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## BACKGROUND

- Nonalcoholic fatty liver disease (NAFLD) can progress to cirrhosis, hepatocellular carcinoma, and end-stage liver failure.<sup>1</sup>
- NAFLD has become a major cause of liver disease including among persons with HIV, but few studies have examined NAFLD incidence in this population.<sup>2-4</sup>
- We aimed to determine NAFLD incidence among persons with and without HIV within the Multicenter AIDS Cohort Study (MACS), a prospective cohort of men who have sex with men.

## METHODS

### Study population and measurements

- Participants of the MACS Coronary Atherosclerosis Progression Study<sup>5</sup> with all the following criteria were included:
  - 2 non-contrast CT scans with complete visualization of the liver and spleen
  - Consumed <3 alcoholic drinks/day on average
  - Had stored cells available for *PNPLA3* testing
- Additional inclusion criteria for the MACS Coronary Atherosclerosis Progression Study: age 40-70, no prior coronary intervention, eGFR >60 mL/min/1.73m<sup>2</sup>
- Baseline CT scans were performed from 2010-2013 and follow-up scans from 2015-2017.
  - NAFLD was defined as liver/spleen HU ratio <1.0.<sup>6</sup>
  - Visceral adipose tissue (VAT) was measured in one axial image obtained between the 4<sup>th</sup> and 5<sup>th</sup> lumbar vertebrae.

### Statistical analysis

- Incident NAFLD was defined as men without NAFLD at baseline who had NAFLD at follow-up.
- Incidence rates (IRs) were calculated as number of incident NAFLD events divided by the total follow-up time (person-years [PYs]).
- Poisson regression was used to compare NAFLD incidence rates.

## RESULTS

- 268 men were eligible: 173 men with HIV (MWH) and 95 men without HIV (MWOH):
  - Median age 57 (IQR 53-62)
  - 53% White non-Hispanic, 35% Black non-Hispanic
- Median time between CT scans was 4.5 years (IQR 3.8-5.0).
- **Incident NAFLD was detected in 30 men (11.1%) with an overall IR of 2.5/100 PYs (95% CI 1.8-3.6).**

The incidence rate of CT-measured NAFLD was high at 2.5/100 PYs. Higher BMI and visceral adiposity, but not HIV, were associated with incident NAFLD.

**TABLE 1. Higher BMI and VAT at baseline but not HIV were associated with incident NAFLD.\***

	Baseline		NAFLD Incidence			
	N	%	N	PYs	IR per 100 (95% CI)	p-value
Population	268	100	30	1186.6	2.5 (1.8, 3.6)	
HIV status						0.76
MWOH	95	35.4	11	403.0	2.7 (1.5, 4.9)	
MWH	173	64.6	19	783.6	2.4 (1.6, 3.8)	
Age (years)						0.72
40-49	82	30.6	8	348.2	2.3 (1.2, 4.6)	
50-59	139	51.9	18	629.9	2.9 (1.8, 4.5)	
60+	47	17.5	4	208.5	1.9 (0.7, 5.1)	
Race/Ethnicity						0.24
White NH	141	52.6	20	613.1	3.3 (2.1, 5.1)	
Black NH	94	35.1	7	429.9	1.6 (0.8, 3.4)	
Other race/ethnicity	33	12.3	3	143.7	2.1 (0.7, 6.5)	
BMI (kg/m <sup>2</sup> )						0.03
<25	109	46.4	6	481.5	1.3 (0.6, 2.8)	
25-30	84	35.7	11	370.3	3.0 (1.7, 5.4)	
>30	42	17.9	9	187.8	4.8 (2.5, 9.2)	
Abdominal VAT (mm <sup>2</sup> )						0.003
Quartile 1	66	24.7	4	291.4	1.4 (0.5, 3.7)	
Quartile 2	67	25.1	2	295.3	0.7 (0.2, 2.7)	
Quartile 3	67	25.1	8	290.1	2.8 (1.4, 5.5)	
Quartile 4	67	25.1	16	305.5	5.2 (3.2, 8.6)	
Diabetes						0.21
No	168	62.7	15	728.0	2.1 (1.2, 3.4)	
Yes	100	37.3	15	458.6	3.3 (2.0, 5.4)	
On lipid-lowering agent						0.08
No	151	63.2	13	666.7	2.0 (1.1, 3.4)	
Yes	88	36.8	15	394.3	3.8 (2.3, 6.3)	
PNPLA3 (rs738409)						0.49
CC	153	57.1	14	681.4	2.1 (1.2, 3.5)	
GC	100	37.3	14	436.0	3.2 (1.9, 5.4)	
GG	15	5.6	2	69.1	2.9 (0.7, 11.6)	
HCV+						0.32
No	241	92.3	28	1063.3	2.6 (1.8, 3.8)	
Yes	20	7.7	1	92.1	1.1 (0.2, 7.7)	
HBV+						0.27
No	253	96.9	27	1123.0	2.4 (1.7, 3.5)	
Yes	8	3.1	2	33.4	6.0 (1.5, 23.9)	

\*Additional covariates not significantly associated with NAFLD incidence include: HOMA-IR, abdominal SAT, HDL, LDL, triglycerides, hypertension, undetectable HIV RNA, CD4 cell count <500 cells/mm<sup>3</sup>, current HAART, cumulative HAART, and cumulative NNRTI, NRTI, and PI use.

**TABLE 2. Higher abdominal VAT at baseline was associated with increased risk of NAFLD on multivariable analysis.**

	Unadjusted		Adjusted*	
	IRR (95% CI)	p-value	IRR (95% CI)	p-value
Age (per 10 years)	0.9 (0.6, 1.4)	0.66	0.63 (0.33, 1.18)	0.15
Black NH (ref=White/Other)	0.56 (0.3, 1.3)	0.16	0.77 (0.30, 2.02)	0.60
Infection Status				
MWH (ref=MWOH)	0.95 (0.5, 1.9)	0.88	0.77 (0.33, 1.79)	0.55
Chronic hepatitis B virus	2.6 (0.8, 8.8)	0.13	2.57 (0.56, 11.82)	0.22
Chronic hepatitis C virus	0.42 (0.1, 3)	0.39	0.44 (0.06, 3.43)	0.43
PNPLA CG/GG (ref=CC)	1.52 (0.8, 3)	0.22	1.47 (0.70, 3.13)	0.31
Abdominal VAT (per 10 cm)	1.06 (1, 1.1)	<.001	1.05 (1.00, 1.11)	0.04
ln(HOMA-IR)	2.1 (1.3, 3.3)	0.002	1.33 (0.61, 2.91)	0.48

\*Adjusted for the variables listed and MACS site

## CONCLUSIONS

- Visceral adiposity, but not HIV infection, was associated with incident NAFLD as determined by serial non-contrast CT scans.
- Although MWH were not at higher risk of NAFLD than MWOH, the incidence of NAFLD among MWH in the study (2.4/100 PYs) was higher than the IRs previously published for hepatitis B virus (1.5/100 PYs) and hepatitis C virus (0.4/100 PYs) among MWH in the larger MACS cohort.<sup>7,8</sup>
- The high incidence of ≥moderate steatosis suggests that NAFLD will continue to increase as a cause of liver disease in persons with HIV.

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