# NON-INVASIVE IDENTIFICATION OF SEVERE NAFLD AND RISK STRATIFICATION OF CLINICAL OUTCOMES USING FIBROSCAN-AST (FAST) SCORE IN 1683 PEOPLE WITH HIV

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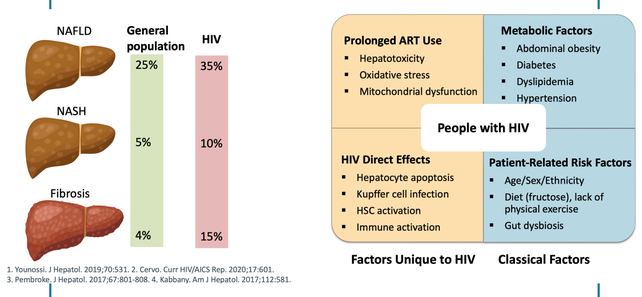
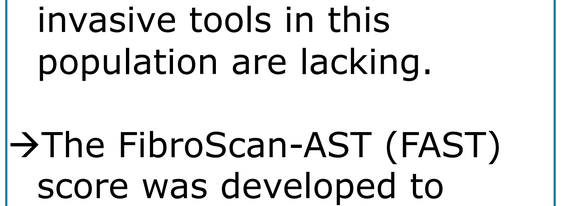
## Background

→Non-alcoholic fatty liver disease (NAFLD) is very frequent in people with HIV (PWH)




1. Younossi. J Hepatol. 2019;70:531. 2. Cervo. Curr HIV/AICS Rep. 2020;17:601.
3. Pembroke. J Hepatol. 2017;67:801-808. 4. Kabbany. Am J Hepatol. 2017;112:581.

→The European AIDS Clinical Society Guidelines recommend screening for NAFLD-associated liver fibrosis in PWH.




→However, longitudinal studies investigating outcomes and identifying optimal non-invasive tools in this population are lacking.

→The FibroScan-AST (FAST) score was developed to identify patients with NASH and significant fibrosis, associated with higher risk of end-stage liver disease.

## Aim

***Primary***: To estimate prevalence and evolution to outcomes of severe NAFLD defined by FAST score in a multicenter cohort of PWH

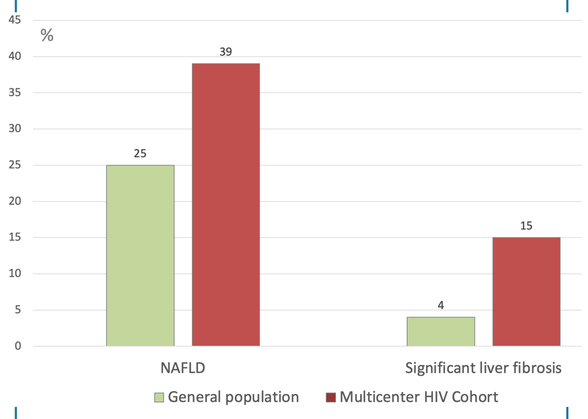
***Secondary***: To compare diagnostic value of FAST score to FIB-4, NAFLD fibrosis score, APRI to predict clinical outcomes

## Methods

→Participants of 3 prospective cohorts in Canada (LIVEHIV) and Italy (Modena and Palermo) as part of a routine screening program for NAFLD

→Almost 2,000 consecutive PWH included

→Patients with HBsAg pos, chronic HCV or alcohol abuse excluded




**Diagnostic tools**

- Vibration controlled transient elastography performed from January 2014 to December 2021
- FAST computed from liver stiffness measurement, controlled attenuation parameter, AST categorized as:

≤0.35 low-risk NASH zone
0.35-0.67 intermediate risk
>0.67 high-risk NASH zone

**Cross-sectional phase**

-Prevalence of FAST categories
-Multivariable logistic regression analysis: factors associated with intermediate-high risk NASH zone (FAST>0.35)

**Longitudinal phase**

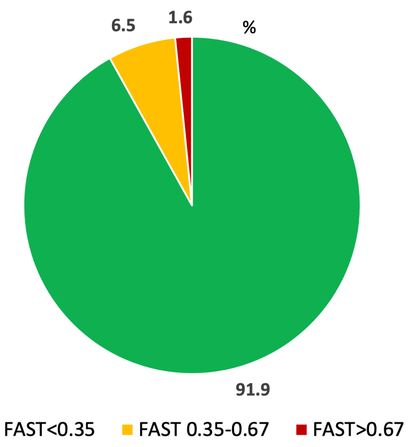
-Survival analysis: incidence of liver-related events (ascites, encephalopathy, variceal bleeding, HCC) and extra-hepatic events (cancer, cardiovascular disease) by FAST score category
-Multivariable time-dependent Cox proportional hazard models: predictors of liver-related events
-Time-dependent AUROCs: performance of FAST score compared to serum fibrosis biomarkers in predicting outcomes

$$\text{FAST score} = \{\exp(-1.65 + 1.07 \times \ln(\text{LSM}) + 2.66 \times 10^{-8} \times \text{CAP}^3 - 63.3 \times \text{AST}^{-1})\} / \{1 + \exp(-1.65 + 1.07 \times \ln(\text{LSM}) + 2.66 \times 10^{-8} \times \text{CAP}^3 - 63.3 \times \text{AST}^{-1})\}.$$

## Results

**Crossectional phase**

| Variable (mean or %) | Total (n=1683) |
|---|---|
| Age | 50 ± 10 yrs |
| Male sex | 74% |
| White/Caucasian | 55% |
| Diabetes | 32% |
| BMI | 25 ± 5 Kg/m$^2$ |
| Time since HIV diagnosis | 16 ± 10 yrs |
| CD4 | 688 ± 315 cells/mL |
| ALT | 39 ± 18 IU/L |
| AST | 28 ± 23 IU/L |
| CAP | 237 ± 57 dB/m |
| Liver stiffness | 6.5 ± 5.8 kPa |
| FIB-4 | 1.67 ± 1.41 |



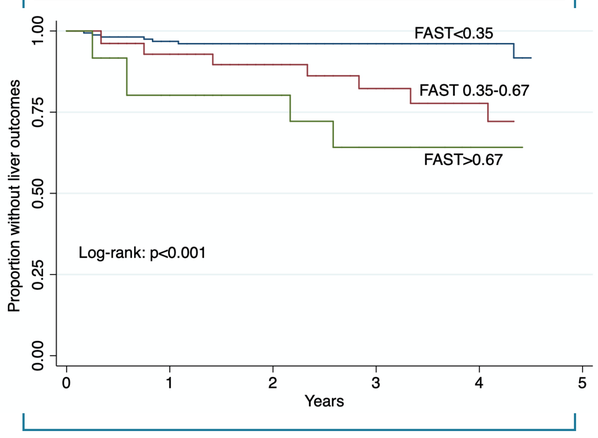

**Factors associated with intermediate-high NASH zone by FAST**

| Variable | Adjusted Odds Ratio | 95% CI | p |
|---|---|---|---|
| BMI (per Kg/m$^2$) | 1.14 | 1.10-1.19 | <0.001 |
| Male sex (Y vs N) | 1.96 | 1.16-3.32 | 0.012 |
| Time since HIV diagnosis (per 10 years) | 1.57 | 1.26-1.997 | <0.001 |
| Diabetes (Y vs N) | 0.96 | 0.77-1.20 | 0.712 |
| CD4 cell count <200 cells/mL (Y vs N) | 3.73 | 1.58-8.82 | 0.003 |

**Longitudinal phase**

Median follow-up → 3.5 years (IQR 2.2-4.5)
Incidence of liver-related outcomes → 7%
Incidence of extra-hepatic outcomes →11.5% (30% extrahepatic cancer; 70% cardiovascular)

| Incidence rates (per 100 PY) | FAST<0.35 | FAST>0.35 |
|---|---|---|
| Liver-related outcomes | 1.6 (0.7-3.4) | 7.6 (4.2-13.7) |
| Extra-hepatic outcomes | 4.5 (2.8-7.4) | 7.2 (3.7-13.8) |



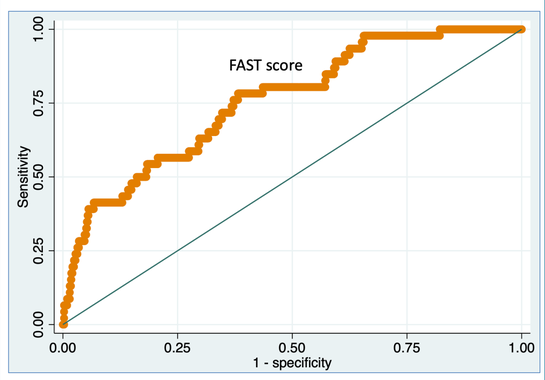

## Results (cont.)

FAST score >0.35 predicted liver-related outcomes (adjusted hazard ratio 4.44, 95% CI 1.66-11.9; p=0.001)

Model adjusted for sex, BMI, diabetes, duration of HIV infection, protease inhibitors exposure and CD4 <200 cells/mL

**Accuracy for liver outcomes**

| Non-invasive test | AUROC | Standard error | 95% CI |
|---|---|---|---|
| FAST score | 0.77 * | 0.03 | 0.70-0.84 |
| FIB-4 | 0.68 | 0.04 | 0.59-0.75 |
| NAFLD Fibrosis Score | 0.60 | 0.04 | 0.52-0.68 |
| APRI | 0.71 | 0.04 | 0.63-0.78 |




## Limitations

→Limited number of deaths to assess mortality
→Competing risk analysis not performed
→Relatively limited representation of women and ethnical diversity
→Could not account for individual antiretroviral regimens

## Conclusion

→PWH without viral hepatitis are at risk for severe NAFLD, supporting the recent EACS guidelines on screening for liver fibrosis
→Although BMI seems the main associated factor, HIV-related (CD4, HIV duration) affect NAFLD severity
→FAST score predicts liver-related outcomes in this population
→Prognostic accuracy of simple serum biomarkers suboptimal
→*Ad hoc* models should incorporate HIV-related factors

**References**
Younossi. J Hepatol. 2019;70:531. Cervo. Curr HIV/AICS Rep. 2020;17:601; Pembroke. J Hepatol. 2017;67:801-808. Kabbany. Am J Hepatol. 2017;112:581; Newsome et al, Lancet Gastro Hepatol 2020;5:362-373 2019; Price et al, Clinical Infectious Dis 2022; May 3; Sebastiani et al, HIV Medicine 2020;21:96-108; Cervo et al, Clinical Infectious Diseases 2020;71:e694-e-701

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