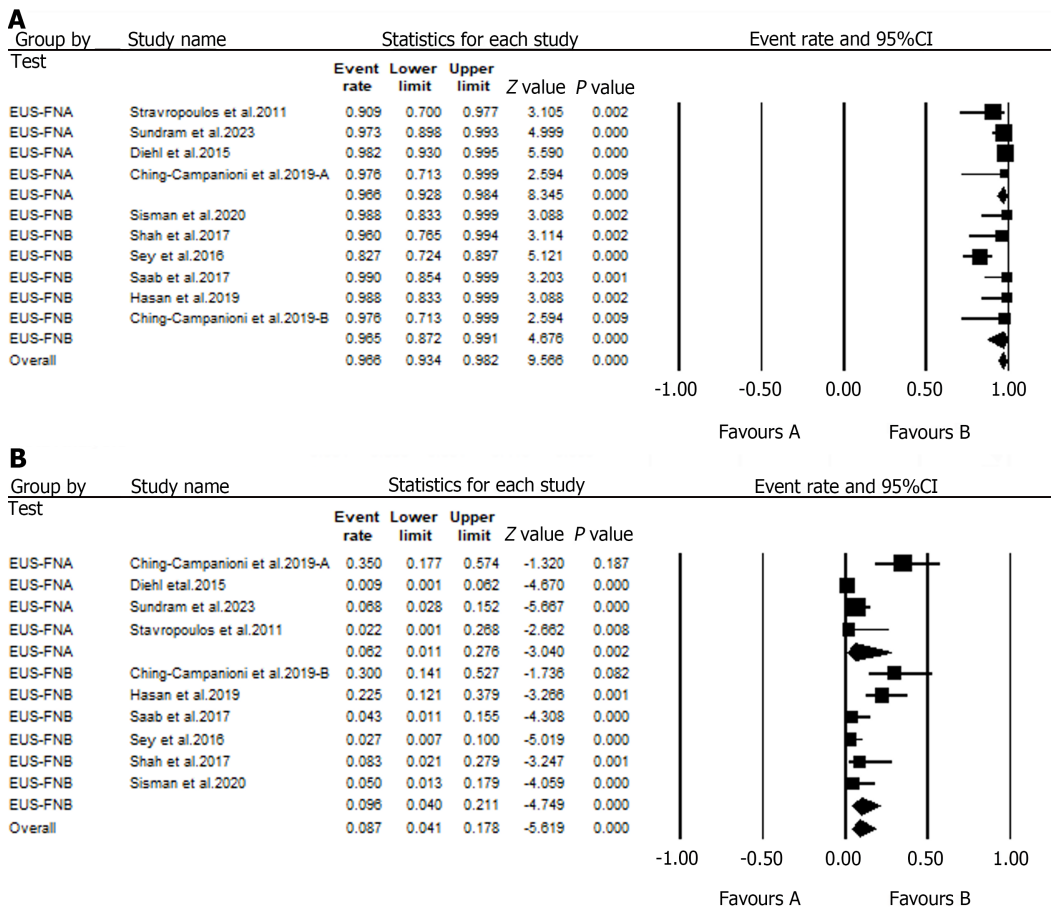
EUS has also been used to treat FLL using various techniques. However, this is a relatively new and expanding field, with the majority of information obtained from case reports and animal research. In the present study, only two studies



**Figure 3 Forest plot of diagnostic and complications accuracy.** A: Forest plot of diagnostic and accuracy in focal liver lesion detection (FLL); B: Forest plot of complications in FLL diagnosis. EUS: Endoscopic ultrasound; CEH-EUS: Contrast-enhanced endoscopic ultrasound; FNA: Fine-needle aspiration; FNB: Fine-needle biopsy.

reported EUS-guided interventions for solid liver lesions. A case series by Jiang *et al*[52] reported that EUS-guided iodine-125 brachytherapy was a safer and more effective treatment modality than EUS-guided ethanol injection for refractory left-sided liver lesions[52]. However, this finding warrants further large-scale clinical trials and comparative studies. In contrast, Nakaji *et al*[39] revealed that EUS-guided ethanol injection may be an effective and safe treatment option for early-stage HCC located in the caudate lobe[39].

GV in portal hypertension and cirrhosis can be catastrophic if not managed appropriately. Currently, therapeutic methods for managing GV include medical techniques, endoscopic interventions, and interventional radiology-guided procedures, such as transjugular intrahepatic portosystemic shunt and balloon retrograde transvenous obliteration. However, in recent years, EUS-guided interventions, such as EUS-guided coil embolization, thrombin, and CYA injections, have gained interest. Our pooled analysis has shown that EUS-guided interventions for GV had high technical success (98%), high obliteration rates (84%), low complications (15%), and low rebleeding events (17%). Furthermore, the subgroup analysis revealed that EUS-guided coil embolization alone was associated with fewer complications than EUS-guided CYA alone (10% vs 20%, respectively). Additionally, we noticed that combining CYA with coil embolization was associated with improved technical success, obliteration rates, and complication rates compared to EUS-guided CYA



**Figure 4 Forest plot of diagnostic accuracy and complications in parenchymal liver disease detection.** A: Forest plot of diagnostic accuracy in parenchymal liver disease (PLD) detection; B: Forest plot of complications in PLD diagnosis. EUS: Endoscopic ultrasound; FNA: Fine-needle aspiration; FNB: Fine-needle biopsy.

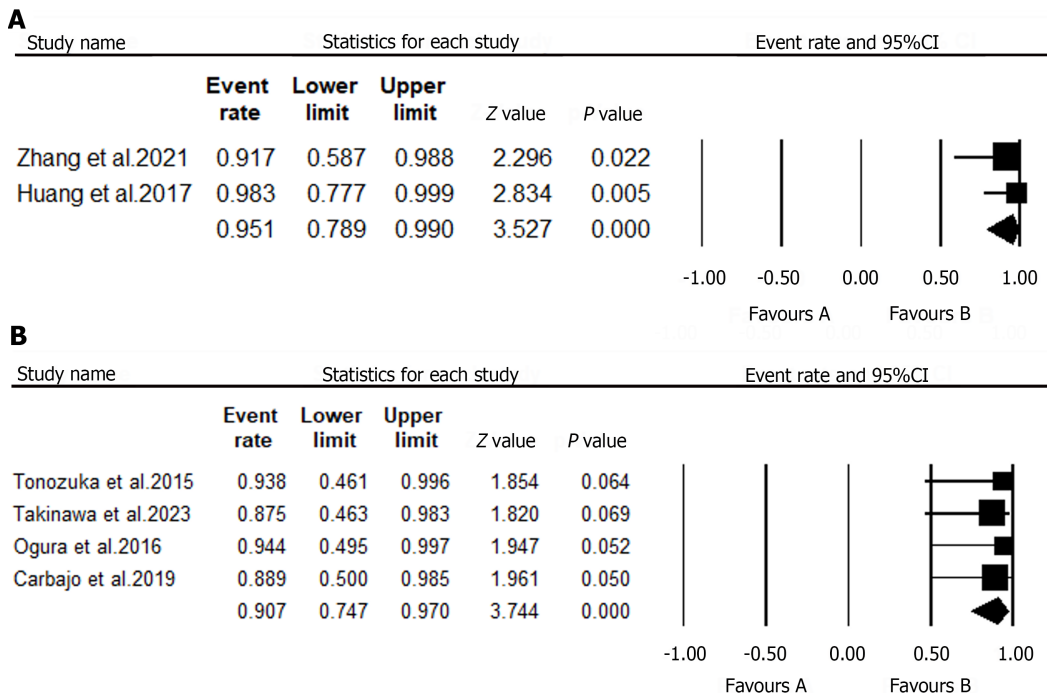
alone.

**Limitations**

Similar to other scientific research articles, our review has several limitations that should be considered when interpreting our findings. First, we observed high inter-study heterogeneity in our statistical analysis, which may be due to the varied and limited sample sizes. However, we used a random-effects model to account for this heterogeneity and obtained conservative results. Second, most studies included in the present research were conducted in single centers; hence, they are not entirely representative of the general population and community. Third, most studies were retrospective or prospective in nature, indicating that they were subject to selection and confounding biases. Finally, conference abstracts and articles published in different languages were eliminated, indicating that the data from these studies improved the scientific and statistical power of the meta-analysis.

**CONCLUSION**

EUS plays a significant role in the diagnosis and treatment of hepatic disorders. Notably, EUS-LB with FNA or FNB provides excellent diagnostic precision for FLL and PLD. Accumulated evidence indicates that EUS-FNB may be more effective than EUS-FNA for FLL diagnosis, and the addition of contrast enhancement can improve the diagnostic accuracy of EUS. However, these findings need extensive validation through larger clinical trials and comparative studies. EUS-guided interventions tend to be effective in the treatment of liver abscesses, GV, and FLL, with reduced complication risks. Nevertheless, the potential efficacy of EUS-guided interventions requires further large-scale randomized trials.



**Figure 5 Forest plot of the technical success rate of endoscopic ultrasound.** A: Forest plot of the technical success rate of endoscopic ultrasound (EUS) in detecting portal hypertension; B: Forest plot of the technical success rate of EUS-guided liver abscess drainage; C: Forest plot of the clinical success rate of EUS-guided liver abscess drainage.

## ARTICLE HIGHLIGHTS

### Research background

Endoscopic ultrasound (EUS) is a diagnostic and therapeutic procedure. The use of the EUS in the field of liver disease is recognizably increasing. However, the safety and efficacy are not well addressed.

### Research motivation

We aimed to explore the safety and accuracy profile of the EUS in hepatology by comparing 28 articles evaluating the diagnostic role and 17 evaluating the therapeutic role of EUS.

### Research objectives

To examine and explore the accuracy and efficacy of the role of the EUS in liver disease including the international aspects.

### Research methods

We independently conducted an extensive systematic review using an electronic search on PubMed, Medline, Cochrane Library, Web of Science, and Google Scholar databases were extensively scoured for studies until October 2023. The methodological quality of the eligible articles was performed using the Newcastle-Ottawa scale or Cochrane’s Risk of Bias tool. In addition, statistical analyses were performed with the comprehensive meta-analysis software.

### Research results

The pooled analysis demonstrated that EUS diagnostic tests have an accuracy of 92.4% for focal liver lesions (FLL) and 96.6% for parenchymal liver diseases. In addition, the cumulative analyses showed that EUS-guided liver biopsies with either fine needle aspiration or fine needle biopsy have low complication rates when sampling FLL and parenchymal liver diseases (3.1% and 8.7%, respectively). Furthermore, analysis of data from four studies has shown that EUS-guided liver abscess has a high clinical (90.7%) and technical success (90.7%) without significant complications. Similarly, EUS-guided interventions for the treatment of gastric varices (GV) have a high technical success (98%) and GV obliteration rates (84%), with low complications (15%) and rebleeding events (17%).

### Research conclusions

The role of EUS in the liver disease is well established with promising accuracy and efficacy profile. We found that EUS-guided interventions are effective and safe in treating liver diseases.

## Research perspectives

EUS in liver diseases is a promising technique with the potential to be considered as a first-line therapeutic and diagnostic option in selected cases.

## FOOTNOTES

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