Determinants of liver steatosis in people living with HIV on antiretroviral therapy

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Riebensahm C[1,2], Berzigotti[3,4], Surial B[1], Günthard H[5,6], Tarr, P.E.[7], Furrer H[1], Rauch A[1], Wandeler, G[1,8], Swiss HIV Cohort Study

[1]Department of Infectious Diseases, Bern University Hospital, University of Bern, Switzerland, [2]Graduate School of Health Sciences, University of Bern, Switzerland, [3]Department for Visceral Surgery and Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, Switzerland, [3]Hepatology, [4]Department of BioMedical Research, University of Bern, Bern, Switzerland, [5]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, [6]Institute of Medical Virology, University of Zurich, [7]University Department of Medicine, Kantonsspital Bruderholz, University of Basel, [8]Institute of Social and Preventive Medicine, University of Bern, Switzerland

BACKGROUND

Given the impact of new antiretroviral therapy (ART), including integrase strand inhibitors (InSTI) and tenofovir alafenamide (TAF), on weight and metabolic parameters, their potential contribution to the development of liver steatosis is of concern. We evaluated the determinants of liver steatosis among people living with HIV (PLWH) in a single center of the Swiss HIV Cohort Study (SHCS), and described the proportion of individuals with metabolic dysfunction-associated fatty liver disease (MAFLD), according to the 2020 definition[1].

METHODS

Between November 2019 and August 2021, we enrolled consecutive PLWH at Bern University Hospital. Individuals with active or past viral hepatitis co-infection and pregnant women were excluded. All participants were asked to undergo liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) using transient elastography (TE). Liver steatosis was defined as follows: S1 (mild steatosis) if CAP 248-267dB/m, S2 (moderate steatosis) if CAP 268-279dB/m, and S3 (severe steatosis) if CAP ≥280dB/m. Liver fibrosis was categorized according to Metavir equivalent stage: F0-1 (no or mild fibrosis) if LSM <7.1kPa, F2-3 (significant fibrosis) if LSM 7.1-11kPa, and F4 (cirrhosis) if LSM ≥ 11.1kPa 2.

We used multivariable logistic regression to explore factors associated with steatosis.

RESULTS

Table 1. Baseline characteristics, stratified by BMI category

Characteristics	BMI <25 kg/m²	BMI ≥25 kg/m²
	N= 204	N= 212
Median age, years (IQR)	51 (42-59)	52 (46-59)
Female sex (%)	52 (25.5)	61 (28.8)
Region of origin (%)		
Europe	154 (75.5)	151 (71.2)
Africa	27 (13.2)	52 (24.5)
Other	23 (11.3)	9 (4.2)
HIV transmission group (%)		
MSM	112 (54.9)	90 (42.5)
Other	92 (45.1)	122 (57.5)
Arterial hypertension (%)	49 (24.0)	72 (34.0)
Diabetes (%)	9 (4.4)	28 (13.2)
Dyslipidemia (%)	59 (28.9)	98 (46.2)
Median BMI, kg/m² (IQR)	22.1 (20.8-23.9)	29.6 (26.6-31.5)
Median ALT, U/L (IQR)	28.0 (19.0-30.5)	33.2 (22.0-40.0)
Hazardous alcohol consumption (%)	41 (22.2)	42 (22.0)
Median current CD4+ count, cells/µl (IQR)	740 (535-897)	792 (577-985)
Median eGFR in mL/min (IQR)	91 (75-104)	89 (71-100)
ART duration, years (IQR)	13.3 (7.0-20.0)	12.0 (6.0-19.0)
Exposed to TAF (%)	103 (50.5)	126 (59.4)
Exposed to InSTI (%)	141 (69.1)	138 (65.1)

Abbreviations: IQR, interquartile range; MSM, men who have sex with men; PWID, patients who inject drugs; BMI, body mass index; CV, cardiovascular; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ART, antiretroviral therapy; TAF, tenofovir alafenamide; InSTI, integrase-strand transfer inhibitor.

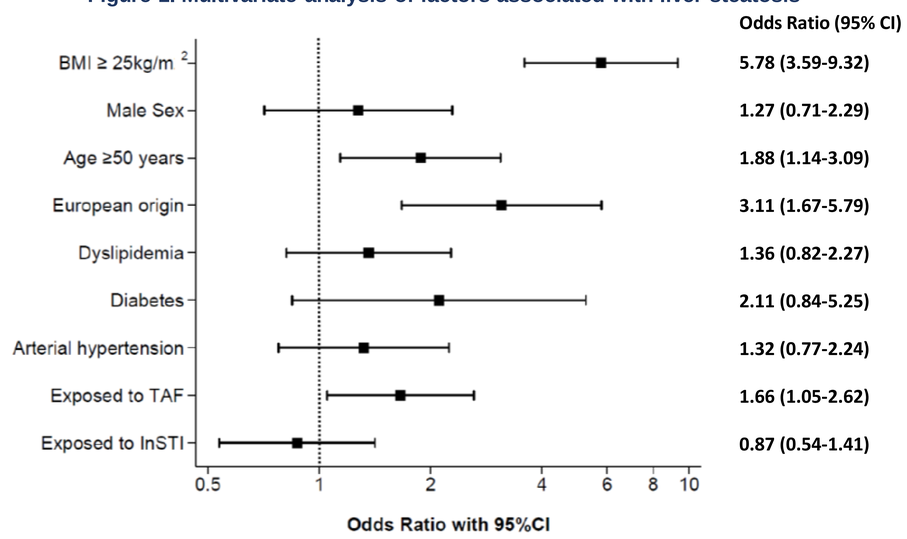
- **This single center study suggests that half of the patients on ART in Switzerland have any degree of liver steatosis and over one third have severe steatosis**
- **In addition to well-established risk factors, our results indicate an association between the use of TAF and liver steatosis**

RESULTS

Of 480 eligible individuals, 416 (86.7%) agreed to participate and had a reliable TE measurement. Cardio-metabolic risk factors were more common in patients with a BMI ≥25 kg/m². A similar proportion of participants was exposed to InSTI in both groups (69% and 65%, respectively). Among individuals with a BMI <25 kg/m², 50.5% were on a TAF-containing regimen, whereas this proportion was 59.4% among patients with a BMI ≥25 kg/m². Baseline characteristics are shown in Table 1.

Overall, 212 (51.0%) participants had liver steatosis, including 143 with severe steatosis. The proportion of individuals with liver steatosis was 69.8% in patients with a BMI ≥25 kg/m² and 31.4% in individuals with a BMI <25 kg/m². Of all participants, 179 (43.0%) met the criteria for MAFLD.

Figure 1. Multivariate analysis of factors associated with liver steatosis



Abbreviations: BMI, body mass index, TAF; tenofovir alafenamide; InSTI, integrase-strand transfer inhibitor; OR, odds ratio; CI, confidence interval

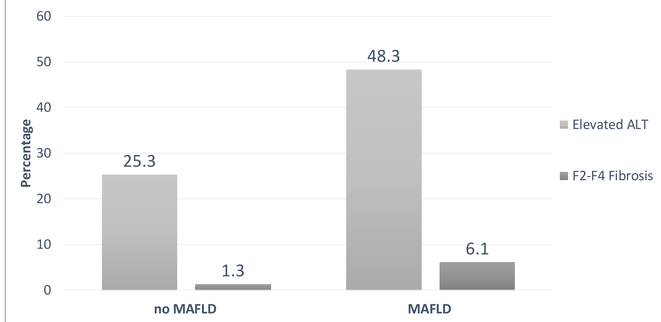
In multivariable analyses, patients were more likely to have liver steatosis if they were ≥50 years, of European origin, or had a BMI ≥25 kg/m². Whereas we found no association between InSTI exposure and liver steatosis, participants currently on a TAF-containing regimen were more likely to have steatosis than those not on TAF (Figure 1). The latter association did not depend on the time spent on a TAF-containing regimen.

When we included weight increase of 10% as a further risk factor to our multivariable model, both weight gain (aOR, 3.12; 95% CI, 1.42-6.83) and exposure to TAF (aOR, 1.65; 95% CI, 1.03-2.65) remained significantly associated with liver steatosis.

RESULTS

Of 212 individuals with S1-S3 steatosis, 6 (2.8%) had a LSM compatible with significant fibrosis (F2-F3) and 5 (2.4%) a measurement compatible with cirrhosis (F4). Among the full study population, 146 (35.2%) patients had elevated ALT. The proportion of individuals with elevated transaminases was higher in patients with steatosis compared to those without steatosis (44.6% vs. 25.5%).

Figure 2. Distribution of significant fibrosis or cirrhosis and elevated ALT by MAFLD category



Abbreviations: ALT, alanine aminotransferase, MAFLD, Metabolic associated fatty liver disease

Figure 2 shows the distribution of ALT elevation and significant fibrosis or cirrhosis by MAFLD classification. Among lean PLWH with liver steatosis, who did not meet the criteria for MAFLD, 8 (24.2%) had elevated transaminases and none had fibrosis.

Conclusion

Our data show a high prevalence of liver steatosis among PLWH on ART in Switzerland.

In addition to well-established risk factors such as age, ethnicity and obesity, the use of TAF was significantly associated with hepatic steatosis.

Overall, MAFLD was diagnosed in 43% of participants, including in 17% of individuals with a BMI <25 kg/m² and liver steatosis.

References

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Contact: Riebensahm, Carlotta, MD | carlotta.riebensahm@insel.ch

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