

Review article

The role of EUS in liver transplantation

Running title: EUS, liver transplantation

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ABSTRACT

Endoscopic ultrasound (EUS) is being increasingly used for both diagnostic and therapeutic purposes in various settings in gastroenterology and hepatology. Similarly, it has also been adopted in liver transplantation (LT), and its utilization is steadily increasing. EUS strengthens LT care in both the pre-transplant and post-transplant periods. Specifically, EUS is valuable in the evaluation of liver parenchyma, portal hypertension assessment and variceal management, tissue sampling when percutaneous or transjugular approaches are contraindicated or impractical, detection and characterization of hepatic and nodal metastases—thereby refining staging and sometimes even eligibility for LT—management of postoperative collections, and enabling biliary and pancreatic interventions in altered anatomy by creating access routes. In this review, we discuss these applications of EUS, along with its current limitations and its evolving role in the setting of LT.

Keywords: Endohepatology; endoscopic ultrasound; EUS; liver diseases; liver transplantation.

Introduction

Liver transplantation (LT) is the only curative therapy for end-stage liver disease.[1] Endoscopy is an essential tool in peritransplant care. In this setting, endoscopic ultrasound (EUS) has become an increasingly important tool, providing high-quality imaging, diagnostic sampling, and minimally invasive therapeutic approaches. Compared with percutaneous or transjugular approaches, EUS offers advantages in patients with challenging anatomy, ascites, coagulopathy, or inconclusive imaging findings.[2,3]

EUS supports diagnosis and risk stratification through the evaluation of portal hypertension, varices, cirrhosis, and focal liver lesions, while also guiding therapeutic procedures such as drainage of hepatic collections and treatment of variceal bleeding. Evidence consistently demonstrates its diagnostic accuracy, safety, and ability to integrate multiple steps into a single procedure.[2–4] The role of EUS in LT continues to expand steadily, and this review aims to provide a comprehensive overview of the diagnostic and therapeutic applications of EUS in LT candidates and recipients[4]

Pre-Transplant Role of EUS

Candidate Assessment for Liver Transplantation

LT assessment should be pursued for patients with decompensated liver cirrhosis who fail to respond to medical therapies.[5] The model for end-stage liver disease (MELD) score is the primary tool for prioritizing patients for LT; a score of ≥ 15 generally indicates a survival benefit from LT. In patients with hepatocellular carcinoma (HCC), LT eligibility is determined according to the Milan criteria.[6]

For patients with suspected cirrhosis or chronic liver disease, pre-transplant evaluation may integrate endoscopic variceal screening, EUS elastography, EUS-guided portal pressure gradient (EUS-PPG) measurement, and EUS-guided liver biopsy (EUS-LB), often within a single session when clinically indicated.[7]

Portal Hypertension: Definitions, Noninvasive Pathways, and Where EUS Fits

Portal hypertension (PH) results from architectural distortion due to fibrosis/cirrhosis and drives decompensation (varices, ascites, bleeding). The hepatic venous pressure gradient (HVPG) remains the gold standard for assessing PH; it is typically ≤ 5 mm Hg in healthy individuals, >5 mm Hg in cirrhosis, and ≥ 10 mm Hg in clinically significant PH (CSPH), at which point varices and decompensation become likely, especially after 12 mm Hg.[8]

Upper endoscopy is the gold standard for diagnosing gastroesophageal varices, which may serve as a surrogate for PH.[9] To reduce unnecessary procedures in compensated advanced chronic liver disease (cACLD), the Baveno VI consensus proposed a noninvasive approach using transient elastography (TE) for liver stiffness measurement (LSM) and platelet count to assess CSPH.[10] Baveno VII advanced this approach with LSM/platelet criteria to rule out (LSM <15 kPa and platelets $>150 \times 10^3/\mu\text{L}$) and to rule in CSPH (LSM ≥ 25 kPa) in alcohol-, viral-, or non-obese NASH-related cACLD.[11,12] Additionally, the presence of portosystemic collaterals on imaging studies also implies CSPH in cACLD, supporting their use as a component of noninvasive assessment.[13]

Despite these advances, HVPG remains the only valid tool for directly assessing PH severity and hemodynamic response to treatment beyond the presence or absence of CSPH in cACLD.[13]

EUS has recently emerged as an adjunct in this setting, offering advantages over conventional upper endoscopy and imaging.[14] EUS demonstrates substantially higher sensitivity for detecting gastric and deep varices than routine endoscopy. It also helps characterize collateral pathways such as periesophageal, paraesophageal, and perforating veins and provides more accurate measurements of variceal size and wall thickness, which are important for bleeding risk assessment.[15–17]

Doppler capability further allows assessment of hemodynamic changes in the left gastric, portal, and azygos venous systems.[16] In addition, EUS-PPG correlates closely with HVPG, providing a minimally invasive alternative when transjugular access is not feasible, and can be performed in the same session as liver biopsy when indicated.[18] These features position EUS as a complementary modality that enhances risk stratification and therapeutic planning in patients with PH, particularly in LT candidates and recipients.

A clinical study in 33 LT candidates further emphasized this role. EUS detected large deep esophageal varices in 36% of patients, 42% of which had not been identified as large on routine endoscopy. Similarly, EUS revealed large deep gastric varices in 36% of patients, 33% of which were not identified at all on routine endoscopy, while 25% had been classified as small varices.[19] These findings indicate that EUS can reveal clinically important varices missed by routine endoscopy, allowing for more accurate bleeding risk assessment and better guidance of preventive strategies in LT candidates.

Therapeutic EUS for Varices

Endoscopic injection of cyanoacrylate (CYA) remains the guideline-recommended conventional approach for cardiofundal varices, but limitations include imprecise targeting, risk of embolization, and the need for repeat sessions.[20,21]

EUS-guided therapy addresses these challenges by enabling direct visualization of the varices and feeding perforators, Doppler confirmation of obliteration, and more controlled delivery of CYA. This precision offered

by EUS becomes particularly important in the setting of complex vascular anatomy and active bleeding, where visualization is often poor.[22,23]

Notably, combination therapy with coil plus CYA has demonstrated superior efficacy and durability compared with either modality alone, with higher rates of variceal obliteration and lower rebleeding rates than standard endoscopic CYA injection.[20]

Focal Liver Lesions and Tissue Acquisition

EUS improves the detection of small hepatic lesions, particularly those <10 mm, which can be missed on conventional imaging.[24,25] This was demonstrated in a large prospective study of 730 patients undergoing cancer staging. EUS detected focal liver lesions in 20.5% and metastases in 16.2% of patients, compared with 13.6% and 11.2% by CT or MRI, respectively. Importantly, EUS identified 42 cases of metastases that were missed by CT/MRI, while its miss rate was less than 1%.[24]

EUS real-time elastography (RTE) further refines the distinction and characterization between benign and malignant hepatic focal lesions.[2,26] EUS-LB is useful for sampling lesions with difficult access, such as those in the caudate or left lobe, where percutaneous access is limited.[24]

In HCC, cholangiocarcinoma (CCA), or metastatic liver disease, the advantages of EUS in lesion detection and characterization contribute to more accurate staging and improved selection of candidates for LT or surgical resection, which may potentially influence clinical decision-making and improve outcomes in patients being evaluated for transplantation.[27]

EUS also contributes to extrahepatic nodal staging relevant to LT candidacy. In a prospective cohort of 50 LT candidates with HCC and lymphadenopathy, EUS-FNA provided adequate samples in 92% and identified nodal metastases in 30%, thereby precluding LT for this group of patients. Additionally, granulomatous lymphadenopathy was diagnosed in 8%, requiring appropriate treatment before LT.[28]

Within the scope of a nationwide screening protocol for potential LT in unresectable perihilar CCA in the Netherlands, EUS-guided sampling of 84 nonregional nodes in 75 patients identified malignancy in 4% of patients. This is a small but clinically important proportion, given that positive findings precluded LT, suggesting that EUS assessment may change management in a clinically significant proportion of LT candidates.[29]

It should be noted that in unresectable perihilar CCA under evaluation for LT, EUS-guided fine-needle aspiration (EUS-FNA) or EUS-guided fine-needle biopsy (EUS-FNB) should be strictly avoided due to the risk of peritoneal tumor seeding, which can preclude transplant eligibility.[29,30] Therefore, EUS is primarily utilized to assess and sample nonregional or indeterminate lymph nodes and extra-hilar targets in LT candidates with perihilar CCA.

As for HCC, biopsy—including EUS-FNA/FNB—still carries a low risk for seeding, reported in less than 3% of cases across studies.[6,31] Importantly, current evidence shows that this seeding risk is not clearly associated with worse post-transplant outcomes. Accordingly, guidelines do not strictly prohibit biopsy in LT candidates with HCC but recommend reserving it for indeterminate cases on imaging.[6,31,32]

Portal vein thrombosis (PVT) is common in cirrhosis and in patients with suspected or known HCC.[33] The key question is whether the thrombus is bland or tumoral, as this distinction drives staging, transplant eligibility, and choice of locoregional or systemic therapy. EUS guidance provides a transgastric/duodenal route for real-time Doppler-assisted sampling of the portal thrombus, avoiding a transhepatic tract and potentially lowering bleeding risk in coagulopathic patients.

Small series and case reports show high feasibility and meaningful management impact: in a Spanish cohort of chronic liver disease with PVT, EUS-FNA was attempted in eight candidates, technically successful in seven, malignant in six, and it upstaged or altered treatment in six of seven patients, with no reported immediate

adverse events.[34] Earlier reports similarly confirmed malignant thrombus when cross-sectional imaging was inconclusive.[35]

Technical reviews support the safety and practicality of EUS-guided portal venous access in experienced hands, while society guidance still prioritizes conventional imaging techniques such as Doppler/CT/MRI for initial PVT characterization and reserves biopsy for indeterminate cases where results would change management. In the LT pathway, EUS-FNA of PVT is therefore best used as a targeted test to confirm malignancy, clarifying candidacy and directing therapy.[20,36–38]

Beyond diagnosis, EUS is increasingly explored as a therapeutic tool. EUS-guided tumor ablation enables precise targeting with minimal collateral damage, offering a minimally invasive alternative for poorly accessible or high-risk lesions by conventional percutaneous or surgical approaches.[11,39–41]

In a prospective study of 20 patients with 25 caudate lobe tumors, EUS-guided laser ablation achieved 100% complete ablation after one or two sessions, with no procedure-related adverse events. During a median follow-up of 27 months, local tumor progression occurred in 16% and intrahepatic distant recurrence in 75% of patients, with tumor size >2 cm identified as a predictor of local progression.[27] Figure 1 illustrates different EUS techniques mentioned above with target examples.

Post-Transplant Role of EUS

Diagnostic Roles

In the post-LT period, patients may develop graft dysfunction, acute or chronic rejection, surgical complications (e.g., hemorrhage), vascular events, biliary complications, post-transplant lymphoproliferative disorders, de novo solid-organ cancers, infections, and other systemic problems.[42]

In this setting, EUS is used primarily to evaluate biliary and parenchymal complications. When combined with fine-needle aspiration/biopsy (FNA/FNB), EUS provides histological diagnosis of parenchymal disease or malignancy.[4] In addition, EUS-PPG measurement is an emerging tool that is highly consistent with HVPg and may streamline assessment in post-LT patients with suspected portal hypertension or fibrosis.[18,43,44]

As for suspected biliary disease, a cohort of 32 patients with post-LT biliary complications was assessed with both EUS and endoscopic retrograde cholangiopancreatography (ERCP).[45] EUS achieved 94.6% sensitivity and accuracy overall, outperforming ERCP in identifying biliary casts and ischemic cholangiopathy, with potential impacts on management. In contrast, EUS was found to be inferior in identifying anastomotic strictures.

Considering these findings, EUS can serve as a first-look triage tool in post-LT cholestasis unless an anastomotic stricture is more likely. A same-session strategy combining EUS-LB with ERCP is also feasible when both ductal and histological assessments are needed.[43,46,47]

EUS is also being explored in intestinal allograft surveillance, especially for chronic rejection. Assessing graft wall morphology and Doppler resistive indices shows early promise; however, further research is needed.

Therapeutic and Access-Creation Roles

Interventional EUS after LT is used selectively, and the evidence base remains limited to small series and case reports.[4] For post-LT intra-abdominal abscesses, percutaneous or surgical drainage is standard, but EUS-guided drainage offers a minimally invasive alternative when conventional approaches fail or are unsuitable.[48]

Beyond abscesses, EUS-guided aspiration/lavage with sclerosants has been successfully applied to symptomatic hepatic cysts.[49–51]

EUS-guided drainage—including those with lumen-apposing metal stents (LAMS)—demonstrates high efficacy for postoperative fluid collections, including those after LT, with technical and clinical success rates exceeding 90%, while adverse events remain infrequent (<10%) and rarely necessitate surgery. Importantly, outcomes are consistent across timing, size, and access route, with most collections resolving without recurrence.[52–54]

EUS also enables creation of access routes for biliary or pancreatic duct interventions in altered anatomy, achieving >90% technical success, with outcomes at least comparable to percutaneous or surgical options and fewer complications with shorter hospital stays. This is especially valuable in post-transplant patients with Roux-en-Y hepaticojejunostomy and in those after pancreaticoduodenectomy, when ERCP is not feasible.[30,55–57] Figure 2 schematizes and provides an overview of EUS usage in the pre-transplant and post-transplant setting.

Comparison of EUS-Guided Liver Biopsy Versus Percutaneous Liver Biopsy

Percutaneous liver biopsy (PC-LB) remains the conventional approach for hepatic histology, but pain, bleeding risk, sampling error, and post-procedure monitoring are well-recognized drawbacks.[58] EUS-LB offers an endoscopic, Doppler-guided route under the same sedation used for GI evaluation, with easy access despite ascites or large body habitus, and the option to combine multiple tests in one session.[59,60] In terms of post-procedure logistics, PC-LB typically requires 2–4 hours of right decubitus positioning for tamponade of the puncture site, whereas EUS-LB usually involves about 1 hour of routine recovery without positional restrictions.[62]

Across randomized and observational comparisons, both techniques achieve high diagnostic yield, with largely comparable performance. Randomized controlled trials (RCTs) consistently report less pain, shorter observation time, and better tolerability with EUS-LB. One RCT favored PC-LB for median complete portal tract (CPT) yield (17 vs. 13; $p=0.031$) [62], whereas another favored EUS-LB for total specimen length (TSL) (2.35 vs. 1.75 cm; $p=0.01$) and adequacy (TSL ≥ 2 cm and presence of ≥ 11 CPT) (70.4% vs. 32.6%; $p<0.001$), with similar CPTs but more fragmentation after EUS-LB.[63] A meta-analysis of four RCTs showed no difference between EUS-LB and PC-LB for diagnostic adequacy, CPTs, longest or total specimen length, or overall adverse events, while post-procedure pain was lower with EUS-LB.[64,65]

In an observational study, diagnostic adequacy, accuracy, and CPT counts were high and comparable between groups; however, PC-LB had longer TSL (2.74 vs. 1.85 cm; $p=0.02$) and a shorter procedure time.[66] Yet, in another observational study, EUS-LB was shown to achieve similar or better samples with fewer needle passes and faster overall recovery than PC-LB or transjugular biopsy.[27,67]

EUS-LB was also compared with interventional radiology-guided biopsy (IR-LB) (percutaneous or transjugular), and it was reported that IR-LB yielded more CPTs (13.6 vs. 10.8; $p\leq 0.01$), whereas EUS-LB achieved longer total core length (4.6 cm vs. 3.6 cm; $p\leq 0.01$), had more fragmented cores, and was associated with fewer complications.[68]

As for LT recipient-specific evidence, a retrospective single-center study suggests that EUS-LB can offer practical advantages without sacrificing tissue quality.[69] The study included 77 LT recipients—31 in the EUS-LB group and 46 in the PC-LB group. The two groups were similar in age, sex, and reason for transplantation. All EUS-LB cases sampled the left hepatic lobe via a transgastric approach, whereas PC-LB targeted only the right lobe. The interval between LT and biopsy was longer in the EUS-LB group (44.1 vs. 24.4 months, $p=0.029$). EUS-LB yielded longer median aggregate specimen length (7.2 vs. 2.0 cm; $p<0.001$), longer longest core (1.85 vs. 1.24 cm; $p<0.001$), and more CPTs (12.0 vs. 7.2; $p<0.001$), with higher adequacy (61.3% vs. 10.9%; $p<0.001$).

Regarding symptom burden, the EUS-LB group had less abdominal pain (6.5% vs. 52.2%; $p<0.001$) and a higher rate of no post-procedural adverse effects (83.9% vs. 47.8%; $p=0.001$), while no severe events occurred in either group.

Finally, despite rapid growth in EUS expertise in recent years, PC-LB remains more widely accessible compared to EUS-LB.[59,70] Overall, current evidence supports EUS-LB as a safe, diagnostically reliable alternative to PC-LB, and its wider adoption into clinical practice can be expected in the future if further studies continue to confirm its safety and efficacy.

Conclusion

This review synthesizes how EUS complements and, in selected scenarios, improves upon conventional approaches, with an emphasis on its use in the LT setting. Table 1 summarizes the information in this article about the opportunities, successful areas, and limitations of EUS.

For LT candidates with portal hypertension, EUS detects deep varices and identifies collateral pathways that routine endoscopy may miss. Doppler assessment and EUS-PPG add hemodynamic context that closely approximates the gold standard HVPg, which is especially valuable when the transjugular approach is impractical.

In the post-transplant setting, EUS serves as a practical tool for evaluating cholestasis—outperforming ERCP for biliary casts and ischemic cholangiopathy but being less sensitive for anastomotic strictures. EUS also supports post-LT portal hypertension assessment with EUS-PPG, as in the pre-transplant period.

In LT candidates with oncological conditions, EUS improves detection of subcentimeter or difficult-to-access hepatic lesions and enables extrahepatic nodal sampling, refining staging and, at times, transplant candidacy by identifying otherwise occult hepatic or nodal metastases.

Additionally, in cirrhotic patients with PVT and suspected or known HCC, thrombus sampling with EUS-FNA may distinguish benign from malignant thrombi when imaging is equivocal, thereby directly impacting management—including transplant eligibility and therapy selection.

Studies comparing biopsy approaches show broadly similar diagnostic performance between EUS-LB and percutaneous or transjugular techniques. Current evidence favors EUS-LB for lower post-procedure pain and faster recovery, whereas some studies report more CPTs or longer cores with PC-LB. In practice, the choice of approach can be individualized according to the clinical question, target lobe, required concomitant procedures, and local expertise.

Within the therapeutic landscape, EUS-guided therapies offer minimally invasive options when surgery or percutaneous techniques are not feasible or have failed. Targeted therapy of varices with coil and CYA improves obliteration and durability. Postoperative collections can be drained with high technical and clinical success and infrequent adverse events. EUS-created access can enable biliary or pancreatic interventions in altered anatomy. EUS-guided tumor ablation has emerged as a promising option, particularly for lesions in difficult-to-access locations such as the caudate lobe. It enables precise targeting with a low rate of immediate adverse events, although outcomes appear size-dependent, and long-term durability requires further validation. Importantly, many diagnostic and therapeutic capabilities can be integrated into a single session, potentially reducing reinterventions and hospital utilization in carefully selected patients.

Besides its advantages, there are also several limitations regarding its use: EUS access to the right hepatic lobe can be constrained; core fragmentation may be greater in EUS-LB compared to other techniques; and procedure duration may be longer, even if recovery is typically shorter. For biliary evaluation, EUS is also less informative than ERCP when an anastomotic stricture is suspected. Complications are uncommon but are considerably influenced by patient factors and operator experience, highlighting the need for structured training, protocolized patient selection, and multidisciplinary planning.

For instance, cervical esophageal perforation—though rare—illustrates these concerns: a national survey linked risk to older age, operators with <1 year of experience, difficult prior intubations, and prominent cervical osteophytes.[71] Even so, multicenter studies and broader reviews indicate that diagnostic and interventional EUS are safe when performed with appropriate selection and technique.[72,73]

In LT candidates and recipients, who often have altered anatomy and coagulopathy, risk reduction should include competency-based training; explicit pre-procedure review of prior imaging/endoscopy and the potential therapeutic implications of EUS/EUS-FNB findings; careful appraisal of clinical status with clear indications and contraindications; an individualized, team-based procedural plan; and optimization of prerequisites such as anesthesia support, coagulation management, and equipment readiness.[73–75]

In summary, EUS has developed into a versatile tool, providing safe and minimally invasive options for both diagnosis and treatment. Its role is steadily expanding and is increasingly being integrated into routine care within the peritransplant period, complementing and occasionally exceeding conventional methods. Going forward, more research, wider training, and better access will likely make EUS even more central and help improve outcomes for transplant patients.

Abbreviations:

cACLD: compensated Advanced Chronic Liver Disease

CCA: Cholangiocarcinoma

CPT: Complete Portal Tracts

CSPH: Clinically Significant Portal Hypertension

CT: Computer Tomography

CYA: Cyanoacrylate

ERCP: Endoscopic Retrograde Colangiopancreatography

ESLD: End-stage Liver Disease

EUS: Endosonographic Ultrasonography

EUS-EG: EUS-guided Elastography

EUS-FNA: EUS-Fine-Needle Aspiration

EUS-FNB: EUS-Fine Needle Biopsy

EUS-GD: EUS-guided Drainage

EUS-LAMS: EUS-Lumen-Apposing Metal Stent

EUS-LB: EUS-guided Liver Biopsy

EUS-PPG: EUS-guided portal pressure gradient

GV: Gastric Varices

HCC: Hepatocellular Carcinoma

HVPG: Hepatic Venous Pressure Gradient

IR-LB: Interventional Radiology-guided Biopsy

LB: Liver Biopsy

LSM: Liver Stiffness Measurement

LT: Liver Transplantation

MELD: Model of End-Stage Liver Disease

MRI: Magnetic Resonance Imaging

PC-LB: Percutaneous Liver Biopsy

PH: Portal Hypertension

PVT: Portal Vein Thrombosis

RCTs: Randomized Controlled Trials

RTE: Real Time Elastography

TE: Transient Elastography

TSL: Total Sample Length

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Table 1. Advantages and Disadvantages of EUS

Advantages (opportunities and successful areas)	Disadvantages (limitations)
Reaching risky areas easily	Large device size
Taking adequate, high quality and great proportion material	Less effective on diagnosing anastomotic structures

Detecting metastatic lymph nodes with high specificity	Longer procedure performing period than PC-LB
Staging HCC	Limited usage on right lobe liver analysis
Detecting varices which cannot be identified by other methods	Less complete portal triad obtaining (Compared with PC-LB)
Gastroesophageal lumen and organ observing	Some studies stated lower effectiveness on drainage usage (considered in different ways)
Positioning nearby liver	Possibility of perforation
Analyzing vascular changes outstanding	-
High specificity measurement of PH	-
No special position required after process	-
Short recovery time	-
Upper anatomy management	-
Bypass removal (when cannot be done by ERCP)	-
Efficient drainage usage (considered in different ways)	-
Capable when other techniques are unavailable	-
Opportunity of usage with different methods at the same time	-
Less complication	-
EUS: Endoscopic ultrasonography; HCC: Hepatocellular carcinoma; PH: Portal hypertension; ERCP: Endoscopic Retrograde cholangiopancreatography; PC-LB: Percutaneous liver biopsy.	

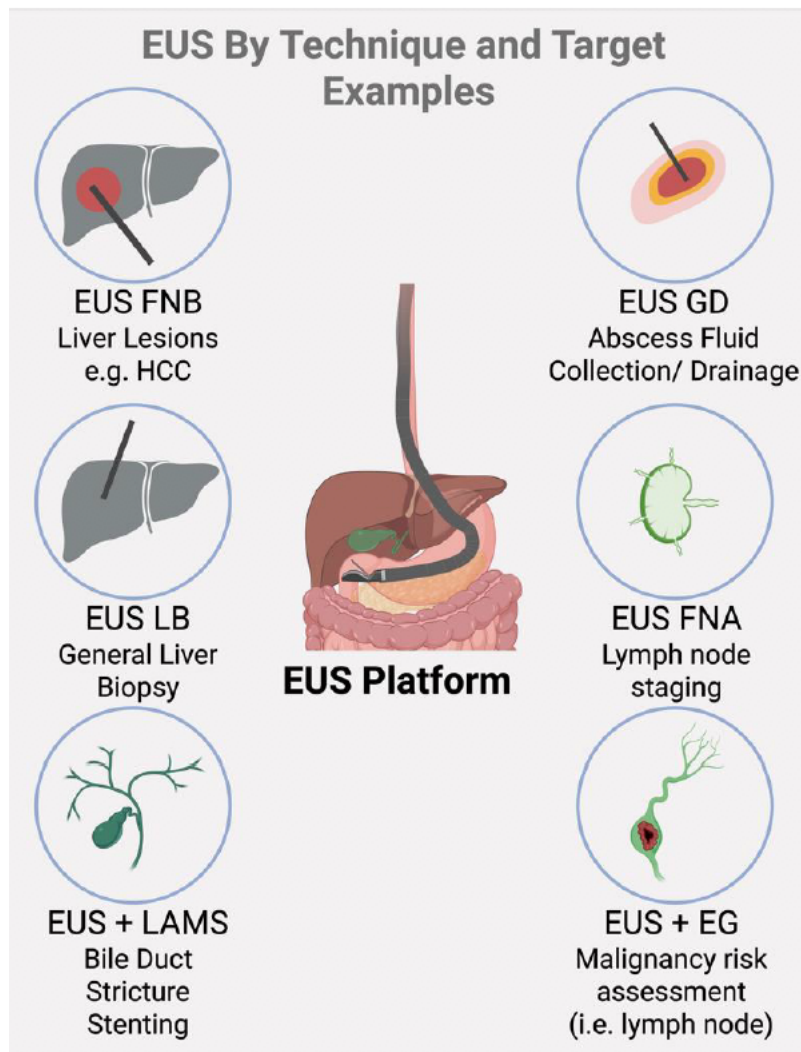


Figure 1. EUS By technique and target examples

EUS is used in different techniques for various purposes. This figure exemplifies diagnostic and therapeutic opportunities given by EUS. EUS: Endosonographic Ultrasonography, EUS-FNB: EUS-Fine-Needle Biopsy, EUS-LB: EUS-guided Liver Biopsy, EUS-LAMS: EUS-Lumen-Apposing Metal Stent, EUS-GD: EUS-guided Drainage, EUS-FNA: EUS-Fine-Needle Aspiration, EUS-EG: EUS-guided Elastography

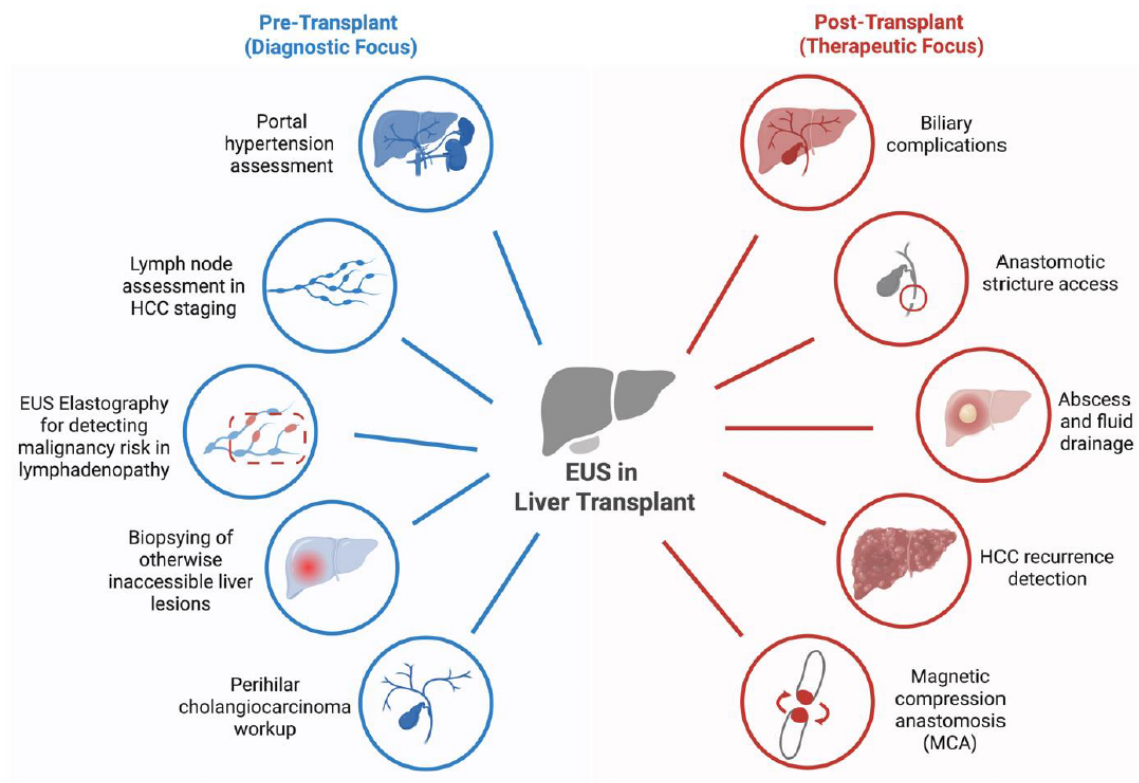


Figure 2. EUS in liver transplant

This figure illustrates EUS use in LT recipients in pre- and post-transplant settings. EUS can be used prior to LT for diagnostic purposes and after LT for therapeutic purposes. For example, pre-transplant EUS is mainly utilized for evaluation of varices and masses, whereas post-transplant EUS is primarily used for biliary complications, and abscess and fluid drainage. LT: Liver transplantation, EUS: Endosonographic Ultrasonography