Barriers and Opportunities for Early HCC detection in Patients with Hepatitis B

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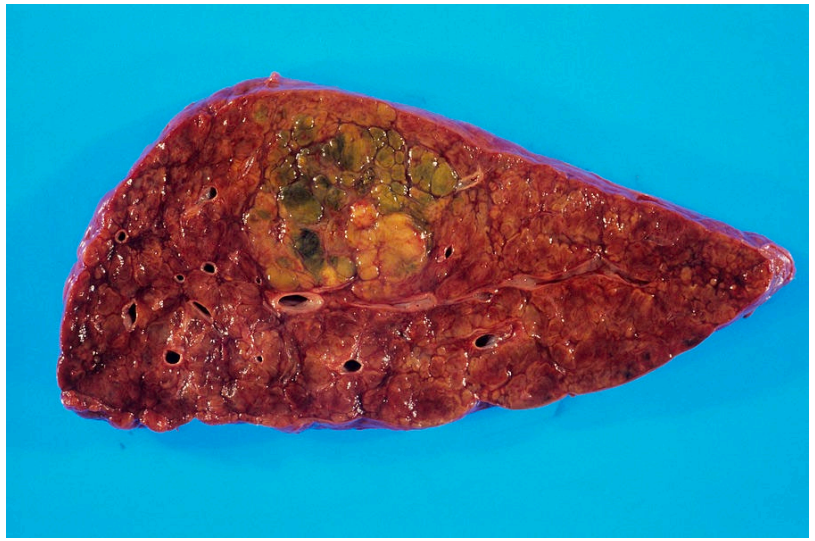
DISCLOSURE SLIDE

- I have no relevant financial relationships to disclose.
- Co-PI of an aMRI HCC screening RCT
- I will discuss investigative use of novel HCC screening tests



Early detection fails across a cascade

Three barriers compound each other to limit early detection.

1. Identify who is at risk

- Undiagnosed HBV
- Incomplete linkage to care
- HCC risk not recognized even when HBV is known.

2. Sustain longitudinal HCC surveillance

Surveillance is a repeated longitudinal process, not a one-time order.

Poor adherence due to:

- Access
- Cost
- Inconvenience

3. Improve current HCC surveillance strategies

- Ultrasound/AFP are imperfect
- One-size-fits-all strategy misses opportunities for better risk-based care.

Central thesis:
improving early detection of HBV-related HCC requires a system-level approach
(patient + provider + healthcare system)
implemented across the cascade continuum 1-2-3.

Barrier 1: the at-risk population is often invisible

In HBV, the first “screening test” is finding and labeling the patient as needing HCC surveillance.

HBV diagnosis → HCC risk recognition

Undiagnosed HBV

Many patients remain undiagnosed or untreated: no diagnosis, no staging, no antiviral decision, no surveillance pathway.

Diagnosed, but HCC risk unrecognized

HBV can confer HCC risk even without cirrhosis. Risk varies by age, sex, family history, country of origin, viral activity, fibrosis and risk scores.

EHR problem + Linkage to Care

HBsAg positivity may be buried in labs, problem lists may be absent surveillance eligibility/need may not be clearly documented .

Care-fragmentation problem

HBV diagnosis, liver staging, primary care, hepatology, radiology, and follow-up often sit in different workflows or different health care systems

Opportunity 1: Diagnose HBV & document HCC surveillance eligibility & plan surveillance

Screen for HBV

- Universal one-time screening recommended in all adults by the CDC since 2023!!

- Emphasize additional screening of high-risk individuals:
  - Endemic-regions
  - High-risk behaviors
  - Family/community members with HBV

Document who needs HCC surveillance

- Cirrhosis or advanced fibrosis
- Family history of HCC
- Africa
- Women age ≥ 50 + Endemic
- Men age ≥ 40 + Endemic
- PAGE-B ≥10
- Important coinfections or cofactors

Actionable outputs

- Start or continue q6momth surveillance
- Use shared decision-making when risk is very low or borderline criteria

Barrier 2: adherence leaks at every surveillance cycle

HCC surveillance is longitudinal: every 6-month cycle creates opportunities for delay and loss to follow-up.

1

Order placed
Requires risk recognition and clinician action

q6 months

3

Result acted on
Requires tracking, abnormal-result escalation, and recall

2

Test completed
Requires access, coverage, transportation, time, and affordability

4

Next cycle scheduled
Surveillance succeeds only if repetition is engineered

→ Success requires buy-in from: Patients + Providers + Healthcare System

Opportunity 2: Optimize the HCC surveillance care pathway

1. **Registry + Recall**
   Identify eligible HBV patients and automatically generate due/overdue lists.

2. **Navigation**
   Close gaps in scheduling, transportation, language, and financial barriers.

3. **Convenience**
   Pair ultrasound/AFP with HBV visits, labs, antiviral monitoring, or local imaging.

4. **Closed-loop tracking**
   Measure completion, abnormal findings, and diagnostic follow-up.

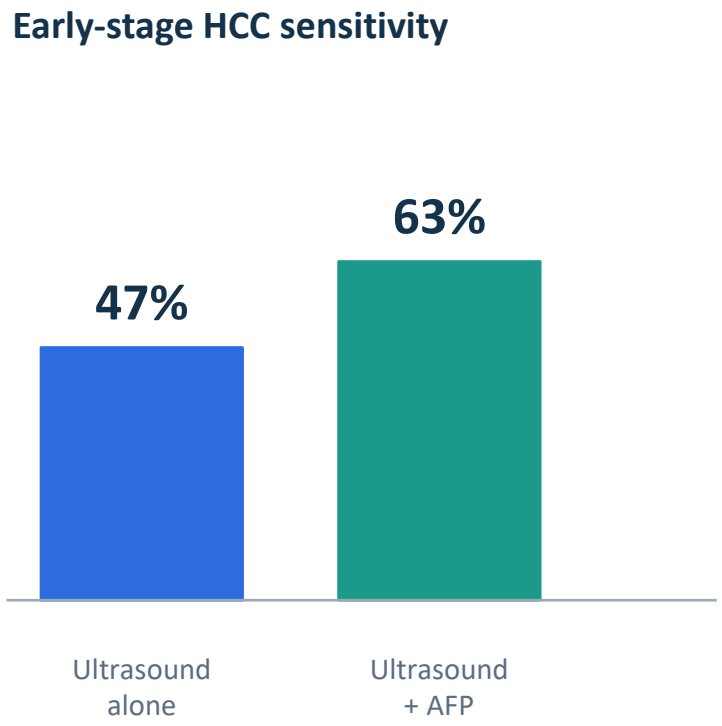
A useful quality metric

“Covered time” in surveillance

Percent of follow-up time protected by a completed surveillance test, rather than a simple yes/no annual count.

Measure the program, not just the order.

Barrier 3A: our standard surveillance tests (ultrasound + AFP) are imperfect



Why ultrasound struggles

Operator dependence, body habitus, heterogeneous cirrhotic liver texture, and poor visualization can all reduce sensitivity for small tumors.

Why AFP is inadequate

Some tumors do not produce AFP; elevations can reflect inflammation or regeneration.

What is emerging

BIOMARKERS: Blood-based biomarkers and biomarker panels; ctDNA/methylation approaches;
ABBREVIATED MRI protocols:
short protocols but maintain high performance.

Opportunity

Improve detection with better modalities while preserving access, adherence, and affordability.

Opportunity 3A: improve HCC screening tests (tests in ongoing trials)

Dynamic contrast-enhanced abbreviated MRI

Dynamic contrast-enhanced phases: arterial, portal-venous, delayed
Acquisition time = 10 minutes

Promise

Very early-stage detection
Highest sensitivity & specificity
Enables LI-RADS
Enables HCC diagnosis (LR5) without recall

Caution

Capacity, cost, contrast, reimbursement

Non-contrast Abbreviated aMRI

DWI + T1 + T2; no contrast
Acquisition time =8-10 minutes

Promise

No gadolinium
Shorter scan
Better sensitivity than ultrasound

Caution

Capacity, Lower sensitivity than DCE aMRI

Protein biomarkers panel

GALAD and related panels

Promise

Blood draw
Easier repeat testing
Better adherence

Caution

Needs prospective validation
Low sensitivity

ctDNA biomarker panels

Oncoguard (EXACT Sciences)
HelioLiver (HELIO Genomics)
Multicancer Early Detection panels

Promise

Blood draw
Novel biology
Better adherence

Caution

Cost, false positives, Sensitivity unknown, MRI-negative workups

Barrier 3B: one-size-fits-all surveillance is hard to justify

HBV-related HCC risk is heterogeneous; surveillance strategy can be matched to risk and test performance.

Current default

Eligible HBV patients

→ ultrasound + AFP every 6 months

Same test. Same pathway.
No matter the risk

Opportunity 3B: Risk Stratification & Risk Based Surveillance

HBV-related HCC risk is heterogeneous; surveillance strategy can be matched to risk and test performance.

Current default

Eligible HBV patients

→ ultrasound + AFP every 6 months

Same test. Same pathway.
No matter the risk

Calculate HCC Risk: REACH-B , PAGE-B, mPAGE

Lower risk	No surveillance or delayed start, with annual reassessment + shared decision-making
Intermediate risk	ultrasound + AFP Consider biomarkers where validated
Highest risk or poor US quality	aMRI or intensified strategy when feasible and cost-effective

Goal: allocate surveillance resources where:

- **they produce the most early-stage detections per burden, dollar, and false-positive cascade OR**
- **they produce the greatest benefit in reducing HCC-related mortality**

Take-home: build an engineered early-detection system

1

Find the population

- Systematically detect HBV
- Stage risk
- Create actionable surveillance eligibility labels.

2

Keep them engaged

Treat surveillance as a longitudinal program with:

- Registries & Recall
- Navigation
- Convenience
- Closed-loop tracking

3

Upgrade the strategy

- Improve test performance with biomarkers & aMRI
- Replace one-size-fits-all strategy with risk-based surveillance.

Take Home Message

In HBV-related HCC, early detection is not limited by a single barrier → it is limited by a cascade that must be improved end-to-end.

Questions?

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