

The logo for the Chronic Liver Disease Foundation (CLDF) features the letters "CLDF" in a bold, dark blue, sans-serif font. The letters are closely spaced and have a slight shadow effect.

CLDF

Chronic Liver Disease Foundation

*Unparalleled expertise,
unprecedented access*

2024

YEAR IN REVIEW

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Embassy of Education

The infographic features a light purple map of the United States in the background. Three teardrop-shaped callouts are positioned over the map: a dark purple one on the left, an orange one in the center, and a teal one on the right. Each callout contains a number and a label. Below these callouts is a grey rectangular box with a dark purple border containing a paragraph of text.

182
ambassadors

49
states

Academic
and
Community
Education

The Embassy of Education is a dedicated working group led by hepatologists, committed to educating healthcare professionals about the latest advancements in managing chronic liver disease. The Embassy of Education network will actively disseminate the CLDF's Continuing Medical Education (CME) initiatives within their respective communities.

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CLDF Committees

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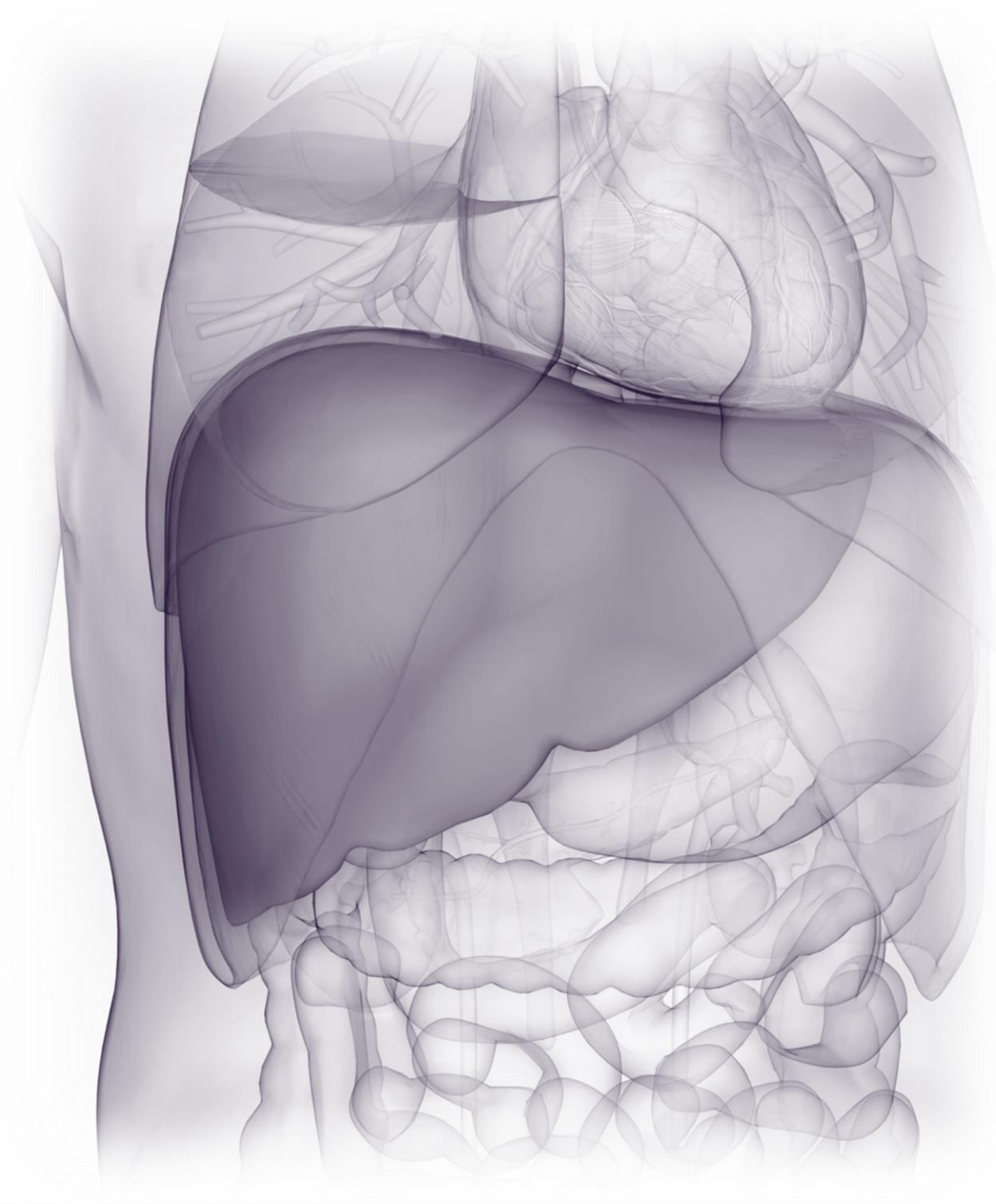
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Tatyana Kushner, MD, MSCE	Kali Zhou, MD
Michelle Lai, MD, MPH	

2024 Educational Initiatives



Advances in Non-Invasive Assessment and Management of MASLD

UC Irvine, DOM Research Retreat

Rohit Loomba, MD, MHSc

Professor of Medicine
Director, MASLD Research Center
Chief, Division of Gastroenterology and Hepatology
Department of Medicine
University of California at San Diego
Email: roloomba@ucsd.edu



MASH-PATH: **A 2024 NASH-TAG Satellite Symposium**

*A satellite symposium experience that will provide
education on the latest emerging data for the management
and treatment of patients with MASLD/MASH*

Friday, January 5, 2024 at 12:45 PM

The Chateaux Deer Valley
7815 Royal Street East
Park City, Utah, 84060

Speaker:

Rohit Loomba, MD, MHSc

Director, NAFLD Research Center
Director of Hepatology, Professor of Medicine
Vice Chief, Division of Gastroenterology
University of California at San Diego
La Jolla, CA

This activity is jointly provided by Medical Education Resources and the Chronic Liver Disease Foundation.



Supported by an educational grant from Madrigal Pharmaceuticals.





Participants in Liver Connect 2024 conference



of attendees who completed an evaluation determined that the learning objectives were met



of attendees who completed an evaluation rated the speakers 'Excellent' or 'Very Good'



of attendees who completed an evaluation form started the education was free of commercial bias and matched their current scope of practice



of attendees who completed an evaluation form agreed that the education presented would cause them to make a change in their practice



of attendees who completed an evaluation form agreed that the activity improved their ability to perform as a more efficient healthcare team member

4th ANNUAL CONFERENCE **LIVER** **CONNECT**



Innovations IN THE Management of **MASH**

Breakthroughs in MASH
Diagnosis and Management
A Liver Connect City Series



THE GLOBAL
NASH COUNCIL



GHAPP

Gastroenterology & Hepatology
Advanced Practice Providers

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MAJOR ADVANCEMENT IN MASH MANAGEMENT

Navigating New Horizons:
Evolution of MASH Care



Supported by an educational grant from Madrigal Pharmaceuticals.

MAJOR ADVANCEMENT IN MASH MANAGEMENT



Supported by an educational grant from Madrigal Pharmaceuticals.

Innovations IN THE Management OF MASH



Breakthroughs in MASH Diagnosis and Management

A Liver Connect City Series



**Breakthroughs in MASH
Diagnosis and Management**
A Liver Connect City Series

Stay at the forefront of liver health advancements and earn up to 3.0 AMA PRA Category 1 Credits™!

Thursday, February 13, 2025
6:00 PM–9:30 PM

Morristown, NJ
The Westin Governor Morris Hotel
2 Whippany Road
Morristown, NJ 07960

Speakers

- Nikolaos Pysopoulos, MD, MBA, PhD**
NYU Langone Health
New York, NY
- Ilan Weisberg, MD**
NewYork-Presbyterian
Brooklyn Methodist Hospital
New York, NY
- Colin Brown, MD**
Middlesex Monmouth
Gastroenterology
Freehold, NJ

Educational Objectives

- Assess the epidemiologic impact of the spectrum of SLD and MASLD
- Discuss the Use of NITs in MASLD Risk Stratification and Monitoring in clinical practice
- Explain initial treatment of MASLD with Lifestyle Modification and approved medication to manage cardio-metabolic risks (obesity and type 2 diabetes)
- Review data on the currently approved medication for MASH
- Review data about the most promising drugs in Phase 2 and 3 clinical trials of MASH

www.mashallianceeducation.org
info@mashallianceeducation.org

Jointly provided by Medical Education Resources, the Chronic Liver Disease Foundation, Gastroenterology and Hepatology Advanced Practice Providers, and the Global NASH Council.

Supported by an educational grant from Madrigal Pharmaceuticals.

MASH ALLIANCE
CLDF
GHAPP
THE GLOBAL NASH COUNCIL



14
Cities

562
Participants

Atlanta, GA

Houston, TX

Chicago, IL

Kansas City, MO

Cleveland, OH

Menlo Park, CA

Coral Gables, FL

Morristown, NJ

Dallas, TX

New York, NY

Denver, CO

Pasadena, CA

Detroit, MI

Scottsdale, AZ

Supported by an educational grant from Madrigal Pharmaceuticals.

Navigating New Horizons: Evolution of MASH Care

Virtual and Live Meetings



146
Outreach
Meetings

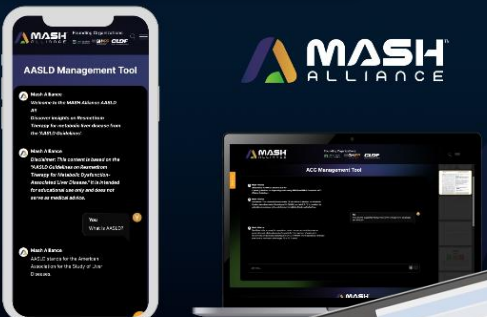
4
Virtual
Broadcasts

1,680
Participants

MASH Alliance: Digital Education Hub



AI Management Tools



Instant Answers with Our AI Chatbot

Our AI MASH Guidance Chatbots are designed to deliver precise, tailored responses to your specific questions on the management of MASH and use of Resmitemor. There are two Chatbots options, one is based on the recent update to the AASLD Practice Management Guidance on MASH (2024), and the other is based on the recent Expert Panel Recommendations for MASH/NASH from ACG (2024).

[Visit AI Management Tools](#)



Symposium Vignettes

EXPERT PERSPECTIVES

POST CONFERENCE HIGHLIGHTS ON MASLD/MASH FROM...

DDW



Rohit Loomba,
MD, MHSc



Nadege Gunn,
MD, CPI



HoChong Gilles,
DNP, FNP-BC

ACG



Nadege Gunn,
MD, CPI



Marcelo Kugelmas,
MD



Christine Hanson,
FNP-C

LIVE BROADCASTS



LIVE OUTREACH

EASL



Kimberly Brown,
MD



Sujit Janardhan,
MD, PhD



Patrick Horne,
MSN, ARNP

AASLD



Nancy Reau,
MD



Joseph Ahn,
MD



Ann Moore,
NP

Enduring Webcasts



ACCREDITED WEBCAST ARE NOW AVAILABLE

EXPERT PERSPECTIVES ***POST CONFERENCE HIGHLIGHTS ON*** ***MASLD/MASH***

View All Four Post-Conference Webcast Highlights on MASLD/MASH

Earn up to **4.0 CME Credits** and stay updated on the latest advancements presented at leading hepatology and gastroenterology conferences.



Accredited Webcasts Available Updates on MASLD/MASH:
<https://www.ghapp.org/expert-perspective-webcasts/post-conference>

Supported by an educational grant from Novo Nordisk Inc.

14th Annual International Clinical Exchange

170
Participants

DATE

Wednesday, June 5, 2024

VENUE

Terrazza Duomo 21

P.za del Duomo, 21, 20122 Milano MI, Italy

14th Annual

CHRONIC LIVER DISEASE FOUNDATION CLINICAL EXCHANGE RECEPTION

**Wednesday,
June 5, 2024**

6:00 - 8:00 PM

Venue:

Terrazza Duomo 21
Piazza del Duomo,
21 20121, Milano

Milan, Italy

Scan Here to Register!



**For Health Care Providers
Additional details to follow!*

Thank you to our sponsors:



If you have any questions, please contact us at:

info@chronicliverdisease.org or call **+1-973-664-9777**

CLDF

Chronic Liver Disease Foundation

Join us for the 14th

Annual CLDF Clinical Exchange Reception

Thursday, November 14, 2024

6:00 PM – 8:30 PM

**Andaz San Diego
The Roof Top by STK**

600 F Street
San Diego, CA 92101

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Pharmaceuticals

novo nordisk

Salix
PHARMACEUTICALS

202

Participants



AASLD Abstracts 2024 – Advisors Review

MASLD / MASH

Type	Abstract No.	Title	Grade (A, B, C)
Oral	0112	EFFECT OF RESMETIROM OR PLACEBO IN NASH FIBROSIS PATIENTS WITH < 5% OR ≥ 5% WEIGHT LOSS AND/OR ON BASELINE GLP-1 THERAPY IN THE MAESTRO-NASH 52 WEEK SERIAL LIVER BIOPSY STUDY	
Oral	0004	2070 RESMETIROM EFFECTS ON NASH WITH LIVER FIBROSIS IN PATIENTS WITH NASH GENETIC RISK ALLELES	
Oral	0147	520 METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) IS SIGNIFICANTLY ASSOCIATED WITH BIOLOGICAL AGE AND ITS ACCELERATION AS ASSESSED BY METHYLATION CLOCK	
Oral	0203	USE OF GLUCAGON-LIKE PEPTIDE 1 RECEPTOR AGONISTS (GLP-1 RA) IN PATIENTS WITH MASLD IN A REAL-WORLD SETTING IS ASSOCIATED WITH SLOWER DISEASE PROGRESSION AND LOWER ALL CAUSE MORTALITY	

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59
Live Independent Reviewers



Publications

HCC Care Cascade Decision-Support Tool

**NEW FEATURES &
UPDATED RESOURCES!**

**CLDF HCC CARE CASCADE
DECISION SUPPORT TOOL**

LEARN MORE



March 2024

This whitepaper was supported by an unrestricted educational grant to the Chronic Liver Disease Foundation from Exelixis, Inc., Mallinckrodt Pharmaceuticals, and Salix Pharmaceuticals. The selection of the authors and the creation of this whitepaper were done independently, and Exelixis, Inc., Mallinckrodt Pharmaceuticals, Salix Pharmaceuticals did not play a role.

PBC Expert Perspectives Algorithm and ChatBot

March 2024

Expert Perspectives on PBC: Interactive Management Algorithm and Chatbot

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Chronic Liver Disease Foundation

CLDF Xpert Perspectives PBC Bot
By community builder

Application of the Latest Advances in Evidence-Based Medicine in Primary Biliary Cholangitis

Tell me about PBC treatment options.

Explain the diagnosis process for PBC.

What are the latest advances in PBC?

Can you discuss PBC symptoms?

Message AI Bot, ask anything! ↑

Powered by Focus Medical

Featured Resources

Application of the Latest Advances in Evidence-Based Medicine in Primary Biliary Cholangitis

Diagnosis and Management of Primary Biliary Cholangitis

Primary biliary cholangitis: 2021 practice guidance

~sp100 Gp210

*Fenofibrate is not currently approved for the treatment of PBC and use is considered off-label.

Figure abbreviations: AMA: antimicrobial antibodies; ANA: antinuclear antibodies; ALP: alkaline phosphatase; CPC: Child-Pugh Class; CSPH: clinically significant portal hypertension; HCC: hepatocellular carcinoma; MRE: magnetic resonance elastography; OCA: obeticholic acid; TE: transient elastography; UDCA: ursodeoxycholic acid; VCTE: vibration controlled transient elastography

PBC diagnosis confirmed by >AMA, >ANA- or biopsy

The CLDF expert panel proposed the following criteria for the diagnosis of PBC (1):

- Scenario 1: Chronic elevation of ALP with a positive antimitochondrial antibodies (AMA); immunofluorescent assay titer of > 1:40 or EIA > 25 units in the absence of other liver and systemic diseases
- Scenario 2: Chronic elevation of ALP with negative AMA but positive PBC-specific antinuclear antibody (ANA; sp-100, gp-210) tests, or reticular pattern of ANA
- Scenario 3: Chronic elevation of ALP with negative AMA and ANA tests, but a liver biopsy showing nonsuppurative cholangitis and destruction of the interlobular bile ducts

In 2021, EASL published an update to the Clinical Practice Guidelines on NITs for the evaluation of liver disease severity and prognosis. For PBC, these guidelines endorse the importance of fibrosis staging for prognosis, independent of biochemical response to therapy. The guidelines state that in patients with PBC, serum biomarkers are not recommended for fibrosis staging in clinical practice. For staging purposes, LSM by

In 2021, EASL published an update to the Clinical Practice Guidelines on NITs for the evaluation of liver disease severity and prognosis. For PBC, these guidelines endorse the importance of fibrosis staging for prognosis, independent of biochemical response to therapy. The guidelines state that in patients with PBC, serum biomarkers are not recommended for fibrosis staging in clinical practice. For staging purposes, LSM by TE, using a cut-off of 10 kPa, was proposed as a criterion for ruling in severe fibrosis/compensated advanced chronic liver disease (17). Previously published liver stiffness values that correlate to histologic stage are 7.1, 8.8, 10.7, and 16.9 kPa for F1, F2, F3, and F4, respectively (18). Both TE and MRE outperformed the biochemical markers for the prediction of advanced fibrosis, with an optimal threshold to predict hepatic decompensation of 10.2 kPa on TE and 4.30 kPa on MRE (1, 13).

In summary, we recommend that TE or MRE be used for staging PBC at the baseline. We recommend that a TE of > 10 kPa and an MRE > 4.3 kPa would be acceptable in identifying PBC patients with advanced fibrosis and at an increased risk of hepatic decompensation in the future (1). Blood-based NITs have not gained wide acceptance by physicians or regulatory agencies regarding staging liver disease (1, 19).

Start UDCA 13-15 mg/kg/day for: 12 months if VCTE

or TE < 10 kPa, MRE < 4.3 kPa or 6 months if VCTE or TE ≥ 10 kPa, compensated liver disease and no signs of portal hypertension

PBC patients with a lower stage of fibrosis (VCTE or TE < 10 kPa, MRE < 4.3 kPa) may continue UDCA monotherapy for 12 months prior to determining response (ALP < 1.5 x ULN and bilirubin < 1 x ULN) and the need for second-line therapy. For patients with more advanced fibrosis stage (VCTE or TE ≥ 10 kPa), compensated liver disease and no signs of portal hypertension, response (ALP < 1.5 x ULN and bilirubin < 1 x ULN) and the need for second-line treatment should be assessed at 6 months. Based on recent data, clinicians may consider the more stringent criteria (ALP < ULN and bilirubin < 0.6 mg/dL) to assess response in patients with more advanced disease (1).

At 6 months, ALP < 1.5 x ULN + bilirubin < 1.0 x ULN

or at 12 months, ALP < 1.5 x ULN + bilirubin < 1.0 x ULN

Lack of biochemical response to UDCA is reported in 25–50% of treated patients (20) and has been associated with a >5-fold increase in risk of progression to cirrhosis, as well as a 3-fold increase in age-adjusted mortality (21). At this time, clinicians are encouraged to use two liver biochemistries as the anchor for clinical judgment when determining candidates for second-line therapy in PBC: ALP and bilirubin levels (2, 5, 22). If elevated above the ULN, bilirubin is more important than ALP for prognosis and in identifying advanced stage of PBC in the absence of Gilbert's syndrome or another explanation. However, most patients will have elevated ALP levels rather than elevated bilirubin levels. For example, in a patient with a normal ALP, advanced fibrosis stage and bilirubin > ULN, adding a second-line therapy can be considered. Additional factors to consider include the patient's age and acceptance of additional medications (1).

When evaluated after 12 months of treatment with UDCA, serum ALP and bilirubin levels correlate closely with the risk of liver transplant or death. Current guideline documents do not recommend a specific cut-off value for serum ALP or bilirubin beyond which a second drug should be initiated, although it is important to remember that long term survival of patients with PBC whose serum ALP is < 1.5 x ULN and bilirubin is normal is similar to that of the general population (22). However, more recent data suggest that there is additional survival benefit in obtaining normalization of serum ALP and achieving a bilirubin level < 0.6 mg/dL (23).

Of note, the response to UDCA has been characteristically assessed at 12 months (24); however, there is growing evidence that the response can be reliably predicted after a shorter period of UDCA treatment. A study presented at the 2021 AASLD annual meeting, which included 3,516 UDCA-treated

CLDF PBC Disease Content

GHAPP E-Newsletter Series: PBC

Find an Expert

CLDF Embassy of Education

GHAPP Faculty Advisors, APP Network

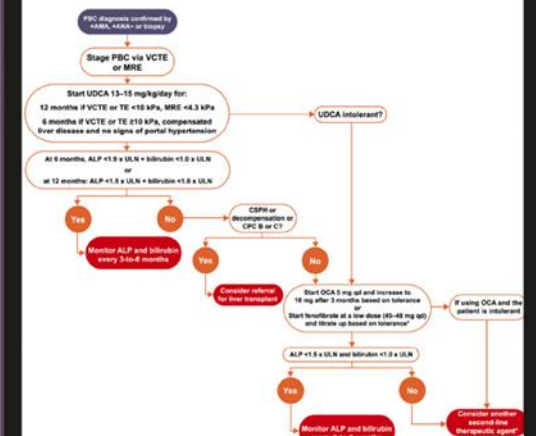
1:44

chronicliverdiseasefoundation.org

provide recommendations regarding the diagnosis and treatment of PBC (2-4).

CLDF Published Algorithm for the Treatment of PBC (1)

Click on select boxes in the algorithm for additional information



~sp100 Gp210

*Fenofibrate is not currently approved for the treatment of PBC and use is considered off-label.

Figure abbreviations: AMA: antimicrobial antibodies; ANA: antinuclear antibodies; ALP: alkaline phosphatase; CPC: Child-Pugh Class; CSPH: clinically significant portal hypertension; HCC: hepatocellular carcinoma; MRE: magnetic resonance elastography; OCA: obeticholic acid; TE: transient elastography; UDCA: ursodeoxycholic acid; VCTE: vibration controlled transient elastography

Supported with an unrestricted educational grant from Ipsen.

Hepatocellular Carcinoma (HCC) Surveillance Beyond the Guidelines: Surveillance in Non-Cirrhotic Viral Hepatitis and Metabolic Dysfunction-Associated Steatohepatitis, and the Role of HCC Biomarkers

July 2024



Hepatocellular Carcinoma (HCC) Surveillance Beyond the Guidelines: Surveillance in Non-Cirrhotic Viral Hepatitis and Metabolic Dysfunction-Associated Steatohepatitis, and the Role of HCC Biomarkers

Robert J. Wong, MD, MS^{1,2}, Ira M. Jacobson, MD¹, Aljaz Ahmed, MD¹, Paul Kwo, MD¹

¹Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Palo Alto, CA

²Gastroenterology Section, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA

³Division of Gastroenterology and Hepatology, NYU Langone Health, New York, NY

Introduction

Hepatocellular carcinoma (HCC) remains a leading cause of morbidity and mortality in the United States (US) and worldwide.^{1,2} In 2023, the American Cancer Society estimated that over 40,000 new individuals were diagnosed with liver cancer, and nearly 30,000 people died from it.³ While cirrhosis is the primary risk factor for HCC development, it can also develop in patients with chronic liver disease without cirrhosis, particularly those with chronic hepatitis B (CHB). There is also increasing concern about noncirrhotic HCC (NCHCC) in patients with metabolic dysfunction-associated steatotic liver disease/metabolic dysfunction-associated steatohepatitis (MASLD/MASH).⁴ HCC surveillance leads to diagnosing tumors at earlier stages, which translates into more options for potentially curative treatments and improved overall survival.⁵⁻⁸ However, effective implementation of HCC surveillance remains a challenge. Additionally, there remains confusion and conflicting approaches to HCC surveillance in certain high-risk groups of individuals with non-cirrhotic chronic liver disease. In this review, we examine the existing literature and provide consensus expert guidance on practical approaches to implementing HCC surveillance in non-cirrhotic individuals with CHB, chronic hepatitis C (CHC), and MASLD/MASH.

The recently updated practice guidance from the American Association for the Study of Liver Diseases (AASLD) recommends HCC surveillance for individuals with cirrhosis of any etiology, except for those with Child-Pugh-Turcotte (CPT) class C cirrhosis who are ineligible for liver transplantation or those with life-limiting conditions or co-morbidities that cannot be improved with liver transplantation or targeted therapies.² The guidance also recommends HCC surveillance in non-cirrhotic chronic hepatitis B (CHB) patients who meet the following criteria: men over 40 years and women over 50 years from regions with high CHB endemicity (i.e., regions with an HBsAg seroprevalence > 8%).⁹ Individuals from Africa in their third decade of life, those with a family history of HCC, and people with a PAGE-B score > 10.¹⁰ However, little guidance is provided regarding individuals with non-cirrhotic CHB outside of the aforementioned criteria. The AASLD guidelines specifically recommend against routine HCC surveillance for individuals with non-cirrhotic CHC or MASLD/MASH with F3 fibrosis. However, the European Association for the Study of the Liver (EASL) guidelines recommend surveillance for HCV patients with F3 and F4 fibrosis, including after a sustained virologic response (SVR).¹¹ Individuals in these categories, for whom AASLD guidelines do not recommend HCC surveillance, can still develop HCC. Additionally, significant heterogeneity exists in real-world surveillance practices. In the following sections, we will address each of these challenging scenarios.

Surveillance for HCC among patients at risk remains suboptimal. A recent meta-analysis of 29 studies involving 118,799 patients with chronic hepatitis reported a pooled estimate of 24.0% for HCC surveillance utilization.¹² Another recent analysis in a cohort of over 2,000 cirrhosis patients found that the proportion of time covered by surveillance was 24.9%, with only 16% of patients having semi-annual surveillance in the year prior to HCC diagnosis.¹³ Low utilization of HCC surveillance in patients with cirrhosis, coupled with data from the National Cancer Institute's Surveillance Epidemiology and End Results database showing overall five-year survival in patients with HCC less

1

Hepatocellular Carcinoma (HCC) Surveillance Beyond the Guidelines

Hepatocellular Carcinoma (HCC) Surveillance Beyond the Guidelines

an urgent need for improvement reasons for low HCC surveillance are complex and multifactorial, reflecting a system-level failure.¹⁴⁻¹⁶ While alarmingly underutilized, equally important barriers observed in effective surveillance are particularly notable in underserved populations, including low socioeconomic and safety-net populations, which face disproportionate impacts on HCC mortality rates.¹⁷⁻¹⁹ HCC in these groups, contributing to

Table 1. WHO Wilson and Junger's Principles of an Ideal Screening Test²⁰

- Condition being screened for is an important health problem
- Accepted treatments should be available for individuals diagnosed with the condition
- Facilities for diagnosis and treatment should be readily available
- Condition is in a recognizable early or latent phase during which to implement screening should be easily identifiable
- Test should be suitable and perform accurately
- Test should be acceptable to the population
- The natural history of the condition, including disease progression from early/latent phase to disease state, should be adequately understood
- There should be agreed policy or practice guidance on who should be tested
- The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
- Case-finding should be a continuous process and not a "once and for all" project (i.e., surveillance)

HCC and Hepatitis B and C Virus Infections

Globally, 292 million people are infected with CHB, with 2.2 million cases reported in the US.²¹⁻²³ CHC affects 50 million people worldwide,²⁴ with an estimated 2.7 to 3.9 million people in the US.²⁵ CHB and CHC account for an estimated 75% to 80% and 10% to 20%, respectively, of cases of virus-associated HCC.²⁶ In general, chronic hepatitis B virus (HBV) infection and chronic hepatitis C virus (HCV) infection lead to repeated cycles of cellular inflammation-necrosis-fibrosis, and potential clonal expansion of dysregulated hepatocytes, that culminate in malignancy.²⁴⁻²⁶

According to an authoritative review, 70%-90% of patients with CHB-associated HCC have cirrhosis.²⁷⁻²⁸ A study within the US Veterans Administration system found that 9.5% of patients with HBV-associated HCC did not have cirrhosis, with African-Americans and Asians at higher risk than other groups.²⁹ The role of demographic factors in determining the frequency of HCC in non-cirrhotic CHB patients was underscored in a study conducted in China that highlighted the association of HBV with NCHCC.³⁰

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arch is ongoing into the mechanisms of clonal transformation caused by the viral DNA into human chromosomes, genetic dysregulation that can culminate in hepatitis B x protein has also been redispensing to HCC through various ways.³¹ These features of CHB infection distinct from HCV, and while certainly a risk in cirrhosis, are also presumed in the higher risk of NCHCC in CHB. Furthermore, they contribute to guidelines for HCC screening and even these two viral infections.

that increase the risk of HCC HBV and HCV-infected patients have a classic study conducted by Chen in Taiwan followed over 3,600 HBsAg-als for a mean of 13 years. The study elevated serum HBV DNA levels (> or mL) were a strong predictor of HCC. In a, several studies and meta-analyses viral therapy with tenofovir for HBV sk of HCC compared to entecavir a similar number of studies report no demographic and other factors are the analyses considered. However, no tested the opposite, i.e., that entecavir h lower risk.³² Notably, coinfection with D virus infection (HDV) increases the risk of HCC development > to six-fold compared with HBV mono-

in patients infected with HBV or HCV, ar is imperative. However, it is important to n treatments will reduce but not completely risk of developing HCC.³³⁻³⁵ This is like factors not influenced by treatment, inclu of cellular damage that occurred prior t The goal of HCV treatment is to achiev is defined as undetectable HCV RNA after the end of treatment. This is no tantamount to virologic "cure," making H very different from HBV treatment, w chronic suppression rather than cure. Dat achieving SVR in HCV-infected patients with a reduced risk of HCC development liver-related outcomes.^{33,34}

Per the AASLD guidance, HCC su recommended for patients with cirrhosis c including HCV, even after SVR is achieve therapy.² However, there is no recom surveillance in patients with F3 fibrosis. Inc recommends HCC surveillance for patie and F3 fibrosis, citing the risk of these understated and further noting that "the advanced fibrosis and cirrhosis cannot defined." EASL further recommends the should continue after SVR has been attai

PAGE-B calculator).² Although patients under 40 years old do not meet the threshold warranting surveillance of an annual HCC incidence over 0.2%, many clinicians have encountered such patients. Consequently, clinicians prefer to discuss surveillance in adult CHB patients, regardless of age, individualized decisions.³⁶

For chronic HCV infection, male sex, a (> 60 years), genotype 3 infection, viral (HBV, HIV), F3 fibrosis, steatosis (especie 3 patients), metabolic syndrome, elevat end of treatment, and history of alcohol abuse have all been reported to potentia to HCC risk.^{34,40} One study found that Black/African American patients develop stages of liver disease compared to other further data are needed to elucidate the biological mechanisms.⁴¹

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Hepatocellular Carcinoma (HCC) Surveillance Beyond the Guidelines

Our literature search on HCC surveillance in CHC F3 patients post-SVR provided mixed results (Table 2), but, as one study concluded, "more cost-effective models that could better identify at-risk individuals, especially among patients with F3 fibrosis are warranted."⁴² It is also important to point out that, following the approval of direct-acting antiviral (DAA) treatment for HCV infection, one controversial study suggested a time-related association between DAA treatment and HCC recurrence.⁴³ However, a recent meta-analysis demonstrated no such association. The study did demonstrate that patients treated with DAAs remain at risk of developing HCC and that DAAs do not necessarily improve survival rates when administered in patients already treated for HCC,⁴⁰⁻⁴¹ however, recent studies focusing on patients treated for HCC with curative intent demonstrated improved survival if treated with antiviral therapy for HBV or HCV infection.⁴²

Table 2. Highlights of a Literature Search on HCC Surveillance in CHC Patients Post-SVR with F3^{34,40-47}

Study Design	Results
A Markov model evaluated the cost-effectiveness of biannual or annual HCC ultrasound surveillance vs. no surveillance in 50-year-old patients with advanced fibrosis after achieving SVR with anti-HCV therapy. ⁴²	HCC surveillance after achieving SVR to HCV treatment was found to be cost-effective for patients with cirrhosis. However, it was not cost-effective for F3 patients.
A study prospectively followed 481 patients with HCV and F3 fibrosis or higher after achieving SVR with interferon-free therapies. Clinical-biological parameters and LSM were performed before starting treatment and at SVR, and HCC surveillance was conducted. Two predictive models based on LSM (ModelA) or FIB-4 score (ModelB) were proposed. ⁴⁴	During a median follow-up of 48.8 months, 29 patients developed HCC (incidence 1.6 per 100 person-years). The study suggested that incorporating multiple factors, including age, serum albumin, FIB-4 score, and transient elastography measurements, could better risk stratify and identify patients with a low risk of HCC (<1%/year). For these patients, HCC surveillance could be discontinued.
A total of 6,796 patients with advanced fibrosis (F3/F4) who developed incident post-SVR HCC between March 2015 and October 2021 were identified from 30 sites in Europe, North America, South America, the Middle East, South Asia, East Asia, and Southeast Asia. ⁴⁶	After adjusting for geographic region, HCC surveillance was associated with early-stage detection (Barcelona Clinic Liver Cancer stage I/II, 71.0% vs. 21.3%, P < .001) and lower mortality rates (adjusted hazard ratio, 0.29, 95% CI 0.18-0.48). The authors concluded that the clinical characteristics, including early-stage detection and prognosis of post-SVR HCC, differed significantly across geographic regions. Surveillance utilization appears to be a high-yield intervention target to improve prognosis among patients with post-SVR HCC globally.
31 studies, from January 1, 2014 to December 31, 2020, assessing HCC incidence or outcomes by cirrhosis status in adults with HCV who achieved SVR after DAAs were identified and analyzed. ⁴⁵	In patients without cirrhosis, including F3 fibrosis, HCC incidence was lower than the thresholds associated with cost-effective HCC screening in patients with F3 fibrosis, the lack of between-study heterogeneity provides strong evidence that HCC screening may not be warranted.
A multicenter, observational, and retrospective study was conducted to describe the post-SVR follow-up in clinical practice for patients with F3 fibrosis (n=219) and determine the predictive factors for the development of HCC. ⁴⁷	The analysis adjusted for sex, age, presence of diabetes and alcohol consumption and found that a post-SVR FIB-4 ≥ 3.25 was associated with a 12-fold increase in HCC risk (p < 0.001).
A systematic review and meta-analysis identified 44 studies (107,548 person-years of follow-up) assessing the incidence of HCC after HCV cure among patients with F3 fibrosis or cirrhosis. ⁴³	The incidence of HCC was 0.5 per 100 person-years (95% CI, 0.3-0.7) among patients with F3 fibrosis, which is below the recommended threshold for cost-effective screening.

DAAs, direct-acting antiviral; F3, stage 3 fibrosis; F4, stage 4 fibrosis; FIB-4, FIBrosis-4 Index; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LSM, liver stiffness measurement; SVR, sustained virologic response.

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