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CLONAL HEMATOPOIESIS, INFLAMMATION, AND CORONARY ARTERY DISEASE IN PERSONS WITH HIV

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BACKGROUND

Persons living with HIV (PLWH) have increased risk of an ageing-related expansion of blood cell subpopulations with specific somatic mutations termed clonal hematopoiesis (CH). CH is associated with both inflammation and cardiovascular disease in uninfected populations. We aimed

- to investigate the distribution of coronary artery disease (CAD) in well-treated PLWH.
- Explore if CH and inflammatory markers were associated with CAD in older, well-treated PLWH.

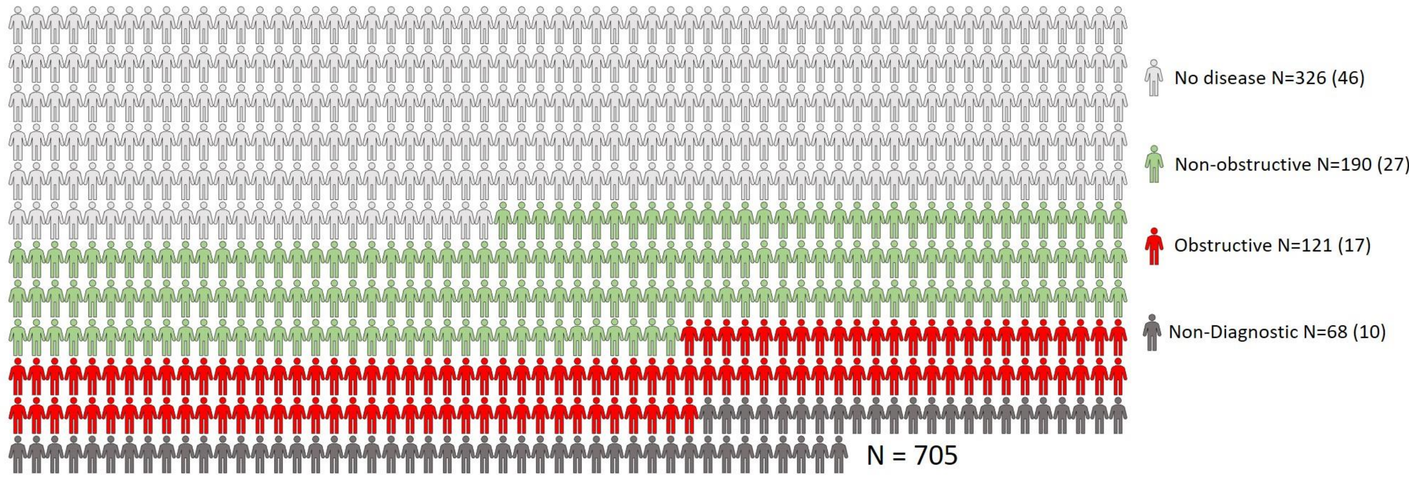

Figure 1. Distribution of Non-obstructive and onstructive disease among participants. Numbers, N, and percentages (%)

METHODS

PLWH with a coronary computed tomography angiography were recruited from the Copenhagen comorbidity in HIV infection (COCOMO) study. In a random subset of 171 participants older than 55 years, targeted gene sequencing was performed.

CAD severity in CT-scans were categorized as

- No disease (no atherosclerosis<)
- Non-obstructive (<50% stenosis)
- Ostructive (≥50% stenosis).

High concentration of inflammatory markers (IL-6, IL-1β, soluble CD14 and soluble CD163) was defined as concentration above the 75th percentile of each marker, respectively.

Gene sequencing was done using targeted sequencing of 21 CH-associated genes and CH was defined as variant allele frequency >2%.

RESULTS

Coronary CT angiographies were performed in 705 PLWH of whom 171 were also analyzed for CH.
Mean age was 51 (SD: 11) years, 77 (11%) were women, and 669 (96%) had suppressed viral replication.

Among individuals who had gene sequencing performed, 46 (27%) had CH. The most common CH-related mutations were in DNMT3A (n=22, 13%) and TET2 (n=12, 7%).

Clonal Hematopoiesis and CAD

Of individuals with CH, 138 (81%) had no CAD, 21 (46%) had non-obstructive CAD, 9 (20%) had obstructive CAD and 3 (2) had non-diagnostic scans. CH was not associated with CAD in unadjusted or adjusted analyses.

Demographic characteristics	
Men, n (%)	628 (99)
Age, mean (SD)	51 (11)
Smoking status, n (%)	
• **Current**	196 (28)
• **Former**	248 (35)
Hypertension, n (%)	299 (45)
Diabetes, n (%)	19 (3)
Obese (BMI>30)	46 (7)
Dyslipidemia	135 (22)
Use of antiretroviral therapy	696 (99)
Undetectable HIV RNA	669 (95)
CD4 group	
• **<200 cells per mm^3**	10 (1)
• **200-349 cells per mm^3**	40 (6)
• **350-500 cells per mm^3**	102 (15)
• **>500 cells per mm^3**	553 (78)

Inflammatory markers and CAD

High concentration of IL-6 was associated with higher odds of obstructive CAD (odds ratio, OR:3.24 [2.08, 5.03], P<.001) in unadjusted analyses and after adjusting for age and sex (OR:1.95 [1.19-3.19], P=.008).

IL-1β, soluble CD14, and soluble CD163 were not associated with CAD in unadjusted or in adjusted analyses.

CONCLUSIONS

- More than half of well-treated PLWH had evidence of coronary atherosclerosis.
- High levels of IL-6 were associated with obstructive CAD.
- No other inflammatory markers were associated with CAD.
- CH was not associated with CAD.

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