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

Gadour *et al*. Role of EUS in liver diseases

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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 varies obliteration which was successful in 84% with only 15% rebreeding risk.

**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 pancreatobiliary 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.

**MATERIALS AND METHODS**

***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 I2 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.

**RESULTS**

***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).

***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.

***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 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 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 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 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.

**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.

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**Figure Legends**



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



**Figure 2 Risk of bias summary.**

  

**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.

   

**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.

    

**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.

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

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

**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 *et al*[9], 2022 | Single-arm observational study | Romania | 30 | 17/13 | 64.3 | FLL | EUS-FNA | Diagnostic accuracy: 97% |
| Complications: 1 patient |
| Minaga *et al*[10], 2021 | Retrospective study | Japan | 426 | 248/178 | 69 (63–75) | FLL | CEH-EUS | Diagnostic accuracy: 98.4% |
| Takano *et al*[11], 2021 | Retrospective study | Japan | 106 | 60/46 | 68 (32–87) | FLL | EUS-FNA | Diagnostic accuracy: 96% |
| Complications: 1 patient |
| Ichim *et al*[12], 2020 | Prospective study | Romania | 48 | 27/21 | 66.3 (40–83) | FLL | EUS-FNA | Diagnostic accuracy: 98% |
| Complications: None |
| Facciorusso *et al*[13], 2021 | Retrospective study | Italy | 116 | 70/46 | NR | FLL | EUS-FNB | Diagnostic accuracy: 88.8% |
| Complications: None |
| Chon *et al*[14], 2019 | Retrospective study | Korea | 58 | 35/23 | 68.1 (42–86) | FLL | EUS-FNB | Diagnostic accuracy: 89.7% |
| Complications: 1 patient |
| Akay *et al*[15], 2021 | Retrospective study | Turkey | 25 | 15/10 | 62.73 ± 15.24 | FLL | EUS-FNA | Diagnostic accuracy: 86.3% |
| Complications: None |
| Gheorghiu *et al*[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 *et al*[16], 2020 | Retrospective study | China | 38 | 35/3 | 55.7 ± 11.8 | FLL | EUS-FNB | Diagnostic accuracy: 90% |
| Complications: 3 patients |
| Hollerbach *et al*[17], 2003 | Prospective study | Germany | 41 | NR | 66 ± 7 | FLL | EUS-FNA | Diagnostic accuracy: 94% |
| Complications: 2 patients |
| Singh *et al*[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 *et al*[19], 2002 | Retrospective study |  | 26 | NR | NR | FLL | EUS-FNA | Diagnostic accuracy: 89% |
| Complications: 6 patients |
| Lee *et al*[20], 2015 | Retrospective study | Korea | 21 | 9/12 | 63 (37–81) | FLL | EUS-FNB | Diagnostic accuracy: 90.5% |
| Complications: None |
| Oh *et al*[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 *et al*[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 *et al*[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 |
| Complications: None |
| Ching-Companioni *et al*[51], 2019 | Prospective RCT | United States | 40 | NR | NR | PLD | EUS-FNA and EUS-FNB | Diagnostic accuracy: 100% |
| Complications: 13 patients |
| Hasan *et al*[24], 2019 | Prospective study | United States | 40 | 14/26 | 61 (46.7–68.2) | PLD | EUS-FNB | Diagnostic accuracy: 100% |
| Complications: 9 patients |
| Bhogal *et al*[25], 2020 | Retrospective study | United States | 513 | 244/269 | NR | PLD | EUS-FNA and EUS-FNB | Diagnostic accuracy: 99% |
| Diehl *et al*[26], 2015 | Prospective study | United States | 110 | 48/62 | 53 (9–87) | PLD | EUS-FNA | Diagnostic accuracy: 98% |
| Complications: 1 patient |
| Sundaram *et al*[27], 2023 | Retrospective study | India | 74 | 37/37 | 44.5 (18–79) | PLD | EUS-FNA | Diagnostic accuracy: 97.3% |
| Complications: 5 patients |
| Saab *et al*[28], 2017 | Retrospective study | United States | 47 | 16/31 | 54 | PLD | EUS-FNB | Diagnostic accuracy: 100% |
| Complications: 2 patients |
| Sey *et al*[29], 2016 | Cross-sectional study | United States | 75 | 24/51 | 51 | PLD | EUS-FNB | Diagnostic accuracy: 82.7% |
| Complications: 2 patients |
| Shah *et al*[30], 2017 | Retrospective study | United States | 24 | NR | NR | PLD | EUS-FNB | Diagnostic accuracy: 96% |
| Complications: 2 patients |
| Sisman *et al*[31], 2020 | Retrospective study | Turkey | 40 | 24/16 | 44 (22–72) | PLD | EUS-FNB | Diagnostic accuracy: 100% |
| Complications: 2 patients |
| Stavropoulos *et al*[32], 2012 | Prospective case series | United States | 22 | 6/16 | 61 (32–79) | PLD | EUS-FNA | Diagnostic accuracy: 91% |
| Complications: None |
| Zhang *et al*[33], 2021 | Prospective Study | China | 12 | 9/3 | NR | PH | EUS-PPG | Technical success rate: 91.7% |
| EUS-PPG correlates well with HVPG (r = 0.923) |
| Complications: None |
| Huang *et al*[34], 2017 | Prospective study | United States | 28 | 18/10 | 63 (30–80) | PH | EUS-PPG | Technical success rate: 100% |
| EUS-PPG correlates well with clinical parameters of PH |
| Complications: None |

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.

**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 *et al*[35], 2016 | Retrospective study | Japan | 27 | 20/7 | Liver abscess | EUS-AD | Clinical success: 100% |
| Technical success: 100% |
| Complications: None |
| Tanikawa *et al*[36], 2023 | Retrospective study | Japan | 8 | 4/4 | Liver abscess | EUS-AD | Clinical success: 87.5% |
| Technical success: 87.5% |
| Tonozuka *et al*[37], 2015 | Retrospective case series | Japan |  |  | Liver abscess | EUS-AD | Clinical success: 100% |
| Technical success: 100% |
| Complications: None |
| Carbajo *et al*[38], 2019 | Retrospective study | Spain | 9 | NR | Liver abscess | EUS-AD | Clinical success: 88.9% |
| Technical success: 88.9% |
| Nakaji *et al*[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 *et al*[52], 2016 | Case series | China | 26 | 17/9 | Solid liver lesions | EUS-guided ethanol injection and iodine-125 brachytherapy | Complications: None |
|
| Frost *et al*[40], 2018 | Case series | Ireland | 8 | 7/1 | GV | EUS-guided thrombin injection | Complications: None |
| Obliteration: 75% |
| Rebleeding: 1 patient |
| Bhat *et al*[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 *et al*[42], 2019 | Retrospective study | United States | 104 | 62/42 | GV | EUS-guided CYA | Obliteration: 79% |
| Rebleeding: 12 patients |
| Complications: 13 patients |
| Binmoeller *et al*[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 *et al*[44], 2020 | Prospective study | United States | 40 | 27/13 | GV | EUS-Guided coil embolization | Technical success: 100% |
| Obliteration: 100% |
| Complications: 1 patient |
| Lôbo *et al*[53], 2019 | RCT | Brazil | 32 | 13/19 | GV | EUS-guided CYA and coil embolization | Complications: 13 patients |
| Obliteration: 93.3% |
| Mukkada *et al*[45], 2018 | Retrospective study | India | 30 | NR | GV | EUS-Guided coil embolization | Rebleeding: 6 patients |
| Lee *et al*[46], 2000 | Prospective study | China | 101 | 69/32 | GV | EUS-guided CYA | Obliteration: 79.6% |
| Complications: 22 patients |
| Rebleeding: 19 patients |
| Gubler *et al*[47], 2014 | Retrospective study | Switzerland | 40 | 25/15 | GV | EUS-guided CYA | Complications: 2 patients |
|
| Kozieł *et al*[48], 2019 | Retrospective study | Poland | 16 | 9/7 | GV | EUS-guided CYA and coil embolization | Technical success: 94% |
| Complications: 6 patients |
| Romero-Castro *et al*[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.