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## LIVER ABLATION IN CIRRHOTIC PATIENTS WITH CLINICALLY SIGNIFICANT PORTAL HYPERTENSION: CURRENT EVIDENCE, CHALLENGES, AND EMERGING ROLE OF ELASTOGRAPHY

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### Summary.

Liver ablation is a cornerstone therapy for early-stage hepatocellular carcinoma (HCC), offering a curative-intent option for patients ineligible for resection or transplantation. However, the presence of clinically significant portal hypertension (CSPH) raises safety concerns due to the increased risk of bleeding, liver decompensation, and technical difficulties. This review aims to critically analyze the safety and efficacy of liver ablation in patients with CSPH, examine conventional and novel risk stratification tools, and highlight the emerging role of liver and spleen elastography in pre-procedural assessment. Integrating elastography assessment with standard clinical indicators may improve patient selection and procedural planning in cirrhotic patients with portal hypertension (PH) undergoing liver ablation. Further prospective validation and risk stratification models are warranted.

**Keywords:** liver ablation, liver cirrhosis, clinically significant portal hypertension, elastography.

**Rezumat. Ablația hepatică la pacienții cu ciroză și hipertensiune portală clinic semnificativă: informații actuale, provocări și rolul emergent al elastografiei.**

Ablația hepatică reprezintă o terapie de bază pentru carcinomul hepatocelular în stadiu incipient (CHC), oferind o opțiune cu intenție curativă pacienților care nu sunt eligibili pentru rezecție sau transplant. Cu toate acestea, prezența hipertensiunii portale clinic semnificative (HPCS) ridică îngrijorări privind siguranța procedurii din cauza creșterii riscului de sângerare, decompensării hepatice și dificultăților tehnice. În acest articol este analizată în mod critic siguranța și eficacitatea ablației hepatice la pacienții cu HPCS, instrumentele tradiționale, cât și cele noi de stratificare a riscului, și este evidențiat rolul emergent al elastografiei ficatului și splinei în evaluarea preprocedurală. Integrarea evaluării elastografice cu indicatorii clinici standard poate îmbunătăți selectarea pacienților și planificarea procedurii la pacienții cu ciroză și hipertensiune portală care urmează să efectueze ablație hepatică. Sunt necesare studii prospective suplimentare și modele de stratificare a riscului.

**Cuvinte cheie:** ablația hepatică, ciroză hepatică, hipertensiune portală clinic semnificativă, elastografie.

**Резюме. Абляция печени у пациентов с циррозом и клинически значимой портальной гипертензией: актуальные данные, проблемы и возрастающая роль эластографии.**

Абляция печени – краеугольная терапия при раке печени на ранних стадиях (HCC), предлагающая лечение с целью излечения пациентам, не годным к резекции или трансплантации. Однако наличие клинически значимой портальной гипертензии (КСПГ) вызывает вопросы безопасности из-за повышенного риска кровотечений, печеночной декомпенсации и технических трудностей. Этот обзор ставит целью критически проанализировать безопасность и эффективность абляции печени у пациентов с КСПГ, рассмотреть как традиционные, так и новые методы стратификации риска, и подчеркнуть развивающуюся роль эластографии печени и селезенки в предпроцедурной оценке. Интеграция оценки эластографии с традиционными клиническими показателями может улучшить отбор пациентов и планирование процедур у пациентов с циррозом печени и портальной гипертензией, которым проводится абляция печени. Требуется дальнейшая проспективная валидация и разработка моделей стратификации риска.

**Ключевые слова:** абляция печени, цирроз печени, клинически значимая портальная гипертензия, эластография.

## Introduction.

Liver ablation methods, such as radiofrequency ablation (RFA) and microwave ablation (MWA) are often used to treat the early stages of hepatocellular carcinoma (HCC). For patients with cirrhosis, these methods are curative options in cases where surgical resection or transplant is not possible. Still, clinically significant portal hypertension (CSPH) is a debated relative contraindication due to its associated markers of thrombocytopenia, splenomegaly, varices, and portal vein changes where the risks of post-operative bleeding, ascites, and liver failure are possible.

**The aim of this study** is to evaluate the role of liver ablation in patients with liver cirrhosis with CSPH and early stage HCC, analysing current evidence, present challenges and the emerging role of elastography.

## Materials and Methods.

This narrative review synthesizes evidence on the safety and effectiveness of liver ablation in cirrhotic adults with CSPH, with emphasis on the pre-procedural role of liver and spleen elastography. We searched PubMed and Google Scholar for articles published in the last 10 years that addressed CSPH diagnosis (hepatic venous pressure gradient (HVPG) or validated non-invasive surrogates), elastography parameters (liver stiffness measurement (LSM); spleen stiffness measurement (SSM)), and ablation outcomes (complications, post-ablation decompensation, local tumor progression, survival). Observational studies and relevant guidelines/consensus documents were eligible; editorials and case reports with non-extractable data were excluded. Data were extracted into a structured template and summarized thematically by ablation modality (RFA/MWA), CSPH definition, and elastography thresholds.

## Results and discussions.

### Safety and Efficacy of Ablation in CSPH Patients

HCC frequently arises in the setting of liver cirrhosis, with approximately 85–90% of HCC patients demonstrating varying degrees of hepatic fibrosis or cirrhosis. Among these, hypersplenism and associated thrombocytopenia are common manifestations of portal hypertension (PH), affecting around 30% of patients [1-3]. Notably, thrombocytopenia with platelet counts (PC) below  $150 \times 10^9/L$  occurs in 64–78% of cirrhotic patients, with moderate ( $50\text{--}75 \times 10^9/L$ ) and severe ( $<50 \times 10^9/L$ ) thrombocytopenia reported in 13% and 1%, respectively [4, 5]. In some Chinese cohorts, the proportion of cirrhotic patients with severe thrombocytopenia rises to 22–25% [6-8].

While hepatectomy remains a curative approach for early HCC, it is often contraindicated in cirrhotic patients with CSPH due to the increased risks of intraoperative bleeding, impaired liver regeneration, and poor synthetic function [9]. Local thermal ablation (LTA), including MWA and RFA, offers a minimally invasive alternative with comparable overall survival and disease-free survival rates in early-stage HCC, and is especially suitable for patients with limited hepatic reserve [10].

Traditionally, a PC below  $50 \times 10^9/L$  has been regarded as a relative contraindication to invasive procedures, including LTA, due to presumed elevated bleeding risk. However, evidence regarding the correlation between thrombocytopenia and post-ablation bleeding remains inconsistent. In a retrospective study involving 709 LTA procedures, 170 patients (24.0%) had severe thrombocytopenia (PC  $<50 \times 10^9/L$ ). The overall incidence of bleeding was 4.37%, aligning with previously reported rates (0.5%–4.87%) from similar cohorts. Notably, patients with PCs between  $30\text{--}50 \times 10^9/L$  who did not receive any prophylactic treatment showed no significant increase in bleeding rates compared to patients with normal PCs, suggesting that this range may still be safe for ablation [10].

For patients with PC  $<30 \times 10^9/L$ , pre-procedural correction measures, including platelet transfusions, recombinant thrombopoietin, and thrombopoietic agents, were used to raise median platelet levels to  $36 \times 10^9/L$  (range  $22\text{--}70 \times 10^9/L$ ). Even within this subgroup, the bleeding risk remained acceptably low, supporting the feasibility of LTA in selected patients with profound thrombocytopenia [10].

Importantly, PC and conventional coagulation parameters (INR, prothrombin activity) were not independently associated with post-ablation bleeding [10]. These findings align with the evolving understanding of a rebalanced but fragile hemostatic system in cirrhosis, where elevated von Willebrand factor levels (VWF) and reduced ADAMTS-13, a plasma reprotolysin-like metalloprotease that regulates thrombogenesis by cleaving VWF, contribute to compensatory primary hemostasis, despite reduced platelet function [11].

Multivariate analysis identified tumor diameter and number of lesions as the only independent predictors for bleeding complications. Mechanistically, bleeding can occur through various pathways including intraperitoneal hemorrhage due to capsular rupture, hemothorax from intercostal artery injury, and hemobilia from bile duct-vascular fistulae [12].

Major complications were observed in 7.8% of procedures, including infections, pleural effusions, liver failure, and renal injury. However, these were not significantly more frequent in patients with PCs below  $50 \times 10^9/L$  or  $30 \times 10^9/L$ . Instead, lower body mass index, hypoalbuminemia, larger tumor size, and multiple ablation sessions were independent predictors for major complications [10].

These results highlight the importance of comprehensive pre-procedural evaluation rather than relying solely on platelet thresholds when assessing ablation eligibility in cirrhotic patients with CSPH. The study [10] also underscores the potential for expanding treatment access to thrombocytopenic patients who might otherwise be denied curative therapy.

### Conventional Risk Stratification in CSPH

#### *Hepatic vein wedge pressure measurements*

The HVPG, measured through hepatic vein catheterization, is the gold standard for diagnosing sinusoidal PH in patients with advanced chronic liver disease (ACLD). An HVPG value up to 5 mmHg is considered normal. Values between 6 and 9 mmHg indicate subclinical PH, while an HVPG of 10 mmHg or higher defines CSPH. This threshold is critical, as patients exceeding it are at increased risk of developing the full spectrum of PH-related complications, including gastro-esophageal varices and other portosystemic collaterals, variceal bleeding, ascites and its related complications, and hepatic encephalopathy [13].

Although HVPG measurement is the gold standard for detecting and quantifying PH, it is a moderately invasive procedure that carries some risks, including potential injury during jugular vein access, the induction of arrhythmias, and exposure to radiation. Additionally, accurate interpretation of HVPG results requires specialized expertise. These limitations have confined the routine use of HVPG to specialized centers, prompting ongoing efforts to validate noninvasive alternatives that can be applied in everyday clinical practice [14].

#### *PC and Splenomegaly*

A common cause of hypersplenism is chronic liver disease. It is a common finding in liver cirrhosis and frequently occurs in patients with PH. Spleen size remains an independent predictor of CSPH in patients with compensated disease and can be used alongside LSM and PC to enhance diagnostic accuracy [13, 15-17]. PC is a simple and widely used blood-based marker for assessing PH. However, when used alone, its diagnostic accuracy for identifying CSPH in patients with compensated advanced chronic

liver disease (cACLD) is limited and not sufficient for clinical decision-making (e.g., AUROC: 0.787). To improve predictive performance, PLT has been incorporated into several widely accepted criteria and prediction models that also include ultrasound elastography measurements, such as Baveno VII [18], ANTICIPATE  $\pm$  NASH [19], and NICER model, which combines SSM at 100 Hz, LSM, and body mass index (BMI) [20].

#### *Doppler ultrasound*

Doppler ultrasound findings—such as reduced portal vein flow velocity, increased resistance index in the hepatic, splenic, and renal arteries, decreased resistance index in the superior mesenteric artery, and a flattened flow pattern in the hepatic veins—have been associated with the presence of CSPH. However, in patients with compensated disease, these indicators lack sufficient accuracy to reliably confirm or exclude the condition [21].

#### *Endoscopic Evidence of Varices*

Since esophageal varices (EV) typically develop when the HVPG reaches at least 10 mm Hg, their presence indicates CSPH by definition. However, CSPH is also found in approximately 50–60% of patients with compensated cirrhosis who do not yet have EV. Consequently, EV absence does not indicate CSPH absence [22].

### Elastography in the Assessment of PH

#### *LSM*

LSM by transient elastography (TE) correlates well with HVPG and the presence of EV, making it a valuable noninvasive tool for assessing the severity of PH. The latest EASL guidelines on noninvasive testing for assessing liver disease severity and prognosis recommend a risk stratification algorithm for cACLD based on the Baveno VI criteria: patients with LSM below 20 kPa and PCs above  $150 \times 10^9/L$  are considered at very low risk of having CSPH [9]. CSPH can be presumed when any of the following criteria are met: (1) LSM  $>25$  kPa; (2) LSM between 20–25 kPa with a PC  $<150 \times 10^9/L$ ; or (3) LSM between 15–20 kPa with a PC  $<110 \times 10^9/L$  [14].

#### *SSM*

When HVPG exceeds 10 mm Hg, SSM by TE demonstrates a stronger correlation with HVPG than LSM [14]. The Baveno VII consensus introduced dual cut-offs for SSM at 50 Hz: an SSM-50 Hz value below 21 kPa effectively rules out CSPH, while a value above 50 kPa confirms its presence [18]. Additionally, an SSM value  $\leq 46$  kPa may be especially useful for ruling out varices needing treatment and avoiding unnecessary endoscopy in patients who would otherwise meet Baveno VI screening criteria

(LSM  $\geq 20$  kPa and PC  $< 150 \times 10^9/L$ ). However, the clinical applicability of SSM remains limited due to several factors: (1) studies have primarily included patients with chronic viral hepatitis, restricting generalizability to alcohol-related liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD); (2) SSM has a high technical failure rate (15%–27%); and (3) the need for further validation of a novel 100 Hz spleen-specific probe [14].

### **Integrating Elastography and Hematologic Markers**

In patients with HCC and coexisting cirrhosis, particularly those with CSPH, accurate risk stratification is essential to safely guide local therapeutic interventions such as RFA or MWA. When elastography findings are integrated with conventional hematologic indices such as PC and spleen size, a more robust framework for procedural risk assessment and candidate selection emerges.

This integrated approach enhances clinical decision-making in three critical domains: 1) Improved Selection of Ablation Candidates, 2) Prediction of Post-Procedural Complications and 3) Optimizing the Timing of Prophylactic Measures.

#### ***Improved Selection of Ablation Candidates***

Patients with low PCs ( $< 50 \times 10^9/L$ ) and elevated LSM or SSM values are often excluded from thermal ablation due to presumed risk of bleeding. However, evidence suggests that such thresholds may be overly conservative. Several studies have shown that patients with moderate thrombocytopenia ( $30\text{--}50 \times 10^9/L$ ) and stable elastography profiles may safely undergo ablation without increased bleeding complications [10, 12, 24]. Therefore, combining LSM/SSM with hematologic data may allow for a more individualized selection of eligible candidates.

#### ***Prediction of Post-Procedural Complications***

Elevated LSM and SSM have been associated with a higher risk of procedure-related complications, including hemorrhage, ascites, and hepatic decompensation [24]. In a large cohort study of 709 ablation procedures, PC and INR alone did not predict bleeding risk, while tumor size and lesion number were independent predictors [10]. Incorporating elastography parameters could thus aid in early identification of high-risk individuals and stratify post-ablation surveillance intensity.

#### ***Optimizing the Timing of Prophylactic Measures***

In cases of borderline PC or elevated SSM, prophylactic interventions—such as platelet transfusion, thrombopoietin analogues, or non-selective beta-blockers—may reduce procedural risk. The timing and necessity of such interventions can

be optimized through elastography-guided decision-making. For example, elevated SSM may warrant pre-ablation beta-blocker initiation to modulate portal pressure, whereas transient thrombocytopenia without elevated SSM might not require transfusion. This integrative approach reflects the growing recognition that the hemostatic system in cirrhosis is rebalanced rather than simply impaired, with compensatory mechanisms such as elevated VWF and reduced ADAMTS-13, contributing to hemostatic function. Hence, isolated laboratory abnormalities should not be used as absolute contraindications without considering elastography context [25, 26].

In conclusion, the combination of LSM, SSM, PC, and spleen size offers a more comprehensive assessment of procedural risk and patient suitability for ablation.

### **Challenges and Limitations**

Although the integration of elastography and hematologic markers represents a significant advancement in the management of HCC patients with CSPH, several challenges limit its widespread adoption in routine clinical practice. One of the primary concerns is the operator dependence and variability associated with elastography measurements. Techniques such as TE, point shear wave elastography, and two-dimensional shear wave elastography are highly sensitive to technical factors including probe positioning, acoustic window quality, and patient cooperation. Variations in operator experience and patient anatomy, particularly in cases of obesity or ascites, can lead to inconsistent results and reduced reproducibility of LSM and SSM values, as demonstrated in studies analyzing intra- and inter-observer variability in ARFI and SWE assessments [27].

Another important limitation is the lack of universally accepted cutoff thresholds for procedural risk stratification. While several studies have proposed elastography values associated with the presence of PH and EV—such as LSM  $> 20\text{--}25$  kPa or SSM  $> 40\text{--}50$  kPa—there is no consensus regarding optimal stiffness thresholds specifically applicable to ablation safety or bleeding risk. This absence of standardized and validated parameters restricts the clinical utility of elastography in guiding invasive treatment decisions [28].

Moreover, much of the supporting evidence for using elastography in this context is derived from retrospective, single-center studies, with limited representation of real-world patient heterogeneity. Prospective, multicenter trials specifically evaluating the predictive value of elastography parameters for procedural safety and complication rates in

HCC patients undergoing ablation remain scarce. Without high-level validation, the incorporation of elastography into procedural risk stratification algorithms and clinical practice guidelines remains tentative [29].

Finally, the presence of confounding anatomical and hemodynamic variables such as portal vein thrombosis (PVT) and advanced nodular transformation of the liver parenchyma can significantly distort stiffness measurements. PVT may artificially elevate SSM by altering portal hemodynamics, while multinodular cirrhosis may lead to heterogeneous and potentially misleading LSM values. These structural alterations reduce the reliability of elastography metrics and necessitate careful interpretation within the broader clinical context [30].

### Future Directions

The integration of elastography parameters and hematologic markers in guiding loco-regional therapies for HCC in cirrhotic patients with CSPH represents a promising advancement. However, further development and clinical validation are essential to optimize its application. One key area for progress lies in the design and implementation of prospective, multicenter studies that evaluate the predictive value of LSM and SSM in the context of ablation planning. Such studies are needed to establish evidence-based cutoff values for stiffness parameters that can stratify procedural risk and guide clinical decision-making with greater precision [29].

Another important direction is the development of composite scoring systems that combine elastography data with conventional laboratory markers (e.g., PC, INR, albumin), imaging features (e.g., tumor size, vascular invasion), and clinical parameters (e.g., Child-Pugh or ALBI score). These multimodal models could provide a more comprehensive assessment of patient-specific procedural risk and post-ablation outcomes. A risk stratification tool that integrates both hemodynamic and structural parameters would support more refined patient selection and procedural planning.

In addition, the use of advanced imaging technologies, such as contrast-enhanced ultrasound (CEUS), offers potential for real-time intra-procedural assessment of ablation efficacy and vascular integrity. CEUS can aid in identifying subcapsular tumors at higher risk of bleeding or incomplete ablation and may improve safety in patients with borderline risk profiles [31].

Finally, these innovations align with the broader movement toward personalized medicine in oncology and hepatology. Tailoring the ablation strategy—

such as energy modality, number of sessions, and preprocedural optimization—to the individual patient's risk profile based on integrated elastography, hematologic, and radiologic data may improve outcomes while minimizing complications. Such personalized approaches may also facilitate access to curative therapy for patients traditionally considered high-risk, such as those with severe thrombocytopenia or borderline hepatic function.

Consequently, these future directions underscore the need for a paradigm shift from empirical ablation decision-making toward algorithmic, risk-adjusted strategies informed by multimodal assessment.

### Conclusion.

Cirrhotic patients suffering from CSPH can still consider liver ablation as a treatment. The integration of liver and spleen elastography with pre-existing clinical indicators might improve their protection evaluation and help in creating structured ablation plans. To establish criteria and confirm the reliability of the risk prediction models, additional prospective studies are necessary.

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