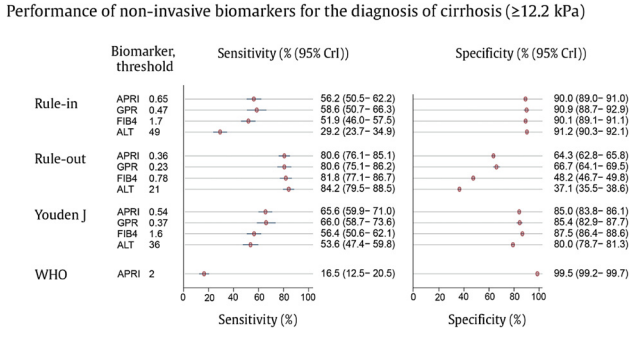
Low-cost non-invasive biomarkers of liver fibrosis are needed to identify patients at risk of HBV-related mortality who therefore require antiviral treatment. We evaluated the performance of the biomarkers APRI (AST to platelet ratio index), FIB-4 and GPR (GGT to platelet ratio) in an individual patient data (IPD) meta-analysis.

Method: We included data from HEPSANET, a network comprised of 12 cohorts of HBsAg-positive individuals in 8 sub-Saharan African countries. We used transient elastography as a reference test for cirrhosis (≥12.2 kPa) and significant fibrosis (≥7.9 kPa). We excluded patients who were pregnant, had hepatitis C, D, or HIV co-infection, were on hepatitis B therapy or had acute hepatitis. Upper limits of normal were 40 U/L for AST/AST and 61 U/L for GGT. We fitted a bivariate Bayesian IPD model with patient-level covariates and study-level random effects.

Results: We included 3549 patients. Median age was 33 years (IQR 28–41) and 60% were male. The prevalence of significant fibrosis and cirrhosis among included cohorts was 18% and 7% respectively. APRI and GPR had the best discriminant performance (area under curve 0.81 and 0.82) relative to FIB-4 (0.77) or ALT alone (0.70) for cirrhosis. The World Health Organization (WHO) threshold of APRI>2.0 was associated with sensitivity of 16.5% (95% credible interval 12.5–20.5) and specificity of 99.5% (99.2–99.7) for cirrhosis. At rule-in thresholds for cirrhosis APRI (cut-off 0.65) had sensitivity of 56.2% and specificity of 90.0%; GPR (cut-off 0.47) had sensitivity of 58.6% and specificity 90.9%. At rule out-thresholds for cirrhosis APRI (0.33) had sensitivity and specificity of 80.6% and 64.3%; GPR (0.23) had sensitivity 80.6% and specificity of 66.7% (Figure). The subset of asymptomatic patients who were diagnosed with HBV through routine screening had a mean cirrhosis prevalence of 2.5%, and APRI (cut-off 0.65) had a positive predictive value (PPV) of 13.2% and negative predictive value (NPV) of 98.8%. Among patients diagnosed with HBV due to suspected liver disease, cirrhosis prevalence was 27%; with APRI cut-off 0.65, PPV was 59.6% and NPV 84.5%.

Conclusion: APRI at the WHO-recommended threshold of 2.0 has a poor sensitivity for the diagnosis of cirrhosis in sub-Saharan Africa; WHO guidelines should be revised for the WHO African region to reflect these findings. APRI and GPR had equivalent diagnostic performance and performed best at ruling out cirrhosis but were less good at correctly identifying cases. Programs need to be aware of the significant trade-offs between under- and over-diagnosis of liver cirrhosis when implementing low-cost fibrosis markers in hepatitis B programs in sub-Saharan Africa.



OS016

Prediction of ten-year risk of severe liver disease in the general population using commonly available biomarkers

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Background and aims: Estimating risk for severe liver disease, including cirrhosis, in the general population is complicated in part due to the rarity of this outcome. Existing prediction tools are suboptimal and there is a need for improvement. Here, we aimed to identify subgroups of persons in the general population with high risks for development of severe liver disease using commonly available biomarkers.

Method: We used laboratory and clinical data on 126, 925 individuals aged 35–79, in Stockholm, Sweden, with clinical examinations between 1985 and 1996. No individuals had known chronic liver disease, a drug- or alcohol use disorder at baseline. Nationwide registries were used to ascertain ten-year cumulative incidence of severe liver disease, a composite of diagnoses corresponding to cirrhosis or its complications. Candidate biomarkers were selected based on if they meaningfully improved prediction of severe liver disease in addition to the established FIB-4 score. They were then categorized and combined, creating subgroups with different risk profiles.

Results: During a follow-up of average 9.3 years, we ascertained 630 incident cases of severe liver disease (0.5%). On top of the FIB-4 score we identified age, impaired glucose, and gamma-glutamyl transferase (gGT) to meaningfully improve a classification of risk. 24 risk groups were created, with a cumulative incidence of severe liver disease at ten years ranging from 0.2% (age 35–65, low FIB-4, no impaired glucose and normal gGT) to 32.1% (age 35–65, high FIB-4, impaired glucose and high gGT). A heatmap of these risk groups was created (Figure 1).

Cumulative incidence of severe liver disease at ten years			FIB-4 Low	FIB-4 Intermediate	FIB-4 High
gGT high	Impaired glucose	age ≥66	13.0	13.7	29.1
		age 35-65	2.6	10.7	32.1
	No Impaired glucose	age ≥66	3.6	0.0	22.7
		age 35-65	2.2	7.4	25.4
gGT normal	Impaired glucose	age ≥66	1.3	2.8	12.5
		age 35-65	0.6	1.0	6.0
	No Impaired glucose	age ≥66	0.6	0.7	2.5
		age 35-65	0.2	0.4	5.5

Figure 1: Heatmap of subgroups with differing risk for severe liver disease at ten years, in percent.

Conclusion: Estimates of risk of severe liver disease in the general population using the FIB-4 score can be substantially improved by adding age and biomarkers commonly available in the primary care setting.

OS017

Gadoxetic acid-enhanced MRI-derived Functional Liver Imaging Score (FLIS) and spleen diameter provide complementary information for risk stratification in ACLD

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Background and aims: The Functional Liver Imaging Score (FLIS) derived from gadoxetic acid-enhanced MRI (GA-MRI) correlates with hepatic function in chronic liver disease (CLD) patients. Splenic metrics, i.e., volume and craniocaudal diameter (SCCD) are markers of portal hypertension, a key driver of disease progression.