GUT MICROBIOTA ASSOCIATED WITH STENOCTIC CORONARY ARTERY DISEASE IN HIV INFECTION

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BACKGROUND

We aimed to assess the potential impact of gut microbiota alterations and related pathways, on the presence and severity of stable coronary artery disease (CAD) in people living with HIV (PLWH).

METHODS

Gut microbiota profiles from participants of the Copenhagen Comorbidity in HIV infection (COCOMO) study were determined by 16S rRNA sequencing, and CAD severity was assessed by a high-resolution research coronary CT angiography. Sequencing was performed on the Illumina MiSeq platform. Alpha diversity, beta diversity and bacterial abundances were analyzed on a rarefied (subsampled) dataset, and differentially abundant bacterial genera were adjusted for False Discovery Rate (FDR) using the Benjamini-Hochberg method. Associations between CAD-related microbiota alterations and stenotic CAD were tested using logistic a priori defined regression models adjusted for age, gender and smoking.

The **CAD-related microbiota** profile in **PLWH** identified in our study has more similarities with CAD-related microbiota profiles in the **general population** than microbiota profiles previously reported in HIV cohorts

RESULTS

In a total of 254 participants with available microbiota samples and CT angiography, n=60 were categorized as having stenotic CAD, n=80 had non-stenotic CAD, and n=114 had no CAD. Participants with stenotic CAD had gut microbiota profiles with significantly lower alpha diversity and higher beta diversity compared to both non-stenotic CAD and no CAD. Participants with stenotic CAD also had distinct compositional microbiota profiles, including increased relative abundance of Ruminococcus Gnavus, known to produce pro-inflammatory polysaccharides and Veillonella, potentially linked to fibrosis, as well as reduced abundance of several bacterial genera, some with potential for butyrate production, important for gut barrier integrity.

These bacterial genera (all QFDR<0.05) were used to define a CAD-related microbiota index: Loge (Veillonella + Ruminococcus Gnavus + Alistipes)/(Prevotella_9+ Megashpaera + Moryella + Catenibacterium + Fusicatenibacter + Ruminococcacea_UCG_005 + Ruminococcacea_UCG_009 + Lachnospiracea_ND3007_group + Eubacterium_xylanophilum_group), which was associated with stenotic CAD independent of age, gender and smoking (adjusted p<0.001). We observed no differences in gut microbiota composition between PLWH with non-stenotic CAD and no CAD.

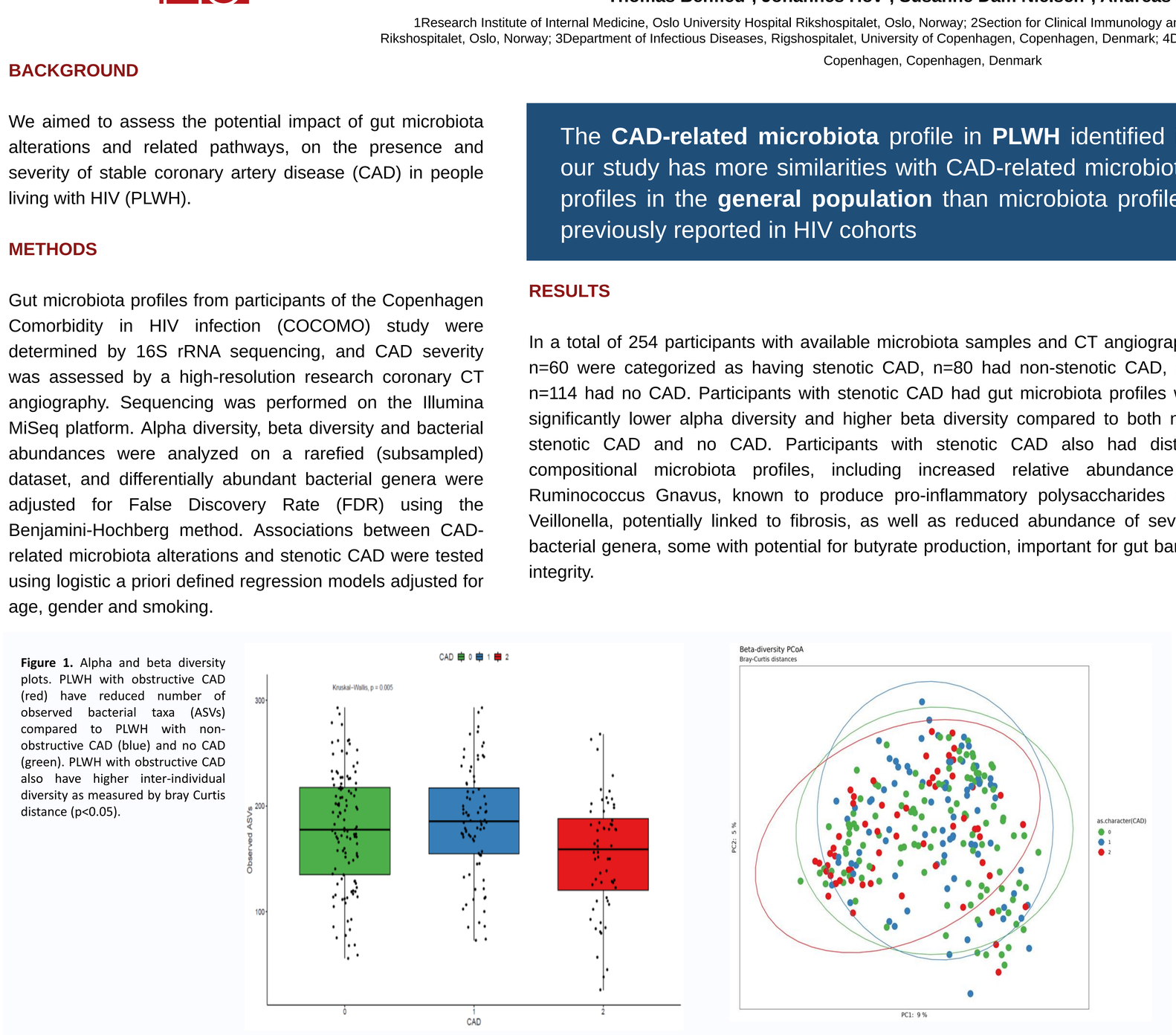

Figure 1. Alpha and beta diversity plots. PLWH with obstructive CAD (red) have reduced number of observed bacterial taxa (ASVs) compared to PLWH with non-obstructive CAD (blue) and no CAD (green). PLWH with obstructive CAD also have higher inter-individual diversity as measured by bray Curtis distance (p<0.05).

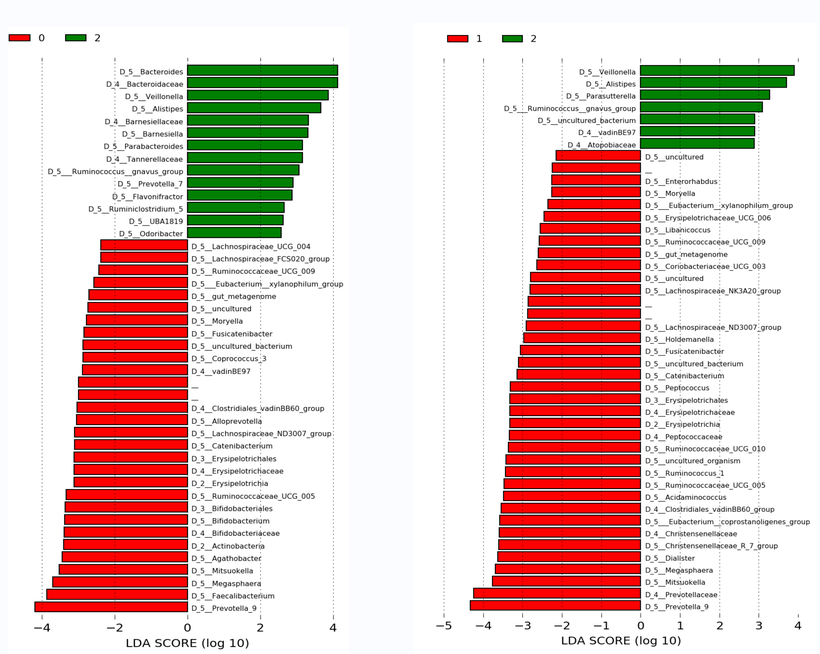

Figure 2. Compositional microbiota changes. PLWH with obstructive CAD (group 2) compared to PLWH without CAD (group 0) and non-obstructive CAD (group 1), respectively. Data as Lefse plot. Taxa with increased relative abundance in PLWH with obstructive CAD in green, taxa with reduced relative abundance in red, all $Q_{FDR} < 0.05$.

CONCLUSIONS

PLWH with obstructive CAD have distinct gut microbiota profiles compared to PLWH with non-stenotic CAD and no CAD. Future studies from this longitudinal cohort will determine whether these CAD-related microbiota profiles are predictive of future cardiovascular events in PLWH.

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