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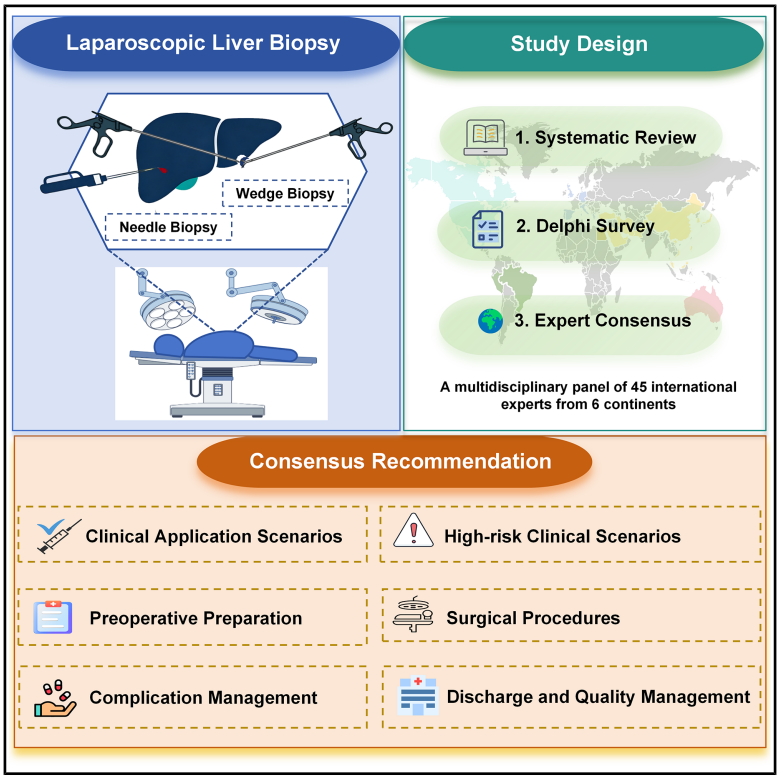
An international multidisciplinary consensus statement on laparoscopic liver biopsy

Graphical abstract



Highlights

- An international consensus on laparoscopic liver biopsy was established
- Standardized recommendations cover applications, procedures, and management
- LLB is valuable when other approaches are limited in complex cases

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In brief

Si-Yi Lei et al. present an international consensus for laparoscopic liver biopsy. This consensus standardizes clinical practice and supports safe, accurate liver tissue acquisition to aid clinical decision-making in complex diseases.

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Report

An international multidisciplinary consensus statement on laparoscopic liver biopsy

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SUMMARY

Laparoscopic liver biopsy (LLB) provides a way to obtain liver tissue samples under direct visual inspection of the liver surface. It complements percutaneous liver biopsy (PLB) for complex or high-risk cases where PLB cannot be performed. Clinical practices for LLB vary across centers due to the lack of international standards. To improve the procedural quality and diagnostic efficiency of LLB, a multidisciplinary panel of 45 international experts from 6 continents, including hepatology, hepatobiliary surgery, gastrointestinal surgery, and metabolic and bariatric surgery, developed this consensus statement through three rounds of a modified Delphi process. This consensus covers clinical application scenarios, high-risk clinical scenarios, preoperative preparation, surgical procedures, complication management, and discharge and quality management. It aims to promote the standardization, safety, and rational clinical application of LLB; support the management of complex cases; and facilitate the appropriate implementation of this important diagnostic procedure.

INTRODUCTION

Liver biopsy (LB) is a cornerstone for obtaining liver tissue samples to diagnose liver diseases and guide treatment.[1] While open surgical biopsy is highly invasive, ultrasound- or computed tomography (CT)-guided percutaneous liver biopsy (PLB) has become a widely adopted minimally invasive technique. However, PLB is often inadequate in technically challenging cases. Emerging techniques, such as endoscopic ultrasound-guided liver biopsy (EUS-LB) and transvenous liver

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biopsy (TLB), have expanded options but carry inherent limitations (Table S1).[1–8]

Laparoscopic liver biopsy (LLB) and other biopsy techniques (including PLB, EUS-LB, and TLB) are mutually complementary in clinical practice. The most appropriate modality for the individual patient should be guided by patient characteristics, lesion anatomy, and institutional capabilities. PLB remains the priority choice due to its low cost, minimal trauma, and ease of use. In contrast, LLB is indicated for complex or high-risk scenarios where other techniques are contraindicated or technically unfeasible. LLB enables direct visual inspection, multi-site sampling, and the retrieval of high-quality specimens for advanced pathological analyses,[9–11] thereby enhancing diagnostic precision and safety by avoiding critical structures.

Given that LLB increases treatment costs and entails additional surgical/anesthetic trauma, a multidisciplinary team (MDT) assessment is essential to select the appropriate biopsy approach for complex cases. To standardize its application and optimize patient outcomes, we developed this international consensus via a Delphi process, establishing protocols for technical performance, specimen quality, and risk minimization.

RESULTS

The Delphi methodology used in this consensus process is depicted in Figure 1. A total of 46 consensus statements were formulated and thematically organized into 6 core domains of LLB by the final expert panel, which comprised 45 international

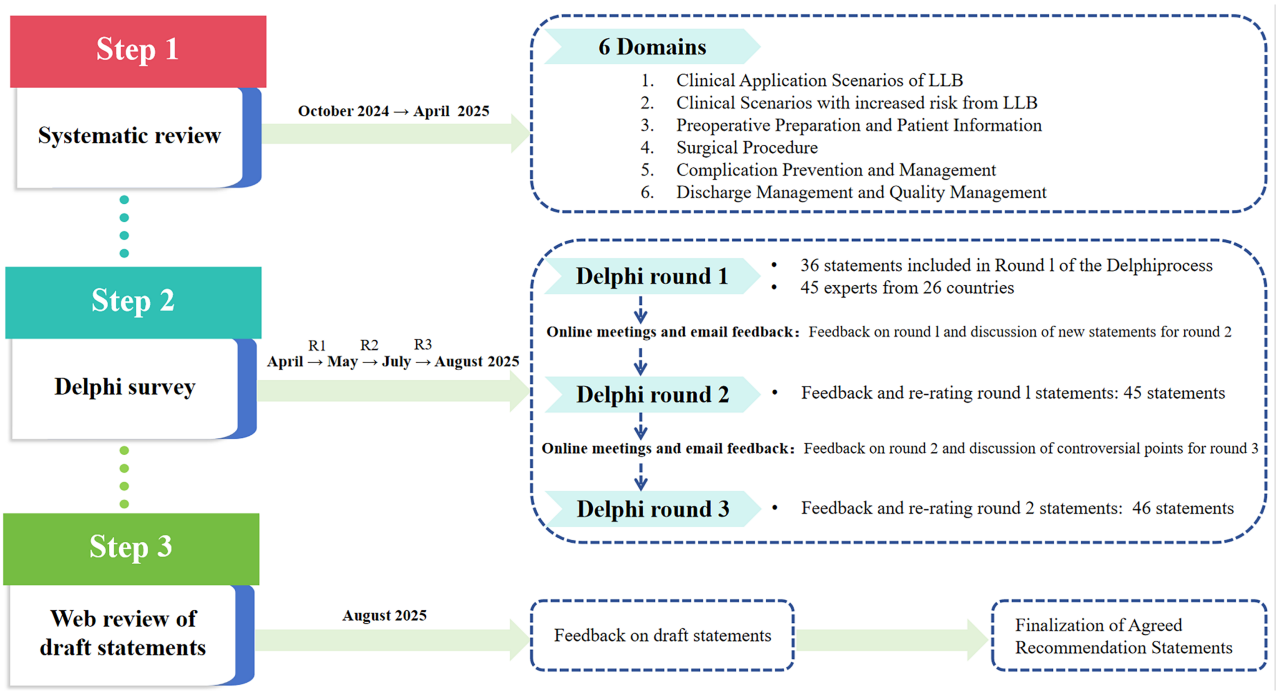

Figure 1. Flowchart of the Delphi procedure adopted for developing a consensus statement on LLB

specialists. Detailed information on the expert panel is provided in Table S2. Consensus on all proposed statements was progressively enhanced across the three rounds of the modified Delphi process, with the mean percentage of expert responses marked as "Agree" and the combined proportion of "Agree or Somewhat agree" showing a consistent upward trend (Figure S1). All statements achieved an agreement rate of ≥78%, with no C-level ratings. Specifically, 25/46 statements received a grade of "U" (100% agreement), 20/46 received "A" (90%–99% agreement), and 1/46 received "B" (78%–89% agreement), with the detailed grade distribution shown in Table 1 and the corresponding agreement percentages (grade levels) for each round provided in Tables S3, S4, and S5.

DISCUSSION

Clinical significance of the consensus

This international consensus provides consistent standards for LLB practice. Clinical approaches to LLB vary across global centers, and consistent standards can support clinical decision-making. In daily clinical practice, we frequently observe inconsistent decision-making for high-risk patients (e.g., morbid obesity and coagulopathy) and variable technical performance of LLB, which has led to wide variability in complication rates and diagnostic yield. This consensus provides a standardized framework for LLB practice, directly addressing these variabilities.

Core domain recommendations

Clinical application scenarios of LLB

This consensus defines the application scenarios of LLB (Table 1; Figure 2) and provides guidance for choosing LLB instead of PLB or TLB. In clinical practice, many centers either underutilize LLB in high-risk cases or overutilize it in low-risk cases, leading to unnecessary costs or missed diagnoses. The consensus' clear triggers for LLB use (e.g., morbid obesity and abnormal gastric anatomy precluding EUS-LB) provide a practical triage tool for clinicians, ensuring that LLB is used only when it provides clear safety or diagnostic benefits.

Conditions limiting PLB, TLB, or EUS-LB applicability, such as morbid obesity (which prolongs percutaneous puncture trajectories and raises visceral injury risk[1,12]), thoracic deformities or narrow intercostal spaces (which limit access to target liver lobes), and hepatic agenesis, atrophy, or congenital vascular malformations (which reduce imaging accuracy and sampling precision[13]), all hinder the performance of traditional biopsies. Moreover, strict contraindications further narrow the applicability of these methods. PLB is contraindicated in local puncture-path infection (risk of dissemination) or massive ascites (visceral injury risk).[1,2,14] TLB is limited in patients with intrahepatic vascular obstruction (e.g., liver vein thrombosis) or inaccessible subcapsular locations,[7,15] and EUS-LB is contraindicated in abnormal gastric anatomy or portal hypertension.[16] In contrast, LLB allows laparoscopic exploration to avoid high-risk areas, with concurrent management (ascites drainage and infection isolation).[17,18]

For complex anatomical lesions, LLB offers distinct advantages over traditional biopsy modalities. For focal lesions in complex anatomical locations (gallbladder-adjacent nodules [Figure S2A], hepatic hilar masses [Figure S2B], subdiaphragmatic lesions [Figure S2C], and caudate lobe lesions [Figure S2D]), PLB potentially leads to biliary fistula, bile duct hemorrhage, vascular injury and gallbladder perforation,[19,20]

Table 1. Consensus statements on LLB (using a Delphi procedure)

Domain and statements	Grade[a]
1. Clinical application scenarios of LLB	
1.1 Use of LLB when other diagnostic approaches are unavailable or inadequate (including percutaneous, transvenous, endoscopic ultrasound, or CT-guided biopsy and non-invasive tests). Limitations include but are not limited to the following factors: ① Challenging patient anatomy (e.g., morbid obesity, narrow intercostal spaces, hepatic lobe agenesis or atrophy, congenital anomalies); ② Technical or equipment-related limitations (e.g., unavailability or malfunction of image-guided biopsy tools); ③ Non-diagnostic or inadequate previous biopsy (e.g., insufficient tissue, poor sample quality, sampling error, complications from prior attempts); ④ Contraindications to percutaneous access (e.g., local infection, ascites, vascular obstruction, inaccessible lesion location); ⑤ Discordance between findings (e.g., discrepancies between clinical, laboratory, imaging, and histological data);	A
1.2 Focal lesions in complex anatomical locations. Lesions located in anatomically complex regions, including but not limited to the following: ① Lesions adjacent to the gallbladder or hepatic hilum (with caution to avoid bile duct and vascular injuries); ② Subdiaphragmatic lesions, especially in segments VII and VIII, where pneumothorax risk with percutaneous biopsy is high; ③ Caudate lobe lesions;	A
1.3 Need for multiple-site sampling. LLB allows direct visualization and multiple-site sampling of multiple liver regions under direct vision or combined with intraoperative ultrasound, reducing the inherent sampling variation of unilateral tissue biopsy and enabling timely hemostasis after sampling. Recommendations include but are not limited to the following scenarios, which should be determined based on the patient's condition: ① Imaging suggests multiple focal or diffuse heterogeneous lesions; ② Initial single-site biopsy results are negative or nonspecific.	A
1.4 Coagulopathy. For patients with coagulopathy, TJLB remains the preferred approach due to superior safety in high-bleeding-risk settings. However, in experienced centers and under directed laparoscopic visualization, LLB may be cautiously considered in select patients when TJLB is contraindicated or unavailable and appropriate correction of coagulopathy is achieved preoperatively.	A
1.5 Intraoperative opportunistic liver biopsy. In patients undergoing laparoscopic surgery for another indication, opportunistic liver biopsy may help assess underlying liver disease or clarify incidental findings. Including but not limited to the following scenarios: ① Patients with pre-existing liver disease undergoing any laparoscopic procedure may undergo concurrent liver biopsy during surgery to evaluate liver disease progression; ② During any laparoscopic surgery, if incidental discovery of suspected lesions of unknown nature or patients at risk of liver-related events occurs, concurrent liver biopsy may be considered.	A
1.6 Special populations:	
1.6.1 Liver transplant Recommend that transplant teams establish center-specific protocols before adopting LLB routinely. ① Liver transplant donors For living liver transplant donors (especially ECDs), LLB may be considered. This method allows for the acquisition of histological samples and visual assessment of the liver surface and abdominal cavity conditions, enabling the detection of abnormalities that are difficult to identify via imaging. However, for deceased donors (especially DCD donors), LLB is not recommended; clinically, open laparotomy is more preferred, with biopsy performed as appropriate. The decision to adopt LLB should be based on a comprehensive assessment of clinical needs, donor conditions, and procedural risks. ② Liver transplant recipients Postoperative follow-up strategies should focus on the management of immunosuppressive regimens (including monitoring of immunosuppressant concentrations and individualized adjustments). LLB can be used as one of the supplementary methods when non-invasive examinations are difficult for	A

(*Continued on next page*)

Table 1. *Continued*

Domain and statements	Grade[a]
differential diagnosis; however, specific protocols need to be comprehensively evaluated by the transplant team based on conditions such as bleeding risk, infection risk, and abdominal adhesions.	
1.6.2 Patients with unexplained liver disease complicated by ascites For patients with unexplained liver disease complicated by non-infected ascites (after preoperative evaluation to exclude infection or after infection control), when the transjugular approach is not feasible, LLB combined with intraoperative drainage may be considered as one of the alternative options. Preventive measures should be taken to minimize the risk of complications (such as hepatic encephalopathy or spontaneous bacterial peritonitis).	A
1.6.3 Patients with NCPF/IPH For patients with NCPF or IPH at high risk of bleeding, transjugular liver biopsy remains the preferred method of biopsy. However, in cases where transjugular access is unavailable or insufficient, and with bleeding control measures in place, laparoscopic biopsy under direct vision may be cautiously considered as an alternative.	U
2. Clinical high-risk scenarios of LLB	
2.1 Severe cardiopulmonary insufficiency. LLB is generally contraindicated in patients with ASA IV–V due to poor tolerance to anesthesia and pneumoperitoneum. If necessary, it may be cautiously considered only when no diagnostic alternatives exist, histology is essential for decision-making, and the procedure is done after a comprehensive multidisciplinary assessment, with input from the anesthesiology, cardiology, hepatology, and intensive care teams in an ICU/high-dependency unit with full cardiopulmonary and anesthetic support.	B
2.2 Severe hemorrhagic disorders that are difficult to correct. LLB is contraindicated in patients with uncorrected coagulopathy due to high bleeding risk. TJLB is preferred. If not feasible and histology is essential, LLB may be cautiously considered only in expert centers with full intraoperative hemostatic capacity and after MDT approval.	A
2.3 Uncontrolled severe intra-abdominal infection. LLB should be avoided in the presence of active intra-abdominal infection. The biopsy should be postponed, which may be reconsidered until only after documented infection control (clinical and laboratory resolution).	A
2.4 Shock or hemodynamic Instability. LLB is contraindicated in patients with shock or unstable hemodynamics due to the risk of worsening hypotension from pneumoperitoneum. If absolutely necessary, biopsy should be done only in an ICU setting with invasive hemodynamic monitoring and anesthetic support.	A
2.5 Pregnancy. First and second trimesters of pregnancy (up to 28 weeks): LLB may be cautiously considered after multidisciplinary assessment. Third trimester of pregnancy: due to enlarged uterus and limited surgical space, LLB is generally not recommended unless there are strong indications.	A
2.6 Extensive intra-abdominal adhesions. LLB may be attempted only by experienced surgeons with advanced laparoscopic skills when severe adhesions exist, and after failed or infeasible image-guided or transjugular approaches. Visual adhesiolysis must be performed with readiness for conversion to open surgery.	U
2.7 Patients with multiple underlying diseases or poor surgical tolerance. For patients at high perioperative risk, LLB may be considered only when the potential benefits clearly outweigh the risks following evaluation by the multidisciplinary team specializing in relevant diseases.	A
3. Preoperative preparation and patient information	
3.1 Preoperative assessment. A complete medical history (anticoagulant/antiplatelet medication use, allergy history, underlying medical conditions, etc.) and relevant examinations before surgery to evaluate disease status, surgical tolerance, anesthesia risks, and airway risks should be available.Examinations include but are not limited to the following, which should be adjusted based on the patient's condition: infectious disease screening, blood type, complete blood count, coagulation function, liver and kidney function, electrolytes, blood glucose, blood pressure, electrocardiogram, chest X-ray or CT, and abdominal imaging (ultrasound as the initial examination, with CT/MRI recommended for complex cases).	U
3.2 Timing of imaging examinations before LLB.It is recommended that baseline imaging examinations (CT/MRI/ultrasound) be performed within 1 month before LLB. For clinically stable patients without	A

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Table 1. *Continued*

Domain and statements	Grade[a]
significant comorbidities or suspected malignant tumors, imaging examinations may be extended to within 3 months if no obvious progression of the condition is suspected. If there is a change in the clinical status or the previous imaging examinations are deemed unsuitable for the surgical plan, further imaging examinations should be considered.	
3.3 Patient informed consent. Explain to the patient the purpose, procedure, potential risks (including but not limited to anesthesia-related complications, postoperative pain, hemorrhage, and infection), alternatives and complications of LLB. Obtain documented informed consent. For patients lacking decision-making capacity, adhere to institutional policies and local legal guidelines. Preoperatively, maintain fasting as follows: 6 h for dairy and starchy solids, 8 h for fatty solids, and 2 h for clear liquids.	A
3.4 Perioperative management of anticoagulant and antiplatelet medications. For patients taking long-term antiplatelet or anticoagulant medications before surgery, a comprehensive assessment of the surgical bleeding risk and underlying disease risk is required to determine whether and how to discontinue relevant medications and whether bridging therapy is needed. When necessary, multidisciplinary experts from cardiology, pharmacy, anesthesiology, and hematology, should be consulted.	A
4. Surgical procedure	
4.1 Anesthesia: general anesthesia is recommended to ensure smooth intraoperative procedures with adequate abdominal muscle relaxation, full control of ventilation and respiratory function, and painlessness.	U
4.2 Positioning: the patient should be placed in a head-up, foot-down (reverse Trendelenburg) position with left-side tilting as the initial position to facilitate liver exposure. The surgical position can be adjusted intraoperatively based on actual conditions.	U
4.3 Pneumoperitoneum establishment and laparoscope insertion: pneumoperitoneum is established by entering the abdominal cavity using a Veress needle, open Hasson technique, or visual trocar (Visiport). The pressure is typically maintained at 10–12 mmHg, reduced to 8–10 mmHg for patients with cardiopulmonary diseases, balancing visualization needs with minimizing hemodynamic impact on patients with poor general condition. The approach site and method (single-port/multi-port) should be individually selected, prioritizing safety and surgical objectives. Continuous intraoperative monitoring of vital signs remains essential for managing intra-abdominal pressure and preventing complications.	A
4.4 Laparoscopic exploration: insert the laparoscope for a comprehensive abdominal exploration. Observe for vascular injury during abdominal access, and assess liver morphology, color, surface nodules, and adhesions. Meanwhile, other abdominal organs should be inspected for abnormalities. If unexpected lesions are identified, document them promptly and evaluate their impact on the planned procedure.	U
4.5 Biopsy site selection: for diffuse liver diseases, liver biopsy is typically performed at the inferior margin of the intersegmental boundary between liver segments V and VI, or at the inferior margin of liver segment III. For biopsies of suspicious focal lesions, the site should be selected and integrated with preoperative imaging data, IOUS, and intraoperative laparoscopic findings.	U
4.6 Procedure of LLB: for diffuse liver diseases, needle biopsy combined with wedge biopsy is recommended. For needle biopsy, the biopsy needle (16G/18G) should be directed parallel to the diaphragmatic surface of the liver and inserted perpendicularly to the inferior liver margin to avoid injuring the deep Glisson's sheath; perform wedge liver tissue resection at the same site. For lesions of unknown nature, two-point sampling (5 mm from the lesion margin + central area) under intraoperative ultrasound guidance is recommended.	U
4.7 IOUS-guided biopsy: IOUS-guided biopsy can enhance the accuracy and safety of LLB, especially for deep or non-visible lesions. It enables real-time lesion localization, clear definition of lesion boundaries, and helps avoid major blood vessels or bile ducts. IOUS is particularly useful in cirrhotic livers, for targeting focal lesions, and for detecting additional lesions not identified by preoperative imaging. Although it may slightly increase operation time, it can significantly improve the diagnostic positivity rate in specific cases.	U
4.8 Tissue acquisition: for needle biopsy, at least 2–3 complete tissue cores should be obtained each time, with each core $\geq$1.5 cm in length and containing more than 10 portal tracts considered adequate. Wedge biopsy typically requires resection of a wedge-shaped liver tissue specimen approximately 5 $\times$ 15 mm.	U
	U

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Table 1. *Continued*

Domain and statements	Grade[a]
4.9 Hemostasis after tissue acquisition: depending on the severity of bleeding and anatomical location, different techniques are useful for bleeding control, including local hemostatic agents and monopolar electrocoagulation (suitable for superficial oozing), bipolar electrocoagulation (safer near major vascular structures), and suturing or clip application.	
4.10 Conversion to open surgery In cases where laparoscopic procedures are difficult to complete due to factors such as lesion size, anatomical location, handling difficulties, or intraoperative occurrence of severe bleeding, organ injury, conversion to open surgery may be performed after adequate evaluation to ensure patient safety.	A
4.11 Management of intraoperatively suspected malignant lesions. For lesions of unknown nature, preoperative MDT discussion should be completed and documented, and the informed consent form should cover the possibility of decision-making for lesion resection based on the location and size of intraoperative clinical suspicious lesions and/or the results of intraoperative frozen section biopsy. A coaxial biopsy technique and other methods should be adopted during the biopsy.	A
4.12 End-of-procedure assessment: ① Repeatedly inspect the puncture or resection site for bleeding, and check the abdominal cavity for signs of hemorrhage or bile leakage. If necessary, raise blood pressure to identify bleeding points. ② Based on intraoperative conditions, consider placing a drainage tube postoperatively for observation when indicated.	U
4.13 Postoperative monitoring: closely monitor the patient's vital signs and abdominal symptoms postoperatively. For patients with an indwelling abdominal drainage tube, observe the volume and characteristics of the drainage.	U
4.14 Operation time: the operation time is typically 15–30 min, but may vary in complex or challenging cases.	U
5. Complication prevention and management	
5.1 For complications (pneumoperitoneum-related, intraoperative, postoperative), the modified Clavien-Dindo classification system stratifies risks as follows: High risk: gas embolism, pneumomediastinum, major vascular injury. Moderate risk: pneumothorax, delayed hemorrhage (liver biopsy site/abdominal wall), delayed visceral perforation. Mild risk: cholecystocardiac reflex, infection, subcutaneous emphysema, local pain, postoperative abdominal distension. Very low-risk: needle tract seeding metastasis.	U
5.2 Key treatment timing recommendations for complications of different risks: high risk: $\leq$5 min; moderate risk: $\leq$24 h; mild risk: 4–48 h. However, the timing of intervention should still be adjusted according to the patient's clinical status. Complications are generally uncommon when performed by skilled operators.	A
5.3 Core measures for high-risk complications management: ① Disposal protocol: immediately terminate pneumoperitoneum, rapidly stabilize the circulatory system, and perform emergency thoracotomy/laparotomy only when strictly indicated. ② Prevention strategies: continuously monitor $ETCO_2$ during the procedure. Avoid excessive Trendelenburg positioning. Strictly control pneumoperitoneum pressure and prioritize intraoperative ultrasound-guided puncture techniques. ③ Monitoring requirements: synchronously monitor arterial blood gas analysis, CVP, and cardiac output. Dynamically assess changes in the patient's condition.	U
5.4 Core measures for moderate-risk complications management: ① Disposal strategies: pneumothorax: prioritize closed thoracic drainage; combine with thoracoscopic exploration if necessary. Delayed re-bleeding: implement hemostatic techniques; administer blood transfusion support for massive hemorrhage. Delayed hemorrhage/visceral perforation: Perform timely diagnostic laparoscopy to accurately identify bleeding/perforated lesions. ② Prevention measures: ensure the accuracy of pneumoperitoneum needle placement. Strictly control pneumoperitoneum inflation rate. Execute low-pressure (8 mmHg) wound inspection postoperatively. ③ Monitoring requirements: dynamically track hemoglobin trends to identify occult bleeding early. Routinely assess abdominal symptoms to capture signs of disease progression.	U
5.5 Core measures for mild-risk and special complications management: (1) Prevention and management strategies: ① Cholecystocardiac reflex (bradycardia): correct arrhythmia with intravenous atropine, maintain	U

(*Continued on next page*)

Table 1. ***Continued***

Domain and statements	Grade[a]
gentle tissue manipulation intraoperatively, consider preoperative prophylactic atropine. ② Infection: perform specimen culture for targeted antibiotic therapy, enforce strict aseptic protocols, administer prophylactic antibiotics when indicated. ③ Pain: evaluate severity using VAS dynamically, administer analgesics if necessary. ④ Subcutaneous emphysema/postoperative abdominal distension: encourage early mobilization and prokinetic agents, control pneumoperitoneum pressure intraoperatively, conduct structured assessment of subcutaneous swelling. ⑤ Needle tract tumor seeding: perform extended lesion resection; ensure en-bloc extraction via specimen bag. (2) Monitoring requirements: ① Vital signs: continuous monitoring of BP and HR. ② Infection indices: regular review of temperature, white blood cell count, neutrophil ratio, and CRP. ③ Symptom-specific assessment: grade and record subcutaneous emphysema range/degree, timely collection of VAS scores for pain.	
6. Discharge management and quality management	
6.1 Discharge criteria: ① Stable vital signs; ② VAS pain score $\leq$3, effectively controlled by oral NSAIDs; ③ No bleeding at the puncture site, hemoglobin decrease from preoperative values $\leq$ 1 g/dL; ④ Able to consume liquid diet independently 4 h postoperatively; ⑤ The specific discharge time should also be determined by the patient's condition, wishes, local medical insurance policies, etc.	U
6.2 Day surgery: for simple diagnostic LLB cases or those undergoing cholecystectomy combined with LLB that meet the discharge criteria.	U
6.3 Delayed discharge: recommend extending hospital observation and discharging after liver function stabilizes for cases with complex intraoperative conditions during LLB, patients developing complications, those undergoing combined surgery of grade III or above; and patients with Child-Pugh class B/C.	U
6.4 Standardized patient discharge education: Before discharge, patients must be clearly informed of: ① Warning signs (persistent abdominal pain with VAS >4, fever >38.5°C, etc.); ② Activity and medication; ③ Follow-up arrangements; ④ For special populations (elderly, diabetic patients, bariatric surgery cases, etc.), intensified targeted guidance is required, with multidisciplinary collaboration needed when necessary.	U
6.5 Follow-up schedule: Recommend implementing a standardized stratified follow-up based on postoperative time and disease risk: ① Short-term follow-up (1 week postoperatively): complete wound assessment, review blood routine and liver function tests if indicated, and formulate a diagnosis and treatment plan based on pathological reports.② Medium-term follow-up (1–3 months postoperatively): perform corresponding reexaminations according to the primary disease and review abdominal ultrasound/CT/MRI if indicated. ③ Long-term follow-up (6–12 months postoperatively): evaluate the progression of chronic liver diseases. ④ For low-risk individuals, telemedicine follow-up may be considered.	A
6.6 Training for LLB competence ① It is recommended to implement a standardized training program. Trainees must complete core training content under supervision, including theoretical learning and application of standardized intraoperative complication checklists to strengthen risk prevention awareness, mandatory simulation training, and specialized drills for complications, with surgical teams operating in high-risk environments required to focus on reinforcing this module. ② Qualification assessment: trainees are required to independently perform at least 10 LLB procedures under appropriate supervision. A formal competency-based assessment must be conducted by experienced surgeons, synchronously incorporating indicators such as biopsy adequacy rate, complication rate, and procedure time to ensure operational quality and safety.	U
6.7 It is recommended to capture intraoperative photographs and videos for traceable quality control.	U
	U

(*Continued on next page*)

Table 1. *Continued*

Domain and statements	Grade[a]
6.8 Recommendation for multidisciplinary collaboration model A full-cycle multidisciplinary collaboration system (preoperative, intraoperative, postoperative) is recommended, with quality ensured via joint outpatient assessment, real-time multidisciplinary feedback, and postoperative joint ward rounds. ① LLB as the primary procedure: hepatologists lead preoperative indication assessment, liver function reserve analysis, and postoperative plan formulation. Surgeons perform precise puncture, interventional radiologists or ultrasound physicians optimize intraoperative guidance and screen postoperative complications, anesthesiologists develop personalized anesthesia plans, pathologists evaluate frozen section quality and guide sampling, nursing teams manage perioperative education and rehabilitation. ② LLB as an additional procedure (e.g., combined with bariatric/metabolic surgery): the primary surgical department leads the process, with hepatologists assisting in liver disease assessment and postoperative management. ③ Patients with comorbidities: relevant specialties (e.g., cardiology and endocrinology) are consulted based on conditions to refine the comprehensive treatment plan.	

LLB, laparoscopic liver biopsy; ECDs, extended criteria donors; DCD, donation after circulatory death; NCPF, non-cirrhotic portal fibrosis; IPH, idiopathic portal hypertension; ASA, American Society of Anesthesiologists; INR, international normalized ratio; TJLB, transjugular liver biopsy; MDT, multidisciplinary team; ICU, intensive care unit; CT, computed tomography; MRI, magnetic resonance imaging; IOUS, intraoperative ultrasound; $ETCO_2$, end-tidal carbon dioxide; CVP, central venous pressure; VAS, visual analog scale; BP, blood pressure; HR, heart rate; CRP, C-reactive protein; NSAIDs, non-steroidal anti-inflammatory drugs.

Consensus statements were revised based on expert suggestions. Detailed original items from each round are available in the supplementary materials.

[a]Grade: U, unanimous (100%) agreement; A, 90%–99% agreement; B, 78%–89% agreement, C = 67%–77% agreement.

and high pneumothorax risk.[21] In contrast, LLB enables direct visualization of lesion-anatomy relationships and precisely identifies vascular structures around caudate lobe lesions, making it the preferred approach for these complex cases.

Multi-site sampling addresses pathological heterogeneity in diseases like metabolic dysfunction-associated steatotic liver disease (MASLD), a condition where disparities in hepatic steatosis, inflammation, and fibrosis necessitate multi-site sampling to accurately characterize overall disease burden.[22,23] It also improves early hepatocellular carcinoma (HCC) detection in cirrhotic livers with coexisting regenerative and malignant nodules,[24] while enabling precise inflammation/fibrosis staging in diffuse fatty liver with focal necrosis.[25] In patients with unexplained elevations in liver enzymes, multi-site sampling may reveal interface hepatitis indicative of autoimmune hepatitis or characteristic lesions of drug-induced liver injury when initial single-site biopsies are unrevealing.[26–28]

In coagulopathic patients, including those with an elevated international normalized ratio (INR) or platelets $\leq 50 \times 10^9$/L, LLB serves as an alternative when transjugular liver biopsy (TJLB) is limited.[15,29–32] This approach also improves the diagnostic safety and accuracy of acute liver failure.[33] With pre-procedural coagulation optimization (intraoperative thromboelastography [TEG]/ROTEM[34]) and correction of coagulation profiles using 4-factor prothrombin complex concentrate (4F-PCC), platelets, vitamin K, or adjustment of anticoagulant medications,[35] LLB can be safely performed in patients with hemostatic disorders. Targets for correction should be individualized according to the underlying disease and lesion location, with multidisciplinary input from a hematologist.

Intraoperative opportunistic LLB during concurrent laparoscopic surgeries (e.g., cholecystectomy, bariatric surgery) enables dynamic disease assessment without additional trauma, such as MASLD fibrosis staging in bariatric patients and[36–38] intrahepatic inflammation and fibrosis data in chronic hepatitis B patients[39]; diffuse liver nodules during cholecystectomy warrant concurrent biopsy to differentiate cirrhotic nodules from early HCC[40–43]; and biopsy in people living with obesity during bariatric surgery enables early metabolic dysfunction-associated steatohepatitis diagnosis,[36,38,44,45] preventing missed postoperative liver disease progression.

In special populations, for living donors, particularly expanded criteria donors (ECDs) such as elderly individuals or those with fatty liver or hepatic fibrosis,[46] LLB clarifies steatosis degree via histological grading to better assess risks.[47,48] In post-transplant recipients with unexplained graft dysfunction, such as suspected rejection, or infection,[49] LLB is an important supplemental tool, with multidisciplinary assessment mandatory pre-procedure given their immunosuppression-related bleeding and infection risks. Routine LLB is not recommended for deceased donors, especially donation after circulatory death (DCD) donors. For patients with unexplained liver disease complicated by ascites, TJLB is an important alternative to severe ascites when PLB is unfeasible.[50] However, TJLB is limited by equipment availability, technical demands, and small samples. LLB enables safe sampling via direct visualization, with concurrent ascites drainage achieving diagnosis and decompression simultaneously. And LLB proceeds only if infections are excluded or controlled.[51] Intraoperatively, clinicians should control ascites drainage volume and rate to avoid hepatic encephalopathy, prevent elevated intra-abdominal pressure, and reduce cardiorespiratory complications. Use low-pressure CO2 pneumoperitoneum to prevent elevated intra-abdominal pressure and reduce cardiorespiratory complications.[52,53] For patients with non-cirrhotic portal fibrosis

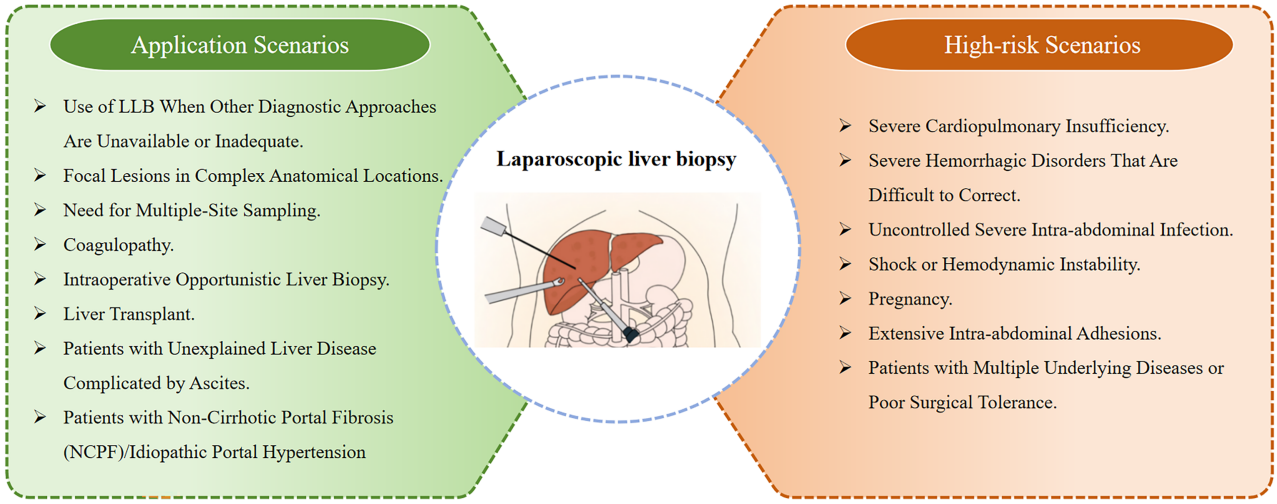

Figure 2. Application scenarios and high-risk scenarios of LLB

and idiopathic portal hypertension (IPH), pathological diagnosis is important for differentiating etiologies (e.g., vascular liver disease and pre-sinusoidal portal hypertension) and formulating therapeutic strategies (e.g., assessment for shunt surgery).[54] Traditional PLB risks massive hemorrhage (dense vascular puncture trajectory)[55,56] and may miss core lesions, causing misdiagnosis. TJLB measures hepatic venous pressure gradient to directly assess portal hypertension severity and confirm IPH, making it first line.[57] When TJLB is technically limited or diagnostically inadequate, LLB is an alternative with adequate hemostatic preparation and direct visualization.

Clinical high-risk scenarios of LLB

The high-risk scenario recommendations (Table 1; Figure 2) address the major clinical challenge of balancing diagnostic need with procedural safety in vulnerable patients. Prior to this consensus, many centers avoided LLB in American Society of Anesthesiologists (ASA) IV–V patients entirely, leading to diagnostic delays, while others performed it without standardized precautions, resulting in high hemodynamic instability rates. The consensus' stratified approach (contraindication vs. cautious use with modifications) provides clear guidance.

ASA IV–V patients with end-stage cardiopulmonary failure, multiple organ dysfunction syndrome, or hepatic failure have poor tolerance to anesthesia and pneumoperitoneum.[58] LLB is justified only in exceptional cases requiring urgent pathological diagnosis, with intensive care unit (ICU) invasive monitoring[33,59,60] and use of low-pressure pneumoperitoneum ($\leq$10 mmHg) or gasless techniques.[61] LLB is contraindicated in patients with shock or hemodynamic instability, as pneumoperitoneum exacerbates circulatory collapse—particularly detrimental in septic or cardiogenic shock.[62] Urgent cases require ICU invasive monitoring, hemodynamic stabilization, and low-pressure/gasless laparoscopy.[60,63–65] Active intra-abdominal infections increase dissemination and hemostasis impairment risks. For instance, LB is contraindicated in acute suppurative peritonitis, as it may induce infection spread or sepsis.[2,66] LLB should, therefore, be deferred until infection is controlled.

LLB is generally contraindicated in patients with refractory coagulopathy due to extremely high bleeding risk,[67] with TJLB preferred. A study of 7,469 TJLB procedures showed 0.6% major complications and 0.2% severe bleeding.[7] LLB may be cautiously considered only if TJLB is unavailable and histological diagnosis is critical, with TEG monitoring[68,69] and ICU surveillance.

No standardized LB guidelines exist for pregnancy. Unlike the American College of Obstetricians and Gynecologists' (ACOG's) general laparoscopic surgery guidelines, this consensus provides the specific recommendations for LLB in pregnancy. According to the ACOG, the second trimester (<28 weeks) is the suitable period for non-emergent laparoscopic procedures, as it is associated with the lowest rates of preterm birth and miscarriage.[70] LLB may be cautiously considered after MDT assessment, with invasive procedures only initiated if histology is indispensable for treatment guidance (e.g., differential diagnosis of pregnancy-associated acute liver disease).[2,71] Regimens should be jointly developed by obstetric and anesthetic teams, with fetal-safe medications selected. A 30° left lateral tilt should be adopted to avoid uterine compression of the inferior vena cava, and pneumoperitoneum pressure should be controlled at 8–10 mmHg.[72] Guidelines from the British Society for Gynaecological Endoscopy/Royal College of Obstetricians and Gynaecologists note that laparoscopic surgery has low adverse fetal and maternal complication rates.[73] However, LLB is not recommended in the third trimester ($\geq$28 weeks) due to limited surgical exposure. Biopsy should ideally be delayed until postpartum. LLB may be unavoidable only in life-threatening maternal conditions, following MDT confirmation of benefit exceeding risk, with emergency cesarean section capability and postoperative tocolysis.[74] Future research should focus on prospective validation of these pregnancy-specific LLB recommendations to further refine safety and efficacy in this high-risk population.

Extensive intra-abdominal adhesions increase iatrogenic injury risk,[75] with LLB reserved for cases in which PLB or TJLB has failed, and requires a highly experienced laparoscopic

surgeon,[76] and standardized adhesiolysis is mandatory.[77] If dense adhesions cannot be safely released, immediate conversion to open surgery is imperative. Patients with multiple comorbidities (ASA III–IV, Charlson comorbidity index ≥3) have elevated postoperative complication rates.[78,79] These patients require MDT confirmation that diagnostic benefits substantially outweigh the surgical risks, with individualized anesthesia and organ functional reserve assessment.[80–82]

Preoperative preparation and patient information

The preoperative preparation recommendations (Table 1) standardize the variable pre-procedure practices across centers. The anticoagulation management guidelines, aligned with the 2025 American College of Cardiology (ACC) update, address the common clinical dilemma of balancing bleeding risk with thromboembolic risk.

Comprehensive preoperative history taking focuses on anticoagulant/antiplatelet use, allergies, and underlying cardiovascular, respiratory, or renal disorders,[1] and a tailored diagnostic panel is used to evaluate surgical tolerance and anesthetic risk. Mandatory tests include infectious pathogen screening (hepatitis B virus/hepatitis C virus, syphilis, human immunodeficiency virus) for cross-infection prevention, blood group typing for transfusion preparedness, complete blood count (CBC) (platelet count $<50 \times 10^9$/L indicates elevated bleeding risk), coagulation tests (INR >1.5 suggests impaired hemostasis), and hepatic/renal function tests to assess metabolic capacity. Hypertensive patients require preoperative blood pressure control (≤140/90 mmHg) to reduce cerebrovascular risk, with electrocardiography screening for arrhythmias and chest imaging for pulmonary risk assessment. Ultrasound is the initial liver imaging modality, with contrast-enhanced CT/MRI recommended for complex cases (multifocal lesions, unclear anatomy[83]) to optimize biopsy trajectories and reduce iatrogenic injury.

During the first round of expert voting, specific intervals for preoperative imaging were established (Table S3). Regarding the "maximum interval between imaging studies (CT/MRI/ultrasound) and LLB," a majority (50%) of experts voted for "≤1 month." Based on this vote, the consensus recommends baseline imaging (CT/MRI/ultrasound) within 1 month before LLB, with flexibility to extend to 3 months for stable patients (e.g., no suspected malignancy, no disease progression, no severe comorbidities like decompensated cirrhosis). Unlike existing LB guidelines[1,2] that do not specify imaging intervals for LLB, this consensus provides evidence-based, flexible intervals tailored to patient stability, filling a critical gap in standardized LLB practice. Future research should validate these imaging intervals in multicenter prospective cohorts to further refine their safety and efficacy, particularly in patients with rapidly progressive liver disease.

Written informed consent is required after disclosing the procedure's purpose, risks (anesthesia complications, bleeding, and infection), and alternatives.[84] Preoperative fasting follows international standards: 6 h for solids and 2 h for clear liquids to reduce aspiration risk.[85] Perioperative anticoagulant/antiplatelet management follows ACC guidelines[79,86]: aspirin continuation for low-bleeding-risk procedures, 5–7 days P2Y12 inhibitor discontinuation for moderate-to-high-risk cases,[87] warfarin cessation 5 days preoperatively with low-molecular-weight heparin bridging,[88] and direct oral anticoagulant discontinuation 24–36 h preoperatively.[89,90] Standard laparoscopic equipment, biopsy needles (16G/18G), and intraoperative ultrasound are required,[91,92] with immediate specimen fixation and labeling ensuring pathological analysis quality.

Surgical procedure

The surgical procedure recommendations (Table 1) target the technical variability in LLB performance, to improve procedural safety and specimen retrieval accuracy. General anesthesia via endotracheal intubation or laryngeal mask airway is administered, with bispectral index monitoring to prevent delayed emergence.[93,94] Hepatorenal-protective agents with non-hepatic metabolism are prioritized. The initial patient position is 15°–30° head-up tilt (reverse Trendelenburg) combined with a 10°–15° left lateral tilt to optimize liver exposure,[95] with adjustments tailored to lesion location (increased right tilt for left LB and 10°–20° head-down Trendelenburg for right LB).

Pneumoperitoneum is established via the Veress needle (non-adhesion patients, >95% success for non-adhesion patients, 0.23%–0.31% injury risk[96]), open Hasson (layered incision for prior abdominal surgery or suspected adhesions[97]), or visual trocars (reduces insertion complications[98]), selected by abdominal surgery history, BMI-defined obesity, and surgeon experience. Pressure is maintained at 10–12 mmHg (8–10 mmHg for cardiopulmonary comorbidities[99]), with single- or multi-port laparoscopy used per patient condition (port details in Table S6). After laparoscope insertion, intra-abdominal exploration rules out puncture/trocar injury; evaluates liver morphology, color, texture, and lesions (intraoperative ultrasound improves differentiation between cirrhotic nodules and early HCC); releases perihepatic adhesions; and examines other abdominal organs (biliary tract, gastrointestinal tract, and peritoneum). Unexpected lesions are documented and evaluated intraoperatively.

The key steps of LLB are illustrated in Figure 3. For non-mass lesions, biopsy is typically performed at the inferior margin of the intersegmental boundary between hepatic segments V and VI or at the inferior margin of segment III. The biopsy needle (16G/18G) is inserted parallel to the diaphragmatic surface of the liver to avoid damage to the deep-seated Glisson's sheath (Figure S3A). For special lesions, direct laparoscopic guidance allows puncture at the site closest to the liver lesion, avoiding large blood vessels and bile ducts. Multi-point sampling is performed based on disease status, with at least 2–3 tissue strips (≥1.5 cm each) recommended.[2] Alternatively, wedge biopsy (excising a 5 × 15-mm wedge-shaped liver tissue block) is used to evaluate lesion margin status (Figure S3B). For mass lesions, biopsy sites are selected based on preoperative imaging and intraoperative laparoscopic observations. Image-guided two-point sampling (5 mm from lesion margin + central region) is recommended with intraoperative ultrasound. For focal lesions suspected of malignancy (e.g., primary or metastatic HCC), intraoperative indocyanine green staining improves puncture site accuracy.[100–102]

Hemostasis is stratified by bleeding type: superficial oozing is managed with topical agents or monopolar electrocoagulation, bleeding near critical vessels uses bipolar electrocoagulation, and persistent hemorrhage requires combined hemostatic agents. A 3- to 5-min observation period confirms no rebleeding.

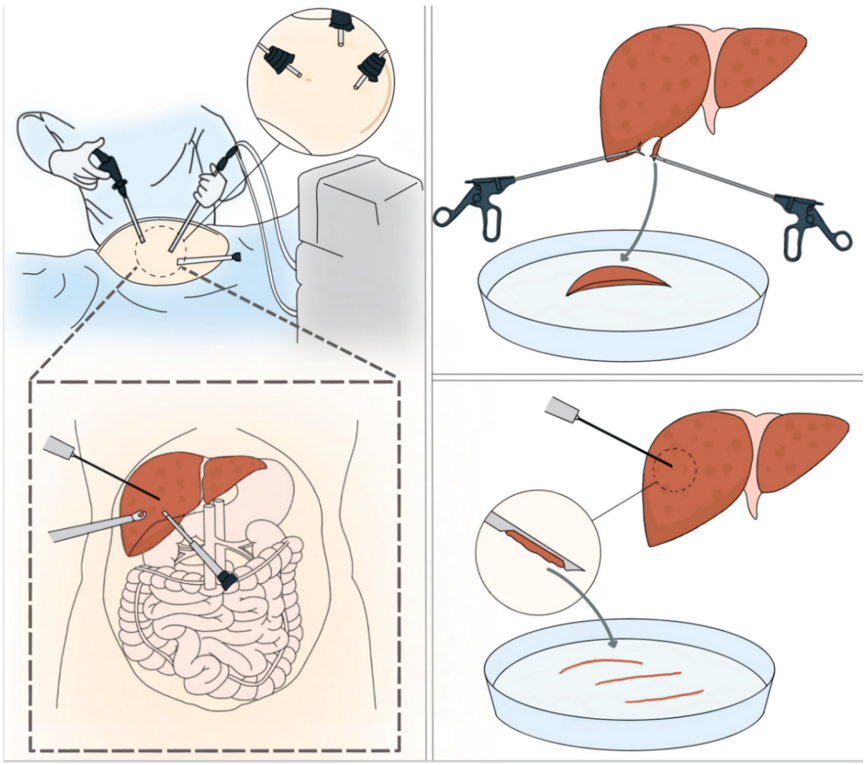

Figure 3. Schematic diagram of surgical procedure

Conversion to open surgery is indicated for anatomical complexity, severe bleeding, or organ injury.[103]

Preoperative MDT discussion is mandatory for lesions of unknown nature.[104] Intraoperative coaxial biopsy reduces tumor seeding risk,[105,106] with frozen section analysis guiding real-time decisions.[107] Postoperatively, vital signs are monitored for 4–6 h, with CBC testing at 6–8 h to detect delayed hemorrhage.[2] LLB operative time is typically in the range 15–30 min, with surgeon experience correlating with shorter duration and lower complications.[108] Specimens must be immediately fixed, labeled, and sent for pathological analysis.[1] Tissue fragility varies across liver disease stages, manifesting as unclear tissue architecture and broken or distorted fibrous septa on pathological examination, which compromises overall tissue structural stability (Figures S4A and S4B). Laparoscopic wedge biopsy can complement specimen integrity in such cases (Figures S4C and S4D).

Complication prevention and management

Although laparoscopic surgery is minimally invasive, the main complications are pneumoperitoneum-related events, intraoperative injuries, and postoperative sequelae.[21,103,109–116] The consensus establishes a stratified complication management framework (Table 1) aligned with the modified Clavien-Dindo classification system (Table S7),[117] with precise intervention timing critical for improving patient outcomes.

(1) High-risk complications

Gas embolism occurs when gases (e.g., CO_2) enter the bloodstream. Immediate pneumoperitoneum termination and circulatory stabilization (mean arterial pressure [MAP] $\geq$65 mmHg) are mandatory. Survival rates improve significantly with intervention within 5 min of onset.[118–120] Pneumomediastinum arises from excessive pneumoperitoneum pressure (15 mmHg) or traumatic puncture, impairing cardiopulmonary function. Continuous end-tidal CO_2 ($ETCO_2$) monitoring detects early embolism via abrupt $ETCO_2$ reductions; extreme Trendelenburg positioning should be avoided to reduce gas entrainment, with pneumoperitoneum pressure maintained at 12–15 mmHg and ultrasound-guided puncture used to avoid vascular injury.[121,122]

(2) Moderate-risk complications

Iatrogenic pneumothorax is managed first with closed drainage; thoracoscopy is indicated for persistent air leakage (>7 days) or complex lesions.[123] Delayed hemorrhage (from inadequate hemostasis or coagulopathy) requires laparoscopic electrocoagulation, hemostatic agents, or transarterial embolization; transfusion is reserved for hemodynamic instability.[2,124] Delayed visceral perforation is addressed via laparoscopic or open repair based on perforation characteristics and patient status.[125] Prophylactic measures include ultrasound-guided pneumoperitoneum needle placement (for patients with abdominal wall varices or adhesions[126]), controlled insufflation (1 L/min initially), and postoperative wound inspection at 8 mmHg to detect occult bleeding/gas leakage.[127,128] Serial hemoglobin monitoring (6–8 h postoperatively, then every 12–24 h) and abdominal imaging identify delayed complications.[129]

(3) Low-risk complications

Cholecystocardiac reflex (bradycardia/cardiac arrest from gallbladder traction) is managed with immediate procedure pause and intravenous atropine 0.5–1 mg, with resolution typically within 1–2 min[116] Surgical site infections are mitigated via sterile technique; prophylactic antibiotics are given 30 min preoperatively for immunocompromised patients, diabetics, or procedures >2 h[130,] Subcutaneous emphysema (from $\geq$15 mmHg pressure or poor trocar sealing) resolves spontaneously in 3–5 days; early ambulation (4 h postoperative) is encouraged with chest imaging for severe cases. Postoperative abdominal distension is relieved via early liquid intake and prokinetics, with decompression if needed.[131] Pain is controlled to visual analog scale (VAS) $\leq$3, with renally excreted analgesics preferred for cirrhotic patients.[132] Needle tract tumor seeding (incidence <0.1%) is mitigated via coaxial biopsy and leak-proof retrieval bags[106]; suspected seeding requires wide excision

(1–2 cm margin) plus adjuvant therapy. Management must be individualized: clinicians should integrate patient age, comorbidities (e.g., coronary artery disease [CAD], diabetes, and chronic obstructive pulmonary disease [COPD]), and functional status; aggressive intervention may be needed for elderly/multimorbid patients even for low-risk complications. Surgeon experience reduces overall complication rates via precise technique and early risk detection.[133]

Discharge management and quality management

The discharge and quality management recommendations (Table 1) address the post-procedure variability that has led to inconsistent patient recovery and follow-up, a key consideration for resource-constrained centers. The stratified follow-up approach ensures that high-risk patients receive appropriate monitoring while reducing unnecessary visits for low-risk patients. The standardized discharge criteria, stratified care pathways, and quality control protocols are grounded in Enhanced Recovery After Surgery (ERAS) principles.[134] The core requirements—stable vital signs within ±10% of preoperative baselines ($SpO_2 \geq 95\%$ on room air) to mitigate cardiopulmonary complications, VAS pain scores ≤ 3 managed with oral non-steroidal anti-inflammatory drugs (with heightened monitoring for bleeding and acute kidney injury in cirrhotic patients[135]), no active bleeding defined by ≤ 1 g/dL hemoglobin decline within 6–8 h post-procedure (with vigilance for occult hemorrhage if declines exceed 2 g/dL[136]), tolerance of clear liquids by 4 h post-procedure to enable ERAS-aligned early enteral nutrition (shortening hospital stays by 1–2 days and reducing infection rates[134]), and individualized assessment of underlying disease control (e.g., 24-h extended observation for portal hypertension patients)—balance postoperative safety with healthcare resource efficiency.

For uncomplicated diagnostic LLB or combined cholecystectomy-LLB (cholecystectomy class I–II, no intraoperative complications), same-day discharge is feasible with non-inferior safety to inpatient care, shortening hospital stays and reducing costs.[137–139] Delayed discharge is indicated for patients with unstable liver function or controllable complication risk, stratified by (1) preoperative factors: age >65 years (45% same-day discharge success vs. 78% for younger patients), ASA III–IV status, uncontrolled diabetes/hypertension, prior upper abdominal surgery, choledocholithiasis, acute cholecystitis, complex combined surgeries, Child-Pugh B/C cirrhosis, or lack of home support; (2) intraoperative factors: open conversion, complications, or anatomical complexity; and (3) postoperative factors: inadequate pain control, gastrointestinal dysfunction, complication signs, or patient anxiety.[140]

Standardized discharge education covers red-flag symptoms (persistent pain VAS > 4, fever > 38.5°C, worsening jaundice, hematemesis/melena) and activity restrictions (avoiding 5-kg lifting for 1 week). Stratified follow-up includes 1-week assessment of wound healing, CBC/liver function, and MDT discussion for confirmed malignancy; 1–3 months of liver disease surveillance (liver stiffness/alpha-fetoprotein [AFP] for cirrhotic patients); and 6–12 months of therapy guidance, with telemedicine improving low-risk patient adherence.[141,142] Specialized guidance is provided for elderly patients, diabetics (glycemic control to prevent infection[143]), and post-bariatric patients (nutritional support via MDT).

LLB training includes theoretical education (standardized checklists to reduce complications[144,145]) and simulation training for basic and emergency skills.[146,147] Establishing a surgical learning curve should occur under the supervision of experienced surgeons. As no previous studies have established standardized training requirements specifically for LLB, this consensus recommends that trainees complete at least 10 supervised LLB procedures before independent practice. Competency assessment (biopsy adequacy ≥ 1 cm/≥ 6 portal tracts, complication rate $\leq 5\%$, operative time ≤ 30 min) by senior surgeons.[148,149] Intraoperative photographs/videos of key steps are recommended for traceable quality control, stored encrypted in a patient-identified database.

A full-cycle preoperative-intraoperative-postoperative MDT model is recommended. For isolated LLB, hepatologists lead preoperative assessment, with surgeons, radiologists, anesthesiologists, pathologists, and nurses collaborating to ensure safety and specimen quality. For opportunistic LLB (e.g., combined with bariatric surgery), the lead surgical department coordinates planning, with hepatologists evaluating hepatic steatosis to guide postoperative management. Multidisciplinary rounds with documented responsibilities ensure care continuity.

Limitations of the study

A potential concern associated with LLB is the risk of tumor seeding due to pneumoperitoneum during specimen retrieval, which has been reported in a small number of studies on laparoscopic liver surgery for malignant lesions. The positive pressure of CO_2 pneumoperitoneum may facilitate the dissemination of tumor cells into the peritoneal cavity or blood circulation during biopsy needle insertion/retrieval. To mitigate this risk, the consensus recommends (1) using coaxial biopsy needles to reduce the number of punctures, (2) minimizing the duration of pneumoperitoneum and maintaining low-pressure pneumoperitoneum (≤ 12 mmHg) for malignant lesions, and (3) retrieving the biopsy specimen in a sealed bag to avoid direct contact between tumor tissue and the peritoneal cavity. Notably, the overall incidence of tumor seeding related to LLB is extremely low, and the benefit of accurate diagnosis for malignant lesions outweighs the potential risk in most clinical scenarios.

Despite the notable advantages of LLB in complex LB cases, it has inherent limitations that warrant clinical consideration. First, LLB requires general anesthesia and laparoscopic surgical equipment, which increases the overall medical cost for patients compared with PLB. Second, LLB is an invasive surgical procedure that entails additional anesthetic and surgical trauma, which is not negligible for patients with poor general condition or multiple comorbidities. Thus, LLB is not recommended as a first-line biopsy modality, and clinical decision-making must balance the diagnostic benefits against the procedural costs and trauma via MDT assessment, in line with the principle of "individualized treatment."

With ongoing advances in laparoscopy, pathology, and contemporary diagnostic and therapeutic practice in hepatology, this consensus distills the essential elements of LLB into practical, standardized guidance. Centers should adapt these recommendations to their resources and patient populations to

safeguard patients and to strengthen diagnostic yield and subsequent clinical decision-making. This international consensus provides a standardized framework that will enhance the safety and diagnostic accuracy and widen the adoption of LLB in clinical and research settings.

RESOURCE AVAILABILITY

Lead contact

Further information and requests for all the resources in this study should be directed to and will be fulfilled by the lead contact, Ming-Hua Zheng (zhengmh@wmu.edu.cn).

Materials availability

This study did not generate new, unique reagents.

Data and code availability

- Researchers interested in accessing the data are required to submit a formal request along with a brief research proposal to the corresponding author. Upon approval by the authors and the relevant institutional panel, a data transfer agreement will need to be signed before data can be shared.
- This manuscript does not report original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

CONSORTIA

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AUTHOR CONTRIBUTIONS

Conceptualization and methodology, S.-Y.L., Y.H., W.Y., J.N., and M.-H.Z.; Questionnaire design and writing – original draft, S.-Y.L., F.T., W.Y., J.N., M.-H.Z. and Y.H.; writing – review and editing, all authors; supervision, W.Y., J.N., and M.-H.Z.; project administration, S.-Y.L., Y.H., and M.-H.Z.; investigation, D.C.R., K.A., V.W.-S.W., N.J., C.J.T.-H., S.T., M.E.-K., J.G., M. Muthiah, O.G., M.Y., D.V.H., G.S., G.P., A.A.-A., A.G.R., S.H.K., R.W., K.M., A.S., M.K., R. Rajan, Y.S., H.E.T., S.S., E.O., C.P., Q.C., O.T., E.R.-Ú., R.O., R. Ribeiro, M. Musella, A.C.R., S.-w.R., T.A., W.J.L., M.P.C., J.E.G.F., J.S., A.M., S.W., W.Y., J.N., and M.-H.Z.; All authors reviewed and commented on the manuscript and approved the final version.

DECLARATION OF INTERESTS

G.P. has served as advisor and/or lecturer for Abbvie, Albireo, Amgen, AstraZeneca, BioArs, Elpen, Genesis, Gilead, GlaxoSmithKline, Ipsen, Janssen, Merck Sharp & Dohme, Novo Nordisk, Roche, Takeda, and Vir Pharmaceuticals and has received research grants from Abbvie, Gilead, Takeda, and Vianex. G.S. has acted as a speaker for Merck, Gilead, Abbvie, Novo Nordisk, and Eli Lilly and served as an advisory board member for Gilead, GlaxoSmithKline, Merck, and Novo Nordisk. F.T.'s lab has received research funding (to the institution) from AstraZeneca, MSD, Gilead, and Agomab. F.T. has received honoraria for consulting or lectures from AstraZeneca, Abbvie, Alnylam, Boehringer, Falk, MSD, GSK, Pfizer, Novo Nordisk, and Sanofi. V.W.-S.W. reported receiving personal speaker fees from Abbott; consultant and speaker fees from AbbVie; personal consultant fees from Boehringer Ingelheim, Echosens, and Gilead Sciences; grants from Gilead Sciences; personal consultant fees from Intercept, Inventiva, Novo Nordisk, Pfizer, Sagimet Biosciences, and TARGET PharmaSolutions; personal speaker fees from Unilab; and personal consultant fees from Virinxa and is a cofounder of Illuminatio outside the submitted work. M.Y. reported receiving honoraria from Kowa and grants from Gilead Sciences. J.G. serves on the advisory boards and receives honoraria for talks from Novo Nordisk, AstraZeneca, Roche, BMS, Pfizer, Cincera, Pharmaxis, Boehringer Mannheim, CSL, Norgine, Gilead, and Eisai. M. Muthiah has served as a consultant to Roche, Astellas, and Gilead. He has been an advisor for LernaBio. M. Muthiah has served as a speaker for Abbott, Perspectum, and Echosens. He also serves as the CMO of LiverGENIX PTE LTD. M.-H.Z. serves as a speaker for AstraZeneca, Hisky Medical Technologies, and Novo Nordisk and as a consultant for Boehringer Ingelheim and Eieling Technology and has received consulting fees from Boehringer Ingelheim.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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SUPPLEMENTAL INFORMATION

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
Google Forms (Web-based)	Google LLC	https://www.google.com/forms
WPS Office (version 12.1.0.24657) - Excel	Beijing Kingsoft Office Software, Inc.	https://www.wps.com/
WPS Office (version 12.1.0.24657) - PowerPoint	Beijing Kingsoft Office Software, Inc.	https://www.wps.com/
Procreate (version 5.3.15)	Savage Interactive Pty Ltd.	https://procreate.com/
Figdraw (version 2.0)	Hangzhou Duotai Technology Co., Ltd.	https://www.figdraw.com/

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

Study design

This study aimed to develop standardized international consensus statements for LLB to address the lack of unified guidelines for its clinical application. A modified Delphi method was adopted to synthesize expert opinions, with the study design adhering to best practices for consensus development.[150]

Conceptual framework

A targeted literature review (covering publications through April 2025, duration: 4 months) was conducted to identify key themes in LLB practice. Combined with input from core hepatology and surgery experts, a conceptual framework was established, encompassing 6 core thematic domains: (1) Clinical Application Scenarios of LLB; (2) Clinical High-risk Scenarios of LLB; (3) Preoperative Preparation and Patient Information; (4) Surgical Procedure; (5) Complication Prevention and Management; (6) Discharge Management and Quality Management. These domains guided the development of initial consensus statements and survey items.

Participants

Expert panel recruitment

Expert panelists were recruited to ensure global representation (6 continents: Asia, Europe, North America, South America, Africa, Oceania) and multidisciplinary expertise. Core members were drawn from the International Obesity Society Working Group on Steatotic Liver Disease, with additional participants selected from international hepatology/surgery societies or researchers with peer-reviewed publications on liver disease and liver biopsy. Eligibility criteria included: (1) $\geq$5 years of clinical/research experience in hepatology, hepatobiliary surgery, gastrointestinal surgery, or metabolic and bariatric surgery; (2) active involvement in liver disease diagnosis and treatment; (3) willingness to participate in all three rounds of surveys and manuscript revision. We developed an email template detailing the study and eligibility criteria for prospective panelists. Experts were enrolled if they responded with interest in participation.

Panel characteristics

To ensure Delphi process transparency and reproducibility, we documented panel size, response rate, and dropout rate per round. Reminder emails were sent 7 or 3 days before each survey deadline to optimize response rates. A total of 56 experts were invited, with 45 completing the first round (response rate: 80.4%). The final expert panel comprised 45 international specialists. Across all three rounds and manuscript reviews, panel size remained unchanged, with a 100% response rate and no dropouts (Table S1). The panel included surgeons (73.3%), hepatologists (22.2%), and gastroenterologists (4.5%). Geographically, 48.8% were from Asia, 22.2% from Europe, 13.3% from North America, 6.7% from South America, and 4.5% each from Africa and Oceania. Regarding work experience: <9 years (2.2%), 10–19 years (40.0%), 20–29 years (35.6%), >30 years (22.2%).

METHOD DETAILS

Delphi process design

The Delphi process consisted of three sequential rounds of anonymous online surveys, followed by consensus finalization. Given the paucity of high-level prospective clinical evidence for LLB, we adopted the methodological approach from Rubino, F. et al.[150] and established a consensus grading system (U/A/B/C) based on the total agreement rate (sum of ''Agree'' and ''Somewhat agree''

responses) of international multidisciplinary experts through the modified Delphi process. This grading system is more suitable for developing clinical consensus in fields with limited high-quality evidence.

Consensus was defined *a priori* based on two tiers: (1) The minimum threshold for consensus was set at >67% total agreement,[150] indicating that the statement had sufficient expert support; (2) For final inclusion, statements were required to achieve ≥78% total agreement (modified based on iterative feedback and consensus progression across three rounds), ensuring high-quality and clinically actionable recommendations. Grading criteria were as follows: "U" (Unanimous, 100% total agreement), "A" (90–99% total agreement), "B" (78–89% total agreement), and "C" (67–77% total agreement). Statements with <78% total agreement underwent revision and re-voting, while those achieving ≥78% total agreement were finalized.

Data collection

Round 1 (R1) data collection lasted six weeks (concluded May 23, 2025) and included six domains, 36 draft statements, and two open-ended items to inform Round 2. The R1 survey was administered via Google Forms. Experts rated each statement on a 4-point Likert scale ("Agree"/"Somewhat agree"/"Somewhat disagree"/"Disagree"), with a free-text comment field for each item. Open-ended items were selected based on their relevance to LLB practice.

Round 2 (R2) data collection concluded July 15, 2025, and provided experts with R1 group results to allow response adjustments if deemed appropriate. To evaluate heterogeneity and stability of revised content, the questionnaire was retained. The revised questionnaire included statements from R1, incorporating expert feedback and focusing on items that did not initially reach consensus.

The R3 survey was completed by August 17, 2025. The final questionnaire focused on revised controversial items from R2. New statements (e.g., management of intraoperatively suspected malignant lesions) were added based on R2 expert comments. The final outcome demonstrated all 46 finalized statements achieved ≥78% agreement, with no C-grade statements.

Consensus finalization

The consensus steering committee reviewed all survey results, expert comments, and revised statements. A subset of experts verified the final statements, with adjustments made based on iterative discussions. Consensus on all proposed statements improved across the three Delphi rounds. The mean percentage of "Agree" and combined "Agree or Somewhat agree" responses increased (Figure S1). The final consensus statements were organized into the six core domains, with concretely corresponding agreement percentages (grade levels) in each round provided in Tables S3, S4, and S5.

QUANTIFICATION AND STATISTICAL ANALYSIS

Descriptive statistics were used to summarize expert demographic characteristics and agreement rates across rounds. Agreement rates for each statement were calculated as the percentage of "Agree" and "Somewhat agree" responses relative to the total number of valid responses. Trends in agreement rates across the three rounds were analyzed to assess consensus progression. The "n" represents the number of expert panel members responding to each round. No additional statistical tests were performed, as this study is a consensus development inquiry using a Delphi methodology. Central tendency and dispersion are reported as percentages and raw counts for all questionnaire items. Data management and preliminary analysis were performed using Excel (WPS Office, version 12.1.0.24657), which is fully compatible with Microsoft Excel. All statistical analyses adhered to the reporting standards for Delphi studies. Google Forms (Web-based) was used for distributing questionnaires and collecting expert responses across all three Delphi rounds. Excel (WPS Office, version 12.1.0.24657) was used for data entry, cleaning, and descriptive statistical analysis. PowerPoint (WPS Office, version 12.1.0.24657) and Figdraw (version 2.0) were used for drawing and chart layout, with surgical procedure schematics created using Procreate (version 5.3.15).

ADDITIONAL RESOURCES

Every round survey was administered via Google Forms: R1 link: https://forms.gle/46GqwRPZpb5xo8iQ6; R2 link: https://forms.gle/L8XBMuXzst4oNLiG8; R3 link: https://forms.gle/dtQBMuG6PgBKXzkf6. This consensus was registered in the International Practice Guideline Registry Platform (PREPARE) under registration number PREPARE-2025CN1539.

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Supplemental information

An international multidisciplinary consensus statement on laparoscopic liver biopsy

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Supplementary Table 1. Comparison of the advantages and disadvantages of different surgical methods of liver biopsy.

Biopsy Method	Advantages	Disadvantages
Percutaneous Liver Biopsy	Relatively simple procedure, feasible in obese patients or those with ascites or coagulopathy.	Significant limitations in patients with severe obesity, massive ascites, or thrombocytopenia.
	Can be performed under local anesthesia, reducing patient burden.	Risk of complications such as bile leakage, especially near major vessels or the gallbladder.
	Direct liver tissue sampling with high diagnostic accuracy for focal lesions.	Limited to certain areas, typically the right lobe; lesions in the left lobe may be missed.
	Low equipment requirements, generally guided by ultrasound or CT, cost-effective.	Small tissue samples may affect diagnostic accuracy.
Transvenous Biopsy	Preserves liver capsule; safer for lesions near hepatic veins.	Complex procedure requiring advanced interventional skills and DSA guidance.
	Allows simultaneous angiography to assess vascularity of lesions.	Risk of vascular injury, thrombosis, and severe circulatory complications.
	Facilitates portal hypertension assessment and HVPG measurement.	Blood contamination may affect pathological diagnosis.
		Difficulty in sampling focal lesions due to distal anatomical constraints.
Endoscopic Ultrasound-Guided Biopsy	Clear visualization of the digestive tract and adjacent structures, high accuracy for pancreatic, biliary, and liver lesions.	Requires specialized training for endoscopists.
	Avoids interference from gastrointestinal gas, real-time ultrasound guidance reduces complications.	May cause significant patient discomfort, such as nausea and vomiting.
	Allows simultaneous observation of gastrointestinal conditions.	Smaller tissue samples may be insufficient for certain diagnoses.
Laparoscopic Biopsy	Direct visualization of liver and surrounding structures, accurate assessment of lesion characteristics.	Requires general anesthesia, with associated risks and longer recovery times.
	High accuracy and sufficient sampling and suitable for difficult-to-diagnose lesions.	Risk of postoperative complications such as infection.
	Allows simultaneous management of other abdominal conditions.	Higher costs, including surgery, anesthesia, and hospitalization.

HVPG: hepatic venous pressure gradient; *DSA:* digital subtraction angiography.

Supplementary Table 2. Demographic composition of the expert panel

Characteristics	Round 1	Round 2	Round3
Surveys sent, n	56	45	45
Total respondents, %	80.4 (45/56)	100 (45/45)	100 (45/45)
Participant type, %			
Surgeon	73.3		
Hepatologist	22.2		
Gastroenterologist	4.5		
Age group, %			
<40 yrs	11.1		
40-65 yrs	77.8		
>65 yrs	11.1		
Gender, %			
Women	8.9		
Men	91.1		
Region of practice, %			
Asia	48.8		
North America	13.3		
South America	6.7		
Europe	22.2		
Africa	4.5		
Oceania	4.5		
Working Experience, %			
< 9 yrs	2.2		
10-19 yrs	40.0		
20-29 yrs	35.6		
> 30 yrs	22.2		

Supplementary Table 6. Comparison of puncture sites for laparoscopic liver biopsy.

Category	Single-Port Laparoscopy	Multi-Port Laparoscopy
Lesion Location & Depth	Suitable for superficial, well-defined lesions (e.g., subcapsular cysts, focal nodular hyperplasia). Limited to lesions accessible via a single port.	Preferred for deep-seated or extensive lesions (e.g., diffuse hepatic fibrosis with nodules, multifocal metastases). Multiple ports enable access to diverse anatomical regions.
Lesion Size & Number	Optimal for small, solitary lesions. Minimizes hepatic trauma due to restricted instrumentation.	Ideal for large or multifocal lesions. Concurrent use of multiple instruments improves biopsy efficiency.
Disease Complexity	Suitable for straightforward cases (e.g., benign cysts/hemangiomas confirmed by imaging). Limited to uncomplicated lesions requiring minimal exploration.	Preferred for complex lesions (e.g., suspected malignancy, adhesions). Enables detailed exploration, adhesion dissection, and evaluation of lesion-tissue relationships.
Patient Comorbidities	Lower physiological burden; advantageous for elderly patients or those with comorbidities (e.g., cardiopulmonary dysfunction, diabetes).	Requires better patient tolerance for prolonged surgery. Not ideal for high-risk patients due to increased procedural complexity.
Cosmetic Outcome	Single small incision minimizes scarring, meeting aesthetic expectations.	Multiple incisions result in visible scars, particularly with four-port approaches.
Operational Space	Limited space causes instrument interference, hindering deep tissue biopsy or large lesion management.	Expanded workspace reduces instrument conflict, facilitating biopsy of deep or complex lesions.
Surgical Field	Narrow visualization due to coaxial instrument and camera placement; potential for visual obstruction.	Enhanced panoramic view with multi-angle instrument/camera placement, improving lesion detection and biopsy precision.
Technical Difficulty	Steep learning curve; demands advanced single-port proficiency.	Technically mature; easier to master (e.g., classic three-port approach).
Complication Risk	Lower incision-related risks (infection, bleeding, seroma). However, restricted space may increase hepatic parenchymal injury.	Higher incision-related complications. Improved visualization reduces inadvertent tissue damage.
Specimen Acquisition	Narrow channel limits retrieval of large/intact specimens.	Multiple instruments facilitate retrieval of adequate tissue samples for pathological analysis.

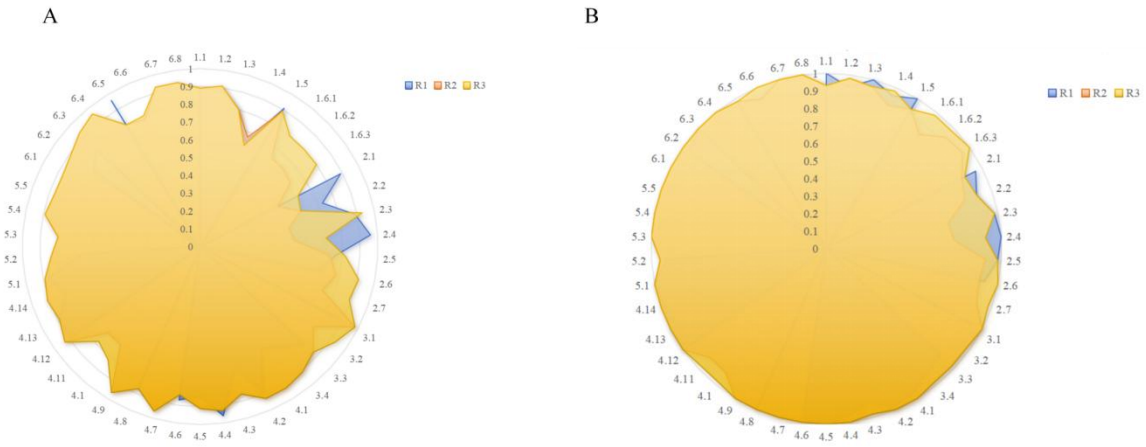
Supplementary Table 7. Risk-stratified complication management in LLB.

Risk Level	Complication Type	Critical Treatment Time	Management Measures	Preventive Strategies	Monitoring Parameters
Grade IV-V (High)	• Gas embolism	≤5 minutes	1. Immediate termination of pneumoperitoneum	• Real-time $ETCO_2$ monitoring	• Arterial blood gas analysis
	• Mediastinal emphysema		2. Maintain circulatory stability	• Avoid extreme Trendelenburg position	• Central venous pressure
	• Major vascular injury		3. Emergency thoracotomy/laparotomy	• Pneumoperitoneum pressure 12-15 mmHg • Intraoperative ultrasound-guided needle insertion	• Cardiac output
Grade III (Moderate)	• Pneumothorax	≤24 hours	1. Chest tube drainage ± thoracoscopic exploration (pneumothorax)	• Confirm proper pneumoperitoneum needle placement	• Hemoglobin trends
	• Delayed rebleeding (e.g., liver biopsy site/abdominal wall)		2. Angioembolization ± blood transfusion (hemorrhage)	• Controlled insufflation rate	• Abdominal pain assessment
	• Delayed visceral perforation		3. Diagnostic laparoscopy (hemorrhage/perforation)	• Postoperative low-pressure (8 mmHg) wound inspection	• CRP levels
Grade I-II (Mild)	• Cholecardiac reflex	4-48 hours	1. Intravenous atropine 0.5-1 mg (bradycardia)	• Gentle tissue manipulation	• Vital signs BP/HR
	• Infection		2. Pathogen-targeted antibiotics after culture	• Preoperative atropine prophylaxis	• Body temperature/WBC/neutrophil count
	• Subcutaneous emphysema		3. NSAIDs PRN (pain)	• Strict aseptic technique	• Infection markers (CRP)
	• Local pain		4. Early ambulation ± prokinetic agents	• Prophylactic antibiotics when indicated	• Subcutaneous swelling assessment
	• Postoperative abdominal distension			• Reduced pneumoperitoneum pressure	• VAS pain score • Bowel sounds
Special Risk	• Needle tract tumor seeding	Case-specific	• Extended resection of affected area	• Specimen retrieval bags for suspected malignancies	• Serial AFP measurements
				• Postoperative tumor marker surveillance	• Biopsy site monitoring

$ETCO_2$, end-tidal carbon dioxide; BP, blood pressure; HR, heart rate; CRP, C-reactive protein; VAS, visual analogue scale; NSAIDs, non-steroidal anti-inflammatory drugs; AFP, alpha-fetoprotein.

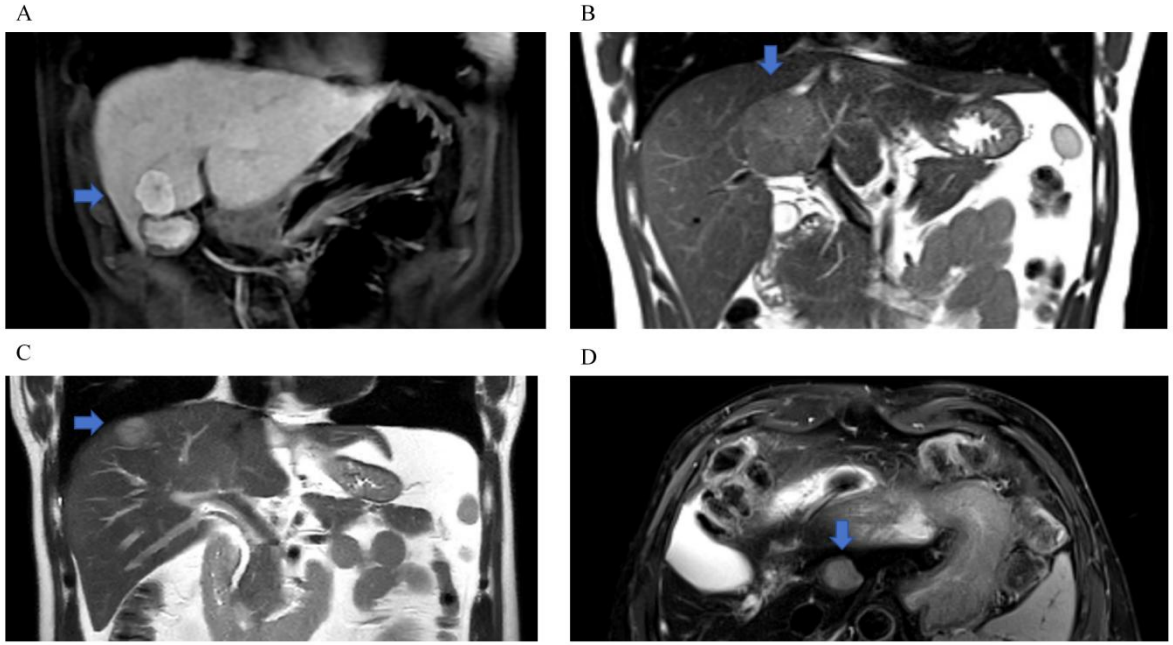
Supplementary Figure S1. Scores for agreement during the consensus development process.

(A) Scores for agreement by experts in Round 1 and Round 2 surveys. **(B)** Total scores for "agree" and "somewhat agree" by experts in Round 1 and Round 2 surveys.

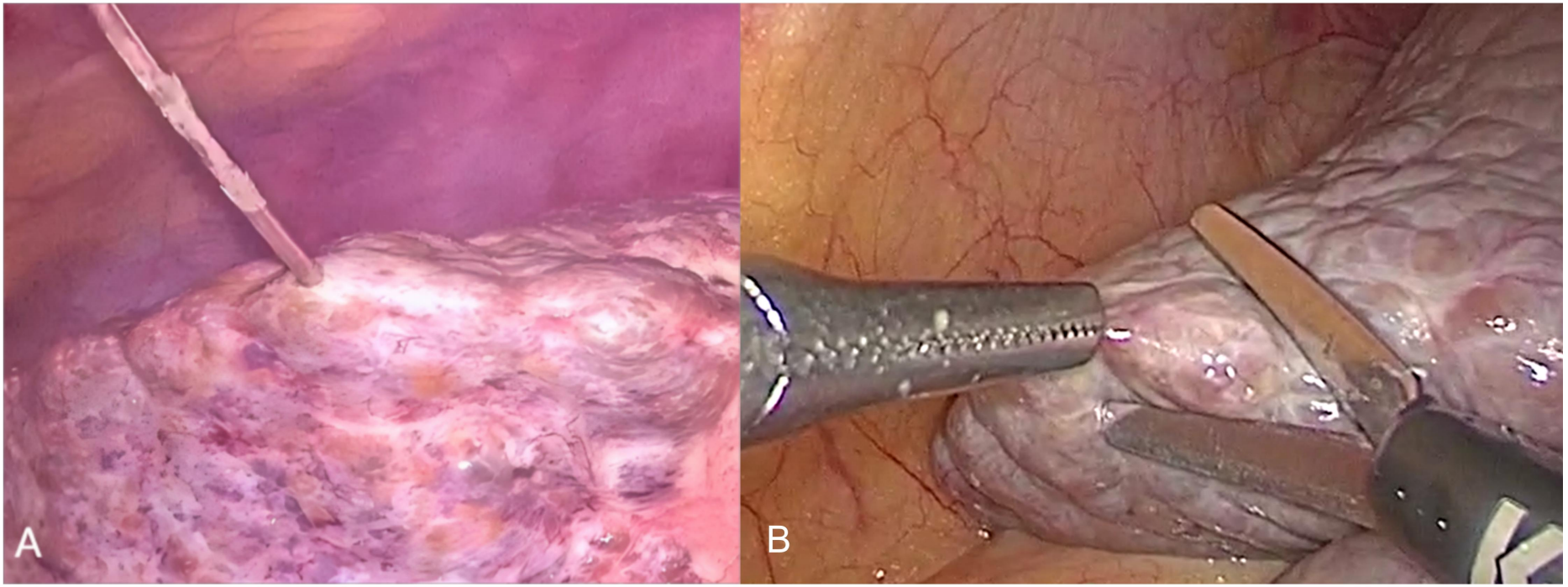


Supplementary Figure S2. Focal lesions in complex anatomical locations on MRI imaging.

(A) MRI demonstrates a nodule adjacent to the gallbladder fossa in the left medial segment of the liver (S4 segment). **(B)** Mass in the perihilar region of the liver. **(C)** Nodule below the diaphragmatic dome of the right liver lobe. **(D)** Caudate lobe nodule of the liver.



Supplementary Figure S3. Laparoscopic needle biopsy (A) and wedge biopsy (B).



Supplementary Figure S4. Laparoscopic needle biopsy pathology (A, B) and wedge biopsy pathology in patients with liver disease (C, D).