Gut Microbiota, Circulating Inflammation Markers, and Cardiac Dysfunction in Women and Men with HIV

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BACKGROUND

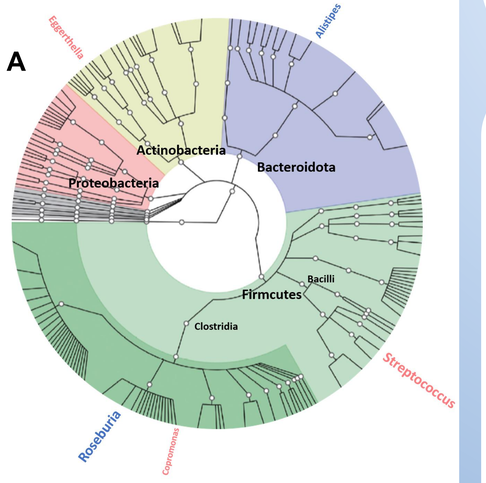
- The relationships among gut microbial alterations, host inflammation, and cardiac dysfunction are not fully elucidated, particularly in the context of HIV.
- We hypothesized that higher abundance of pro-inflammatory gut bacteria is associated with higher levels of host circulating inflammatory markers and cardiac dysfunction.

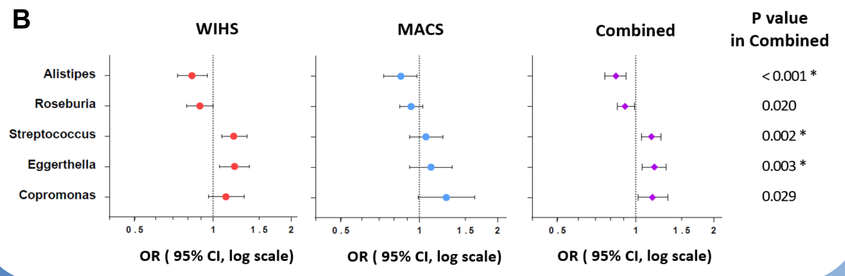
METHODS

- We examined associations of gut microbial features (16S rRNA sequencing) with cardiac dysfunction (left ventricular systolic or diastolic dysfunction, via echocardiography) in 1570 participants (973 women, 68% HIV+; 597 men, 54% HIV+) from the MACS/WIHS Combined Cohort Study (MWCCS).
- In a subset (397 women and 359 men), we further integrated cardiac dysfunction–associated microbial features(shotgun metagenomic sequencing) with 59 circulating proteomic inflammation markers (Olink platform) in relation to cardiac dysfunction and HIV.

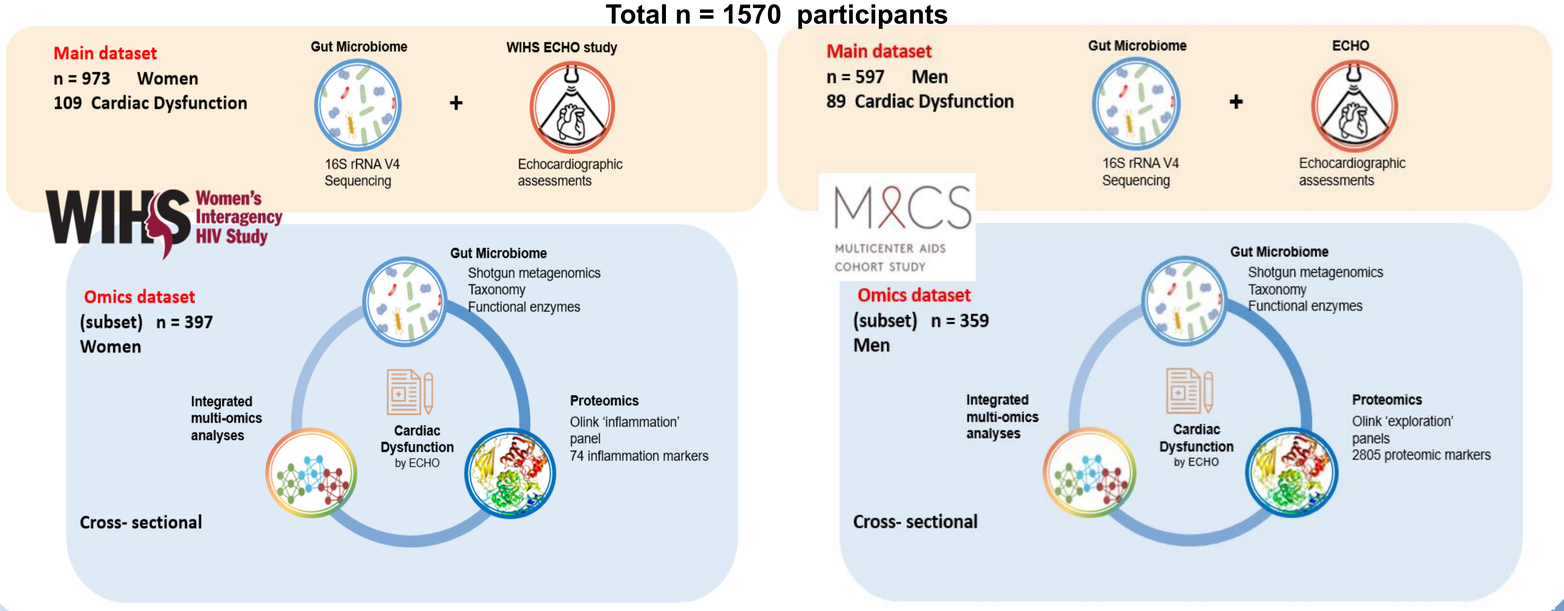
RESULTS

Figure 1. Associations of gut microbial features with cardiac dysfunction.
(A) Integrated phylogenetic tree. Red/blue font represent positive/negative associations between microbial taxa and cardiac dysfunction.
(B) Data are odds ratios (ORs) and 95% CIs for cardiac dysfunction per SD increment of CLR transformed abundance of gut bacterial genus, adjusted for age, race/ethnicity, study site, antibiotic use, income, education, BMI, current smoking, alcohol use, HIV status and ART use. "*", FDR<0.1.



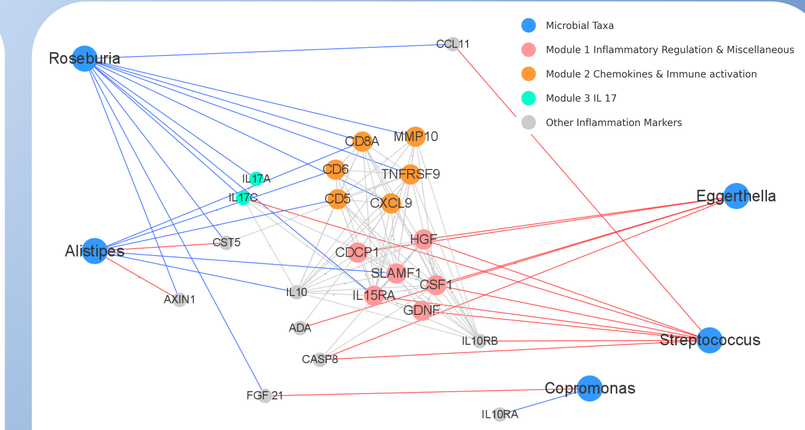


Study Design
Total n = 1570 participants



- The potentially pathogenic bacteria *Streptococcus*, *Eggerthella, and Copromonas* were associated with higher odds of cardiac dysfunction, whereas the beneficial genera *Roseburia* and *Alistipes* were associated with lower odds.
- Results were consistent in women and men, and those with and without HIV.
- These cardiac dysfunction-associated bacteria were associated with 23 inflammation markers. The protective and pathogenic bacteria were linked to distinct modules of inflammation markers.
- HIV+ serostatus, particularly detectable viremia, was associated with lower levels of the beneficial *Roseburia* and higher levels of microbial-related inflammation markers (e.g., CXCL9, TNFRSF9).

Figure 2. Network analysis of cardiac dysfunction-associated bacterial genera and related inflammation markers.
Red/blue lines indicate positive/inverse associations between bacterial genera and proteomic inflammation markers.



CONCLUSIONS

- We identified several gut bacteria, along with related inflammation markers, associated with cardiac dysfunction. Lower abundance of beneficial *Roseburia* and higher levels of inflammation markers were also associated with HIV+ status, suggesting potential mechanistic clues and therapeutic targets for improving cardiac health in people living with HIV.