

HelioLiver Dx Detects Hepatocellular Carcinoma Missed by Ultrasound and AFP in Surveillance-Adherent Patients: A Three-Patient Real-World Case Series

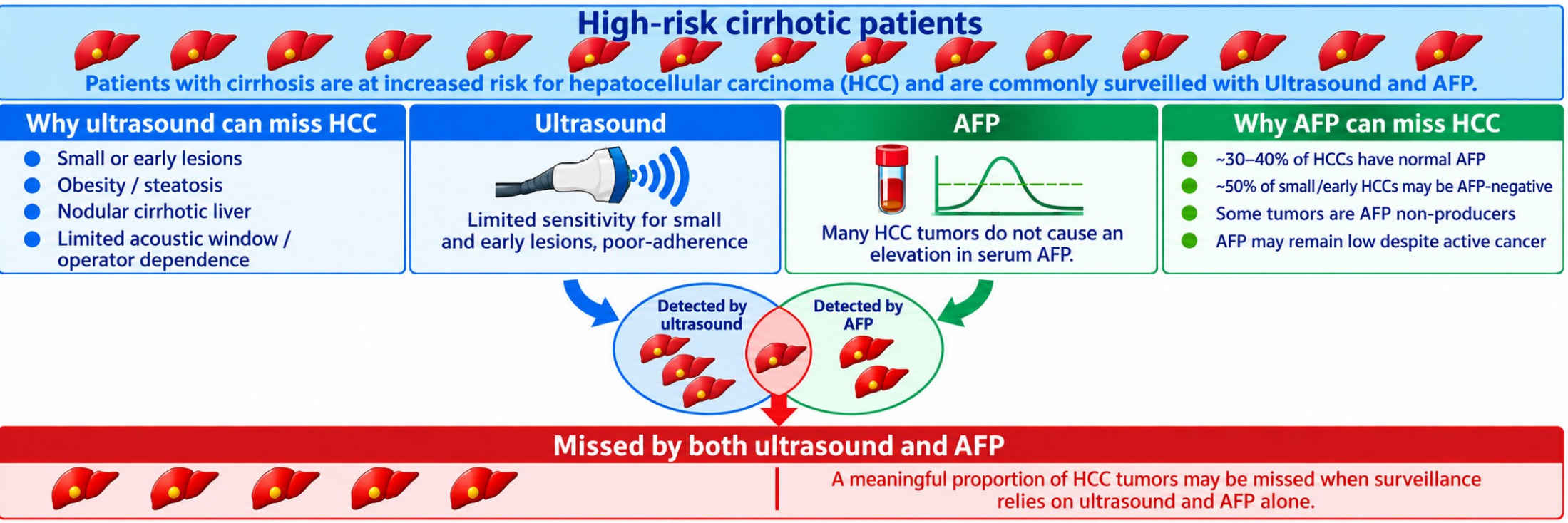
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OVERVIEW

Even with routine HCC surveillance, ultrasound and AFP can miss early-stage disease. Ultrasound may be limited by visualization and operator dependence, while many HCCs do not show elevated AFP. We present three real-world cases in which HelioLiver identified HCC missed by standard surveillance, prompting closer follow-up and earlier diagnosis while potentially curative treatment options remained available.

INTRODUCTION

Earlier detection of hepatocellular carcinoma (HCC) increases the likelihood that patients remain eligible for effective, potentially curative treatment. However, HCC surveillance remains substantially underused¹. Importantly, even patients who adhere to routine surveillance may have early-stage disease missed by standard-of-care ultrasound and alpha-fetoprotein (AFP). Ultrasound performance is operator- and equipment-dependent and may be compromised by obesity, cirrhotic liver morphology, suboptimal visualization, and small tumor size. AFP also has limited sensitivity for early HCC and up to 40–50% of HCCs may not demonstrate elevated AFP². HelioLiver™ Dx is a multi-analyte blood-based test that integrates cell-free DNA (cfDNA) methylation with serum protein biomarkers and demographic variables. In the prospective, blinded, multicenter CLiMB study, HelioLiver demonstrated greater sensitivity than ultrasound, with its largest performance advantage observed in small and T1 tumors³. Here, we present real-world patient cases illustrating the clinical utility of HelioLiver in identifying HCC missed by routine ultrasound and AFP surveillance.



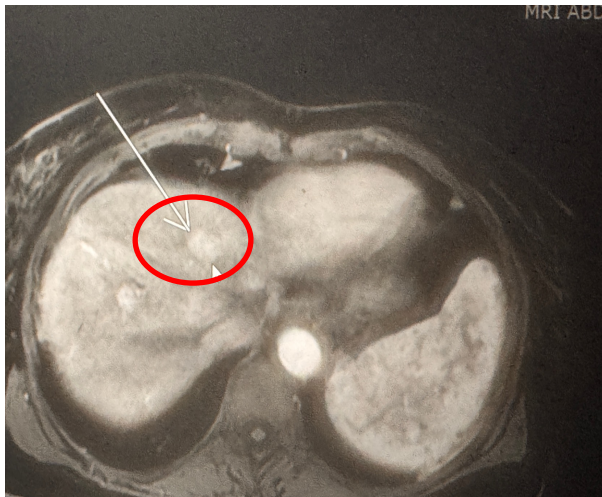
METHODS

We present three patients with cirrhosis and elevated HCC risk in whom HelioLiver was incorporated into routine surveillance. Patient characteristics, comorbidities, ultrasound and confirmatory magnetic resonance imaging (MRI) findings, AFP levels, HelioLiver results, tumor features and pathology, and longitudinal clinical outcomes were reviewed. The impact of HelioLiver on follow-up intensity, clinical management, treatment decisions, and patient outcomes was assessed descriptively.

RESULTS

Case #1

77-year-old woman with decompensated cirrhosis, including ascites managed with diuretics and grade 2 esophageal varices on EGD. Underwent serial ultrasound surveillance for the past 3–4 years, with no hepatic lesions detected.



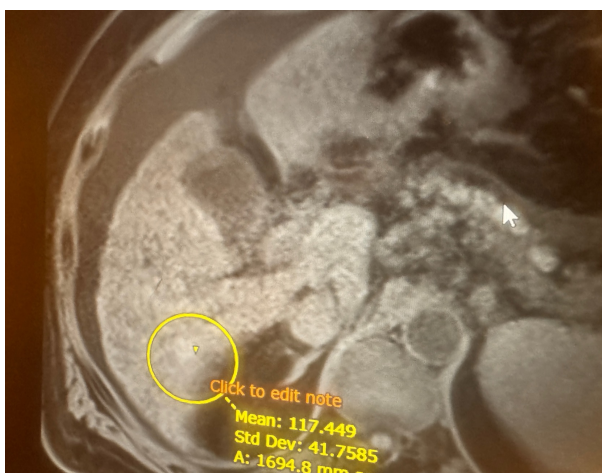
HelioLiver Result: Abnormal/Positive

Test	Value
AFP	14 ng/mL (ref range 0.3 – 12.1 ng/mL)
AFP-L3%	18.1 % (ref range <10 %)
DCP	78 ng/mL (ref range < 7.7 ng/mL)
Methylation score	0.95 (ref range < 0.57)

- MRI prompted by the abnormal HelioLiver result identified a 19 mm LR-4 lesion in the left hepatic lobe, with arterial phase enhancement and no washout.
- Patient was not considered a transplant candidate due to advanced age and comorbidities.
- Given the positive HelioLiver result, preserved liver function, and ability to tolerate locoregional therapy, the clinical team elected to proceed with Y-90 radioembolization.

Case #2

59-year-old male with MASLD-related cirrhosis (MELD 13). Comorbidities: diabetes, obesity, COPD. No decompensation and hepatic function is within normal limits. Ultrasound surveillance over 4 years revealed no liver lesions.



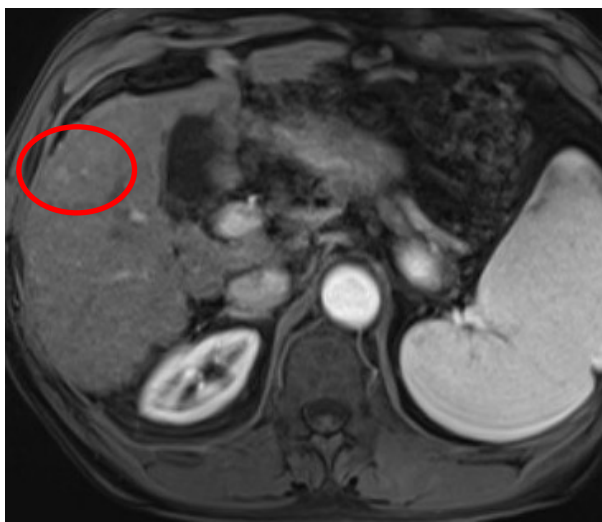
HelioLiver Result: Abnormal/Positive

Test	Value
AFP	12.2 ng/mL (ref range 0.3 – 12.1 ng/mL)
AFP-L3%	16.2 % (ref range <10 %)
DCP	80.6 ng/mL (ref range < 7.7 ng/mL)
Methylation score	0.85 (ref range < 0.57)

- MRI prompted by the abnormal HelioLiver result identified an 8 mm LR-3 lesion.
- The lesion is suspected to be very early HCC but does not yet meet radiographic criteria for a definitive diagnosis.
- The patient will undergo close imaging surveillance with repeat MRI every 3 months.

Case #3

62-year-old male with alcoholic cirrhosis with symptomatic ascites and encephalopathy, referred for liver transplant. Ultrasound did not detect any hepatic lesions. CT around the same time was also negative for any hepatic lesions.



HelioLiver Result: Abnormal/Positive

Test	Value
AFP	1.1 ng/mL (ref range 0.3 – 12.1 ng/mL)
AFP-L3%	NC
DCP	0.3 ng/mL (ref range < 7.7 ng/mL)
Methylation score	0.70 (ref range < 0.57)

- MRI was done due to abnormal HelioLiver, which noted a 9 mm lesion with arterial enhancement and washout in segment V.
- The lesion will be closely monitored with MRI every 3 months until it reaches 2 cm, at which point treatment and liver transplant listing are planned.
- MRI will be used for surveillance rather than CT, as the lesion was not visualized on the initial CT.
- cfDNA methylation is the only biomarker that is elevated.

CONCLUSIONS

These real-world cases demonstrate HelioLiver's ability to detect HCC when routine surveillance with AFP and ultrasound remains negative.

By leveraging cfDNA methylation biomarkers that capture early tumor-associated epigenetic changes, HelioLiver identifies cancers that conventional surveillance can miss, providing clinicians with an opportunity for earlier diagnosis and intervention.

REFERENCES

1. Tang NSY, et al. Meta-analysis: utilisation of hepatocellular carcinoma surveillance. Aliment Pharmacol Ther. 2026;63(1):8-16. doi:10.1111/apt.70403.
2. Singal AG, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology. 2023;78(6):1922-1965. doi:10.1097/HEP.0000000000000466.
3. Taggart DJ, et al. A multi-analyte cfDNA-based blood test for early detection of hepatocellular carcinoma. J Hepatol. 2026;85(3):528-536. doi:10.1016/j.jhep.2026.04.012.