ISSN: 1859 - 431X

VIETNAM ASSOCIATION FOR THE STUDY OF LIVER DISEASES (VASLD)
In Collaboration with the Vietnam Society of Hepatobiliary and Pancreatic Surgery (VSHBPS) and
The Vietnam Society of Minimally Invasive Treatment for HBP Diseases (VASLD - MIT)

CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF HEPATOBILIARY AND PANCREATIC DISEASES IN VIETNAM WITH REPRESENTATIVE CLINICAL ILLUSTRATIONS

Một số Khuyến cáo hướng dẫn về Chẩn đoán, Điều trị bệnh lý Gan mật tuỵ ở Việt Nam & Hình ảnh lâm sàng tiêu biểu

15th World Congress of IHPBA
in New York, USA - April 2022

Hanoi 2026

Vietnam Delegation in A-PHPBA in Seoul, Korea - September 2019

HBP Surgery Week 2023 in Busan, Korea - March 2023

ASIAN Transplantation Week in Seoul, Korea - November 2023

The VSHBPS Delegation at the IHPBA Congress in Cape Town, South Africa,

May 2024, featuring presentations by young surgeons.

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(Tài liệu tiếng Anh phục vụ Hội nghị khoa học Quốc tế
của Hội Gan mật Việt Nam & Hội Phẫu thuật Gan mật tuỵ Việt Nam)

Hanoi 2026

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Publishing

Assoc. Prof. Đao Viet Hang MD, PhD, Assoc. Prof. Tran Thi Khanh Tuong MD, PhD, Assoc. Prof. Tran Manh Hung MD, PhD, Assoc. Prof. Le Van Thanh MD, PhD, Assoc. Prof. Pham Van Thuong MD, PhD, Assoc. Prof. Vu Van Quang MD, PhD, Assoc. Prof. Nguyen Thai Binh MD, PhD, Assoc. Prof. Nguyen Thanh Xuan MD, PhD

Secretariat

Dang Nhu Thanh MD MS (Chief Copyeditor)

Ly Ngoc Bich MD - Nguyen Trung Hieu MD - Pham Thi Dieu Anh BA

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FOREWORD

In recent years, the hepatobiliary and pancreatic (HBP) specialty in Vietnam has undergone remarkable development, with significant advances in the diagnosis and treatment of HBP patients. Leveraging this extensive experience and collaborating with international experts, we have developed 14 clinical guideline recommendations in Vietnam. These include:

Diagnosis and Treatment of HCC (2019)

Prevention and Treatment of Hepatitis (2020)

Treatment of Biliary Stones (2020)

Diagnosis and Treatment of Pancreatic Cancer (2021)

Liver Transplantation (2021)

Application of Indocyanine Green (ICG) Fluorescence in Hepatobiliary Surgery (2023)

Digital Transformation and AI for HBP Diseases (2024)

Diagnosis and Treatment of Perihilar Cholangiocarcinoma (PHC) (2024)

Diagnosis and Treatment of Acute-on-Chronic Liver Failure (ACLF) (2025)

Fatty Liver Disease (2025)

Advances in Minimally Invasive Treatment (MIT) for HBP Diseases (2025)

Dual-Medicine Combinations in the Prevention and Treatment of Viral Hepatitis, Liver Cirrhosis, and HBP Cancer (2025)

Prevention, Nutritional Intervention, and Regimens for HBP Diseases (2025)

Treatment of Pancreatitis and Pancreatic Cysts (2025).

In this publication, we are pleased to introduce the updated 2026 versions of four primary guidelines: ACLF, Liver Transplantation, HCC, and Advances in Minimally Invasive Treatment (MIT) for HBP Diseases. Additionally, we present about more than 60 representative clinical illustrations from the Vietnamese HBP specialty.

These recommendations are formatted as clinical questions and answers, incorporating specialized content and Vietnam's unique clinical experiences. Our objective is to provide information that is concise, accessible, and easy to implement. These guidelines will be continually updated by both Vietnamese and international experts.

Looking forward, we remain committed to developing new recommendations to further advance the HBP specialty and enhance patient care.

On behalf of the Scientific Council and the Clinical Practice Guidelines Editorial Board.

Major General Professor Le Trung Hai, MD, PhD

President of VASLD

Founding President of VSHBPS

President of VASLD-MIT

CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) IN VIETNAM

(2026 Updated Version: Including 18 Clinical Recommendations)

A. Diagnostic Concepts and Approaches to Patients with ACLF (with 2 recommendations):

** **Clinical Question 1**: What is the diagnostic definition of Acute-on-Chronic Liver Failure (ACLF) according to the Asian Pacific Association for the Study of the Liver (APASL)?*

*** Recommendation 1:** Acute-on-Chronic Liver Failure (ACLF) is characterized by an acute hepatic insult manifesting as jaundice (serum bilirubin ≥ 85 µmol/L or 5 mg/dL) and coagulopathy (INR ≥ 1.5 or prothrombin activity < 40%), complicated within 4 weeks by clinical ascites and/or hepatic encephalopathy (HE) in a patient with previously diagnosed or undiagnosed chronic liver disease. Common underlying chronic liver disease includes chronic hepatitis B or C, metabolic-associated fatty liver disease (MAFLD), alcoholic hepatitis, and potentially drug-induced liver injury, autoimmune hepatitis, or Wilson's disease, as well as compensated or decompensated cirrhosis. The condition often progresses over several weeks, potentially leading to multi-organ failure and a high mortality rate.

** **Clinical Question 2**: What are the clinical approaches to managing patients with Acute-on-Chronic Liver Failure (ACLF)?*

*** Recommendation 2:** The clinical approach to managing ACLF patients includes:

- Establishing a definitive diagnosis of ACLF.

- Providing nutritional intervention and supportive care.

- Identifying and treating precipitating factors and the underlying liver disease.

- Preventing and managing organ failure, including assessment of organ damage, severity, prognostic factors, and treatment response.

- Utilizing liver support and bridging therapy.

- Evaluating for liver transplantation.

- Coordinating Post-ACLF recovery and long-term management.

B. Etiology, Precipitating Factors, Classification, Severity, and Prognostic Factors in ACLF (with 4 recommendations):

** **Clinical Question 3:** What are the common causes and precipitating factors of ACLF?*

*** Recommendation 3:** Common causes and precipitating factors of ACLF include:

- Viral Hepatitis: Spontaneous flare-ups of chronic hepatitis B; reactivation following the discontinuation of antiviral therapy or after chemotherapy; and superinfection with hepatitis A, D, E, or C viruses.

- Alcoholic hepatitis: History of ongoing alcohol consumption, AST/ALT ratio > 1.5, jaundice, and exclusion of other causes.

- Hepatotoxic agents: Anti-tuberculosis drugs, antiparasitic agents, etc.; herbal medicines, traditional medicines, and dietary supplements; neurotoxic drugs (sedatives, analgesics); nephrotoxic drugs, etc.

- Autoimmune hepatitis: History of autoimmune hepatitis, irregular medication adherence, dose reduction, or postpartum onset.

- Other causes such as gastrointestinal bleeding (hematemesis, melena, tachycardia, hypotension, decreased hemoglobin, confirmed by endoscopy, etc).

*** ***Clinical Question 4:*** *What is the classification of ACLF according to the Asian Pacific Association for the Study of the Liver (APASL)?*

*** Recommendation 4:** The Asian Pacific Association for the Study of the Liver (APASL) classification of ACLF is based on clinical presentation and organ dysfunction:

- ACLF Grade 1: Decompensated liver failure with damage to 1-2 organs, with a mortality rate of 20% to 40% within 28 days.
- ACLF Grade 2: Decompensated liver failure with damage to 3-4 organs, with a mortality rate of 30% to 60% within 28 days.
- ACLF Grade 3: Decompensated liver failure with damage to ≥ 5 organs, with a mortality rate of 50% to 90% within 28 days.

*** ***Clinical Question 5:*** *How is the severity of ACLF assessed?*

*** Recommendation 5:** Assess ACLF severity using five parameters: Bilirubin, grade of hepatic encephalopathy (coma), INR, lactate, and creatinine, with each scored from 1 to 3. The total score determines the severity level: Level I (5-7 points), Level II (8-10 points), Level III (11-15 points).

APASL ACLF Assessment Scale:

Points	**Bilirubin** (mg/dL)	**HE levels**	**INR**	**Lactat** (mmol/L)	**Creatinin** (mg/dL)
1	<15	0	<1.8	<1.5	<0.7
2	15-25	1-2	1.8-2.5	1.5-2.5	0.7-1.5
3	>25	3-4	>2.5	>2.5	>1.5

*** *Clinical Question 6*:** *What are the prognostic factors in ACLF?*

*** Recommendation 6:** The prognosis for ACLF is poor if the following factors are present:

- Sepsis and ≥ 2 organ failures, or uncontrolled infection.
- Progressive uremia and/or serum creatinine > 4 mg/dL.
- Acute Respiratory Distress Syndrome (ARDS) or hepatic encephalopathy requiring mechanical ventilation for > 72 hours.
- Failure of at least four organs at any given time.
- Active gastrointestinal bleeding.
- Hemodynamic instability requiring >3 mg/h of noradrenaline.
- Ongoing hemodialysis.
- Diabetes mellitus.
- Patients over 60 years of age.

C. Specific treatment, management of organ failure, supportive liver care, and bridging for liver transplantation (with 4 recommendations):

**** Clinical Question 7***: *What are the specific treatments for the underlying causes of ACLF?*

*** Recommendation 7:** Specific treatments for the underlying causes of ACLF include:

- ***Infection control:*** Infection is a major precipitating factor and a serious complication of ACLF; inappropriate antibiotic therapy increases mortality by 9.5 times. Administer antibiotics early upon the onset of Systemic Inflammatory Response Syndrome (SIRS) or when infection is suspected; utilize broad-spectrum (strong) antibiotics promptly. Perform diagnostic paracentesis (ascites fluid

aspiration) to monitor treatment response. Screen for Clostridium difficile if diarrhea is present. If there is no clinical response, consider antibiotic-resistant bacteria or fungal infections (based on clinical assessment, cultures, and biomarkers).

- Treatment of HBV-related ACLF:

+ Initiate antiviral therapy, specifically TAF, TDF, or Entecavir.

+ Re-evaluate after 2 weeks to monitor the decrease in HBV DNA levels.

+ Liver transplantation is indicated in severe cases.

- Treatment of Alcoholic ACLF:

+ Corticosteroids should not be used in patients with severe alcoholic hepatitis, Grade 3 ACLF, nor in cases where infection is not controlled.

- Treatment of drug-induced liver injury (DILI): In Asia, approximately 6.5% of ACLF cases are drug-induced. Immediately discontinue the suspected agent and initiate plasmapheresis.

+ Common causes include herbal remedies, dietary supplements, and anti-tuberculosis drugs.

+ Mortality rates are high (> 60%). Key prognostic factors for mortality include hepatic encephalopathy, ascites, and elevated levels of creatinine, INR, and lactate.

+ In cases where no specific precipitating factor is detected, management focuses on monitoring, supportive care, treatment of complications, and consideration for liver transplantation.

- Autoimmune hepatitis*:* Initiate corticosteroid therapy.

- Wilson's disease*:* Plasma exchange (plasmapheresis) may be utilized.

**** Clinical Question 8:*** *What are the primary considerations in the treatment strategy for Hepatitis B-related Acute-on-Chronic Liver Failure (HBV-ACLF)?*

*** Recommendation 8:** Hepatitis B-related Acute-on-Chronic Liver Failure (HBV-ACLF) is a severe syndrome characterized by the acute decompensation of chronic liver disease or cirrhosis. HBV-ACLF frequently results from a reactivation of the hepatitis B virus (HBV), leading to rapid multi-organ failure and high short-term mortality. The pathogenesis of HBV-ACLF is primarily driven by an excessive systemic inflammatory response and viral reactivation. Therefore, current treatment strategies focus on potent antiviral therapy to suppress HBV replication, comprehensive supportive care for failing organs, and early evaluation for liver transplantation as a definitive treatment option. Standardizing HBV-ACLF treatment protocols is essential to provide targeted strategies tailored to each individual patient.

*** *Clinical Question 9*:** *What is the management strategy for organ failure in ACLF?*

*** Recommendation 9:** The prevention and comprehensive management of organ failure in ACLF should include: treatment of hepatorenal syndrome (including management of cirrhosis with ascites); prevention and treatment of hepatic encephalopathy; and supportive care for respiratory, circulatory, and coagulation disorders.

*** *Clinical Question 10*:** *What are the liver support treatments, clinical outcomes, and bridging management strategies for liver transplantation?*

*** Recommendation 10:** Liver support treatments and bridging therapies awaiting liver transplantation include: paracentesis (large-volume drainage should be performed slowly, typically 3–4 liters at a time); plasma exchange (PEX) or high-volume plasma exchange

(HVPE) combined with continuous veno-venous hemofiltration (CVVH). The 28-day survival rate is approximately 40% for patients undergoing extracorporeal liver assist device (ELAD) therapy, bioartificial liver (BAL) support, or artificial liver support systems such as the molecular adsorbent recirculating system (MARS) and double plasma molecular adsorption system (DPMAS). However, the mortality rate for ACLF remains high even with MARS and DPMAS therapy. In severe cases (Grade 3 ACLF), the mortality rate is significantly higher, particularly when liver transplantation is not performed.

D. Liver Transplantation for ACLF (with 5 recommendations):

** **Clinical Question 11**: What is the role of living donor liver transplantation (LDLT) in the management of ACLF?*

*** Recommendation 11:** Living donor liver transplantation (LDLT) for ACLF is safe and associated with a high survival rate. Multidisciplinary care before, during, and after transplantation, combined with early clinical decision-making, are crucial factors in improving survival for ACLF patients.

** **Clinical Question 12**: When should liver transplantation be performed for ACLF?*

*** Recommendation 12:** Liver transplantation is indicated when ACLF is severe, demonstrates a worsening clinical course despite optimal medical therapy, remains unresponsive to treatment, involves irreversible liver failure, or carries a poor prognosis (based on MELD or CLIF-C ACLF scores). In cases of acute-on-chronic liver failure, transplantation is the most effective intervention and is recommended within the "golden window" of 4–7 days from ACLF

onset. Emergency liver transplantation offers long-term benefits across all levels of ACLF severity. Patients with Grade 1 and Grade 2 ACLF typically have favorable post-transplant outcomes, with 1-year and 3-year survival rates near 90%, and 5-year survival rates exceeding 75%. However, Grade 3 ACLF requires specialized perioperative management and intensive post-transplant care.

***** ***Clinical Question 13*****:** *What precautions should be taken before liver transplantation for Grade 3 Acute-on-Chronic Liver Failure (ACLF)?*

*** Recommendation 13:** Grade 3 Acute-on-Chronic Liver Failure (ACLF) is the most severe clinical form, often requiring liver transplantation as a definitive life-saving intervention. Grade 3 ACLF is characterized by multi-organ failure involving the liver, kidneys, brain (neurological), coagulation, circulatory, and respiratory systems, with mortality rates as high as 80% in the absence of transplantation. Patients require robust hemodynamic resuscitation and a meticulous assessment of transplant feasibility. This includes evaluating the patient's general clinical status, the degree of hepatic dysfunction, and associated complications, alongside MELD and CLIF-C ACLF scores. A multidisciplinary collaboration between hepatologists, transplant surgeons, intensive care specialists, and other relevant experts is essential for the decision-making process. Patients with Grade 3 ACLF require continuous monitoring and must be prepared for emergency transplantation. Bridging therapies, such as extracorporeal liver support systems, may be utilized to maintain clinical stability while awaiting a suitable donor. Early liver transplantation (within $\leq$ 7 days of being listed) should always be prioritized for Grade 3 ACLF patients, as it is associated with significantly better 1-year survival rates compared to delayed transplantation.

*** ***Clinical Question 14:*** *What are the donor considerations in liver transplantation for Grade 3 ACLF?*

*** Recommendation 14:** Donor selection must be performed carefully, with specific consideration given to donor age, degree of hepatic steatosis (fatty liver), and cold ischemia time to ensure optimal graft function. For Grade 3 ACLF, ABO-incompatible living donor liver transplantation (ABOi-LDLT) should not be excluded as a viable option when an ABO-compatible donor is unavailable.

*** ***Clinical Question 15:*** *What are the perioperative and postoperative considerations for liver transplantation in patients with Grade 3 ACLF?*

*** Recommendation 15:** Regarding liver transplantation techniques for patients with Grade 3 ACLF, it should be noted that the use of veno-venous bypass or the "piggyback" technique can help minimize hemodynamic instability. Post-transplantation, close monitoring of liver function tests, coagulation profiles, and bile production is necessary. This includes the prevention and management of surgical complications, coagulation disorders, portal hypertension, and ascites. Comprehensive care requires tailored immunosuppressive therapy, renal replacement therapy, respiratory support, and cardiovascular stabilization. Furthermore, the prevention of severe primary and opportunistic infections is critical for long-term survival.

E. Summary and General Outcomes (with 2 recommendations):

*** ***Clinical Question 16:*** *What is the summary of the diagnosis and management of Acute-on-Chronic Liver Failure (ACLF)?*

*** Recommendation 16:**

- Acute-on-Chronic Liver Failure (ACLF), characterized by jaundice, coagulopathy, ascites, and hepatic encephalopathy, is a

serious complication frequently encountered in Vietnam and carries a high risk of mortality. The most common causes of death include multi-organ failure, hemorrhage, infection, and cerebral edema.

- Early, accurate diagnosis and prompt management are crucial factors for successful treatment.

- The management of ACLF includes standardized medical care and specialized interventions, including liver support systems and, most definitively, liver transplantation. Key management priorities include preventing cerebral edema, maintaining hemodynamic stability, and controlling infection.

- Liver support measures currently applied in Vietnam include plasma exchange (PEX), double plasma molecular adsorption system (DPMAS), molecular adsorbent recirculating system (MARS), and extracorporeal liver assist device (ELAD) therapy. These play a vital role in supporting hepatic recovery and serve as a critical bridge to liver transplantation.

- In cases where the liver is unable to recover spontaneously, liver transplantation is the only definitive treatment. It yields excellent results in ACLF-1 and ACLF-2 cases, with the "golden window" for transplantation occurring between days 4 and 7 of the disease onset. Liver transplantation is a life-saving measure for ACLF patients, even in the presence of multi-organ failure. Living donor liver transplantation (LDLT) for ACLF is safe and associated with high post-transplant survival rates. For well-selected and adequately prepared Grade 3 ACLF cases, post-transplant outcomes are encouraging and clinically acceptable.

**** Clinical Question 17:*** *What are the overall outcomes following liver transplantation for Acute-on-Chronic Liver Failure?*

*** Recommendation 17:**

Post-transplant survival rates are excellent, particularly for ACLF Grades 1 and 2, with short-term survival ranging from 95% to 100% and 3-year survival rates exceeding 90%. While the survival rate

for Grade 3 ACLF following living donor liver transplantation is lower than that of Grades 1 and 2, the results remain acceptable. For carefully selected and clinically optimized Grade 3 ACLF cases, the post-transplant outcomes are highly encouraging.

F. Application Artificial Intelligence (AI) in ACLF (with 1 recommendation):

*** *Clinical Question 18*:** *Application AI for Acute-on-Chronic Liver Failure?*

*** Recommendation 18:** Application artificial intelligence (AI) curently being use for predictive modeling in ACLF with prognostic accuracy. New treatment approaches based on pathophysiological analysis, biological systems, and AI-assisted approaches show great promise. In future of AI in ACLF: Treatment strategy; Organ allocation; Better understanding of physiopathology...

VIETNAM ASSOCIATION FOR
THE STUDY OF LIVER DISEASES,
VSHBPS & VASLD-MIT

SOCIALIST REPUBLIC OF VIETNAM
Independence - Freedom - Happiness

Hanoi, April 5th, 2026

DECISION

Regarding the Promulgation of the "Clinical Practice Guidelines for the Diagnosis and Treatment of Acute-on-Chronic Liver Failure (ACLF) in Vietnam" by the Vietnam Association for the Study of Liver Diseases (VASLD), VSHBPS and VASLD-MIT

President of the Vietnam Association for the Study of Liver Diseases (VASLD),

Founding President of VSHPBS and President of VASLD-MIT

Pursuant to the authorities and responsibilities vested in the President of the Vietnam Association for the Study of Liver Diseases (VASLD), the Founding President of VSHBPS, and the President of VASLD-MIT

HEREBY DECIDES:

Article 1. To officially promulgate the "Clinical Practice Guidelines for the Diagnosis and Treatment of Acute-on-Chronic Liver Failure (ACLF) in Vietnam" (2026 Updated Version), as developed by the Vietnam Association for the Study of Liver Diseases (VASLD), VSHBPS, and VASLD-MIT.

Article 2. The aforementioned Guidelines shall serve as a foundational clinical reference and shall be implemented across all relevant medical and healthcare facilities.

Article 3. This Decision shall take effect immediately upon the date of its signing and official promulgation./.

President of VASLD,
Founding President of VSHBPS
& President of VASLD-MIT

HỘI GAN MẬT TRUNG ƯƠNG HỘI

Major General, Professor Le Trung Hai MD, PhD

CLINICAL PRACTICE GUIDELINES FOR LIVER TRANSPLANTATION IN VIETNAM

(2026 Updated Version: Including 52 Clinical Recommendations)

A. Indications, Recipient and Living Donor Selection, and Timing of Liver Transplantation (with 9 recommendations):

** **Clinical Question 1:** What are the indications for liver transplantation?*

*** Recommendation 1:** Liver transplantation is frequently indicated for patients with hepatocellular carcinoma (HCC), decompensated cirrhosis (typically with a MELD score ≥15) resulting from chronic liver injury (e.g., alcohol-related liver disease, chronic hepatitis B, chronic hepatitis C, autoimmune hepatitis), and acute liver failure, particularly Acute-on-Chronic Liver Failure (ACLF). Additionally, transplantation is indicated for biliary cirrhosis (including Primary Biliary Cholangitis and Primary Sclerosing Cholangitis) and other hepatobiliary conditions such as biliary atresia, Wilson's disease, Neonatal Intrahepatic Cholestasis caused by Citrin Deficiency (NICCD), Budd-Chiari syndrome, Caroli's disease, and perihilar cholangiocarcinoma (following neoadjuvant therapy).

** **Clinical Question 2:** What is the role of liver transplantation in the management of HCC?*

*** Recommendation 2:** Liver transplantation is considered the gold-standard treatment for HCC and is the most common indication globally. It significantly improves survival rates (>80% at 5 years) and reduces the risk of recurrence compared to liver resection. Even for patients with Child-Pugh A function, transplant outcomes

are comparable to or superior to resection. For HCC patients with underlying cirrhosis, transplantation is the treatment of choice as it is the only modality that simultaneously treats both the malignancy and the underlying cirrhotic liver.

**** Clinical Question 3:*** *What are the selection criteria for patients with HCC and Perihilar Cholangiocarcinoma (PHC) undergoing liver transplantation?*

*** Recommendation 3:**

- For hepatocellular carcinoma (HCC): Established criteria include the Milan Criteria (single nodule ≤5 cm or up to 3 nodules, each ≤3 cm), the Up-to-7 Criteria (sum of the number of tumors and the diameter of the largest tumor ≤7), the Kyoto Criteria (≤10 nodules, largest ≤5 cm, and DCP ≤400 mAU/mL), and the Japanese 5-5-500 rule (largest nodule ≤5 cm, ≤5 nodules, and AFP ≤500 ng/mL).

Proposed Vietnam criteria: HCC localized to the liver, without extrahepatic metastasis (e.g., to the peritoneum, lungs, or bone) and without macrovascular invasion of the main portal vein, hepatic veins, or vena cava. Patients within the Milan Criteria are preferred; however, those exceeding these criteria may be considered if there is no extrahepatic spread, regardless of tumor number or size. Consideration is also given to patients ineligible for radical resection (Child-Pugh B or C or diffuse bilobar disease), provided that AFP <500 ng/mL or DCP ≤500 mAU/mL and a partial response to locoregional therapy is observed. A negative PET scan is preferred. The expected minimum 5-year survival rate should exceed 50%.

General Strategy**:** Integrating biomarkers into selection criteria helps mitigate the risk of post-transplant recurrence. Furthermore, downstaging protocols should be considered for patients who initially do not meet these criteria, including the use of immune checkpoint inhibitors or downstaging for limited portal vein infiltration, provided that extrahepatic metastasis is absent.

- For Perihilar cholangiocarcinoma (PHC): Apply the Mayo Clinic criteria, indicated when malignant stricture is present along with at least one of the following: histopathological confirmation of malignancy; a tumor mass <3 cm in diameter; absence of extrahepatic metastasis; a positive FISH (fluorescence in situ hybridization) test for polysomy; or CA 19-9 > 130 U/mL in the absence of acute cholangitis. Additionally, the tumor must be visible on diagnostic imaging and deemed unresectable. The patient must be a suitable transplant candidate (ECOG performance status < 3), aged under 70, and have completed a neoadjuvant chemoradiation protocol.

**** Clinical Question 4:*** *What are the selection criteria for liver transplantation in patients with acute liver failure, acute-on-chronic liver failure (ACLF), and cirrhosis?*

*** Recommendation 4:**

- Fulminant Hepatic Failure: Indicated for patients with Grade II–IV hepatic encephalopathy, a MELD score between 20–40 points, and an INR > 1.5.

- Acute-on-Chronic Liver Failure (ACLF): Characterized by jaundice, coagulopathy persisting for 4 weeks, ascites, and hepatic encephalopathy. Liver transplantation for patients with Grade 1 and Grade 2 ACLF typically yields excellent post-transplant outcomes; however, Grade 3 ACLF requires rigorous evaluation and careful consideration (see Recommendation 8).

- Decompensated cirrhosis: Indicated for patients with a MELD score ≥15. Patients with a MELD score <15 may be considered if they present with complications such as refractory ascites, hepatorenal syndrome, spontaneous bacterial peritonitis (primary peritonitis), hepatic encephalopathy, variceal bleeding due to portal hypertension, or the requirement for a TIPS (transjugular

intrahepatic portosystemic shunt). Cirrhosis Staging: Utilizing the Child-Pugh score (evaluating Bilirubin, Albumin, INR, ascites, and hepatic encephalopathy): Child-Pugh B (7-9 points): Requires specialist transplant consultation. Child-Pugh C (10–15 points): Liver transplantation is indicated.

- ***Primary biliary cholangitis (PBC):*** Indications include Bilirubin > 8 mg/dL, Child-Pugh score > 7, intractable pruritus (severe itching), recurrent cholangitis, or hepatic encephalopathy.

**** Clinical Question 5:*** *What are the considerations and procedures for selecting living liver donors?*

*** Recommendation 5:**

- The ideal age for living liver donors is between 18 and 35 years.

- Most living liver donors should have ABO and Rhesus (Rh) blood group compatibility with the recipient.

- HLA (Human Leukocyte Antigen) compatibility is preferred; hepatic steatosis (fatty degeneration) of the graft should be ≤30%.

- Criteria for the liver volume of selected living liver donors include:

$$\frac{\text{Donor liver volume (ml)}}{\text{Recipient body weight (kg)} \times 10} \geq 0{,}8$$

The selection process must ensure the safety of both the donor and the recipient. Regarding donor safety, the following must be considered: liver donation should not be undertaken if the future liver remnant (FLR) is insufficient, the quality of the liver parenchyma is poor, or the donor is of advanced age. Additional contraindications include the presence of fatty liver disease, cirrhosis, or chronic hepatitis. Donors with metabolic conditions such as morbid obesity, cardiovascular disease, hypertension, malignancies, neurological or psychiatric disorders, or complex socioeconomic factors should be excluded.

The primary stages of the liver donor selection process include:

- Donor Age: Selecting donors typically aged 18-60 years (though some centers extend this to 15-65).

- Initial assessment: Comprehensive liver function tests (LFTs), biochemical and hematological screening, serology, chest X-ray, ECG, and CT volumetry. This stage is designed to exclude candidates with insufficient liver volume or significant comorbid diseases.

- Second-step assessment: Liver MRI (including MR spectroscopy for fat quantification and elastography), HLA typing, cross-matching, Digital Subtraction Angiography (DSA) or CT angiography, coagulation profiles, screening for occult infection or malignancy, echocardiography, pulmonary function tests, and psychological and legal evaluations. This concludes with a multidisciplinary transplant board consultation.

**** Clinical Question 6:*** *What are the criteria for selecting an ideal living liver donor, and what exclusion criteria should be considered when choosing a liver donor?*

*** Recommendation 6:** An ideal living liver donor is typically ≤35 years old, has ABO blood group compatibility, a Graft-to-Recipient Weight Ratio (GRWR) ≥ 0.8, is a candidate for right-lobe donation, and has a hepatic steatosis (fat) percentage < 5%. Generally, a favorable donor is defined by a Remnant Liver Volume (RLV) ≥35%, GRWR > 0.8, absence of fatty liver or cirrhosis, normal vascular/biliary anatomy, excellent physical and mental health, negative DSA (Donor-Specific Antibody) results, negative cross-matching, and non-homozygous HLA status.

Exclusion criteria to consider include: RLV < 30%, especially when combined with hepatic steatosis or advanced age; GRWR < 0.6, hepatic steatosis greater than 15-30%, cirrhosis or significant fibrosis

≥ F2, uncontrolled metabolic disorders or cardiovascular disease, risk of infectious diseases, malignancies or diseases transmissible to the recipient, acute psychiatric problems, active substance abuse, or HLA-homozygous status.

***** ***Clinical Question 7:*** *What are the considerations for selecting a living liver donor in liver transplantation for patients with HCC?*

*** Recommendation 7:** In liver transplantation for HCC, since a small graft relative to the recipient's needs may increase the risk of recurrence, the donor evaluation phase should prioritize selecting a donor with a relatively large graft volume whenever possible. This strategy aims to optimize post-transplant survival and minimize the risk of recurrence in HCC patients.

***** ***Clinical Question 8:*** *What is the optimal timing for liver transplantation in patients with HCC and ACLF?*

*** Recommendation 8:**

- For hepatocellular carcinoma (HCC): Transplantation should be performed promptly for patients meeting the criteria outlined in Recommendation 3. For patients initially exceeding these criteria, locoregional therapies such as TACE, RFA, MWA, PEI, SIRT, SBRT, or liver resection should be employed to downstage the disease or prevent progression. Generally, HCC patients should receive locoregional treatment while on the waiting list, with a target observation period of 6–9 months to assess tumor biology. If a living donor (LDLT) is available, transplantation should ideally be performed after 3 months of stability; for deceased donor (DDLT) transplantation, it should be performed as soon as a suitable organ is available.

- For acute-on-chronic liver failure (ACLF): Liver transplantation is the most effective intervention, with the "golden window" for surgery being 4–7 days from onset. Outcomes for Grade 1 and Grade 2 ACLF patients are excellent, with both 1-year and 3-year post-transplant survival rates exceeding 90%.

**** Clinical Question 9:*** *What are the clinical considerations and general outcomes for liver transplantation in patients with Grade 3 ACLF?*

*** Recommendation 9:**

Grade 3 Acute-on-Chronic Liver Failure (ACLF) is the most severe form, often requiring liver transplantation as a life-saving intervention. Grade 3 ACLF is characterized by multi-organ failure involving the liver, kidneys, brain (neurological), coagulation, circulatory, and respiratory systems, and carries a mortality rate as high as 80% without transplantation. Patients require robust hemodynamic resuscitation and a meticulous assessment of transplant feasibility, including the evaluation of general clinical status, the degree of hepatic dysfunction, and associated complications alongside MELD and CLIF-C ACLF scores. A multidisciplinary approach involving hepatologists, transplant surgeons, intensivists, and other specialists is essential. Grade 3 ACLF patients require continuous reassessment and emergency readiness. Bridging therapies, such as extracorporeal liver support systems, may be used to maintain stability while awaiting a donor. Careful donor selection prioritizing younger age, minimal hepatic steatosis (fatty liver), and short cold ischemia time is vital to ensure optimal graft function. Surgically, the use of veno-venous bypass or the piggyback technique can help minimize hemodynamic instability. Post-transplant monitoring must track liver function tests, coagulation profiles, and bile production, while preventing surgical complications, portal hypertension, and ascites.

Comprehensive care includes tailored immunosuppressive therapy, renal replacement therapy, respiratory support, and cardiovascular stabilization, alongside the prevention of severe and opportunistic infections.

Overall survival following living donor liver transplantation (LDLT) for Grade 3 ACLF is lower than for Grade 1 and 2, yet outcomes remain clinically acceptable. In the absence of a compatible donor, ABO-incompatible (ABOi) LDLT should be considered for Grade 3 patients. In general, optimizing the indications and timing for transplantation in ACLF significantly improves clinical outcomes.

B. Management of Hepatitis B Liver Transplant Recipients, Nutritional Support, and Immunosuppressive Therapy (with 8 recommendations):

**** Clinical Question 10:*** *What are the treatment considerations for liver transplantation in patients with hepatitis B?*

*** Recommendation 10:**

The prevalence of viral hepatitis among liver transplant recipients in Vietnam is approximately 73-86%. Antiviral treatment is mandatory for patients awaiting transplantation. Controlling and preventing the recurrence of hepatitis B post-transplant using antiviral drugs and Hepatitis B Immunoglobulin (HBIG) is essential to enhance passive immunity. The management of acute rejection in hepatitis B patients requires the use of Methylprednisolone at a lower dose compared to patients without hepatitis B. Pediatric transplant recipients should be vaccinated to prevent de novo hepatitis B infection post-transplantation.

**** Clinical Question 11:*** *Which medications are used to treat hepatitis B after liver transplantation?*

*** Recommendation 11:** Priority is given to potent antiviral agents such as Entecavir (ETV) or Tenofovir (TDF/TAF) for lifelong maintenance therapy.

HBIG (Hepatitis B Immune Globulin) Protocol:

- Intraoperative: Administer HBIG during the anhepatic phase or at reperfusion: 10,000 IU if HBV DNA is negative and 20,000 IU if HBV DNA is positive.

- Postoperative: 2,000 IU/day for the first 7 days; 2,000 IU/week for the first month; and 2,000 IU/month for the first year.

Target anti-HBs levels: > 500 IU/L (weeks 0–2); > 250 IU/L (weeks 2–12); and > 100 IU/L (after week 12).

In general, Entecavir or Tenofovir are highly effective. HBIG may be omitted in patients with undetectable HBV DNA at the time of transplantation. Short-term combination therapy with HBIG (approximately one year) should be considered for high-risk patients.

** **Clinical Question 12:** What is the role of albumin in liver transplantation treatment?*

*** Recommendation 12:** Albumin plays a crucial role in both the pre-operative and post-operative phases. Combining albumin with targeted treatments for cirrhosis complications improves clinical outcomes. Maintaining serum albumin levels > 30 g/L helps minimize hemodynamic instability and prevents specific post-transplant complications in recipients.

** **Clinical Question 13:** What are the principles of immunosuppressive therapy in liver transplantation?*

*** Recommendation 13:** The liver is considered an immunologically privileged organ; consequently, acute rejection rates are relatively

low, even in cases of HLA incompatibility. Immunosuppressive agents are essential to reduce rejection rates, increase graft survival, and prolong patient life.

Standard Regimen: Induction therapy + Calcineurin Inhibitors (CNIs) + MMF/mTOR inhibitors.

Maintenance Therapy: Typically, a triple-drug regimen of Tacrolimus + Mycophenolate Mofetil (MMF) + Corticosteroids. Tacrolimus is a cornerstone of this therapy.

Treatment of acute rejection: Typically involves high-dose corticosteroids, potentially combined with Anti-thymocyte Globulin (ATG), Rituximab, or IVIG. Pulse Steroid Protocol: Methylprednisolone 1,000 mg/day IV for days 1-3, followed by a taper (500 - 200 - 160 - 120 - 80 - 40 - 20 mg/day).

** **Clinical Question 14:** How can outcomes be improved regarding HCC recurrence after liver transplantation, and how do immunosuppressive drugs affect this?*

*** Recommendation 14:** Controlling HCC recurrence through locoregional treatments is crucial to improving outcomes; the careful selection of immunosuppressive agents further enhances these results.

Risk Factors for HCC Recurrence: Advanced recipient age, high intra-patient variability (IPV) of Tacrolimus (especially trough levels >10 ng/mL), elevated AFP levels, macro- or microvascular invasion, multifocal tumors, and large tumor size. It is critical to minimize Tacrolimus level variability (IPV) to reduce the risk of HCC recurrence post-transplantation.

** **Clinical Question 15:** What are the considerations for improving outcomes and managing risk factors for HCC recurrence after liver transplantation, and how can immunosuppressive therapy be used to prevent recurrence?*

*** Recommendation 15:** Systemic and immunotherapy treatment after liver transplantation for HCC:

- Use of tyrosine kinase inhibitors (TKIs), such as Sorafenib, Lenvatinib, Regorafenib, etc.

- There are four primary modalities of immunotherapy for HCC:

+ Antibody Therapy: Represented by immune checkpoint inhibitors (ICIs).

+ Cell-Based Therapy: Such as Cytokine-Induced Killer (CIK) cells, Tumor-Infiltrating Lymphocytes (TILs), or CAR-T cell therapy.

+ Cancer Vaccine Therapy.

+ Cytokine Therapy: To enhance the host immune response against the tumor.

**** Clinical Question 16:*** *What are the key strategies for the prevention and management of recurrent hepatocellular carcinoma (HCC) after liver transplantation?*

*** Recommendation 16:** Recurrence of HCC following liver transplantation is a significant clinical concern. Risk factors include tumor stage, macro- or microvascular invasion, preoperative serum AFP levels, and specific immunosuppressive therapy regimens. Strategies to reduce recurrence include the early withdrawal of corticosteroids (steroid-free regimens) or the dose reduction of calcineurin inhibitors (CNIs) in the early postoperative period. Immunosuppressive therapy using mTOR inhibitors (such as Rapamycin/Sirolimus or Everolimus) helps reduce recurrence rates and improve overall survival. A multimodal approach to managing recurrent HCC should be adopted, including adjusting immunosuppressive therapy; surgical resection of recurrent nodules; locoregional therapies (TACE, microwave ablation, radiofrequency ablation); and systemic therapies to extend patient survival.

***Clinical Question 17:** What is the clinical value of early nutritional intervention after liver transplantation?*

*** Recommendation 17:** Liver transplant recipients are at a very high risk of malnutrition. Factors such as anorexia (loss of appetite), unintentional weight loss, and sarcopenia (muscle wasting) within the first month post-surgery are associated with increased metabolic risks. Early nutritional intervention should be implemented to mitigate these risk factors, thereby reducing the risk of glycemic disorders (hyperglycemia) and improving the overall quality of life for liver transplant patients.

C. Anesthesia, Surgical Techniques, Post-Transplant Resuscitation, and Management of Complications (with 13 recommendations):

***Clinical Question 18:** What are the considerations for anesthesia during liver transplantation?*

*** Recommendation 18:** Safe anesthesia during liver transplantation requires meticulous preoperative assessment, comprehensive contingency planning, adequate procurement of blood and blood products, and seamless multidisciplinary coordination. Essential monitoring includes central venous access (for CVP monitoring and fluid administration), at least one large-bore peripheral venous line, and a radial artery line (typically the left) for continuous invasive arterial pressure monitoring. Strategies to maintain normothermia, such as warm infusion fluids and anesthetic gases, must be employed. Exceptional coordination is required during the anhepatic phase and the reperfusion phase to manage hemodynamic shifts.

***Clinical Question 19:** What are the procedures for donor hepatectomy (liver harvesting), flushing, and preservation of the graft?*

*** Recommendation 19:** For adult living donor liver transplantation (LDLT), the donor hepatectomy procedure primarily involves a right hepatectomy. Key steps include intraoperative cholangiography, dissection of the hepatic pedicle and hepatic veins, and parenchymal transection (typically utilizing a CUSA and bipolar cautery).

Graft Flushing and Preservation: The graft is flushed (via the portal vein using a gravitational pressure head of 1.5m, with additional irrigation of the hepatic artery and biliary tree) using 2000 ml of cold HTK solution (Custodiol). The graft is preserved in cold Custodiol or Ringer's Lactate solution at 4°C. Necessary vascular or biliary reconstructions (back-table procedures) are performed during this stage.

**** Clinical Question 20:*** *What are the key technical considerations when performing a right-lobe donor hepatectomy?*

*** Recommendation 20:** During a right-lobe donor hepatectomy, the following technical details are critical:

A right J-shaped incision is made, preserving half of the round ligament on the hilar side (to suspend the remaining left lobe and prevent torsion of the left hepatic vein). A biopsy of the right lobe (typically segments 5–6) is performed to assess the degree of hepatic steatosis. The liver is mobilized, and short hepatic veins draining into the inferior vena cava (IVC) are ligated. The right lobe is suspended using a "liver hanging" tape (or a 12 Fr catheter) passed behind the retro-hepatic IVC (the "hanging maneuver"). Cholecystectomy is performed, and a cystic duct catheter is inserted for intraoperative cholangiography. The hepatic pedicle is dissected.

Parenchymal Transection: Prior to transection, the right portal vein and right hepatic artery are temporarily clamped to identify and mark the ischemic demarcation line. Vascular and biliary branches within the parenchyma are controlled using clips, Hem-o-loks,

or sutures. The middle hepatic vein (MHV) may be harvested with the graft or left with the donor depending on the calculated remnant liver volume (RLV). Segment 1 (caudate process) is resected above the IVC. Intermittent inflow occlusion (Pringle maneuver) may be applied for 15–20 minutes if necessary. Intraoperative C-arm cholangiography is used to identify the precise site for the right hepatic duct division.

Vascular Division: The right hepatic duct, right hepatic artery, and right portal vein are divided. Venous tributaries from segments 5 and 8 to the MHV, and any accessory right hepatic veins, are managed. Finally, the right hepatic vein is resected with a partial clamp applied to the IVC.

** **Clinical Question 21:** What are the primary considerations when performing a recipient hepatectomy?*

*** Recommendation 21:** During the recipient hepatectomy (total hepatectomy), it is critical to meticulously dissect the hepatic hilum to prevent injury to the hepatic artery branches and preserve the peribiliary vascular plexus, which ensures the blood supply to the biliary anastomoses. The bile ducts and hepatic arteries should be clamped and divided close to the liver hilum. The middle and left hepatic veins should be adequately exposed and clamped. The right hepatic vein must be isolated and controlled using a vessel loop or tourniquet.

** **Clinical Question 22:** What are the oncological considerations during recipient hepatectomy for HCC patients?*

*** Recommendation 22:** When performing hepatectomy in patients with HCC, excessive liver manipulation and torsion can cause congestion and ischemia, which may increase the risk of

hematogenous tumor spread and HCC recurrence. Therefore, a "no-touch" or minimally invasive manipulation technique should be prioritized, especially in advanced HCC cases. Particular attention must be paid to avoiding congestion of the middle hepatic vein (MHV) territory; graft congestion and subsequent inflammation can facilitate an environment prone to recurrence. During the recipient hepatectomy, the risk of cancer cell dissemination must be minimized by clamping the hepatic inflow and outflow prior to extensive mobilization of the diseased liver.

*** *Clinical Question 23:* *What are the key technical aspects of liver implantation in recipients using a living donor graft?*

*** Recommendation 23:** In living donor liver transplantation (LDLT), a comprehensive preoperative assessment is mandatory, with specific focus on the presence of portal vein thrombosis. Venous reconstruction using a right-lobe graft is the standard approach, with a strong emphasis on reconstructing the middle hepatic vein (MHV) tributaries (Segments 5 and 8) to prevent graft congestion, hematoma, or outflow obstruction. Hepatic artery anastomosis should be performed using surgical loupes for magnification or microsurgical techniques (mandatory in pediatric cases). Precision in hepatic artery reconstruction is vital for maintaining graft viability and improving long-term survival. For biliary reconstruction, either a duct-to-duct (end-to-end) anastomosis or a Roux-en-Y hepaticojejunostomy should be utilized. The use of an external biliary stent (drainage) is recommended to reduce the incidence of biliary leakage and anastomotic strictures in adult LDLT.

*** *Clinical Question 24:* *What are the key considerations for postoperative resuscitation and management following liver transplantation?*

*** Recommendation 24:**

Following liver transplantation, comprehensive monitoring and intensive care are mandatory, with specific focus on the following areas:

- Respiratory and Hemodynamic Management:

+ Respiratory Care: perform extubation when the patient is conscious, has adequate muscle strength, and meets the following criteria: respiratory rate <30/min, Vt > 5ml/kg, PaO2 >70mmHg, FiO2 <40%, and minute ventilation <10 liters/min. Early extubation reduces the risk of ventilator-associated pneumonia (VAP), improves splanchnic and hepatic perfusion, and shortens the ICU length of stay.

+ Hemodynamic Monitoring: Continuous monitoring via ECG and invasive arterial blood pressure is required. Cardiac output should be assessed using a pulmonary artery catheter, pulse contour analysis (e.g., PiCCO), or transthoracic/transesophageal echocardiography.

- Assessment of Graft Function: *Evaluated through clinical, biochemical, and radiological parameters.*

+ Clinical indicators: Favorable graft function is suggested by stable body temperature, adequate urine output, improving neurological status/consciousness, stable respiration, and a transition of abdominal drainage from serosanguinous to serous/ascitic fluid.

+ Biochemical tests: Monitor transaminases (AST/ALT), which typically peak within the first 48 hours and gradually decline. In cases of small-for-size grafts, significant steatosis, or prolonged cold ischemia time, these enzymes may peak higher but should still trend downward rapidly. Additional critical markers include Prothrombin Time (PT/INR), direct/indirect bilirubin, blood glucose, and serum lactate.

+ Imaging studies: Regular Doppler ultrasound is essential to verify the patency and flow velocities of the hepatic artery, portal vein, and hepatic veins.

- Additional Management Priorities:

+ Renal support: Maintain optimal cardiac output to ensure renal perfusion. Utilize diuretics judiciously, avoid nephrotoxic agents, monitor the levels of immunosuppressive drugs (calcineurin inhibitors), and initiate renal replacement therapy (hemodialysis/ CRRT) when indicated. Closely monitor electrolytes, glucose, hematology, and coagulation profiles.

+ Analgesia and Sedation: Implement multimodal analgesia, typically combining regional catheter-based techniques with intravenous agents (e.g., Fentanyl and Nefopam).

+ Infection Control: Infection remains the most common complication and a leading cause of mortality. Administer prophylactic antibiotics for 5–7 days post-surgery (typically 3rd or 4th generation cephalosporins or broad-spectrum agents). Provide prophylaxis against Cytomegalovirus (CMV), especially during months 1–4 post-transplant. Screen and treat for multidrug-resistant (MDR) organisms in high-risk groups (utilizing Carbapenems or Vancomycin). Provide antifungal prophylaxis (e.g., Fluconazole 400 mg/day for 2–4 weeks for invasive Candida risk). Ensure protocols are in place to prevent HBV/HCV recurrence and manage EBV, VZV, HSV, and latent tuberculosis.

+ Wound and Drain Care: Monitor surgical site integrity. Abdominal drains are typically removed by postoperative day 3 if output is appropriate.

+ Mobilization: Encourage early mobilization (sitting up and progressing to active/passive exercises) to facilitate the return of gastrointestinal motility and reduce drainage volume.

+ Nutritional Support: Maintain NPO (fasting) status with total parenteral nutrition (TPN) on postoperative day 1. Transition to a clear liquid diet and then solid foods in subsequent days; most patients should return to a normal diet by postoperative day 5.

**** Clinical Question 25:*** *What are the general complications encountered after liver transplantation?*

*** Recommendation 25:** The complication rate after liver transplantation typically ranges from 10% to 20%. Critical complications include hepatic artery thrombosis/occlusion (which causes acute graft failure and is primarily diagnosed via Doppler ultrasound, CT angiography, or MRI). Other vascular complications include hepatic vein and inferior vena cava (IVC) stenosis. Common biliary complications include bile leakage (typically occurring early) and biliary stricture (typically occurring later), which can lead to severe sepsis. These are often managed via endoscopic retrograde cholangiopancreatography (ERCP) with high success rates up to 96% most commonly through ductal dilation and stenting. Diagnostic imaging and interventional radiology play a crucial role in the early diagnosis and management of these complications, helping to minimize mortality and the need for re-transplantation.

**** Clinical Question 26:*** *Which specific surgical complications require attention after liver transplantation?*

*** Recommendation 26:** Surgical complications requiring focused monitoring include:

- Postoperative Hemorrhage: Monitor for tachycardia (rapid pulse), hypotension (decreased blood pressure), reduced central venous pressure (CVP), decreased oxygen saturation, abdominal distension, and hematoma visible on ultrasound. Management requires blood product transfusion or reoperation if hemodynamics remain unstable.

- Hepatic Artery Thrombosis (HAT): Manifests as acute graft failure, a rapid rise in AST (GOT) and ALT (GPT) levels, and decreased bile production or “white bile” (clear/mucoid bile).

Diagnosis is confirmed by Doppler ultrasound, angiography, or MRI. Treatment options include urgent thrombectomy, stenting, surgical revision of the anastomosis, or re-transplantation if the graft is necrotic.

- Portal vein thrombosis (PVT): Characterized by hepatic dysfunction, portal hypertension, variceal hemorrhage, and a rapid increase in ascites. Diagnosis is based on Doppler ultrasound, CT scan, or angiography. Treatment involves thrombectomy, bypass procedures, or re-transplantation. Late-onset PVT may be managed with anticoagulants or portosystemic shunts.

- Biliary Fistula: Characterized by worsening right upper quadrant pain, signs of infection/peritonitis, and bile-stained abdominal drainage. CT and MRCP (MRI of the biliary tract) are used to assess the extent. Treatment includes antibiotics, analgesics, ultrasound-guided percutaneous drainage, and ERCP with stent placement. Reoperation is required if conservative measures fail.

**** Clinical Question 27:*** *How is acute rejection diagnosed and treated after liver transplantation?*

*** Recommendation 27:**

The gold standard for diagnosing acute cellular rejection (ACR) is a liver biopsy analyzed according to the Banff classification (1997/ current update). Suggestive clinical signs include fever, jaundice, malaise, abdominal pain, and laboratory elevations in liver enzymes, bilirubin, ALP, white blood cell count, and C-reactive protein (CRP).

- ***Treatment of moderate to severe acute rejection***: Utilize high-dose corticosteroid pulse therapy. For adults (>40 kg), the regimen is:

+ Methylprednisolone: 500 mg IV daily for 3 days.

+ Reduce the dose in increments of 250, 125, 75, 60mg/day → 20mg x 2 times/day for 7 days → to the maintenance dose (20mg prednisolone/day). For patients with hepatitis B or C, reduce the lower dose accordingly: 100 - 80 - 60 - 40 - 20 - 15 - 12.5 - 10mg/day.

In cases of moderate acute cellular rejection, a lower-dose corticosteroid regimen may be utilized: 500 – 250 – 125 – 75 – 60 mg/day. In cases of steroid-resistant rejection (accounting for approximately 10–15% of acute rejection episodes), Anti-Thymocyte Globulin (ATG) is indicated.

***** ***Clinical Question 28:*** *What are the complications of CMV (Cytomegalovirus) infection after liver transplantation?*

***** **Recommendation 28:** The incidence of CMV infection following liver transplantation is over 5%, manifesting with symptoms such as fever, malaise, leukopenia, neutropenia, atypical lymphocytosis, and thrombocytopenia. When the virus invades specific tissues and organs, it progresses to CMV disease. This represents the most common opportunistic infection in liver transplant recipients and significantly increases the risk of post-transplant complications and mortality. It is important to note that a prolonged stay in the Intensive Care Unit (ICU) correlates with a higher risk of CMV infection. Therefore, early diagnosis (using CMV IgG and CMV-DNA PCR tests with a threshold of >100 copies/mL) and aggressive treatment following established protocols (typically Ganciclovir 10 mg/kg/day or Valganciclovir 900 mg twice daily) for a duration of up to 6 months are necessary.

***** ***Clinical Question 29:*** *What is the clinical importance of Enhanced Recovery After Surgery (ERAS), and what are the key considerations for its implementation?*

*** Recommendation 29:** Enhanced Recovery After Surgery (ERAS) plays a crucial role in supporting the rapid recovery of liver transplant recipients by reducing complications, mortality, and hospital length of stay, while simultaneously improving treatment efficacy and lowering healthcare costs.

Implementation Considerations:

Preoperative: Provide pre-transplant counseling, prehabilitation, and optimized nutritional support. Intraoperative: Utilize short-acting anesthetic and analgesic agents during the transplant procedure. Postoperative: Prioritize early extubation (removal of the endotracheal tube), early nasogastric tube removal, and early mobilization (within 24 hours post-surgery). Device Management: Aim for the removal of invasive catheters, including urinary catheters (by postoperative day 3) and abdominal drains (by postoperative day 5). Nutrition: Initiate early enteral feeding within 12–24 hours post-surgery. Monitoring: Maintain vigilant prevention and screening for infection, graft rejection, acute kidney injury, and hepatic artery thrombosis.

*** *Clinical Question 30*:** *What are the recommended post-transplant monitoring protocols for HCC?*

*** Recommendation 30:** During the first three years following liver transplantation for HCC, surveillance should be conducted using AFP, AFP-L3, and DCP (PIVKA-II) biomarkers every three months. Contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen and pelvis should be performed every six months; however, more frequent imaging is required if AFP levels are elevated. Additional CT or MRI of the chest and bone scintigraphy should be considered to rule out extrahepatic spread. PET-CT is recommended for comprehensive metastatic screening. If no metastasis is detected despite rising

markers, the follow-up interval should be shortened to every two months. Diligent postoperative monitoring for HCC recurrence is essential. If recurrence is detected, liquid biopsy may provide molecular insights to guide targeted treatment strategies.

*** *Clinical Question 31:* *What are the key considerations for optimal post-transplant screening for HCC?*

*** Recommendation 31:** The primary focus of these considerations is the correlation between preoperative AFP and PIVKA-II levels and the kinetics of tumor marker normalization post-transplant. A rapid return of tumor markers to baseline levels (within 4–6 weeks) correlates with a lower risk of recurrence and a more favorable overall survival prognosis; conversely, delayed normalization significantly increases the risk of recurrence. For high-risk groups, periodic surveillance every 2–3 months is recommended. Low-risk groups may be safely monitored with imaging every 6 months, provided tumor markers remain stable. Emerging technologies such as liquid biopsy including the analysis of circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and microRNA show potential for the earlier and more precise detection of minimal residual disease (MRD), ultimately improving prognosis and clinical outcomes for liver transplant recipients with HCC.

D. Postoperative complications in liver donors and long-term outcomes (with 3 recommendations):

*** *Clinical Question 32:* *What postoperative complications should be monitored in liver donors?*

Recommendation 32: The perioperative mortality rate for living liver donors globally is approximately 0.01%. The primary cause of death is sepsis, followed by massive intraoperative hemorrhage.

It is critical to remain vigilant for severe complications, particularly hemorrhage resulting from technical failures such as vascular clamp slippage, loosened ligatures, or mechanical stapler failure. The most frequent postoperative issues are surgical site complications (e.g., wound infections or seromas). Additionally, biliary complications occur in approximately 2% of cases, predominantly categorized as Clavien-Dindo Grade III, which require management via endoscopy or interventional radiology, typically with favorable outcomes. In certain instances, percutaneous biliary drainage may be necessary. Vascular complications in the donor are rare and are generally managed through endovascular intervention.

**** Clinical Question 33:*** *What are the long-term outcomes for liver donors?*

*** Recommendation 33:** Long-term postoperative discomfort following living liver donation is primarily related to surgical site issues, gastrointestinal disturbances, fatigue, and chronic pain. To date, there have been no reported donor mortalities in Vietnam. The overall complication rate for donor hepatectomy from living donors is below 9%, with biliary complications being the most frequent, occurring in less than 6% of cases.

Recently, the wide adoption of laparoscopic donor hepatectomy has offered significant advantages, including improved postoperative comfort, enhanced recovery profiles, and a faster return to baseline activities and normal life. Specifically, the laparoscopic approach is associated with fewer wound-related complications, reduced gastrointestinal distress and fatigue, and improved cosmetic outcomes.

**** Clinical Question 34:*** *What are the considerations regarding liver volume regeneration in living donors following donor hepatectomy?*

*** Recommendation 34:** Following a right hepatectomy in a living donor, the future liver remnant (FLR) demonstrates significant regenerative capacity. Specifically, the longitudinal recovery of liver volume is as follows: 7 days post-surgery: The volume of the left lobe increases by nearly 66%, reaching approximately 63% of the donor's original total liver volume. 1-month post-surgery: These figures reach approximately 93% (left lobe expansion) and 73% (of initial total volume). 3 months post-surgery: Approximately 94% and 76%, respectively. 6 months post-surgery: Approximately 129% and 86%, respectively. 12 months post-surgery: Approximately 136% and 89%, respectively. The average length of hospital stay following donor hepatectomy is approximately 11 days.

E. Application of laparoscopic surgery and ICG fluorescence in donor hepatectomy (with 7 recommendations):

*** *Clinical Question 35:*** *What are the fundamental steps in implementing laparoscopic donor hepatectomy for living donor liver transplantation?*

*** Recommendation 35:** The essential steps for performing laparoscopic donor hepatectomy in living donor liver transplantation include: Establishing a surgical team with advanced laparoscopic skills, specifically within the field of hepatobiliary surgery.

Meticulously selecting appropriate cases during the early stages of program implementation to ensure safety and technical success. Utilizing advanced equipment and high-tech surgical platforms to provide optimal intraoperative support. Implementing precise hilar (pedicle) control and specialized parenchymal transection techniques tailored to each individual case.

Laparoscopic donor hepatectomy for living donor liver transplantation is not only a sophisticated new technique but also serves as a testament to the advanced development and specialization of hepatobiliary and pancreatic (HPB) surgery in Vietnam.

*** ***Clinical Question 36:*** *What are the clinical advantages of utilizing laparoscopic surgery for donor hepatectomy (liver harvesting) in living donors?*

*** Recommendation 36:** The implementation of laparoscopic donor hepatectomy is an inevitable global trend. It offers a minimally invasive approach characterized by smaller incisions, superior cosmetic outcomes, a reduced incidence of incisional hernia, and decreased intraoperative blood loss. Furthermore, patients experience a faster return of gastrointestinal motility and a significantly shorter hospital stay, with discharge often occurring within 4–5 days post-surgery, alongside improved postoperative immune function. Recipients and their families should be thoroughly counseled regarding the benefits and risks of this technique during the preoperative phase.

Laparoscopic donor hepatectomy yields clinical outcomes comparable to those of traditional open surgery. However, intraoperative blood loss and the duration of hospitalization are significantly lower in the laparoscopic cohort. The postoperative complication rate for laparoscopic donor hepatectomy is less than 10%. It should be noted that operative time is typically longer in the laparoscopic group, averaging approximately 180 minutes.

*** ***Clinical Question 37:*** *What are the selection criteria, primary surgical techniques, and general outcomes for laparoscopic donor hepatectomy in living donor transplantation?*

*** Recommendation 37:** Initial donor selection criteria focused on simple anatomical cases, without vascular or biliary abnormalities, with a reasonable liver graft volume (700–800g), and a preference for preserving the middle hepatic vein for the donor. Once stabilized, these criteria could be expanded to include cases with anatomical abnormalities, larger graft volumes, and emergency liver transplantation. The main techniques involved accessing the Glissonean pedicle within the liver, performing parenchymal resection using an ultrasonic scalpel and CUSA, utilizing ICG fluorescein imaging, and not placing postoperative abdominal drainage. The results demonstrate high safety profiles with zero donor mortality, low complication rates, and rapid postoperative recovery times.

**** Clinical Question 38:*** *What are the fundamental technical steps for laparoscopic right-lobe donor hepatectomy?*

*** Recommendation 38:** Step 1: Trocar insertion, comprehensive abdominal exploration, and liver biopsy to assess steatosis. Step 2: Division of the hepatic ligaments (coronary, triangular), mobilization of the right lobe, and cholecystectomy. Step 3: Dissection of the hepatic pedicles and placement of vessel loops or bulldog clamps on the right portal vein and right hepatic artery. Step 4: Temporary occlusion of the right hepatic pedicle followed by peripheral intravenous ICG injection to identify and mark the ischemic demarcation line (resection line) under near-infrared fluorescence. Step 5: Parenchymal Transection: Preferably utilizing a CUSA (Cavitron Ultrasonic Surgical Aspirator) to minimize thermal injury to hilar structures. Branches of the middle hepatic vein (MHV) from segments 5 and 8 are identified and clipped/ligated. The right hepatic vein (RHV) is isolated and controlled. The right hepatic duct

is divided, guided by real-time ICG fluorescent cholangiography. Step 6: A transverse suprapubic incision (Pfannenstiel incision) is made, and a specimen retrieval bag is inserted into the abdominal cavity. The right lobe is placed inside the bag while maintaining pneumoperitoneum. Step 7: Following systemic heparinization, the right hepatic artery and right portal vein are divided. The right hepatic vein is then divided using an endoscopic vascular stapler. The graft is extracted through the Pfannenstiel incision and immediately transferred to the back-table for flushing and cold preservation. Step 8: The biliary stump is sutured or clipped, hemostasis is verified, the abdominal cavity is irrigated, the falciform ligament is repaired to prevent lobe torsion, and the incisions are closed.

* ***Clinical Question 39:*** *What are the critical considerations for implementing laparoscopic donor hepatectomy in living donor transplantation?*

* **Recommendation 39*:*** Laparoscopic donor hepatectomy should be performed by experienced surgical teams supported by adequate specialized equipment. It is important to note that a donor BMI >25 kg/m², an estimated graft weight >1000 g, and the presence of anatomical variants are not absolute contraindications for the laparoscopic approach. Meticulous dissection and handling of vascular and biliary structures are essential to minimize postoperative complications. To progressively enhance the safety and efficacy of minimally invasive donor hepatectomy, it is necessary to standardize and simplify technical protocols, supplemented by structured hands-on training and advanced medical education.

* ***Clinical Question 40:*** *What are the clinical advantages of utilizing the Glissonean approach for donor hepatectomy in living donor liver transplantation?*

*** Recommendation 40:** The advantages of the Glissonean approach for donor hepatectomy in living donor liver transplantation include: ensuring the secure and anatomical control of the hepatic pedicle during transection, minimizing the risks associated with complex vascular or biliary anatomical variations, allowing for the definitive dissection of hilar components to proceed after the initial parenchymal transection, providing a more ergonomically convenient and technically straightforward dissection plane, significant shortening the duration of arterial exposure and handling, minimizing the risk of air embolism or vascular injury during hilar dissection, optimizing the critical relationship between the hepatic artery and the bile duct and facilitating the mobilization and precise resection of the bile duct without compromising its delicate blood supply (peribiliary vascular plexus).

**** Clinical Question 41:*** *What is the clinical application of ICG fluorescence in living donor liver transplantation?*

*** Recommendation 41*:*** In living donor liver transplantation (LDLT), the use of Indocyanine Green (ICG) fluorescence administered via intravenous injection at a clinically precise timing serves to identify the ischemic demarcation boundaries for parenchymal transection accurately. Furthermore, ICG fluorescence facilitates the clear visualization of the biliary tree at the hepatic hilum, enabling the surgeon to determine the optimal resection points for the bile ducts (crucial note: a final inspection of the biliary anatomy must be performed immediately following ductal division). Additionally, ICG imaging is an effective tool for assessing the adequacy of graft flushing (lavage) and verifying post-reperfusion tissue perfusion during the transplantation procedure.

F. Pediatric Liver Transplantation, Living Donor vs. Deceased Donor (Brain-Dead) Advantages, Split-Liver Transplantation, ABO-Incompatible Transplantation and Dual Graft Liver Transplantation (with 7 recommendations):

***** ***Clinical Question 42:*** *What are the considerations for liver transplantation in pediatric patients?*

***** **Recommendation 42*:*** Pediatric liver transplantation is primarily performed using living donor grafts and is most frequently indicated for biliary atresia (typically following the failure of a Kasai portoenterostomy and resulting in end-stage liver disease). Other indications include acute liver failure, Wilson's disease, Neonatal Intrahepatic Cholestasis caused by Citrin Deficiency (NICCD), Caroli's syndrome, and Budd-Chiari syndrome. Graft Selection by Age: Typically, a left lateral segment graft (Segments II and III) is utilized for children aged 6 months to 3 years. For children aged 3–12 years, a reduced-size graft, a modified left lobe (Segments II, III, and IV), or occasionally a right posterior segment graft (Segments VI and VII) may be considered. For older children (12–16 years), a full right-lobe graft (Segments V, VI, VII, and VIII) is generally required. Surgical Technique: In pediatric recipients, microsurgical techniques are mandatory for hepatic artery anastomosis and, in some cases, biliary anastomosis. Postoperative Management: Maintenance immunosuppression typically involves Calcineurin Inhibitors (CNIs) such as Tacrolimus or Cyclosporine. If portal vein stenosis (PVS) develops post-transplant, it should be managed through endovascular stent placement.

***** ***Clinical Question 43:*** *What are the advantages and disadvantages of living donor liver transplantation?*

***** **Recommendation 43*:*** The advantages of living donor liver transplantation (LDLT) include the ability to perform the procedure as scheduled, elective surgery, a significant reduction in waiting-list

mortality, superior graft quality from a healthy donor, minimal cold ischemia time, and a broader pool of potential donors. Conversely, the disadvantages include the inherent surgical risks to the healthy donor, the challenge of small-for-size grafts (graft size matching), and the increased technical complexity associated with multiple, small, or short vascular and biliary branches. Furthermore, LDLT carries a higher incidence of biliary and hepatic artery complications and a potential risk for hepatic venous outflow obstruction, particularly when utilizing right-lobe grafts.

**** Clinical Question 44:*** *What are the considerations and surgical techniques for liver transplantation from deceased (brain-dead) donors?*

*** Recommendation 44*:*** Liver transplantation from deceased (brain-dead) donors is a safe and highly effective treatment for end-stage liver disease and hepatocellular carcinoma (HCC). In the recipient, the primary surgical steps involve a total hepatectomy with the division of the biliary and arterial structures, followed by the preparation of the hepatic and portal veins for implantation. The reconstruction involves the sequential anastomosis of the hepatic veins, portal vein, hepatic artery, and bile ducts. Regarding venous reconstruction, surgeons may utilize the "Piggyback" technique or the classic orthotopic technique with inferior vena cava (IVC) replacement; however, modifications involving IVC resection can significantly optimize outcomes by reducing warm ischemia time (from 40 to 20 minutes), shortening overall operative time (from 7–10 hours to 4–6 hours), reducing blood loss, and minimizing the risk of post-reperfusion syndrome, thereby promoting faster recovery. In most cases, a common orifice anastomosis of the three hepatic veins is recommended to ensure adequate outflow. Biliary

reconstruction is typically achieved via an end-to-end (duct-to-duct) anastomosis, with the optional placement of an external biliary stent. Furthermore, advancements in this field allow for split-liver transplantation (dividing one graft for two recipients, ideally an adult and a child) and multi-organ procedures, such as simultaneous liver-kidney or heart-liver transplantation.

Clinical Question 45: *What are the considerations and technical strategies for split-liver transplantation from deceased (brain-dead) donors?*

*** Recommendation 45*:***

Split-liver transplantation involves dividing a single deceased donor liver into two functional grafts for two recipients (typically one adult and one child, or two adults). This procedure optimizes the limited deceased donor pool and significantly expands access to transplantation in Vietnam, particularly for pediatric patients. Donor selection criteria should prioritize ages 10-35, hemodynamic stability, an ICU stay of ≤5 days, and laboratory parameters including hepatic steatosis <30%, GGT <50 U/L, ALT (GPT) <60 U/L, and serum sodium <160 mmol/L. Pediatric recipient criteria include age <15 years, weight <30 kg, and no history of complex abdominal surgery. In-situ splitting is preferred as it shortens cold ischemia time, provides superior anatomical visualization, and facilitates better hemostasis; however, ex-situ splitting is a viable alternative when rapid procurement is necessary or when specialized teams are not available at the donor site. In splitting for an adult-child pair, the adult receives the right trisegment (Segments IV-VIII and I) along with the right hepatic artery, portal vein trunk, right hepatic vein, and IVC. The child receives the left lateral segment (Segments II-III) with the left hepatic artery, left portal vein, and

left hepatic vein. Technical focus must be placed on the Rex fissure dissection, deep parenchymal transection, and secure vascular/biliary stump closure. While 5-year survival reaches approximately 80%, complications involving the biliary tract and vascular anastomoses remain prevalent. Indicators of poor prognosis include a recipient weight ≤6 kg, advanced donor age, cold ischemia time >6 hours, and insufficient inter-unit coordination. A rigorous, coordinated inter-center protocol is essential to optimize long-term outcomes.

***Clinical Question 46:** What are the technological advancements in whole liver transplantation from brain-dead donors?*

* **Recommendation 46:** Whole liver transplantation has achieved remarkable progress through surgical innovations that have improved survival rates and reduced perioperative complications. Key advancements include: ***(1) Optimization of the clamp release sequence:*** Rather than completing all vascular anastomoses before reperfusion, contemporary techniques prioritize releasing the suprahepatic inferior vena cava (IVC) clamp following the anastomosis of the portal vein and suprahepatic IVC, combined with graft flushing using Ringer's lactate and albumin; this significantly reduces warm ischemia time (WIT), intraoperative blood loss, and ischemia-reperfusion injury. ***(2) Temporary portocaval shunt (TPCS):*** Establishing a connection between the portal vein and the infrahepatic IVC during the anhepatic phase reduces portal hypertension, improves mesenteric venous return, and minimizes intestinal congestion and ischemia. ***(3) Super-rapid procurement technique:*** Utilized immediately following the declaration of circulatory death (DCD), this involves a rapid midline laparotomy, immediate aortic cannulation, and complete liver mobilization in under 10 minutes. These techniques not only minimize cold ischemia time (CIT) but also expand the available donor pool and

mitigate postoperative risks. Overall, orthotopic liver transplantation performed with modified techniques specifically those avoiding the need for veno-venous bypass has proven to be safe, effective, and is currently the clinical standard.

**** Clinical Question 47:*** *How about of ABO-incompatible living donor liver transplantation?*

*** Recommendation 47*:*** Liver transplantation for incompatible blood groups:

- Reasons:

+ Unsuitable relatives for liver donation: Blood group incompatibility, insufficient health, age, hepatitis virus infection...

+ Scarcity of grafts from brain-dead donors

- Previous challenges (Before Rituximab):

+ Hyperacute rejection risk due to antibodies against the blood group (Isoagglutinins).

+ Diffuse biliary necrosis.

+ Significantly lower graft survival rate compared to same-blood group (ABOc).

- Turning point: The application of Rituximab (monoclonal antibody against CD20) has completely changed the prognosis.

- Desensitization Protocol:

+ Rituximab: Dose: 375 mg/m² (or fixed dose 200-500 mg) and Timing: 2-3 weeks before surgery.

+ Plasmapheresis (TPE): The goal is to lower the antibody titer to ≤ 1:16.

+ Immunosuppression: Standard triple therapy (Tacrolimus + MMF + Steroids).

+ Important change: Splenectomy or intravenous fluid administration via portal vein/hepatic artery is no longer necessary.

- Regarding outcomes after incompatible blood group transplantation: Current ABOi transplantation outcomes are completely equivalent to ABOc in terms of long-term survival (with a survival rate of nearly 95% after 1 year and around 90% after 3-5 years). However, additional attention should be paid to complications such as biliary atresia after transplantation, rejection, etc.

**** Clinical Question 48:*** *How about Dual-graft transplantation?*

*** Recommendation 48*:*** Dual-graft transplantation provides sufficient liver volume for larger recipients by implanting two grafts from different living donors into a single recipient. This approach is often indicated when a single donor graft is too small for the patient's body. For indications and considerations: Small-for-size graft syndrome, High-acuity patients, Donor safety... Often performed by laparoscopic surgery, which involves simultaneously harvesting two liver grafts from two living donors and simultaneous liver transplantation using two grafts from two living donors (e.g., two left lobes or one right and one left).

G. Continued Integration of Advanced Techniques, Liver Transplantation During the COVID-19 Pandemic, and the Establishment of Excellent Liver Transplant Centers in Vietnam (with 4 recommendations):

**** Clinical Question 49:*** *What advanced surgical and clinical strategies should be prioritized for future integration into liver transplantation?*

*** Recommendation 49*:*** Future development should focus on the implementation of advanced transplant strategies, including: Robotic-assisted donor hepatectomy and recipient transplantation; Hybrid procedures for living donor liver procurement; Liver transplantation

for critically ill patients (high MELD scores); Immune tolerance induction, particularly in pediatric cohorts; Paired donor exchange (donor "swap" programs); and the use of sub-segmental grafts for small pediatric recipients. For very young patients: The parent's liver graft is too large for the child's body. When the child's body is too small, a liver resection to reduce volume is performed.

***** ***Clinical Question 50:*** *What are the considerations for graft selection and outpatient management during the COVID-19 pandemic?*

***** **Recommendation 50*:*** During the COVID-19 pandemic, living donor liver transplantation (LDLT) emerged as the preferred and primary modality due to the enhanced safety and controllability of living donor sources compared to deceased donor programs. For outpatient management, protocols should include extending follow-up intervals to every 2-3 months to minimize hospital exposure, authorizing designated representatives for medication collection, and prioritizing comprehensive vaccination strategies for transplant recipients.

***** ***Clinical Question 51:*** *What are the criteria and advantages for establishing and coordinating a tiered network of liver transplant centers?*

***** **Recommendation 51*:*** The objective is to achieve a harmonized development of high, medium, and low-volume liver transplant centers across the country. High-volume centers, defined as performing over 55 transplants annually and maintaining a waitlist utilization rate of over 68%, significantly improve transplantation access and reduce post-transplant mortality. These centers benefit

from highly experienced surgical teams proficient in managing complex cases and offer superior expertise in the multidisciplinary management of complications, institutionalized learning, and continuous 24/7 specialized service.

Medium-volume centers (20–55 transplants per year with a 26% waitlist utilization) and low-volume centers (fewer than 20 transplants per year with a 6% waitlist utilization) offer distinct advantages, including improved geographic accessibility, reduced transportation burdens for patients, and localized financial and healthcare policy support. These centers facilitate regional organ distribution and provide expanded treatment options for patients. To ensure success, small and medium-sized centers require coordinated collaboration with high-volume institutions, the development of robust infrastructure, and continuous mentorship. It is essential to build a dedicated core team of transplant surgeons and specialists, foster an organizational culture of academic advancement, and establish a clear strategic plan for incremental growth and implementation.

Clinical Question 52: *What are the requirements for establishing Centers of Excellence (COEs) for liver transplantation in Vietnam?*

*** Recommendation 52*:*** The establishment of Centers of Excellence (COEs) for liver transplantation is essential to advance the field nationwide. These centers must be characterized by a highly skilled workforce, featuring multidisciplinary transplant teams with a proven track record of superior clinical outcomes. Such institutions should serve a leadership role in regional and national transplant development. Critical requirements for a COE include a comprehensive multimodal treatment system, state-of-the-art infrastructure equipped with advanced surgical instrumentation, active engagement in clinical research and professional training, and robust strategic collaborations. Furthermore, these centers must provide high-quality, patient-centered care and specialized services while maintaining cost-effectiveness for the population.

VIETNAM ASSOCIATION FOR
THE STUDY OF LIVER DISEASES,
VSHBPS AND VASLD-MIT

SOCIALIST REPUBLIC OF VIETNAM
Independence - Freedom - Happiness

Hanoi, April 5th, 2026

DECISION

Regarding the Promulgation of the "Clinical Practice Guidelines for Liver Transplantation in Vietnam" by the Vietnam Association for the Study of Liver Diseases (VASLD), the Vietnam Society of Hepato-Biliary-Pancreatic Surgery (VSHBPS), and the VASLD-MIT.

President of the Vietnam Association for the Study of Liver Diseases (VASLD),

Founding President of VSHPBS and President of VASLD-MIT

Pursuant to the functions, duties, and powers vested in the President of the Vietnam Association for the Study of Liver Diseases (VASLD), the Founding President of VSHBPS, and the President of VASLD-MIT;

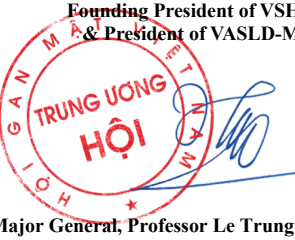
HEREBY DECIDES:

Article 1. To officially promulgate the "Clinical Practice Guidelines for Liver Transplantation in Vietnam" (2026 Updated Version), as ratified by VASLD, VSHBPS, and VASLD-MIT.

Article 2. The "Clinical Practice Guidelines for Liver Transplantation in Vietnam" (2026 Updated Version) shall serve as the authoritative reference and guiding document for clinical application across all medical facilities nationwide.

Article 3. This Decision shall take effect immediately upon the date of signing and formal promulgation./.

President of VASLD,
Founding President of VSHBPS
& President of VASLD-MIT



Major General, Professor Le Trung Hai MD, PhD

CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF HEPATOCELLULAR CARCINOMA (HCC) IN VIETNAM

(2026 Updated Version: Based on the New Guidelines of the Vietnamese Ministry of Health)

(with 52 Evidence-Based Recommendations)

A. Factors and prevention measures for hepatocellular carcinoma (with 2 recommendations):

** **Clinical Question 1:** What are the risk factors, primary oncogenic mechanisms of hepatocellular carcinoma (HCC), and the recommended protocols for surveillance and detection?*

*** Recommendation 1:**

- Risk Factors: The established primary risk factors for HCC include chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections (which increase HCC risk 60-200 times compared to uninfected individuals), chronic liver disease (alcoholic and non-alcoholic), cirrhosis of any etiology, Aflatoxin B1 (AFB1) exposure from contaminated grains, non-alcoholic fatty liver disease (NAFLD/MASLD) which is showing a rising incidence exposure to environmental toxins, autoimmune hepatitis, metabolic disorders, and male gender over 35 years of age. Viral hepatitis and heavy alcohol consumption remain the predominant drivers.

Pathogenesis: The primary mechanism for HCC development within the context of chronic liver disease and progressive cirrhosis involves the activation of hepatic stellate cells. These cells transform into myofibroblast-like cells, creating a pro-carcinogenic microenvironment that facilitates tumor growth, hepatocyte degeneration, and accumulated genetic mutations.

Surveillance of Localized Lesions: To detect HCC early in high-risk patients with chronic hepatitis or cirrhosis, lesions <1 cm identified via ultrasound should be monitored every 3 months. If the lesion remains stable or resolves over 2 years, the interval may be extended to 6 months. For lesions that increase in size to >1 cm, contrast-enhanced computed tomography (CT) and/or magnetic resonance imaging (MRI) must be performed to confirm HCC based on typical vascular hallmarks (arterial phase hyperenhancement and venous/delayed phase washout). The LI-RADS (Liver Imaging Reporting and Data System) should be utilized for standardized reporting. If imaging features are atypical, a core needle biopsy is indicated for histopathological confirmation.

General Screening Guidelines: All patients with cirrhosis or chronic HBV/HCV (aged >35) should undergo surveillance every 6 months using abdominal ultrasound and serum biomarkers, specifically Alpha-Fetoprotein (AFP) and PIVKA-II (DCP).

Advanced Screening: In tertiary centers, screening efficacy can be enhanced by incorporating AFP-L3 testing and shortened CT/MRI intervals (every 3–6 months) where clinically indicated, to optimize the early detection of HCC.

**** Clinical Question 2:*** *What are the recommended preventive measures for hepatocellular carcinoma (HCC)?*

*** Recommendation 2*:***

To effectively prevent HCC, the following public health and clinical measures must be implemented:

- HBV Vaccination and Prevention of Mother-to-Child Transmission (PMTCT): Implement universal hepatitis B vaccination for all infants and high-risk adults. Pregnant women must be screened for HBV; antiviral therapy (e.g., Tenofovir) is indicated if HBV DNA

>2 x 10^5 IU/mL to reduce vertical transmission risk. Newborns of HBsAg-positive mothers must receive both the hepatitis B vaccine and Hepatitis B Immunoglobulin (HBIG) within the first 12 hours of life.

- Chronic Hepatitis Management: Ensure long-term, adherent antiviral treatment for patients with chronic HBV and active necro-inflammatory liver disease. For Hepatitis C, patients should receive Direct-Acting Antiviral (DAA) therapy until a Sustained Virologic Response (SVR) is achieved.

- Management of Metabolic Dysfunction: Actively treat metabolic disorders, specifically Non-Alcoholic Fatty Liver Disease (NAFLD/MASLD) and Non-Alcoholic Steatohepatitis (NASH/MASH), as these significantly elevate HCC risk. Clinical focus is required for metabolic syndrome, particularly diabetes and obesity, which act as synergistic risk factors in NASH patients.

- Harm Reduction and Behavioral Counseling: Educate patients on preventing the transmission of HBV and HCV via sexual contact and blood-borne routes. Strict screening protocols for blood products must be enforced. Patients, especially those with cirrhosis or viral hepatitis, should be counseled on complete abstinence from alcohol and tobacco.

- Medication Safety and Environmental Exposure: Advise against the use of unregulated medications or traditional medicines of unknown origin. Promote safe injection practices to prevent iatrogenic transmission. Minimize exposure to environmental hepatotoxins and industrial chemicals.

- Routine Surveillance: Individuals with chronic liver disease must undergo regular health screenings at least every 6 months. This surveillance should include abdominal ultrasound and serum AFP testing to facilitate the early detection and curative treatment of HCC.

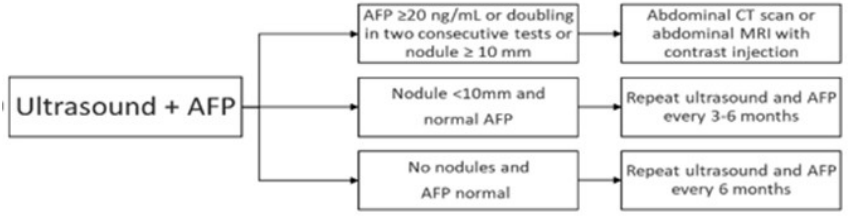
B. Hepatocellular carcinoma screening (with 2 recommendations):

**** Clinical Question 3:*** *Which diagnostic tests and protocols are indicated for the screening of high-risk patients for HCC?*

*** Recommendation 3:**

Hepatocellular carcinoma (HCC) primarily develops in the setting of chronic liver disease, specifically chronic HBV and HCV infections and chronic alcohol abuse. Populations requiring systematic HCC screening include individuals with established cirrhosis and those with chronic hepatitis B, particularly men over 40 years of age and women over 50 years of age.

Standard HCC Screening Protocol: Routine screening consists of abdominal ultrasound and serum AFP testing, conducted according to the clinical algorithm below:



Routine surveillance should be performed every 6 months using hepatobiliary ultrasound, serum Alpha-Fetoprotein (AFP), and Des-gamma-carboxy prothrombin (DCP/PIVKA-II), ideally integrated through the GAAD index (Gender, Age, AFP, and DCP) for improved sensitivity. In tertiary medical centers, screening efficacy can be further optimized by combining ultrasound with a triple-biomarker panel (AFP, AFP-L3, and DCP) and shortened CT or MRI intervals (every 3–6 months), utilizing the GALAD index (Gender, Age, AFP-L3, AFP, and DCP) where resources permit. Clinically, the GAAD index is recommended for broad HCC screening due to its cost-effectiveness and comparable performance to GALAD, whereas the GALAD index is more effectively utilized to support the definitive diagnosis of HCC.

***Clinical Question 4:** What are the clinical benefits of early HCC detection, and what are the essential considerations for achieving an early diagnosis?*

*** Recommendation 4:**

Early detection of hepatocellular carcinoma (HCC) facilitates timely, curative, and cost-effective interventions, significantly increasing the overall survival rate. Detecting HCC at a very early stage, specifically when the tumor size is ≤2 cm, optimizes treatment efficacy and reduces the risk of intrahepatic recurrence, intrahepatic metastasis, or distant extrahepatic metastasis. Overall, early detection and a precise diagnostic approach are the foundation of effective HCC management.

It is essential to strategically and flexibly utilize all available diagnostic modalities, maintaining a comprehensive understanding of the specific advantages and limitations of each method. This ensures that screening tools are applied appropriately, accurately, and effectively to achieve an early diagnosis, which remains the fundamental key to improving the long-term survival and prognosis of patients with HCC.

C. Diagnosis of hepatocellular carcinoma (with 5 recommendations):

***Clinical Question 5:** What is the role of serum biomarkers in the diagnosis of HCC?*

*** Recommendation 5:** The Alpha-Fetoprotein (AFP) marker, at a concentration of ≥ 20ng/ml offers a diagnostic sensitivity of approximately 60% for HCC, whereas an AFP threshold of > 400 ng/ml provides a high specificity of 95%. The inclusion of AFP-L3 > 5/% and DCP > 40 mAU/ml biomarkers further increase specificity and enhances the early detection of HCC. An AFP value of 200 ng/ml

is highly suggestive of HCC, particularly when levels remain ≥200 ng/ml for two consecutive months or reach ≥400 ng/ml for one month; this biomarker also carries significant prognostic weight. Furthermore, monitoring serum AFP is essential for evaluating post-treatment outcomes, especially in patients with elevated baseline levels. In specialized centers, these markers are integrated to calculate the GAAD index (AFP, DCP, age, and sex with a cut-off of 2.57), the GALAD index (incorporating AFP-L3), or the BALAD index (which adds total bilirubin and albumin to the GALAD parameters) to monitor therapeutic response and predict overall survival. Additionally, HBcrAg (hepatitis B core-associated antigen) levels are utilized to predict HCC development, assess the risk of recurrence, and forecast long-term HCC risk in patients with chronic HBV.

***Clinical Question 6:** In cases where AFP levels are not elevated, what diagnostic tests are utilized to confirm HCC?*

* **Recommendation 6:** In patients with HCC where AFP levels remain within normal limits, a definitive diagnosis relies on cross-sectional imaging, specifically contrast-enhanced computed tomography (CT) and/or contrast-enhanced magnetic resonance imaging (MRI). These modalities typically demonstrate the hallmark vascular pattern of HCC: intense arterial phase hyperenhancement followed by rapid washout in the portal venous and delayed phases. If the hepatic lesion exhibits atypical imaging features, a core needle biopsy is mandatory for histopathological confirmation. Specialized centers should utilize the GAAD or GALAD indices, which have demonstrated a sensitivity of over 90% for detecting HCC in early stages. Furthermore, a PIVKA-II (DCP) test should be performed in cases where ultrasound findings are highly suspicious for HCC despite normal serum AFP levels.

**** Clinical Question 7:*** *What is the diagnostic value of imaging modalities in the evaluation of HCC?*

*** Recommendation 7:**

- ***Abdominal ultrasound*** is a minimally invasive, widely available, and cost-effective diagnostic tool, particularly suitable for the clinical context in Vietnam. It demonstrates a sensitivity of 65-80% for HCC and is fundamentally utilized alongside AFP for high-risk patient screening. Ultrasound allows for the assessment of tumor morphology, location, number, and size, as well as the evaluation of underlying liver parenchymal disease, ascites, and associated intra-abdominal lesions. Additionally, Doppler ultrasound enables the evaluation of tumor vascularity and invasion into major vessels, such as the portal vein and inferior vena cava. Where available, Contrast-Enhanced Ultrasound (CEUS) can significantly improve diagnostic accuracy; the hallmark of HCC on CEUS is intense arterial phase hyperenhancement followed by late washout (typically after 60 seconds), whereas non-HCC malignancies often exhibit earlier washout (before 55-60 seconds).

- ***Multidetector Computed Tomography (MDCT) or Magnetic Resonance Imaging (MRI)*** with contrast is indicated to evaluate the vascular dynamics of liver lesions. These modalities provide precise assessment of tumor vascularity, multicentricity, and anatomical relationships with adjacent structures. They are also critical for detecting intrahepatic metastasis (satellite nodules, macrovascular invasion) and extrahepatic spread (hilar lymphadenopathy, adrenal or pulmonary involvement). On CT or MRI, the definitive diagnosis of HCC is based on the characteristic pattern of arterial phase hyperenhancement and portal venous or delayed phase washout. When these typical features are present, a definitive diagnosis can be established without the need for a biopsy. MRI generally offers comparable diagnostic performance to CT, with a sensitivity exceeding 80% and a specificity exceeding 85%.

- The diagnosis of distant metastases requires a multimodal approach, including whole-body MSCT, MRI, or PET-CT with FDG. Furthermore, CT/MRI is utilized for post-treatment surveillance and response evaluation. Lesions that demonstrate Lipiodol retention following Transarterial Chemoembolization (TACE) are also classified as HCC in the appropriate clinical context.

***** ***Clinical Question 8:*** *What is the diagnostic value of hepatobiliary-specific contrast MRI (Primovist/Gd-EOB-DTPA) compared to extracellular agent MRI (ECA-MRI) in HCC?*

*** Recommendation 8:** While multidetector CT and standard MRI are effective diagnostic tools, they may lack sufficient sensitivity for very small lesions, potentially leading to unnecessary biopsies. EOB-MRI (Primovist) is a highly sensitive modality utilizing a liver-specific contrast agent that facilitates the early detection of HCC, even for nodules under 1 cm. The use of hepatobiliary-phase MRI should be encouraged for challenging diagnostic cases to avoid over-reliance on invasive biopsies or passive monitoring. Patients presenting with new nodules on ultrasound and elevated AFP should undergo contrast-enhanced CT or MRI, with EOB-MRI considered as a preferred option if conditions permit particularly when standard imaging is inconclusive. EOB-MRI demonstrates superior sensitivity compared to standard extracellular contrast MRI and CT, enabling the differentiation of small HCC (under 1 cm) from precancerous lesions, such as high-grade dysplastic nodules, in the cirrhotic liver. Generally, hepatobiliary MRI (Gd-EOB-DTPA) is recommended for suspected multifocal disease and complex cases. However, recent comparative studies suggest that Extracellular Agent MRI (ECA-MRI) may be preferred in certain contexts due to its higher specificity in characterizing small HCC nodules by providing a more distinct vascular “washout” assessment.

Clinical Question 9: *What role does artificial intelligence (AI) play in assisting with the early and accurate diagnosis of HCC?*

*** Recommendation 9:** Global data, corroborated by clinical research in Vietnam, demonstrates that artificial intelligence (AI) is a powerful adjunctive tool for the detection and diagnosis of HCC. Specifically, AI algorithms facilitate the early identification of liver lesions enhancing the precision of localization, sizing, and volumetric analysis which leads to more informed therapeutic decisions and a reduction in HCC-related mortality. Studies conducted in Vietnam, validated against the gold standards of clinical and histopathological findings, indicate that AI achieves high diagnostic performance with a sensitivity of 90%, a specificity of 97%, and an overall accuracy of 91% in the diagnosis of HCC.

Clinical Question 10: *What are the definitive criteria for the diagnosis of HCC?*

*** Recommendation 10:**

Hepatocellular carcinoma (HCC) is diagnosed based on the following criteria:

- The presence of a hepatic lesion demonstrating hallmark vascular features on contrast-enhanced CT or MRI (arterial phase hyperenhancement and venous/delayed phase washout), combined with a serum AFP level of ≥400 ng/ml or an elevated AFP level <400 ng/ml in the presence of chronic HBV or HCV infection. In cases where CT/MRI demonstrates typical vascular hallmarks, but AFP is not elevated, or when imaging features are atypical regardless of AFP levels, a core needle biopsy of the liver lesion is mandatory. A positive histopathological result confirms the diagnosis. If the initial biopsy is negative but clinical suspicion remains high, the biopsy should be repeated, and the patient should be closely monitored with follow-up imaging every 2 months.

D. Liver biopsy (with 1 recommendation):

**** Clinical Question 11:*** *What is the role and indications of liver biopsy in the diagnosis of HCC?*

*** Recommendation 11:**

Liver biopsy (core needle biopsy) or fine-needle aspiration (FNA) is indicated when a hepatic lesion >1cm does not exhibit the hallmark vascular characteristics of HCC on contrast-enhanced imaging, or when histopathological and molecular evidence is required to guide systemic targeted therapy.

In clinical practice, a liver tumor biopsy is not mandatory for all patients, particularly when serum biomarkers and typical dynamic CT/MRI findings (arterial enhancement with venous washout) provide sufficient evidence for a definitive diagnosis. Biopsy is reserved for cases where non-invasive diagnostic criteria are not met, as the procedure carries specific risks, including hemorrhage, infection, and needle-track seeding (occurring in 1–3% of cases). While a positive biopsy confirms HCC, a negative result does not definitively exclude malignancy or prove the lesion is benign; such cases require a multidisciplinary review of the imaging and a repeat biopsy after 2–3 months. Biopsies of small or complex lesions should always be evaluated by a specialized hepatopathologist.

E. Staging of Hepatocellular Carcinoma (with 1 recommendation):

**** Clinical Question 12:*** *What are the clinical criteria and systems utilized for the staging of HCC?*

*** Recommendation 12:** Staging HCC requires a comprehensive assessment of tumor burden, underlying liver function, and the patient's performance status. The Barcelona Clinic Liver Cancer (BCLC) staging system is the primary framework used, categorized

as follows: Very Early (Stage 0): A single lesion ≤2 cm no vascular invasion or metastasis, Child-Pugh A, ECOG 0 (good general condition), Okuda score 1, and compensated liver function. Early (Stage A): A single tumor of any size or up to three nodules each ≤3cm, N0 and M0, Child-Pugh A–B, ECOG 0, Okuda 1-2, and compensated liver function. Intermediate (Stage B): Multinodular disease (>3 tumors) without vascular invasion or extrahepatic spread, with liver function and health status similar to Stage A. Advanced (Stage C): Evidence of portal vein invasion, lymph node involvement (N1), or distant metastasis (M1), with an average performance status. Terminal (Stage D): Child-Pugh C, severe physical impairment (ECOG 3-4), Okuda score 3, and decompensated liver function. While BCLC provides a standardized research framework, a more flexible approach following the APASL (Asian Pacific Association for the Study of the Liver) guidelines is recommended for clinical practice in Asia. This allows for broader indications for radical and combination therapies such as expanded liver resection, Hepatic Arterial Infusion Chemotherapy (HAIC), and radiotherapy facilitating an individualized and multimodal treatment transition.

F. Multimodal treatment of HCC (With 2 recommendations):

**** Clinical Question 13:*** *What is the role of multimodal treatment in the management of HCC?*

*** Recommendation 13:** The treatment of HCC requires a multimodal approach facilitated by a Multidisciplinary Team (MDT), including surgeons, hepatologists, gastroenterologists, oncologists, radiologists, interventional radiologists, nuclear medicine physicians, radiation oncologists, pathologists, nutritionists, and psychologists. Curative-intent surgery primarily liver resection and transplantation remains the most critical intervention for achieving long-term survival.

Current modalities include liver resection, transplantation, local ablation (RFA, MWA, PEI), transarterial therapies (TACE, TOCE, DEB-TACE), radiotherapy (SIRT, SBRT), targeted molecular therapy, and immunotherapy. Selecting the appropriate treatment method for patients at different stages of HCC will yield the best results:

- For localized HCC without extrahepatic metastasis or portal vein thrombosis, surgical resection is the optimal choice if complete tumor removal is feasible. Recently, laparoscopic hepatectomy has gained prominence due to its minimally invasive benefits, including faster recovery and oncological outcomes comparable to open surgery.

- For tumors smaller than 3 cm, local ablation is a viable alternative to resection.

- In cases where resection is contraindicated, treatment selection (ablation, TACE, or transplantation) must be individualized through MDT consultation based on tumor burden and liver function. This multimodal strategy improves survival by (1) utilizing a multidisciplinary framework, (2) combining synergistic methods, (3) repeating effective interventions, (4) applying sequential therapies, and (5) tailoring indications to the patient's specific profile and international guidelines.

Following the APASL/BCLC framework: Very Early (0) and Early (A) stages prioritize resection, ablation, or transplantation; Intermediate (B) stage focuses on TACE, SIRT, or radiotherapy; Advanced (C) stage utilizes systemic therapy (first-line: Atezolizumab + Bevacizumab, Sorafenib, or Lenvatinib; second-line: Regorafenib, Pembrolizumab); and Terminal (D) stage focuses on palliative care. The MDT is crucial for deciding on extended resections, pre-transplant staging, and combining TACE with radiotherapy or systemic agents to downstage advanced disease for localized intervention.

***Clinical Question 14:** What is the significance of multidisciplinary collaboration and the move toward holistic integrative management in the treatment of HCC?*

*** Recommendation 14:** Multidisciplinary collaboration integrates diverse specialties including surgical oncology, hepatobiliary surgery, medical oncology, diagnostic and interventional radiology, pathology, gastroenterology, infectious diseases, nuclear medicine, radiation oncology, nutrition, and psychology as well as other specialists relevant to the patient's specific comorbidities. This multidisciplinary consultation board, typically coordinated by a core team of oncologists and surgeons, synchronizes clinical efforts to achieve optimal therapeutic outcomes. Such collaboration is particularly vital in complex cases involving significant comorbidities, where the pooling of collective expertise ensures the most precise and effective treatment plan. Current clinical practice in Vietnam increasingly emphasizes this multidisciplinary framework, evolving toward a holistic, integrative management model for HCC that addresses the patient's entire clinical and psychological profile throughout the continuum of care

G. Surgical Management of Hepatocellular Carcinoma (with 9 recommendations):

***Clinical Question 15:** Which preoperative assessments are utilized to select patients for liver resection in HCC?*

*** Recommendation 15:**

- Liver resection is a potentially curative treatment for HCC, with a 5-year overall survival rate typically ranging from 50% to 70%. Before proceeding, clinicians must assess the technical feasibility of the procedure, the patient's clinical status (specifically performance

status, liver function, and the future liver remnant (FLR) volume), and the oncological prognosis regarding the risk of recurrence. A multidisciplinary team (MDT) approach is essential to accurately evaluate the disease stage and liver reserve.

- Patient selection should align with established guidelines, noting that BCLC criteria are often more restrictive than the standards applied in Asia, which prioritize "attempting liver resection while the tumor is resectable," provided safety is guaranteed. Accurate assessment of hepatocellular function and portal hypertension is mandatory to determine the appropriate extent of resection. The guiding principle must always balance patient safety with oncological efficacy. To prevent postoperative liver failure (PHLF), CT- or MRI-based volumetry must be utilized to ensure an adequate FLR.

- The recommended criteria for surgical selection include: (1) Absence of distant metastasis; (2) Absence of main or diffuse portal vein thrombosis; (3) Child-Pugh class A or select B; (4) Platelet count ≥100,000/μL and total bilirubin ≤1.2mg/dL (5) Absence of high-grade esophageal varices (Grade 1 or 2 is permissible); (6) A Future Liver Remnant (FLR) to Total Liver Volume (TLV) ratio > 30% for a healthy liver or >40% for a cirrhotic/diseased liver. In cases of insufficient FLR, strategies to induce hypertrophy should be employed, such as Portal Vein Embolization (PVE) or Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS). Other adjunctive techniques include combined PVE with Transarterial Embolization (TAE) or Hepatic Vein Embolization (HVE).

**** Clinical Question 16:*** *How should liver function be assessed prior to hepatectomy for HCC?*

*** Recommendation 16:** Preoperative liver functional reserve must be rigorously evaluated using the Child-Pugh score (incorporating serum albumin, bilirubin, INR, and clinical assessment of hepatic

encephalopathy and ascites). In medical centers where the technology is available, the Indocyanine Green (ICG) clearance test specifically the ICG retention rate at 15 minutes (ICG-R15) should be utilized as a highly sensitive and globally accepted quantitative measure. Utilizing ICG for preoperative assessment is a valuable technique that significantly assists in determining the safe extent of resection and preventing the high-risk complication of post-hepatectomy liver failure (PHLF).

**** Clinical Question 17:*** *What is the preferred surgical approach for anatomical hepatectomy using the extra-Glissonean pedicle control technique for HCC?*

*** Recommendation 17:** Currently, the extra-Glissonean (extracapsular) approach for anatomical hepatectomy is considered a preferred surgical strategy for the treatment of HCC. Utilizing Takasaki's anatomical hepatectomy technique, the surgeon can achieve primary control of the three main Glissonean pedicles (right, middle, and left) at the hepatic hilum without opening the liver parenchyma. This technique facilitates the selective isolation and control of the pedicles for the posterior sector (Segments 6 and 7), the anterior sector (Segments 5 and 8), and the left lobe (Segments 2, 3, and 4). The primary advantages of this extra-Glissonean approach include its technical reproducibility, reduced operative time, enhanced safety by minimizing hilar dissection, and the ability to ensure thorough oncological resection through precise inflow control.

**** Clinical Question 18:*** *What is the role of minimally invasive laparoscopic surgery in the execution of Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy (ALPPS)?*

*** Recommendation 18:** In cases of HCC where major hepatectomy is indicated but the future liver remnant volume is insufficient for safe resection, liver hypertrophy is induced using the ALPPS technique. Generally, ALPPS facilitates a rapid and effective increase in liver volume. Performing this technique via a minimally invasive approach is safe and expands curative treatment opportunities for patients who require major hepatectomy for liver cancer.

**** Clinical Question 19:*** *What are the key considerations for trisegmentectomy 5-7-8 using a modified liver hanging technique in large right HCC with right hepatic vein invasion?*

*** Recommendation 19:** HCC with hepatic vein invasion often presents significant surgical challenges, particularly when preserving liver volume is crucial. Triple hepatectomy of segments 5-7-8 is a viable approach, allowing for parenchymal preservation in necessary cases. During surgery, the resection margins are performed in two steps: the first between the right and left lobes, and the second between segments 6 and 7, based on the ischemic area of segment 7 after selective ligation of the Glisson's pedicle. Liver hanging is used during surgery to guide the resection margins, especially in deeper areas. Overall, triple segmentectomy 5-7-8 combined with a modified liver hanging technique is a safe and convenient surgical method, especially for cases with large tumors requiring preservation of remnant liver volume.

**** Clinical Question 20:*** *What are the indications, efficacy, and precautions of liver venous deprivation (LVD) for inducing liver enlargement before major liver resection surgery?*

*** Recommendation 20:** Simultaneous portal vein embolization (PVE), the standard method for liver enlargement, combined with hepatic vein embolization (HVE), which blocks blood flow out of the liver, significantly increases both the rate and extent of liver hypertrophy before major hepatectomy. This combined approach, known as liver venous deprivation (LVD), shortens the preoperative waiting time and reduces the risk of tumor progression. Overall, LVD is a safe and feasible minimally invasive technique that increases the volume of the future liver remnant (FLR). It expands the indications for hepatectomy and reduces the incidence of postoperative liver failure. It is critical to note that PVE must always be performed prior to HVE under ultrasound guidance.

**** Clinical Question 21:** What are the effectiveness and advantages of laparoscopic liver resection?*

*** Recommendation 21:** In recent years, laparoscopic liver resection has developed rapidly and is a preferred minimally invasive method due to its significant clinical advantages. It is a feasible and safe treatment for HCC, particularly for minor resections (left lateral section, peripheral segments) and major anatomical resections. This approach demonstrates a success rate exceeding 95%, a complication rate of approximately 5%, no perioperative mortality, and median intraoperative blood loss of roughly 100 ml. Furthermore, this minimally invasive technique facilitates rapid postoperative recovery and shorter hospital stays, while maintaining high oncological efficacy. Centers initiating a laparoscopic program should initially focus on simple resections, exercising caution to avoid major vascular injury when resecting tumors in Segment 5. In cases of significant intraoperative hemorrhage, early conversion to open surgery is recommended, and the extra-Glissonean pedicle should be carefully monitored. Laparoscopic liver resection can be

safely performed for large tumors in the setting of cirrhosis and portal hypertension when patients are selectively indicated and managed by experienced surgeons. Additionally, the use of ICG fluorescence imaging during laparoscopy assists in detecting small lesions and determining the precise margins for anatomical resection.

*** ***Clinical Question 22:*** *What is the application of ICG fluorescence imaging in liver resection surgery for HCC?*

*** Recommendation 22:**

To clearly define the boundaries within the liver parenchyma, Indocyanine Green (ICG) fluorescent dye is utilized. ICG can be administered via direct staining ***(positive staining)*** under intraoperative ultrasound guidance, where the dye is injected into the portal vein branch supplying the target segment; the entire resected area then fluoresces green under near-infrared light. In general, ICG fluorescence imaging effectively delineates hepatic segment boundaries during both open and laparoscopic anatomical hepatectomy when used in conjunction with intraoperative ultrasound.

In Vietnam, the indirect staining method ***(negative staining)*** is more commonly applied. After clamping the Glissonean pedicle of the segment to be resected, an ICG solution (typically at a dose of 0.05mg/kg body weight) is injected into a peripheral vein. The dye is absorbed by the remaining vascularized liver tissue, which appears green under the fluorescence detection mode of the camera, while the target region remains non-fluorescent. Following this fluorescence boundary allows for precise parenchymal transection and the identification of intersegmental planes. It is crucial to strictly control the target Glissonean pedicle to ensure an anatomically correct and radical resection.

Clinical Question 23: *What are the benefits of using the ICG clearance test (Indocyanine Green Retention rate at 15 minutes - ICG R15) to measure hepatocellular function and estimate the future liver remnant (FLR) after hepatectomy? What is the value of ICG R15 in pre- and post-operative assessment?*

*** Recommendation 23:**

- Integrating the measurement of hepatocellular ICG clearance (ICG R15) with the assessment of the expected future liver remnant (FLR) volume significantly enhances patient safety during hepatectomy. An ICG R15 ≥10% is recognized as one of three independent risk factors associated with post-hepatectomy liver failure (PHLF). The risk of PHLF is substantially reduced when the ICG R15 is <10\% and the expected FLR is ≥30% of the total baseline liver volume.

- The ICG R15 test is a safe and easily performed preoperative procedure that assists in determining the safe extent of liver resection. Postoperatively, ICG R15 values help clinicians monitor the progression of liver dysfunction and contribute to evaluating the effectiveness of treatments for postoperative liver failure.

H. Liver transplantation for the treatment of HCC (with 8 recommendations):

Clinical Question 24: *What are the indications and clinical benefits of liver transplantation for the treatment of HCC?*

*** Recommendation 24:** Liver transplantation is indicated for HCC when other treatment modalities have failed and there is no evidence of extrahepatic metastasis. For patients presenting with both HCC and underlying cirrhosis, liver transplantation is the definitive choice as it is the only intervention capable of simultaneously

treating the malignancy and end-stage liver disease. Currently, liver transplantation is considered the gold-standard treatment for HCC and remains the most common surgical indication. It provides superior survival outcomes (exceeding 80% at 5 years) and significantly lower recurrence rates compared to liver resection. In general, even for patients at the Child-Pugh A stage, the outcomes of liver transplantation are comparable to or better than those of liver resection.

***** ***Clinical Question 25:*** *What are the criteria and selection strategies for liver transplantation in patients with HCC?*

*** Recommendation 25:**

Liver transplantation criteria for HCC consider the number of tumors, tumor size, biomarkers (AFP, AFP-L3, DCP), and other indicators such as negative PET scans. The goal is to ensure a 5-year survival rate greater than 50%. Patient selection is primarily based on the Milan criteria (one tumor ≤5cm or three tumors, with the largest ≤3cm or broader criteria such as the Up-to-7 criteria (sum of the number of tumors and the largest tumor size ≤7. The Kyoto criteria (≤10 tumors, size ≤5cm, and DCP ≤400 mAU/ml) yield a 5-year survival rate of nearly 90%. Other references include the Japanese 5-5-500 rule (tumor size ≤5cm, number of tumors ≤5, and AFP ≤500 ng/ml). Selecting patients based on specific biomarkers helps minimize the risk of recurrence after transplantation.

Proposed criteria:

Any number of tumors, with tumor size ≤5cm. Unresectable disease (Child-Pugh B or C, or multifocal tumors in both lobes). AFP <500 ng/ml or DCP ≤500 mAU/ml before transplantation. Partial response to locoregional treatment (AFP stable or decreasing with treatment).

Clinical Question 26: *When should liver transplantation be performed for HCC?*

*** Recommendation 26:**

Timing of liver transplantation for HCC: Early transplantation is recommended when patients meet the established criteria, primarily the Milan criteria (see Recommendation 25). For cases initially outside these criteria, patients should undergo "downstaging" or "bridging" therapies such as TACE, RFA, MWA, PEI, SIRT, SBRT, or liver resection to reduce the disease stage or prevent disease progression while on the waiting list.

In general, patients with HCC should receive locoregional treatment while awaiting transplantation, with an anticipated waiting period of 6–9 months. If feasible, Living Donor Liver Transplantation (LDLT) should be performed after a 3-month observation period to ensure biological stability, whereas Deceased Donor Liver Transplantation (DDLT) should be performed as early as possible once a graft becomes available.

Clinical Question 27: *What are the technical considerations for living donor liver transplantation (LDLT) in adults with HCC?*

*** Recommendation 27:** Liver transplantation in adults using living donors primarily utilizes the right liver lobe. Critical considerations include a comprehensive preoperative assessment of the patient's general condition and the presence of portal vein thrombosis. Intraoperatively, meticulous reconstruction of the hepatic vein anastomosis particularly the middle hepatic vein is essential to prevent anastomotic stenosis and graft congestion. Optimal hepatic vein and hepatic artery reconstruction significantly improves graft quality and post-transplant survival.

In general, surgical maneuvers in HCC patients must be performed to avoid torsion of the middle hepatic vein, which can lead to graft dysfunction, inflammation due to vascular occlusion, and an increased risk of tumor recurrence. A minimally invasive approach should be employed during the recipient's total hepatectomy to reduce the risk of hematogenous spread of cancer cells into the systemic circulation.

**** Clinical Question 28:*** *What is the role of laparoscopic living donor for transplantation in HCC patients?*

*** Recommendation 28:** The application of laparoscopic living donor hepatectomy is an inevitable trend in transplant surgery. As a minimally invasive procedure, it utilizes small incisions and offers significant advantages, including superior aesthetic results, reduced intraoperative blood loss, faster recovery of bowel motility, and shorter hospital stays. Furthermore, this approach may contribute to improved immune function compared to open surgery. It is essential that donors and their families are comprehensively informed about the benefits and technical aspects of this technique during the preoperative counseling process.

**** Clinical Question 29:*** *What are the common post-liver transplant complications in patients with HCC?*

*** Recommendation 29:** Post-operative complications following liver transplantation occur in 20-30% of cases. Clinical focus must be directed toward vascular complications, including hepatic artery occlusion, hepatic vein stenosis, and inferior vena cava stenosis. Biliary complications are also frequent: bile leakage typically presents early, while biliary strictures often occur late; both can lead to severe infections. Diagnostic radiology, interventional radiology,

and interventional endoscopy are essential for the early diagnosis and management of these vascular and biliary tract complications, ultimately reducing mortality and the necessity for re-transplantation. Biliary tract interventions, in particular, demonstrate high success rates of up to 96%. The most common procedure is angioplasty and stenting via Endoscopic Retrograde Cholangiopancreatography (ERCP) to resolve biliary strictures.

**** Clinical Question 30:*** *What are the post-transplant monitoring protocols for HCC?*

*** Recommendation 30:** During the first three years after liver transplantation for HCC, monitoring should be conducted using AFP, AFP-L3, and DCP tests every three months. Computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen and pelvis should be performed every six months; this imaging is especially indicated for cases with elevated AFP levels. Additional CT or MRI of the chest and bones may be considered. PET-CT should be considered for metastatic screening. If no metastasis is detected but clinical suspicion remains, the follow-up interval should be shortened to two months. Post-operative monitoring for recurrence of HCC is crucial. Upon detection of recurrence, a liquid biopsy will provide information to guide appropriate treatment strategies.

**** Clinical Question 31:*** *What is the optimal screening strategy for HCC after liver transplantation?*

*** Recommendation 31:** The focus of this strategy is the correlation between pre-transplant AFP and PIVKA-II levels and the rate of normalization of these tumor markers post-transplant. A rapid return of tumor markers to normal levels (within 4-6 weeks)

correlates with improved recurrence risk and overall survival prognosis; conversely, slow normalization significantly increases the risk of recurrence. For high-risk groups, periodic monitoring every 2-3 months is recommended. Meanwhile, low-risk groups can safely be monitored with imaging every 6 months, unless there is evidence of rising tumor markers. New technologies such as liquid biopsy including circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and microRNA analysis show potential for earlier and more accurate detection of residual disease, improving the prognosis and treatment outcomes for liver transplant patients with HCC.

I. Percutaneous Intervention for the Treatment of Hepatocellular Carcinoma Using Radiofrequency Ablation (RFA) and Microwave Ablation (MWA) (with 3 recommendations):

**** Clinical Question 32:*** *What are the characteristics, indications, and influencing factors of percutaneous intervention for HCC treatment using RFA and MWA?*

*** Recommendation 32:**

Radiofrequency ablation (RFA) and microwave ablation (MWA) are radical and effective treatments for early-stage HCC that locally destroy the tumor through thermal energy (tumor ablation). These are minimally invasive interventions. Most procedures target easily accessible tumors and are performed percutaneously under ultrasound guidance; other guidance methods include CT, MRI, and DSA. Cases requiring ablation for tumors ≥5 cm require multidisciplinary consultation.

- Percutaneous intervention (RFA and MWA) is indicated for early-stage liver tumors ≤3cm) that are not suitable for hepatectomy (e.g., cases with cirrhosis and portal hypertension). For tumors between 3-5 cm, RFA should be combined with TACE.

- Several factors including viral hepatitis markers, AFP levels, tumor number, and tumor size combine to influence recurrence and disease-free survival (DFS) after local ablation. Close monitoring after local ablation is necessary to improve treatment efficacy.

Clinical Question 33: *What are the efficacy and safety of laparoscopic RFA and MWA for HCC?*

*** Recommendation 33:**

- The effectiveness of radiofrequency ablation (RFA) treatment for HCC is demonstrated by an improvement in clinical symptoms in nearly 70% of patients and an AFP response in over 70% of those with elevated baseline levels. The tumor response rate at 1-6 months post-treatment is approximately 90%. This method effectively improves overall survival time.

- Percutaneous thermal ablation (PTA) offers survival and recurrence rates similar to hepatectomy, particularly for liver tumors ≤3 cm. RFA may be selected as a first-line radical treatment, replacing hepatectomy for HCC cases involving a single tumor ≤3 cm and preserved liver function. Indications may be extended to patients with liver tumors >3 cm who are inoperable; in such cases, a combination of TACE and RFA is recommended.

Clinical Question 34: *What are the results of microwave ablation (MWA) treatment for HCC?*

*** Recommendation 34:** Microwave ablation (MWA) therapy completely destroys tumors after one or two MWA sessions. Survival time is significantly improved. The disease-free survival rate for one year is nearly 80%. Overall, MWA is comparable to RFA and is superior for large tumors.

K. Treatment for HCC with TransArterial ChemoEmbolization (TACE) (with 5 recommendations):

**** Clinical Question 35:*** *What are the indications for TACE and superselective TACE treatment for HCC?*

*** Recommendation 35:**

- Transarterial chemoembolization (TACE) is a minimally invasive method that involves injecting chemotherapy drugs into the microarteries supplying the liver tumor to occlude the tumor's blood vessels, gradually causing necrosis and shrinkage of the tumor. This is a palliative treatment and serves as the standard, first-line therapy for intermediate-stage HCC (BCLC-B). It is also indicated for large or multifocal liver tumors, as a downstaging therapy before surgery, as bridge therapy while waiting for a liver transplant, or in combination with systemic therapy for advanced-stage HCC. Two forms of TACE are commonly used: Conventional TransArterial Chemo-Embolization (cTACE) using Lipiodol and Spongel, and Drug-Eluting Bead Transarterial Chemoembolization (DEB-TACE), which reduces systemic toxicity and increases the retention time of the embolizer within the tumor to improve destruction efficacy. TACE is contraindicated when bilirubin levels exceed 50 μmol/L.

- Superselective Transcatheter Arterial Chemoembolization involves guiding the catheter to the smallest artery supplying the tumor. By accurately identifying the feeding artery, this technique increases the rate of complete response and can potentially lead to radical outcomes similar to surgery, RFA, or MWA. This approach also reduces side effects and minimizes the impact on liver function. Generally, superselective TACE is primarily applied to tumors <5 cm, while curative TACE is applied to tumors in stage BCLC-A.

- Repeated TACE, with or without surgery or ablation, continues to effectively prolong overall survival for patients with inoperable HCC.

**** Clinical Question 36:*** *What are the treatment options for patients with intermediate-stage HCC (BCLC-B) who are not suitable for TACE?*

*** Recommendation 36:**

- Patients with intermediate-stage HCC (BCLC-B) are considered unsuitable for TACE if they meet any of the following criteria:

- High likelihood of becoming refractory to TACE if they fall outside the Up-to-7 criteria (sum of the number of lesions and the largest lesion size in cm ≥7).

- Risk of liver function decline to Child-Pugh B after TACE, especially in cases with bilobar lesions.

- Risk of non-response to TACE due to large or infiltrative tumors, poor differentiation, or sarcomatous transformation following TACE.

Treatment strategies for patients with intermediate-stage HCC (BCLC-B) unsuitable for TACE:

- First-line treatment should involve Tyrosine Kinase Inhibitors (TKIs) or immunotherapy combinations with high response rates. Approved regimens include: Atezolizumab in combination with Bevacizumab, Sorafenib, or Lenvatinib.

- Sequential treatment, such as initial administration of Sorafenib or Lenvatinib followed by selective TACE, may benefit patients due to the synergistic mechanism of action.

- A multidisciplinary consultation is required to assess the patient's condition and determine the optimal timing for treatment switching.

- TACE should be combined with systemic therapy for patients with large, multifocal HCCs who are unsuitable for TACE alone.

- Selective Internal Radiation Therapy (SIRT) may be considered as a curative treatment option.

**** Clinical Question 37:*** *What are the criteria for failure or resistance to TACE in HCC, and what is the management strategy after TACE resistance?*

*** Recommendation 37:**

- Refractory TACE: This is defined as a lack of response after more than 3 TACE procedures within 6 months, particularly when the tumor burden remains over 50%, or after two or more unsuccessful TACE treatments.

***- Criteria for TACE Refractoriness*:** A patient is considered refractory if they meet one of the following criteria:

+ Rapid clearance of Lipiodol in the early stages post-procedure.

+ Appearance of new metastatic tumors within the liver.

+ Poor deposition of embolization material (Lipiodol) in the tumor, resulting in persistent tumor hypervascularity on contrast-enhanced imaging (CT, MRI, or Contrast-Enhanced Ultrasound).

+ Development of portal vein thrombosis following TACE.

+ Technical inability to insert the microcatheter into the feeding artery necessary for embolization.

+ Continuously rising tumor markers (AFP). In specialized centers, AFP-L3 and DCP may also be utilized for assessment.

+ Rapid decline in liver function following the intervention.

+ Appearance of extrahepatic metastases.

**** Clinical Question 38:*** *Treatment options after TACE resistance and the strategies for converting from TACE to SIRT or Hepatic Artery Infusion Chemotherapy (HAIC)?*

*** Recommendation 38:** Continuing TACE after a patient has developed resistance may negatively impact liver function.

- Systemic Therapy: Treatment with Tyrosine Kinase Inhibitors (TKIs) with high response rates, such as Sorafenib, Lenvatinib, or Regorafenib, should be considered immediately upon TACE failure (usually after two unsuccessful attempts). However, TKIs are indicated only for patients with preserved liver function (Child-Pugh A).

- Conversion to SIRT: Switching treatment from TACE to Selective Internal Radiation Therapy (SIRT) is recommended for BCLC stage B HCC when there are predictors of TACE failure, or for advanced-stage HCC presenting with branch or portal vein thrombosis.

- HAIC Alternative: When TACE resistance is diagnosed in BCLC stage B or C HCC, Hepatic Artery Infusion Chemotherapy (HAIC) may be an alternative. In patients with HCC (tumors >7 cm, without vascular invasion or metastasis), HAIC using the FOLFOX regimen provides a higher response rate and improved overall survival compared to TACE, while TACE is associated with more frequent complications.

**** Clinical Question 39:*** *What is the follow-up strategy after transarterial chemoembolization (TACE) treatment for HCC?*

*** Recommendation 39:**

Following TACE treatment, patients are monitored in the ward for 3 days to manage post-embolization syndrome and to ensure early detection and management of any complications. Upon discharge, patients are instructed to manage their underlying chronic liver disease, including the use of antiviral therapy for hepatitis B or C, total abstinence from alcohol, and appropriate lifestyle modifications.

- A follow-up examination is conducted after 1 month to assess the tumor response. This evaluation is based on clinical examination, serum AFP (including AFP-L3 and DCP if available), and dynamic CT or MRI of the liver and biliary tract.

- If the liver tumor exhibits persistent hypervascularity, a second TACE session is indicated, or an alternative appropriate treatment method is selected.

- If a complete response is achieved, periodic monitoring every 3 months is mandatory. This surveillance aims to:

+ Track post-treatment survival time.

+ Assess disease progression to determine the feasibility of curative interventions (hepatectomy, liver transplantation, RFA, or MWA).

+ Detect local recurrence or distant metastasis to facilitate a timely switch to alternative treatment methods through multidisciplinary consultation.

L. Treatment of HCC by selective internal radiation therapy (SIRT) and A-SIRT (with 2 recommendations):

**** Clinical Question 40:*** *What are the mechanisms, indications, efficacy, and advantages of treating HCC with selective internal radiation therapy (SIRT) using Yttrium-90?*

*** Recommendation 40:**

- *Mechanism:* When radioactive Yttrium-90 (^{90}Y) microspheres are injected into the artery supplying the liver tumor, they lodge in the small arterial branches within the tumor, causing embolization. The tumor is destroyed via two mechanisms: the reduction of tumor nourishment (ischemia) and the emission of beta radiation (0,93 MeV) from the radioactive isotope (^{90}Y) attached to the microspheres. This radiation destroys cancer cells and reduces or eliminates the liver tumor with minimal impact on surrounding healthy tissue.

- *Indications:* Selective Internal Radiation Therapy with (^{90}Y) (SIRT) is indicated for patients with HCC who are no longer candidates for surgery and have a median overall survival time of less

than 30 months. This method is equivalent to TACE in efficacy but is associated with fewer complications, fewer required interventions, reduced hospital stays, and lower recurrence rates. It can be applied even in cases involving portal vein thrombosis.

- Optimal Selection Criteria: The best indications for SIRT include liver tumors ≤ 10cm with a single arterial blood supply, no hepatic arteriovenous shunts, and no extrahepatic metastases. Patients should have a good performance status, compensated liver function (Child-Pugh A or B), and a liver-pulmonary shunt <20% as determined by Tc-99m MAA scintigraphy. Additionally, patients should have no prior history of liver radiotherapy and a high likelihood of a favorable prognostic response to radiation.

**** Clinical Question 41:*** *What are the indications, efficacy, and advantages of treating HCC with radiation segmentectomy (A-SIRT)?*

*** Recommendation 41:** The A-SIRT method (also known as ablative SIRT or radiation segmentectomy) involves the super-selective delivery of a high dose of radioactive substances ≥200 Gy into the segmental or subsegmental artery supplying the tumor. This technique maximizes the cytotoxic effect on the tumor region, destroying the malignancy along with the surrounding healthy liver parenchyma within the localized target area. A-SIRT is indicated as an alternative treatment for patients with HCC presenting with a solitary tumor ≤5 cm confined to 1-2 segments, particularly in cases where surgical resection or thermal ablation is no longer clinically indicated.

M. Treatment of HCC using external beam radiation therapy and stereotactic body radiation therapy (with 2 recommendations):

**** Clinical Question 42:*** *Where does external beam radiation therapy (EBRT) play a role in the treatment of HCC?*

*** Recommendation 42:** In recent years, the application of advanced External Beam Radiation Therapy (EBRT) techniques, such as Stereotactic Body Radiation Therapy (SBRT) and Proton Therapy, has provided an additional effective and minimally invasive treatment option for patients with early, intermediate, and advanced-stage HCC. Radiotherapy can be utilized as a bridge therapy for patients awaiting liver transplantation to prevent tumor progression, adjuvant therapy following embolization (e.g., TACE) to enhance local control or as combination therapy with targeted agents or immunotherapy for advanced-stage patients, particularly those presenting with portal vein tumor thrombosis (PVTT).

*** *Clinical Question 43:*** *What is the role of stereotactic body radiation therapy (SBRT) in the treatment of HCC and the efficacy of combining SBRT with TACE for intermediate-stage HCC?*

*** Recommendation 43:** Stereotactic Body Radiation Therapy (SBRT) is a radical treatment option for HCC that is unresectable or unsuitable for thermal ablation (RFA/MWA), such as tumors >3cm or lesions located near critical structures like major blood vessels, the diaphragm, or the gallbladder. SBRT serves as an effective bridging therapy for patients awaiting liver transplantation and is a valuable modality for managing portal vein tumor thrombosis (PVTT). Additionally, SBRT is indicated for treating residual HCC following TACE or in combination with systemic therapies like Sorafenib or Lenvatinib for BCLC-C patients with portal vein invasion. This minimally invasive method is characterized by minimal side effects and a high safety profile. Careful patient selection is essential, considering the BCLC stage, Child-Pugh score, tumor location, tumor size, and the volume of the uninvolved (healthy) liver. Strict adherence to technical protocols is mandatory, including

respiratory motion management (e.g., abdominal compression, 4DCT) and precise dose selection based on the mean liver dose and the functional liver remnant. The combination of SBRT and TACE results in significantly higher long-term survival rates compared to TACE monotherapy for patients with intermediate-stage HCC.

N. Treatment of HCC with systemic chemotherapy (with 1 recommendation):

**** Clinical Question 44:*** *What is the role of hepatic arterial infusion chemotherapy (HAIC) in the treatment of HCC?*

*** Recommendation 44:**

- Hepatic arterial infusion chemotherapy (HAIC) allows for the delivery of chemotherapy at high concentrations directly into liver tumors and portal vein thrombi over an extended period. This approach reduces systemic side effects by utilizing the "first-pass effect" during initial hepatic metabolism. HAIC is a suitable intervention for patients with Child-Pugh B and C stage HCC and serves as an effective locoregional treatment, particularly in advanced stages of the disease.

- Recent clinical evidence suggests that HAIC is as effective as leading systemic therapies or other transarterial interventions for advanced HCC. Furthermore, combining HAIC with systemic treatments, including immunotherapy, demonstrates promising synergistic effects that enhance tumor response and prolong survival. For patients who are ineligible for or have failed systemic therapies, HAIC remains a viable treatment option. Additionally, the use of adjuvant HAIC following hepatectomy has been shown to reduce recurrence rates and improve overall survival. Integrating HAIC into a multidisciplinary management strategy maximizes tumor response and improves patient survival outcomes.

O. Systemic treatment of HCC (with 2 recommendations):

**** Clinical Question 45:*** *What are the indications for systemic treatment in advanced-stage HCC?*

*** Recommendation 45:**

- Systemic therapy is indicated for patients with advanced-stage HCC (BCLC-C) who are no longer candidates for surgery, embolization, or ablation, or for those who have progressed after transarterial chemoembolization (TACE).

- Eligible patients should have preserved liver function (primarily Child-Pugh A, though selected Child-Pugh B cases may be considered) and a favorable performance status (ECOG PS 0-1 or 0-2).

- Systemic therapy offers a significant opportunity to prolong patient survival. Tyrosine Kinase Inhibitors (TKIs) play a foundational role in this setting, although the current clinical trend emphasizes the combination of these agents with immunotherapy to enhance therapeutic outcomes.

**** Clinical Question 46:*** *What are the systemic treatment regimens for advanced-stage HCC?*

*** Recommendation 46:**

- First-line systemic treatment:

+ The preferred first-line regimen is Atezolizumab (1200 mg IV on day 1) combined with Bevacizumab (15 mg/kg IV on day 1, 21-day cycle). Both drugs are highly tolerable with low toxicity. However, patients must undergo gastroscopy to manage the risk of esophageal variceal rupture (e.g., ligation or beta-blockers) prior to treatment. Bevacizumab is contraindicated in patients with severe gastrointestinal bleeding within the past 6 months or platelet counts below 75 G/L. It is a relative contraindication in patients with active autoimmune disease.

+ Another preferred regimen is dual immunotherapy with Tremelimumab + Durvalumab. Durvalumab is a monoclonal antibody that binds to the PD-L1 protein on the surface of cancer cells. This prevents cancer cells from binding to the PD-1 receptor on T cells, thereby releasing and reactivating T cells to attack and destroy the tumor. Meanwhile, Tremelimumab binds to the CTLA-4 protein on the surface of T cells. Therefore, it competes with the B7 protein of antigen-presenting cells (APCs), preventing CTLA-4 from binding to B7 and reactivating T cells. The combination of these two drugs creates a dual immunotherapy effect, enhancing the activation and function of T cells at multiple stages of the immune response, maximizing the immune response against the tumor. Dosage: a single dose of Tremelimumab 300 mg combined with Durvalumab 1500 mg every 4 weeks.

+ Other regimens using small molecule drugs are indicated in first-line treatment such as:

. Lenvatinib is an oral polykinase inhibitor (at a dose of 12 mg/day for adults 60 kg or heavier and 8 mg/day for those under 60 kg).

. Sorafenib (at a dose of 800 mg/day - divided into 2 doses/day). Sorafenib is indicated in patients with Child-Pugh A and B.

- Systemic treatment in step 2: The choice of treatment will depend on the regimen used in step 1:

If step 1 was Atezolizumab/Bevacizumab or Durvalumab/Tremelimumab, then step 2 should be a tyrosine kinase inhibitor (TKI).

If step 1 was a TKI (Sorafenib/Lenvatinib), then step 2 could be another TKI (Cabozantinib is a MET, VEGFR2, AXL, RET inhibitor) and Regorafenib (an oral TKI with a structure similar to Sorafenib), Ramucirumab (a monoclonal antibody that specifically inhibits the VEGFR-2 receptor) along with immune checkpoint inhibitors (Durvalumab, Nivolumab, Pembrolizumab with a monotherapy anti-PD-1 mechanism).

P. Palliative care, supportive treatment, and nutrition in HCC (with 2 recommendations):

**** Clinical Question 47:*** *What are the components of palliative care and supportive treatment for HCC??*

*** Recommendation 47:**

- Palliative Care for HCC (Best Supportive Care): This is administered when the patient reaches the terminal stage (BCLC D), characterized by a very poor performance status (PS 3-4) or severe decompensated liver function (Child-Pugh C), or when specific anti-tumor treatments are no longer appropriate. The primary goal is symptom control and enhancing the quality of life. This includes pain management (utilizing acetaminophen or opioids based on severity), nutritional support, and psychological counseling. Palliative radiotherapy may be indicated to alleviate pain from bone or brain metastases or to reduce symptoms caused by large liver tumors compressing adjacent tissues.

- Supportive treatment: This involves managing underlying chronic liver diseases, providing nutritional interventions to improve general health, and treating co-existing medical conditions.

**** Clinical Question 48:*** *What is the role of nutritional support in patients with HCC?*

*** Recommendation 48:** Nutrition is currently recognized as one of the five essential pillars in the treatment of liver cancer, playing a critical role in improving overall health and enhancing the patient's quality of life. A proper diet helps improve appetite, prevent muscle atrophy (sarcopenia), reduce ascites, and prevent hepatic encephalopathy (hepatic coma), while avoiding liver toxicity or an increased metabolic burden on the organ.

The diet should include adequate calories, carbohydrates, and protein, with a focus on plant-based sources such as beans and tofu as well as lean animal proteins. Patients are encouraged to consume avocados, beans, and nuts containing healthy unsaturated fats. Conversely, unhealthy fats, including saturated fats and certain cooking oils, should be eliminated. Alcohol must be strictly avoided. Adequate intake of B vitamins is recommended to improve appetite and combat fatigue. Additionally, a light meal before bedtime is advised to maintain energy levels and support metabolic health.

Q. Follow-up and re-examination (with 1 recommendation):

**** Clinical Question 49:*** *What are the important considerations regarding post-treatment monitoring and follow-up appointments for HCC?*

*** Recommendation 49:**

- Patients should be monitored regularly after treatment to detect recurrence or disease progression.

- For patients after radical treatment (liver resection, tumor ablation) or local/regional treatment: Monitoring should include clinical examination, liver function tests, biomarkers (AFP and PIVKA-II), and dynamic imaging (CT or MRI). The recommended frequency is every 3–6 months for the first 2 years, followed by every 6 months thereafter. Monitoring should continue for at least 5 years.

- For patients undergoing systemic treatment: Response should be assessed with periodic imaging of the chest, abdomen, and pelvis. Serum AFP levels (if initially elevated) should be monitored, as changes in AFP are closely related to treatment response and survival. If recurrence is detected, the patient should be re-evaluated according to standardized diagnostic procedures.

R. New proposed treatment protocols for HCC, updated research on immunotherapy in HCC, and the issue of HCC in the elderly (with 3 recommendations):

** **Clinical Question 50:** What is the new proposed treatment protocol for hepatocellular carcinoma?*

*** Recommendation 50:** This protocol is applicable for patients with preserved liver function (Child-Pugh A/B), good performance status (PS 0–2), and no evidence of extrahepatic metastases:

- In the Absence of Vascular Invasion:

+ Solitary tumor of any size (Stage IA): Perform surgical resection or thermal ablation (RFA/MWA) if the tumor is ≤ 5cm If resection is not feasible (Stage IB), TACE, DEB-TACE, SIRT, or ablation (if ≤ 5cm) is indicated; liver transplantation should also be considered (based on Up-to-7 criteria).

+ Multifocal tumors (≥2 tumors) of any size (Stage IIA): If resectable, perform surgical resection or ablation (for ≤ 3 tumors and size ≤ 5 cm. Other options include TACE, DEB-TACE, or SIRT for moderately or highly differentiated tumors. Combined approaches such as hepatectomy + TACE, hepatectomy + RFA/MWA, or liver transplantation (per Up-to-7 criteria) are also recommended).

- In the Presence of Vascular Invasion:

+ Solitary tumor of any size (Stage IIIA): If resectable, perform surgical resection or utilize Hepatic Arterial Infusion Chemotherapy (HAIC), SIRT, and systemic therapy. If unresectable (Stage IIIB), prioritize systemic therapy, HAIC, and SIRT.

+ Multifocal tumors (≥2 tumors) of any size (Stage IVA): If resectable, use a combination of systemic therapy, HAIC, SIRT, and surgical resection; combined resection with TACE/DEB-TACE or RFA/MWA should be considered. If unresectable (Stage IVB), the recommended strategy includes systemic therapy, HAIC, SIRT, and SBRT.

Clinical Question 51: *What are the latest research updates on immunotherapy in HCC?*

*** Recommendation 51:** New research focusing on combination immunotherapy and advances in clinical application has significantly enhanced HCC treatment outcomes and patient health. Immune checkpoint inhibitors (ICIs) targeting the PD-1 receptor/PD-L1 pathway and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) have demonstrated substantial clinical benefits, particularly when used in combination therapies. Recent studies have established the combination of anti-PD-L1 and anti-vascular endothelial growth factor (anti-VEGF) as the new first-line treatment standard for advanced HCC. Future directions for immunotherapy include exploring multi-mechanism approaches, bispecific antibodies, and personalized treatment strategies guided by specific molecular biomarkers.

Clinical Question 52: *What are the considerations regarding liver cancer, and hepatobiliary and pancreatic cancers in general, in the elderly?*

*** Recommendation 52:** Advanced age is a major risk factor for cancer in general and specifically for liver, biliary, and pancreatic malignancies. Aging and carcinogenesis share several biological characteristics, suggesting that slowing the biological aging process may be a crucial factor in cancer prevention. It is essential to avoid both undertreatment and overtreatment in elderly patients. Clinicians must recognize that cancer treatment can accelerate the aging process, while aging itself may limit available treatment options due to reduced physiological reserve. Effective prevention, appropriate exercise, and optimized nutrition are fundamental. A combination of traditional and modern medicine in screening, monitoring, and supportive care can significantly improve the health of the elderly and help prevent the development of cancer.

VIETNAM ASSOCIATION FOR
THE STUDY OF LIVER DISEASES,
VSHBPS & VASLD-MIT

SOCIALIST REPUBLIC OF VIETNAM
Independence – Freedom – Happiness

Hanoi, April 5th, 2026

DECISION

Regarding the promulgation of the "Clinical Practice Guidelines for the Diagnosis and treatment of HCC in Vietnam"
(Updated Version following the 2026 Guidelines of the Vietnamese Ministry of Health) by the Vietnam Association for the Study of Liver Diseases (VASLD), VSHBPS, and VASLD-MIT.

President of the Vietnam Association for the Study of Liver Diseases (VASLD),

Founding President of VSHBPS and President of VASLD-MIT

Pursuant to the functions and powers of the President of the Vietnam Association for the Study of Liver Diseases (VASLD), the Founding President of VSHBPS, and the President of VASLD-MIT:

HEREBY DECIDES:

Article 1. To officially promulgate the "Clinical Practice Guidelines for the Diagnosis and treatment of HCC in Vietnam" (Updated Version following the 2026 Guidelines of the Vietnamese Ministry of Health), as jointly developed by the Vietnam Association for the Study of Liver Diseases (VASLD), VSHBPS, and VASLD-MIT.

Article 2. The "Clinical Practice Guidelines for the Diagnosis and treatment of HCC in Vietnam" (Updated Version following the 2026 Guidelines of the Vietnamese Ministry of Health) of the Vietnam Association for the Study of Liver Diseases (VASLD), VSHBPS and VASLD-MIT shall serve as the primary guiding document for clinical application across all medical facilities.

Article 3. This Decision shall take effect immediately upon the date of signing and formal promulgation./.

President of VASLD,
Founding President of VSHBPS
& President of VASLD-MIT

Major General, Professor Le Trung Hai MD, PhD

CLINICAL PRACTICE GUIDELINES: ADVANCES IN MINIMALLY INVASIVE TREATMENT FOR HEPATOBILIARY AND PANCREATIC DISEASES IN VIETNAM

(2026 Updated Version: Including 47 Clinical Recommendations)

A. General recommendations (with 1 recommendation):

*** *Clinical Question 1*:** *What are the recent advancements and demonstrated clinical advantages of minimally invasive therapy for hepatobiliary and pancreatic diseases in Vietnam?*

*** Recommendation 1:** Substantial progress has been made in interventional and minimally invasive surgical approaches for hepatobiliary and pancreatic (HBP) diseases in Vietnam. Key advancements include:

- Minimally Invasive Interventions for Biliary and Pancreatic Diseases:

+ Use of percutaneous (or via Kehr/T-tube tract) laser or electrohydraulic lithotripsy for the management of complex bile duct stones.

+ Minimally invasive management of vascular and biliary complications following liver transplantation.

+ Application of Endoscopic Retrograde Cholangiopancreatography (ERCP) in the treatment of bile duct stones and pancreatic duct pathologies.

+ Bile duct drainage under Endoscopic Ultrasound (EUS) guidance.

+ Endoscopic bile duct drainage for hilar strictures using a combined ERCP–EUS approach, along with minimally invasive management of postoperative biliary and lymphatic fistulas.

+ EUS- or ERCP/EUS-guided pancreatic duct drainage, step-up approaches for necrotizing pancreatitis, and drainage of postoperative pancreatic fistulas.

+ Endoscopic treatment protocol for pancreatic cysts and outcomes of pancreatic cyst ablation under EUS guidance.

+ EUS-guided intratumoral injection therapy for pancreatic cancer and other pancreatic masses.

- Minimally invasive interventions for liver diseases, including portal vein embolization performed prior to hepatectomy in patients with hepatocellular carcinoma (HCC):

+ Radiofrequency Ablation (RFA) and Microwave Ablation (MWA) for the treatment of hepatocellular carcinoma (HCC).

+ Transarterial embolization techniques for the management of HCC.

+ Combined portal vein and hepatic vein embolization (PVE/HVE) to induce future liver remnant (FLR) hypertrophy prior to major hepatectomy in HCC patients.

+ Selective Internal Radiation Therapy (SIRT) for targeted embolization in HCC management.

- High-Intensity Focused Ultrasound (HIFU) therapy for the treatment of liver and pancreatic malignancies.

- Minimally invasive surgery for hepatobiliary and pancreatic diseases:

+ Laparoscopic donor hepatectomy and liver transplantation.

+ Minimally invasive Associating Liver Partition and Portal vein ligation for Staged Hepatectomy (ALPPS) procedure.

+ Laparoscopic surgery for hepatocellular carcinoma.

+ Laparoscopic and robotic surgery for pancreatic cancer.

+ Laparoscopic pancreaticoduodenectomy with superior mesenteric artery (SMA)-first approach.

+ Minimally invasive surgery for chronic pancreatitis.

+ Minimally invasive cystogastrostomy via mini-laparotomy for large pancreatic pseudocysts.

+ Laparoscopic management of gallstone disease.

The advantages of interventional and minimally invasive surgical treatments for hepatobiliary and pancreatic diseases are well established. These approaches demonstrate high efficacy and safety while maintaining minimal invasiveness. Notable benefits include reduced postoperative pain, lower complication rates, accelerated recovery, shorter hospital stays, decreased healthcare costs, improved cosmetic outcomes, and broad applicability across different levels of healthcare facilities.

B. Recommendations on minimally invasive interventions for biliary and pancreatic diseases (with 25 recommendations):

*** *Clinical Question 2*:** *Application of percutaneous laser lithotripsy in the management of bile duct stones?*

*** Recommendation 2:** The holmium laser delivers highly localized and precise energy with strong stone fragmentation capability, thereby reducing the duration of lithotripsy. This technique has been widely adopted in the management of bile duct stones, particularly in cases of intrahepatic bile duct stones and common bile duct (CBD) stones where ERCP is contraindicated or unsuccessful, or for the treatment of residual or recurrent stones. Key technical aspects include the use of regional anesthesia, selection of an appropriate access route, tract dilation, laser lithotripsy, and stone retrieval via basket extraction or irrigation. Outcome assessment is primarily conducted through cholangioscopic evaluation. The reported complete stone clearance rate is approximately 80%, with residual stones observed in about 20% of cases.

*** *Clinical Question 3*:** *Comparative Advantages and Disadvantages of Percutaneous Electrohydraulic Lithotripsy and Holmium Laser Lithotripsy?*

*** Recommendation 3:** In general, holmium laser lithotripsy demonstrates superior performance owing to its faster stone fragmentation, shorter treatment duration, and overall cost-effectiveness. The technique offers additional advantages, including effective fragmentation of small stones, high operational flexibility, minimal energy loss, enhanced safety due to limited tissue penetration depth, and a reduced risk of collateral injury. Conversely, electrohydraulic lithotripsy (EHL) is characterized by its low equipment cost and the use of small, flexible probes that can be easily integrated with flexible endoscopes. However, EHL is limited by lower probe durability, less localized energy delivery, reduced fragmentation efficiency, and slower stone fragmentation rates compared with laser lithotripsy.

*** *Clinical Question 4*:** *Indications, outcomes, and advantages of percutaneous gallbladder lithotripsy?*

*** Recommendation 4:** Percutaneous Gallbladder Lithotripsy with Holmium Laser is a non-surgical, general anesthesia-free technique for the management of gallstones, offering significant value for patients at high surgical risk. This approach enables preservation of a functional gallbladder while effectively achieving stone clearance. Recent advancements have facilitated the application of one-stage percutaneous gallbladder lithotripsy with gallbladder closure, achieving a complete stone clearance rate of approximately 95%. The procedure is minimally invasive, allowing gallbladder preservation, and providing a hospital stay duration comparable to or shorter than that of laparoscopic cholecystectomy. Indications include patients

with high operative risk, elderly individuals, or those seeking gallbladder preservation, provided that strict selection criteria are met. Outcomes demonstrate a stone clearance rate exceeding 95%, low residual stone and complication rates, and a stone recurrence rate below 10%.

***** ***Clinical Question 5:*** *Procedure of percutaneous gallbladder laser lithotripsy?*

***** **Recommendation 5:** One-stage percutaneous gallbladder lithotripsy with gallbladder closure: ***Procedure overview***

The procedure is performed under endotracheal general anesthesia. Using ultrasound guidance, the puncture site is identified, followed by a small skin incision and needle access to the gallbladder. A guidewire is inserted, and the tract is sequentially dilated to approximately 16 Fr. A rigid cholangioscope is introduced into the gallbladder for visualization. Holmium laser lithotripsy is then performed to fragment and remove stones. Ultrasound, fluoroscopy, and direct endoscopic inspection are used to confirm complete stone clearance. Following lithotripsy, the gallbladder wall is closed in two layers, and a Foley catheter drain is placed for bile drainage monitoring. The drain is typically removed after 24 hours, patients are discharged within 1–3 days, and skin sutures are removed after 10 days.

In elderly or high-risk patients, a two-stage procedure is recommended. Stage 1: Insert a gallbladder drain to remove infected bile and administer antibiotics. Stage 2 (after 7 days): Perform gallbladder lithotripsy. In cases with concomitant CBD stones, access through the gallbladder to the CBD may be used, and stones can be pushed into the duodenum with a balloon. After 7 days, repeat imaging and ultrasound are performed; if stable, the drain is removed and the patient discharged.

*** *Clinical Question 6*:** *Management of biliary and vascular complications after liver transplantation using minimally invasive interventions?*

*** Recommendation 6:** The complication rate following liver transplantation ranges from 10% to 20%. The most common biliary complications are bile leaks and biliary strictures, which can result in severe infections. These are often effectively managed with minimally invasive endoscopic techniques, primarily ERCP with balloon dilation and stent placement, achieving success rates of up to 96%. Vascular complications may include hepatic artery thrombosis, as well as hepatic vein or inferior vena cava stenosis. Imaging and interventional radiology are essential for the early detection and minimally invasive management of these vascular and biliary complications, significantly reducing both mortality and the need for re-transplantation.

*** *Clinical Question 7*:** *Application of Endoscopic Retrograde Cholangio-pancreatography (ERCP) in the treatment of bile duct stones?*

*** Recommendation 7:**

- ERCP is the standard treatment for common bile duct (CBD) stones owing to its safety, minimally invasive nature, and high efficacy, with a stone removal success rate of 85–95%.

- Indications include solitary distal CBD stones, residual or recurrent stones after surgery, and combined procedures with laparoscopic cholecystectomy for one-stage management. Optimal indications also encompass emergency conditions such as suppurative cholangitis, acute pancreatitis secondary to CBD stones, and recurrent stones in high-risk surgical patients.

- Main interventions involve endoscopic sphincterotomy and/or sphincter balloon dilation, followed by stone extraction with or without biliary stenting. Mild complications, including post-ERCP pancreatitis, should be carefully monitored.

Clinical Question 8: *Role of ERCP with large-balloon papillary dilation combined with sphincterotomy for difficult CBD stones?*

*** Recommendation 8:** ERCP with Large-Balloon Papillary Dilation Combined with Sphincterotomy is indicated for difficult common bile duct (CBD) stones, including those with diameter >15 mm, multiple stones, periampullary diverticulum, intradiverticular papilla, distal CBD stricture, or coagulopathy. This technique is simple, technically feasible, and relatively safe for managing large or complex stones. Partial sphincterotomy helps reduce bleeding risk and minimizes the need for lithotripsy. The procedure achieves a complete stone clearance rate of approximately 95%.

Clinical Question 9**:** *Advances in managing difficult CBD stones and techniques to enhance ERCP effectiveness?*

*** Recommendation 9:** Currently, most common bile duct (CBD) stones are extracted using baskets or balloon catheters following endoscopic sphincterotomy (EST). Recently, the introduction of new devices and refined procedural techniques has improved the management of difficult CBD stones, enhancing both safety and stone clearance efficiency.

- Difficult common bile duct (CBD) stones occur in approximately 15-20% of cases and include large stones (>1.5 cm), multiple or irregularly shaped stones, intrahepatic branch or cystic duct stones, impacted distal CBD stones, postsurgical biliary alterations, or biliary strictures.

- Enhanced techniques such as sphincterotomy and large-balloon dilation, particularly their combined application, are now widely utilized, achieving high success rates in managing large and complex stones.

- If complete stone clearance cannot be achieved during ERCP, temporary biliary stent placement may be performed to prevent obstruction and cholangitis until repeat ERCP or surgical intervention.

*** *Clinical Question 10*:** *Advantages of ERCP in the treatment of bile duct stones?*

*** Recommendation 10:** ERCP offers several advantages:

- Applicable for elderly patients, individuals with multiple comorbidities, severe infections, or high surgical risk.

- Effective in managing post-cholelithiasis surgery complications, including residual stones, bile leaks, and recurrent stones.

- Provides rapid relief of acute biliary obstruction, thereby reducing disease severity and facilitating subsequent definitive treatment.

*** *Clinical Question 11*:** *ERCP in treatment of CBD stones in patients with altered anatomy?*

*** Recommendation 11:**

- In patients with Billroth II gastrectomy, conventional ERCP is technically challenging, with intubation success rates of 62-100%, papillary cannulation rates of 88.2-100%, and complication rates of 0-12.5%.

- Technical difficulties include a sharp or narrow afferent loop, adhesions hindering papillary access, elongated afferent limb, and reversed papillary orientation. The procedure requires longer intervention time and high operator expertise.

- Outcomes show papillary access rates >90%, cannulation success ~95%, and overall technical success about 90%. Reported complications include pancreatitis <10%, perforation <3%, and bleeding <5%. Overall, ERCP remains a safe and effective approach for CBD stone management in post-Billroth II gastrectomy patients, with high success and low severe complication rates.

*** *Clinical Question 12*:** *ERCP with pancreatic stent placement for pancreatic duct abnormalities?*

*** Recommendation 12:** ERCP with sphincterotomy, pancreatic duct dilation, and pancreatic stent placement is a minimally invasive technique for managing pancreatic duct abnormalities. The procedure is effective, technically straightforward, and associated with minimal discomfort, short hospitalization, and low overall cost.

*** *Clinical Question 13*:** *Types of EUS-guided biliary drainage (EUS-BD)?*

*** Recommendation 13:** EUS-guided biliary drainage includes:

- ***Transluminal stenting:***

+ Choledochoduodenostomy (EUS-CDS).

+ Hepaticogastrostomy (EUS-HGS).

- ***EUS-guided rendezvous technique*** for retrograde stent placement.

*** *Clinical Question 14*:** *Indications for EUS-guided biliary drainage (EUS-BD)?*

*** Recommendation 14:** EUS-guided biliary drainage is indicated when conventional endoscopic biliary drainage is not feasible or has failed, specifically:

- Failure to access the papilla may occur due to tumor infiltration, duodenal stenosis, altered surgical anatomy, or presence of a duodenal stent.
- Failed ERCP biliary cannulation can result from anatomical alterations or periampullary diverticulum.
- Unsuccessful biliary drainage may also arise from high-level or tortuous strictures or hilar obstructions.

*** *Clinical Question 15*:** *Routes of EUS-guided biliary drainage?*

*** Recommendation 15:**

- Intrahepatic approach:

+ Drainage from the stomach (or jejunum) to B2, B3, or B6 segments.
+ EUS-guided hepaticogastrostomy (HGS).
+ EUS-guided hepaticojejunostomy (HJS).

- Extrahepatic approach:

+ EUS-guided choledochoduodenostomy (CDS).
+ EUS-guided hepaticoduodenostomy (HDS).

- Gallbladder drainage:

+ Indicated for acute cholecystitis in non-surgical candidates.
+ EUS-guided gallbladder drainage (EUS-GBD).

EUS-guided biliary drainage (EUS-BD) serves as an effective alternative to ERCP for biliary decompression, particularly in patients with pancreatic cancer.

**** Clinical Question 16*:** *Indications, contraindications, and outcomes of EUS-guided gallbladder drainage (EUS-GBD)?*

*** Recommendation 16:**

- Indications:

+ Gallbladder drainage in high-risk surgical patients with acute cholecystitis.

+ Internal gallbladder drainage after removal of percutaneous drainage tube in patients not undergoing cholecystectomy.

+ Malignant biliary obstruction in patients where ERCP and conventional ultrasound-guided drainage have failed.

- Contraindications: Suspected gallbladder perforation, biliary peritonitis, massive ascites, severe coagulopathy, or contraindications to anesthesia.

- Outcomes:

+ Technical success rate: 90-100%.

+ Clinical success rate: 72-99%.

+ Adverse event rate: 7-50%. Complications may include: stent misplacement, stent occlusion, bile leakage, peritonitis, pneumoperitoneum, intra-abdominal abscess, recurrent cholecystitis.

**** Clinical Question 17*:** *Endoscopic biliary drainage in hilar strictures with combined ERCP and EUS?*

*** Recommendation 17:**

In patients with malignant hilar biliary obstruction (especially those previously surgically treated), trans-luminal puncture and retrograde stent placement with bridging may be considered.

Key considerations:

- Ensure >50% of liver volume is effectively drained.

- Evaluate PTBD versus ERCP for optimal biliary drainage.

- Decide between partial or complete drainage based on anatomy and disease extent.

- Consider combined EUS and ERCP drainage for complex hilar strictures.

***** ***Clinical Question 18*****: *Management of postoperative biliary or hepatic lymphatic fistula using minimally invasive techniques?*

***** **Recommendation 18:**

Postoperative biliary and hepatic lymphatic fistulae are diagnosed by clinical findings, fluid analysis, and MRI.

- Biliary fistula:

+ Drain above the leak site, with abdominal drainage and lavage.

+ If communicating with the main bile duct → provide drainage.

+ If not communicating → create a fistulous tract.

+ If associated with stricture or transection → place a plastic stent (avoid metallic stents).

- Hepatic lymphatic fistula:

+ Perform percutaneous hepatic lymphangiography under DSA, followed by embolization using a sclerosing agent or biological glue.

+ Outcome: Minimally invasive approaches yield high efficacy and favorable clinical results.

***** ***Clinical Question 19*****: *Indications and outcomes of pancreatic duct drainage under EUS guidance (EUS-PD)?*

*** Recommendation 19:**

- Indications: Pain due to obstructive pancreatitis after failed ERCP, such as:

+ Chronic pancreatitis.

+ Anastomotic stricture after Whipple surgery.

- Outcomes:

+ Technical success: 48-100%.

+ Adverse events: 2-35% (including abdominal pain, acute pancreatitis, pancreatic fluid collection, abscess, bleeding, perforation).

*** *Clinical Question 20*:** *Minimally invasive treatment of infected walled-off pancreatic necrosis (WON) after acute pancreatitis using ERCP/EUS guidance?*

*** Recommendation 20:**

Walled-off pancreatic necrosis (WON) is a complication of acute pancreatitis, occurring in approximately 30-50% of patients with pancreatic necrosis and typically developing around the fourth week after onset. When infection of the necrotic cavity or persistent abdominal pain occurs, minimally invasive interventions under ERCP/EUS guidance should be considered, such as: percutaneous catheter drainage (PCD), percutaneous endoscopic necrosectomy (PEN), endoscopic transluminal drainage (ETD), and endoscopic transgastric necrosectomy (DEN), in which necrosectomy is the key therapeutic step.

Minimally invasive percutaneous endoscopic necrosectomy involves creating a percutaneous tract for endoscope insertion, with the use of a lumen-apposing metal stent (LAMS), esophageal stent, or large-bore catheter systems. Necrotic tissue is then completely removed via the endoscopic transgastric or percutaneous route.

Overall, minimally invasive approaches for infected pancreatic necrosis are highly effective, associated with low complication rates, faster recovery, shorter hospital stays, and reduced treatment costs.

*** *Clinical Question 21*:** *Strategy for minimally invasive intervention in necrotizing pancreatitis?*

*** Recommendation 21:**

Necrotizing pancreatitis is a severe complication of acute pancreatitis and can be fatal if not properly managed. The step-up approach is an effective and safe treatment strategy, beginning with percutaneous drainage and proceeding to further interventions only when necessary. This approach significantly reduces complication rates compared to early open surgery. Favorable outcomes are observed in over 55% of patients after initial percutaneous drainage alone, allowing surgery to be avoided and minimizing post-procedural complications.

*** *Clinical Question 22*:** *EUS-guided drainage of postoperative pancreatic fistula (POPF)?*

*** Recommendation 22:** Postoperative pancreatic fistula (POPF) is a severe complication following pancreaticoduodenectomy, with a mortality rate reaching up to 40%. Endoscopic ultrasound (EUS)-guided drainage of this pancreatic fistula offers a faster resolution and is a feasible option in the management of POPF.

*** *Clinical Question 23*:** *Endoscopic management of pancreatic cysts?*

*** Recommendation 23:**

- For pancreatic pseudocysts: generally, the use of LAMS (Lumen-Apposing Metal Stents) can achieve a treatment success rate of up

to 98%. If there is pancreatic duct obstruction, placing plastic stents can help achieve a success rate of up to 100%.

- For walled-off necrosis (WON) with multiple fluid collections, LAMS application yields result greater than 93%. For WON that does not communicate with the pancreatic duct and has a size of 6-10 cm, using a single-port LAMS results in success rates greater than 94%, and it may be transitioned to plastic stents. For larger cysts (WON) exceeding 10 cm, the use of LAMS and multi-port enhanced plastic stent can achieve a success rate of up to 100% and long-term drainage with plastic stents.

- When the walled-off necrosis extends to the lower abdomen/ pelvis, the combined approach (single or multi-port drainage + percutaneous drainage) achieves a treatment success rate greater than 90%.

*** *Clinical Question 24*:** *Outcomes of EUS-guided ablation of pancreatic cystic neoplasms?*

*** Recommendation 24:** The long-term outcomes following EUS-guided ablation of pancreatic cystic tumors demonstrate a short hospital stay, typically reported at a median of 3.5 days, and a low post-ablation complication rate. The success of EUS-guided chemoablation for pancreatic cysts facilitates a reduction in the need for radiofrequency surveillance

*** *Clinical Question 25*:** *Minimally invasive EUS-guided treatment of insulinoma?*

*** Recommendation 25:** Insulinoma is a rare neuroendocrine tumor (NET) originating from the islet cells of the pancreas. This condition causes hypersecretion of insulin, leading to symptoms of

hypoglycemia. Approximately 90% of insulinomas are benign, and only a very small percentage are malignant, typically associated with larger tumor sizes.

- Endoscopic ultrasound (EUS)-guided absolute ethanol (99-100%) ablation of pancreatic insulinoma is a minimally invasive interventional procedure and a promising therapeutic option for patients with: Insulinomas smaller than 2 cm, post-surgical recurrence, multiple comorbidities or frailty (old age), those who refuse or are unfit for surgery. The overall success rate is generally high, at 95%. Potential post-procedural adverse events include abdominal pain, pancreatitis, bleeding, and pancreatic duct obstruction. Generally, this minimally invasive technique is associated with a low incidence of major early complications and a 10-year overall survival rate of 97.1%. In comparison, the corresponding rates for surgical treatment are 11.2% and 90.7%, respectively.

- EUS-guided Radiofrequency Ablation (RFA) for pancreatic insulinoma provides a clinical efficacy of 95.5% (compared to 100% for surgery), but with a shorter hospital stay than surgery. The adverse event rate is 18%, with no major adverse events reported (the corresponding rates for surgery are 61.8% and 15.7% respectively).

- The combined use of EUS-guided RFA and ethanol injection for pancreatic neuroendocrine tumors (PNETs) is an appropriate treatment indication for small tumors, especially in elderly patients who are unsuitable candidates for surgical resection.

**** Clinical Question 26:*** *Outcomes of EUS-guided RFA for pancreatic cancer?*

*** Recommendation 26:**

- EUS-guided Radiofrequency Ablation (RFA) is a minimally invasive measure identified as a potential treatment for precancerous pancreatic cystic lesions. This method also plays a role in palliative treatment for cases of unresectable pancreatic cancer.

- EUS-guided RFA for unresectable Pancreatic Duct Adenocarcinoma (PDAC) has a technical success rate of 95-100%. The adverse event rate is 13%. It helps achieve clinical improvement in symptom palliation and tumor necrosis after 6 months at a rate of 100%.

C. Recommendations on minimally invasive interventions for hepatocellular carcinoma (HCC) (with 10 recommendations):

*** *Clinical Question 27*:** *Characteristics, Indications, and Influencing Factors of Percutaneous Interventions for Hepatocellular Carcinoma (HCC) using Radiofrequency Ablation (RFA) and Microwave Ablation (MWA)?*

*** Recommendation 27:**

- Radiofrequency Ablation (RFA) and Microwave Ablation (MWA) treatments for Hepatocellular Carcinoma (HCC) are considered curative measures that are highly effective for early-stage HCC. Their mechanism involves local tumor destruction using heat (thermal ablation). These are minimally invasive interventions, with the majority performed percutaneously under ultrasound guidance.

- Percutaneous interventions (RFA and MWA) are indicated for early-stage liver tumors (tumor ≤3cm) but are unsuitable for surgical resection (e.g., in cases of liver cirrhosis with portal hypertension).

- For tumors measuring 3 to 5cm, the combination of RFA/MWA with Trans-arterial Chemoembolization (TACE) should be considered.

*** *Clinical Question 28*:** *Effectiveness of RFA in treating HCC?*

*** Recommendation 28:**

- The efficacy of Radiofrequency Ablation (RFA) for treating HCC shows clinical symptom improvement in nearly 70% of patients.

AFP response (in those with elevated levels before treatment) is observed in over 70%, and tumor response at 1–6 months is approximately 90%. This method results in improved survival time.

- Percutaneous tumor destruction offers survival and recurrence rates similar to surgical resection, especially for liver tumors ≤3 cm. RFA can be chosen as a first-line curative treatment, replacing surgical resection, for HCC cases with a tumor size <3 cm, a single tumor, and good liver function. Indications may be extended to liver tumors >3 cm that are unresectable, which will be treated with a combination of TACE and RFA.

*** *Clinical Question 29*:** *Outcomes of MWA in treating HCC?*

*** Recommendation 29:** Microwave Ablation (MWA) treatment helps achieve complete tumor destruction after one or two MWA sessions. Overall survival time is significantly improved. The one-year disease-free survival rate is nearly 80%. Generally, the MWA efficacy is comparable to RFA, and MWA is superior for larger tumors.

*** *Clinical Question 30*:** *Indications for TACE and Superselective TACE in HCC?*

*** Recommendation 30:**

- Transcatheter Arterial Chemo-Embolization (TACE) is a minimally invasive method. It serves as a palliative treatment and is the standard and first-line therapy indicated for Intermediate-stage HCC (BCLC-B). Additionally, it is used for large or multifocal liver tumors, as a downstaging treatment before surgery or liver transplantation, or in combination with systemic therapy for advanced-stage HCC.

- The implementation of superselective TACE involves advancing the catheter into the smallest arterial branch feeding the tumor. This precisely identifies the tumor-feeding artery, increases the complete response rate after TACE, potentially achieving outcomes comparable to curative treatments like surgery, RFA, or MWA, and helps reduce side effects while minimizing impact on liver function post-TACE.

***Clinical Question 31*:** *Indications, efficacy, and advantages of Selective Internal Radiation Therapy (SIRT) with Yttrium-90 for HCC?*

*** Recommendation 31:** Selective Yttrium-90 Radioembolization (SIRT) is indicated for HCC patients who are unsuitable for surgical resection and have a median overall survival time of less than 30 months.

This method is generally equivalent to TACE but is associated with fewer complications, requires fewer interventions, results in shorter hospital stays, and has a lower recurrence rate. SIRT can be applied even in the presence of portal vein branch thrombosis.

SIRT is best indicated for the following patient and tumor characteristics: tumors ≤10 cm, a single feeding artery, absence of a significant arterioportal shunt, no extrahepatic metastasis, good overall performance status, compensated liver function, hepatopulmonary shunt fraction <20%, tumor responsiveness to radiation, which provides a good prognosis.

***Clinical Question 32*:** *Indications and benefits of Radiation Segmentectomy (Ablative SIRT - A-SIRT) in HCC?*

*** Recommendation 32:** Ablative Selective Internal Radiation Therapy (A-SIRT or Radioembolization) method involves the superselective delivery of a highly concentrated dose of radioactive

material (≥200 Gy) into the segmental or subsegmental artery supplying the tumor. This maximized cytotoxic effect targets the tumor area, destroying the tumor and the surrounding healthy liver parenchyma within the target treatment zone. A-SIRT should be indicated as an alternative treatment for HCC patients with a single tumor ≤5 cm and should only be confined to one to two liver segments in cases where surgical resection or ablation is no longer indicated.

Clinical Question 33*: *Role of Liver Venous Deprivation (LVD) before major hepatectomy?

*** Recommendation 33:** Simultaneous Portal Vein Embolization (PVE) - which is the standard method for liver hypertrophy combined with Hepatic Vein Embolization (HVE) - which aims to block the outflow drainage from the liver significantly increases the speed and degree of preoperative liver hypertrophy before major hepatectomy.

This combined approach thus shortens the waiting time for surgery and reduces the risk of tumor progression. Overall, this is a safe and feasible minimally invasive technique that effectively increases the volume of the Future Liver Remnant (FLR) preoperatively, thereby expanding the indications for liver resection and reducing the rate of post-hepatectomy liver failure. It is important to note that the PVE technique must always be performed before the HVE procedure, both under ultrasound guidance.

Clinical Question 34*: *Role of External Beam Radiotherapy (EBRT) in HCC?

*** Recommendation 34:** In recent years, the application of advanced external beam radiation therapy techniques, such as Stereotactic Body Radiation Therapy (SBRT) and Proton Beam

Therapy, has provided an additional effective and minimally invasive treatment option for patients with early-stage, intermediate-stage, and advanced-stage Hepatocellular Carcinoma (HCC). Radiation therapy can serve as bridging therapy for patients awaiting liver transplantation, adjuvant therapy after transarterial embolization, or be combined with targeted therapy and immunotherapy for the advanced stage that involves portal vein thrombosis.

*** *Clinical Question 35*:** *Role of SBRT in HCC and its combination with TACE in intermediate-stage HCC?*

*** Recommendation 35:** Stereotactic Body Radiation Therapy (SBRT) helps provide curative treatment for HCC that is unresectable or unsuitable for RFA/MWA. This method serves as a bridging therapy for patients awaiting liver transplantation and is used as supportive treatment for portal vein thrombosis. SBRT also helps treat residual HCC after TACE, or can be combined with Sorafenib/ Lenvatinib in patients with BCLC-C and portal vein invasion. This is a minimally invasive method with minimal side effects, and is effective and safe in treating HCC.

Appropriate patient selection is necessary, with attention to BCLC staging, Child-Pugh class, tumor location and size, and healthy liver volume. Strict adherence to the treatment protocol is required, particularly regarding motion management (abdominal compression, 4DCT), and selecting the SBRT dose based on the mean liver dose and healthy liver volume. SBRT combined with TACE results in higher long-term survival compared to TACE alone for patients with intermediate-stage HCC.

*** *Clinical Question 36*:** *Role of High-Intensity Focused Ultrasound (HIFU) in treating liver and pancreatic cancers?*

*** Recommendation 36:** High-Intensity Focused Ultrasound (HIFU) is a non-invasive ablation procedure for liver tumors. It works by concentrating ultrasound energy onto the tumor, causing coagulative necrosis through a thermal effect. HIFU can help achieve a 1-year post-treatment survival rate of 80%. Patients must fast from gas-producing foods for 3 days before treatment and are prohibited from drinking water on the morning of the procedure. The location, size, and morphological characteristics of the tumor and adjacent areas are determined using CT, ultrasound, or MRI. The treatment area is localized, and the lesions are destroyed using ultrasound energy. The total ultrasound time is about 10 minutes, and the treatment time is approximately 30 minutes. Potential side effects include: fatigue, abdominal pain, diarrhea, liver abscess, etc. Liver lesions located too close to the lungs should not be treated to avoid lung damage caused by HIFU. Overall, HIFU is considered a safe and effective method for liver cancer.

For pancreatic cancer, the HIFU treatment method significantly helps patients reduce cancer pain and achieves local destruction of malignant tissue.

D. Recommendations on minimally invasive surgery for hepatobiliary and pancreatic diseases (with 11 recommendations):

*** *Clinical Question 37*:** *Application of laparoscopic surgery in living donor hepatectomy?*

*** Recommendation 37:** The application of laparoscopic liver procurement from living donors is an essential trend, offering a minimally invasive approach with smaller incisions and enhanced cosmetic results. It also provides several surgical advantages, including reduced risk of incisional hernia, less intraoperative blood loss, faster recovery of bowel motility, a shorter hospital stays

(typically discharging patients after 4-5 days), and improved immune function. Laparoscopic liver resection in living donors shows results equivalent to open liver resection. Moreover, the laparoscopic group demonstrates significantly less intraoperative blood loss and a shorter hospital stay. The complication rate after laparoscopic liver procurement in living donors is less than 10%. However, the operative time is longer in the laparoscopic group, averaging 180 minutes.

*** *Clinical Question 38*:** *Key considerations in laparoscopic living donor hepatectomy?*

*** Recommendation 38:** Laparoscopic liver resection for living donor graft procurement should be performed by highly experienced surgeons, utilizing fully equipped facilities. It should be noted that a BMI ≥25, a large graft weight (>1000 ml), and anatomical variations are not absolute contraindications for laparoscopic donor hepatectomy. The technique of Glissonian pedicle approach during liver graft procurement is easy to perform, safe for the donor, and facilitates the dissection of the hilar structures to optimize graft quality. Attention to the technique for handling blood vessels and bile ducts during surgery helps minimize postoperative complications. Overall, to progressively enhance the utilization of minimally invasive laparoscopic liver procurement, it is necessary to standardize and streamline technical procedures, as well as provide training through direct hands-on instruction or online learning.

*** *Clinical Question 39*:** *Role of minimally invasive laparoscopic surgery in ALPPS (Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy)?*

*** Recommendation 39:** For cases of HCC requiring major hepatectomy but where the Future Liver Remnant (FLR) volume is insufficient to allow resection, liver hypertrophy can be achieved using the technique of Associating Liver Partition and Portal vein Ligation for Staged hepatectomy (ALPPS). This technique involves liver parenchymal division and portal vein ligation performed laparoscopically. Overall, ALPPS surgery helps to achieve rapid and effective liver volume increase. This is a safe, minimally invasive technique that opens up treatment opportunities for patients needing major hepatectomy for liver cancer.

*** *Clinical Question 40*:** *Effectiveness and advantages of laparoscopic hepatectomy in HCC?*

*** Recommendation 40:** Laparoscopic Liver Resection (LLR) is a feasible and safe option for treating HCC, particularly for minor resections (such as left lateral segmentectomy and peripheral segmentectomies) and major anatomical resections. This minimally invasive surgery demonstrates high efficacy from an oncological standpoint, with a success rate over 95%, an overall complication rate of just 5%, and virtually no in-hospital deaths reported. Key benefits include minimal blood loss during surgery (approximately 100 ml), rapid postoperative recovery, and a shorter hospital stay. Furthermore, LLR can be safely performed even for large liver tumors accompanied by cirrhosis and portal hypertension, provided the indication is selective and the procedure is executed by an experienced surgeon.

*** *Clinical Question 41*:** *Advantages of laparoscopic and robotic surgery in pancreatic cancer?*

*** Recommendation 41:**

- Laparoscopic surgery has numerous advantages compared to classic open surgery, such as a smaller incision, less postoperative pain, reduced wound infection rates, shorter hospital stays, and better cosmetic outcomes. It should be indicated for pancreatic tumors with a diameter less than 5 cm without metastasis or vascular invasion.

- Laparoscopic surgery can be performed using a hybrid technique. In this technique, after dissection and resection are completed laparoscopically, a small incision is made to exteriorize the segment for the biliary-enteric and gastro-jejunal anastomoses. The pancreatic anastomosis (modified Blumgart technique) is simplified and performed extra-corporeally, which reduces postoperative complications, especially postoperative pancreatic fistula (POPF). This hybrid approach offers several benefits, including expanding the indications for laparoscopic pancreaticoduodenectomy, allowing surgeons to improve their maneuvers, experience, and skills. At the same time, patients benefit from the minimally invasive technique, especially when a fully laparoscopic procedure, including the pancreatic anastomosis, can be performed.

- The Robotic Surgical System features instruments with multi-directional rotation (like a miniature hand), 3D visualization, and a dedicated surgeon console. The maneuvers are executed via robotic arms, which facilitates the performance of complex procedures, such as pancreaticoduodenectomy or total spleen-preserving distal pancreatectomy, with a low conversion rate to open surgery (<5%).

*** *Clinical Question 42*:** *Benefits of "SMA-first approach" in laparoscopic pancreatico - duodenectomy (LPD)?*

*** Recommendation 42:** The application of the Superior Mesenteric Artery (SMA) first approach technique in Laparoscopic Pancreaticoduodenectomy (LPD) shows potential clinical benefits.

These benefits include reduced intraoperative blood loss, a significantly increased number of retrieved lymph nodes, and a trend towards a reduction in major postoperative complications. Specifically, the rates of pancreatic fistula and major complications (Clavien-Dindo ≥III) were observed to be lower in the SMA-first approach group (no major complications) compared to the traditional LPD technique (12.3%). These results suggest that the SMA-first approach can improve oncologic and perioperative outcomes in LPD.

*** *Clinical Question 43*:** *Role of minimally invasive surgery in chronic pancreatitis?*

*** Recommendation 43:** Chronic pancreatitis is characterized by persistent pancreatic inflammation. The combination of laparoscopic surgery (using either the modified Frey procedure or the Puestow/ Partington-Rochelle procedure) and endoscopic pancreatic duct laser lithotripsy has demonstrated good efficacy in treating pancreatic duct stones. This combined approach results in all patients achieving significant pain reduction after treatment and a return to normal activities.

*** *Clinical Question 44*:** *Small-incision cysto-gastrostomy for giant pancreatic pseudocysts?*

*** Recommendation 44:** Surgical treatment for large and giant pancreatic pseudocysts (>10 cm) using a mini-laparotomy incision (approximately 4-5 cm) for cysto-gastrostomy is an option alongside laparoscopic surgery and endoscopic interventions. This approach allows for good patient recovery, reduced pain, a shorter hospital stay, and better cosmetic outcomes.

*** *Clinical Question 45*: *Prevention and management of bile duct injury during laparoscopic cholecystectomy for gallstones?***

*** Recommendation 45:**

The use of Indocyanine Green (ICG) fluorescence during laparoscopic cholecystectomy helps visualize and identify important anatomical landmarks of the extrahepatic bile duct, which can aid in reducing iatrogenic bile duct injury. Other diagnostic imaging methods that can be applied include intraoperative cholangiography (which helps reduce the risk of bile duct injury in acute cholecystitis-95% success rate), intraoperative ultrasound, and endoscopic ultrasound.

Early detection of injury during surgery helps reduce costs and improve quality of life. Surgical repair depends on the characteristics of the injury. The most common repair method is hepaticojejunostomy/ choledocho-jejunostomy, followed by suture repair and Kehr drainage tube placement.

Percutaneous endoscopic intervention and Endoscopic Retrograde Cholangio-pancreatography (ERCP) are used when bile duct injury occurs (for simple bile leaks: temporary stent placement, with a 60-90% success rate in cases of bile duct stricture if flow is maintained). 10-30% of cases are managed with delayed surgery.

*** *Clinical Question 46*: *Laparoscopic common bile duct (CBD) exploration without T-tube drainage, or via cystic duct/ choledochotomy, in recurrent CBD stones?***

*** Recommendation 46:**

Laparoscopic surgery combined with flexible choledochoscopy for extrahepatic common bile duct (CBD) stones without bile duct drainage offers several advantages. These include a high stone clearance rate, effective evaluation of the bile duct, and assessment

of the Oddi sphincter status. The conditions for primary closure of the CBD (i.e., suturing the CBD without external drainage) during laparoscopic surgery combined with choledochoscopy are: complete stone clearance from the bile duct, patent Oddi sphincter, absence of bile duct bleeding, dilated CBD (≥1 cm), experienced surgeon.

Laparoscopic common bile duct (CBD) stone extraction via the cystic duct is indicated for patients with a small number of small CBD stones (stones <1 cm, cystic duct >3 mm) who also require cholecystectomy for cholelithiasis or cholecystitis. The technique involves careful cystic duct dilation and the use of a flexible scope, with stone removal performed using a basket.

Recurrent bile duct stones can be treated endoscopically via a Choledocho-Cysto-Cutaneous fistula tract (formed through the CBD–Gallbladder–Skin) by opening the gallbladder fundus (ensuring the CBD–Gallbladder anastomosis diameter is >2 cm) and extracting stones using a basket or lithotripsy.

*** *Clinical Question 47*:** *Benefits of laparoscopic hepatectomy for intrahepatic bile duct stones?*

*** Recommendation 47:** Laparoscopic liver resection for the treatment of biliary stones is a safe surgery that allows for the complete removal of all stones, excision of the entire pathological bile duct system, and preservation of the healthy bile duct segments. This procedure also offers the other advantages of laparoscopic surgery, such as fewer complications, less postoperative pain, faster recovery, excellent cosmetic results, and a shorter hospital stay.

THE VIETNAM ASSOCIATION FOR
THE STUDY OF LIVER DISEASES,
VSHBPS & VASLD-MIT

SOCIALIST REPUBLIC OF VIETNAM
Independence – Freedom – Happiness

Hanoi, April 5th, 2026

DECISION

Regarding the promulgation of the "Clinical Practice Guidelines for Advances in Minimally invasive treatment for Hepatobiliary and Pancreatic Diseases in Vietnam" by the Vietnamese Association for the Study of Liver Diseases (VASLD), VSHBPS and VASLD-MIT

The President of the Vietnam Association for the Study of Liver Diseases (VASLD), Founding President of VSHPBS and President of VASLD-MIT

Pursuant to the authorities and responsibilities vested in the President of the Vietnam Association for the Study of Liver Diseases, the Founding President of VSHBPS, and the President of VASLD-MIT

HEREBY DECIDES:

Article 1. To officially promulgate the "Clinical Practice Guidelines for Advances in Minimally Invasive Treatment for Hepatobiliary and Pancreatic Diseases in Vietnam" (2026 Updated Version), as developed by the Vietnam Association for the Study of Liver Diseases (VASLD), VSHBPS, and VASLD-MIT.

Article 2. The "Clinical Practice Guidelines for Advances in Minimally Invasive Treatment for Hepatobiliary and Pancreatic Diseases in Vietnam" (Updated version 2026) of the Vietnam Association for the Study of Liver Diseases (VASLD), VSHBPS and VASLD-MIT shall serve as a guiding document to be applied across all medical facilities.

Article 3. This Decision shall take effect from the date of signing and promulgation./.

President of VASLD,
Founding President of VSHBPS
& President of VASLD-MIT

HỘI GAN MẬT VIỆT NAM
TRUNG ƯƠNG HỘI

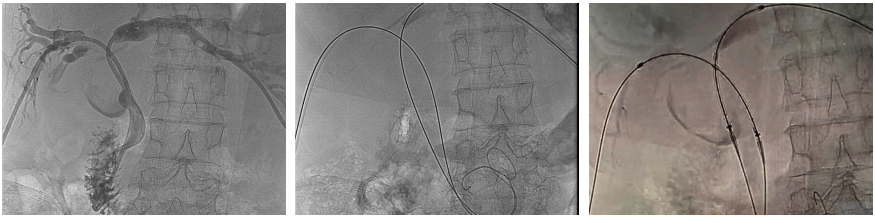
Major General, Professor Le Trung Hai MD, PhD

REPRESENTATIVE CLINICAL ILLUSTRATIONS

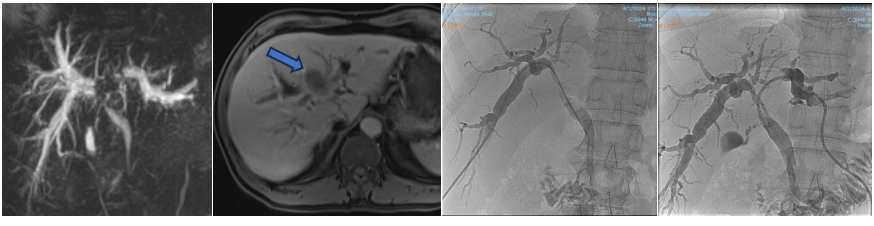
(Featuring clinical imaging from University of Medicine and Pharmacy - Hue University, Hanoi Medical University Hospital, Hue Central Hospital, Cho Ray Hospital, HCMC UMC, Viet Duc Hospital, MCH 108, MH 103, NPH, and other affiliated medical centers)

1. Interventional Radiology in Hepatobiliary and Pancreatic Diseases.

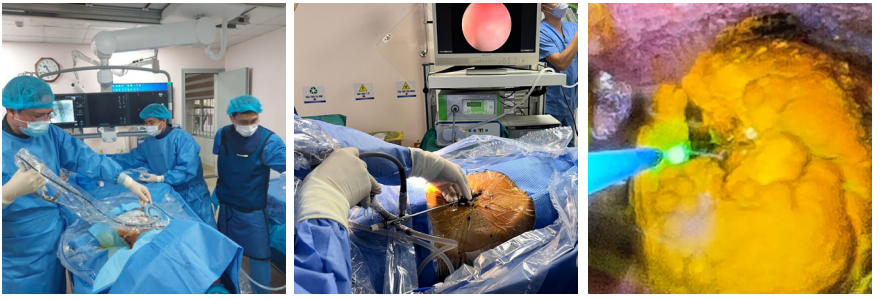
Images 1-3: DEB-TACE for the treatment of hepatocellular carcinoma (HCC) with complete response.



Images 4-6: Bilateral kissing stent placement technique (side-by-side) for Bismuth–Corlette Type IIIA hilar cholangiocarcinoma.

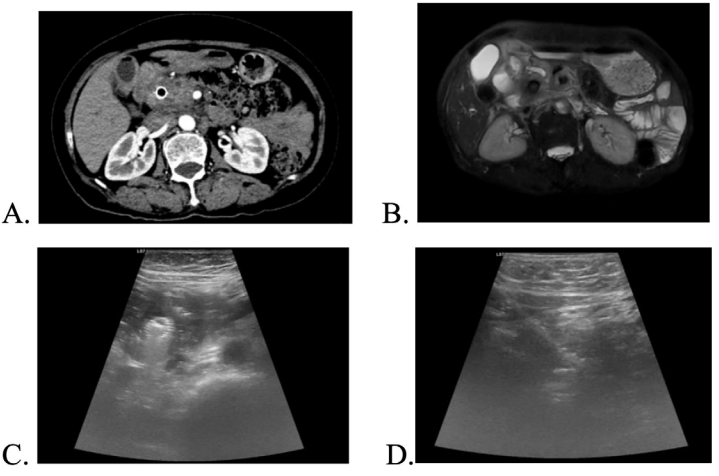


Series of Images 7: Y-stent placement for Bismuth–Corlette Type IIIB hilar cholangiocarcinoma.



Images 8-10: Endoscopic lithotripsy using Holmium laser for the management of cholelithiasis.

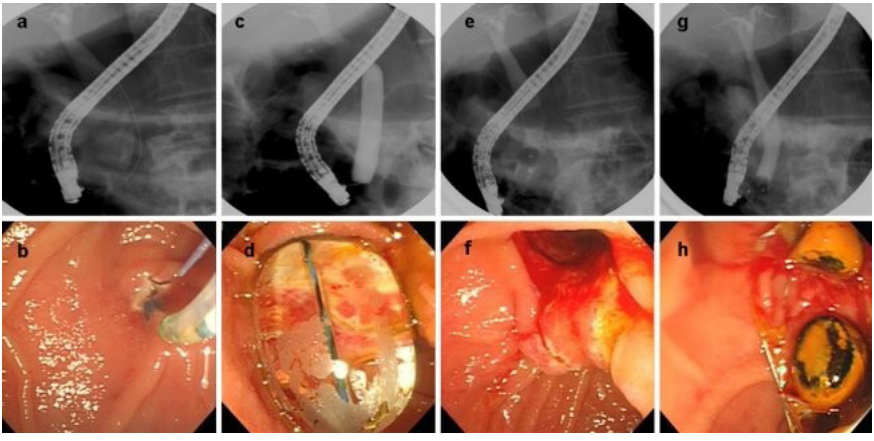
Images 11-13: Percutaneous laser lithotripsy for the management of gallstones.



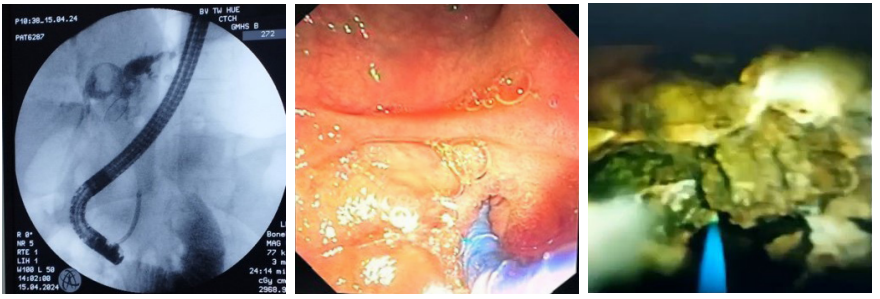
Series of Images 14: Multimodality-guided biopsy for the diagnosis of pancreatic cancer.

2. Interventional Endoscopy in Hepatobiliary and Pancreatic (HBP) Diseases.

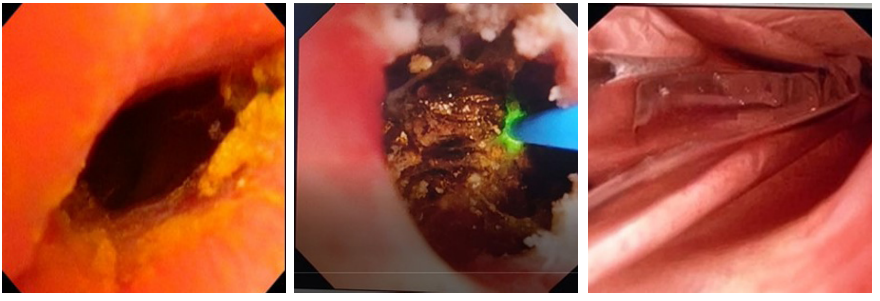
Images 15-17: Extraction of pancreatic duct stones via conventional ERCP.



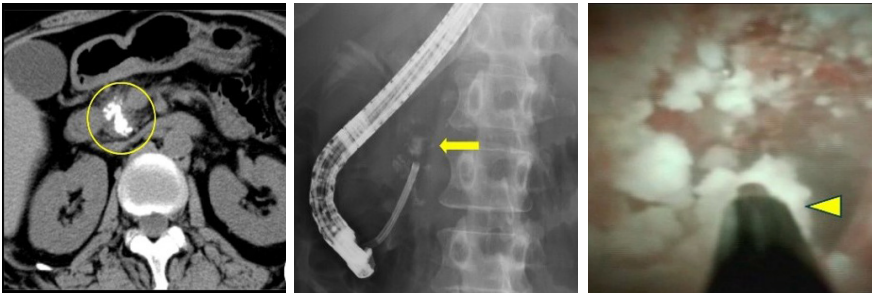
Series of Images 18: Endoscopic sphincterotomy and large-balloon dilation for biliary stone extraction.



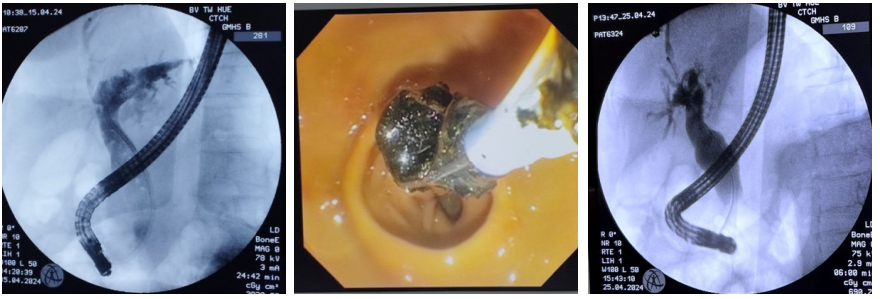
Images 19-23: Management of intrahepatic bile duct stones and associated biliary stricture using SpyGlass™-guided laser lithotripsy.



Images 24-26: Management of intrahepatic stones and associated biliary stricture via lithotripsy and ductal dilation.

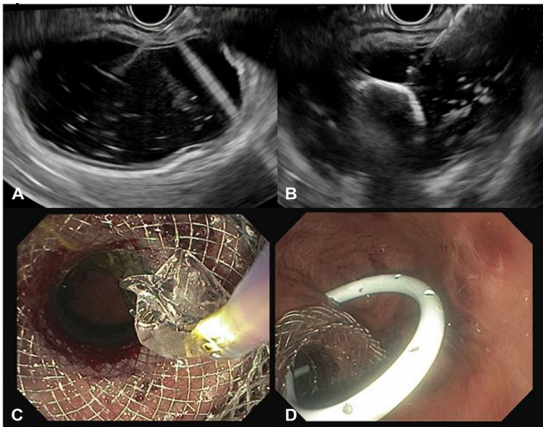


Images 27-29: Endoscopic lithotripsy of pancreatic duct stones.

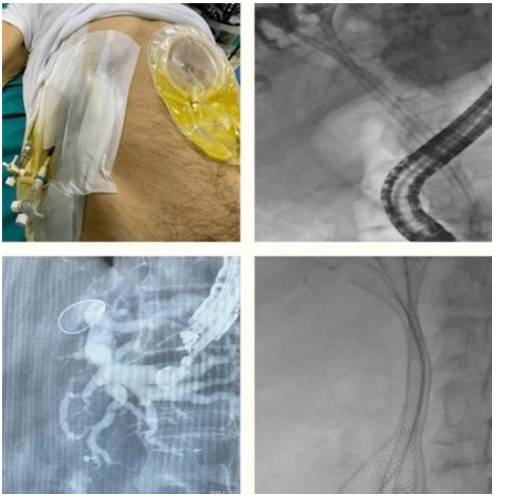


Images 30-32: Fragmentation and extraction of common bile duct (CBD) stones Visualization of the primary stone fragmented into multiple smaller pieces, seen migrating distally toward the lower common bile duct. Deployment of an extraction basket to capture and remove the stone fragments through the expanded papilla into the duodenum. Final cholangiogram confirming complete clearance of all biliary stone remnants and demonstrating restored ductal patency.

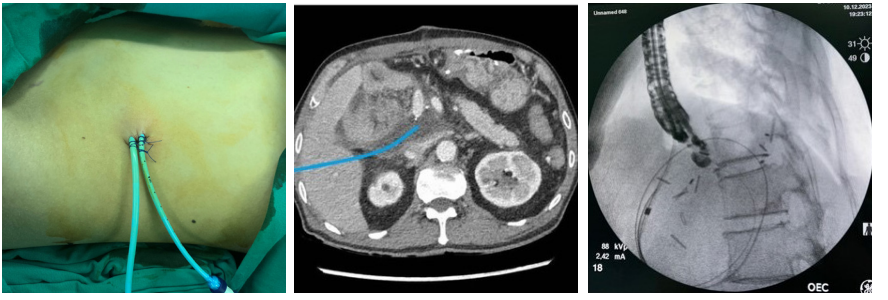
Image 33: EUS - FNA of pancreatic tumor.



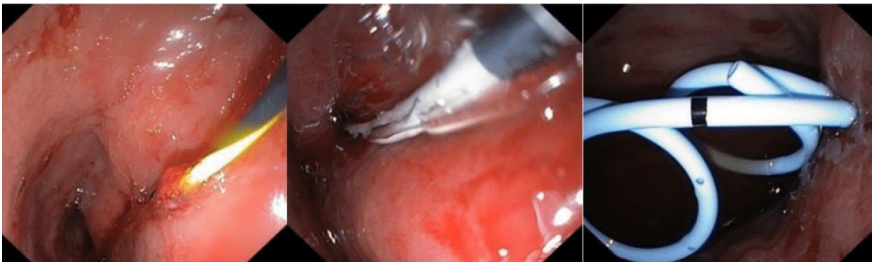
Series of Images 34: EUS-guided drainage of pancreatic pseudocysts into the stomach and duodenum using plastic stents, metal stents, or LAMS (Lumen-Apposing Metal Stents).



Series of Images 35: Endoscopic biliary drainage for malignant hilar obstruction.



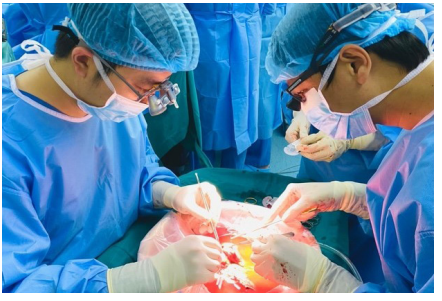
Images 36-38: Percutaneous drainage for pancreatic fistula with effusion to control infection and stabilize the patient's condition, especially in cases where endoscopic access is not feasible.



Series of Images 39: Transmural drainage under endoscopic ultrasound (EUS) guidance following pancreatitis.

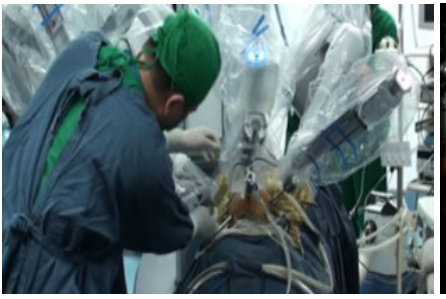
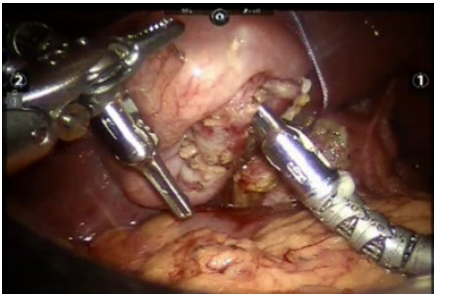
3. Minimally Invasive Surgery in Hepatobiliary and Pancreatic Diseases and Liver Transplantation.

Images 40-41: Laparoscopic liver resection & Laparoscopic pancreaticoduodenectomy.



Images 42-43: Laparoscopic surgery for donor hepatectomy and transplantation.

Image 44: Laparoscopic Klatskin tumor resection.

Images 45-46: Robot-assisted resection of choledochal cyst in children.

4. New advances in Artificial Intelligence (AI) applications, ICG (Indocyanine Green) fluorescence-guided surgery, split-liver transplant, liver transplant from brain-dead donors, ABO-incompatible liver transplant and liver transplant with two grafts from two living donors and technical advances.

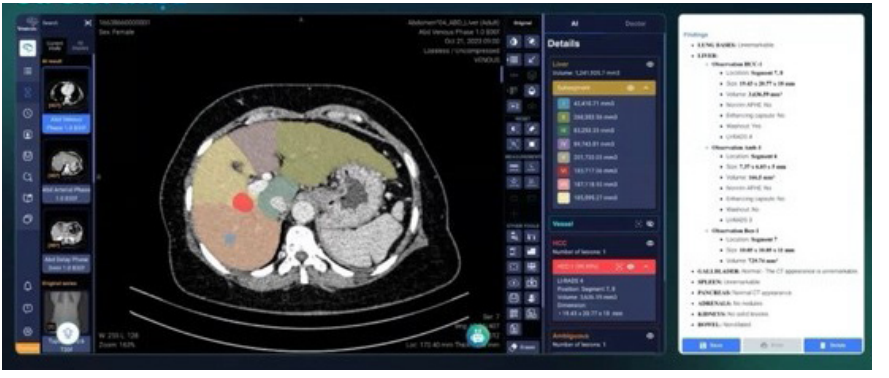
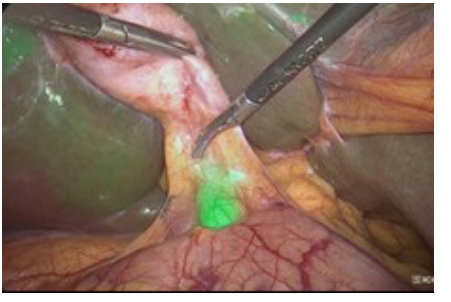
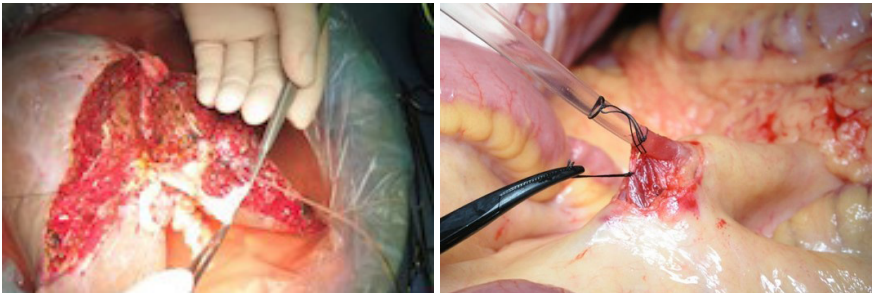


Image 47: Application of artificial intelligence (AI) in the diagnosis of HCC.

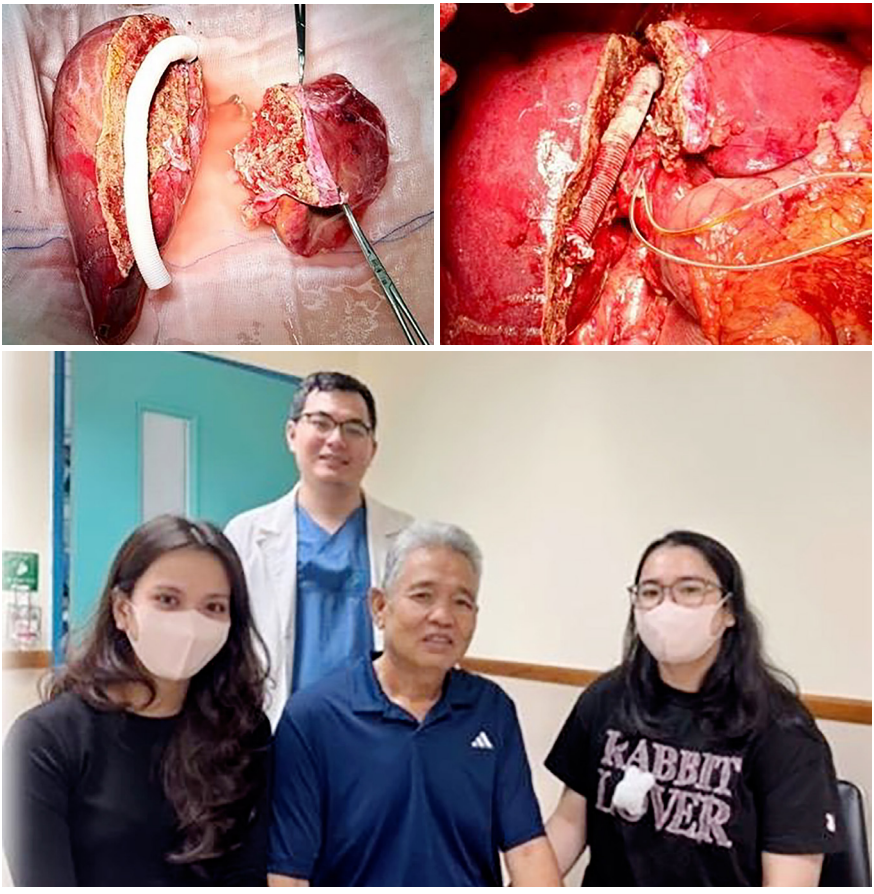
Images 48-49: Application of ICG fluorescence in laparoscopic cholecystectomy.



Images 50-51: Split-liver transplantation and technical advancements in deceased donor liver transplantation.

Images 52-53: ABO-incompatible (ABOi) liver transplantation from a living donor.

Images 54-55: Laparoscopic surgery involved simultaneously harvesting two liver grafts from two living donors.



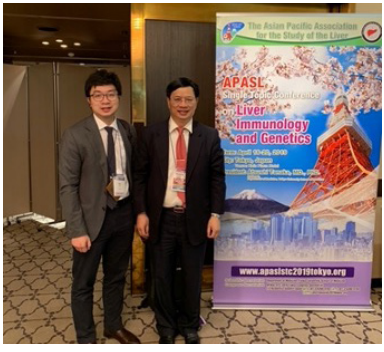
Images 56-58: Liver transplantation with two grafts from two living donors.

Images 59-61: Liver transplantation for very young patients and need a liver resection to reduce volume.

SOME ACTIVITY PICTURES OF VASLD & VSHBPS

Picture 6: Conference on Advances in Surgery and Minimally Invasive Treatment of HPB Disease at Hue Central Hospital (June 2019) with Prof. KK Madhavan - President of APHPBA & 2 Chinese experts

Picture 7: APASL-STC about "Liver immunology & genetics" in Tokyo Japan (April 2019). Prof. Le Trung Hai - President of VASLD with presentation about HCC in Vietnam



Picture 8: Attendance in E-AHPBA Congress in Amsterdam, Holland (June 2019)

Picture 9: VSHBPS Delegation attend Symposium of Pediatric liver transplantation in Seoul, Korea (September 2019)

Picture 10: Prof. Suk Koo Lee from Korea and Vietnam experts in Oncology Conference in Hanoi (January 2021). Release Clinical Practice Guidelines for the Management of Pancreatic Cancer

Picture 11: VSHBPS Delegation at the 15th IHPBA World Congress in New York, USA (April 2022)

Picture 12: Gift presentation for Prof. Brian Goh (from Singapore) and Prof. Rawisak Chanwat (from Thailand) at the Vietnam HPB Conference in Hanoi (May 2022)

Picture 13: HBP Surgery Conference in Busan, South Korea (March 2023). Prof. Le Trung Hai – President of VSHBPS delivering the welcome speech at the Presidential Dinner and serving as a Chairperson for the Asia Symposium on HBP Surgery

Picture 14: Conference of Japan Society of HBP Surgery in Tokyo (June 2023)

Picture 15: World Hepatitis Day's Symposium in National Hospital of Tropical Disease in Hanoi with 4 international experts (July 2023)

Picture 16: Leaders of VSHBPS and Prof. Ki-Hun Kim at the ISLS Conference in Zurich, Switzerland (October 2023)

Picture 17: The ATW Conference in Seoul, Korea (November 2023). Prof. Le Trung Hai, President of VSHBPS, was invited to deliver the Welcome Speech at the Gala Dinner and served as the Chairperson for the Vietnam Symposium on Organ Transplantation

Picture 18: The 17th National Conference of VASLD & VSHBPS at Military Medical University (December 2023) featuring Prof. Kwang Hyub Han from South Korea. Release of the Guideline Recommendations for ICG (Indocyanine Green) Fluorescence Imaging

Picture 19: Prof. Le Trung Hai, Founding President of the VSHBPS, as an invited speaker at the Thai Hepato-Biliary-Pancreatic Association (THPBA) Annual Meeting. His presentation, titled "Liver Transplantation in Vietnam: Achievements & Challenges" in Bangkok, Thailand (February 2024)

Picture 20: Leaders at the 16th IHPBA Congress in Cape Town, South Africa (May 2024)

Picture 21: World Hepatitis Day's Sympoeium in University Medical Center in Hochiminh City with 3 international experts (July 2024)

Picture 22: The Vietnam HPB Conference at Thai Nguyen Central Hospital (October 2024) with attendance of Prof. Tran Van Thuan - Vice Minister of Health and Prof. Jong Man Kim (Korea). Release of the Guideline Recommendations on Digital Transformation & AI in HPB Surgery and the management of Perihilar Cholangiocarcinoma

Picture 23: Asian Oncology Conference in Xi'an, China (November 2024) Prof. Le Trung Hai, President of VASLD, attending the Asian Oncology Conference as an invited speaker with presentation about "Advances in Prevention and Treatment for HCC in Vietnam"

Picture 24: Minimally Invasive Treatment Course for Biliary & Pancreatic Diseases at 108 Military Central Hospital (February 2025) featuring Prof. Ichiro Yasuda, President of the Japan Biliary Association

Picture 25: VSHBPS Conference at Vinmec International Hospital, Hanoi (May 2025), featuring the participation of renowned experts Prof. JS Park and Prof. KW Lee from South Korea. Release of the Guideline Recommendation for Acute-on-Chronic Liver Failure (ACLF) in Vietnam

Picture 26: IHPBA Symposium in MCH 108, Hanoi (November 2025)

Picture 27: The 18th National Conference of VASLD & VSHBPS at Hue Central Hospital (December 2025) with Prof. Shin Ji Hoon, President of the Korean Society of Interventional Radiology, and Prof. Kai-Wen Huang, President of the Asian Association of Tumor Ablation. Release of the Guideline Recommendation for Minimally invasive treatment for HBP diseases in Vietnam

Picture 28: Liver Summit 2026 and Launch of VASLD - Hepatology Chapter in Hochiminh City (April 2026), featuring the participation of Professor Tawesak Tanwandee from Thailand

Picture 29: Vice Minister of Ministry of Health - Associate Prof. Nguyen Tri Thuc appreciated guideline recommendations of VASLD and VSHBPS

Symposium on Liver Transplantation in ASEAN at the ILTS Conference, Suntec City, Singapore (May 2025). Professor Le Trung Hai was co-chair for this symposium

The Vietnam Delegation at the Congress of the International Society of Liver Surgeons (ISLS) in Toronto, Canada (October 2025)

A-PHPBA Congress in Bangkok, Thailand (October 2025). Vietnam Delegation had many presentations and Moderators. Professor Le Trung Hai was Moderator for one HBP Session

ASEAN Symposium of Oncology in Kunming, China (November 2025).

Professor Le Trung Hai was co-chair for this symposium.

The 15th National Conference of VASLD & VSHBPS in Ho Chi Minh City (November 2019). A significant gathering featuring more than 20 international experts, including key leaders from the IHPBA and A-PHPBA. This landmark event saw the official release of the Guideline Recommendations for the Diagnosis and Treatment of HCC, establishing a unified clinical framework for liver cancer management in Vietnam.

Scientific Conference on Liver Transplantation at 108 Military Central Hospital (March 2023)

with 3 Korean professors. The conference focused on providing a comprehensive update on the clinical practice guidelines for Liver Transplantation.

The Council of Update Vietnam New Guidelines 2026 for HCC & Professor Le Trung Hai is President of this Council

Founding Congress of the Vietnam Society of Hepato-Biliary-Pancreatic Surgery (VSHBPS) in Hanoi (February 2026). Professor Le Trung Hai is Founding President of VSHBPS

& Associate Professor Le Van Thanh is President of VSHBPS.