Associations of inflammatory biomarkers with cardiovascular burden and predicted risk in people with HIV

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POPPY Pharmacokinetic and clinical observations in people over 50

BACKGROUND

People with HIV have an elevated risk of cardiovascular disease (CVD), driven in part by persistent systemic inflammation [1]. Specific inflammatory biomarkers, including IL-6, IL-10, TNF-α, CCL2/MCP-1, and CXCL1, have been implicated in CVD pathogenesis [2]. We examined associations between these biomarkers, current CVD burden and predicted 10-year CVD risk in adults with HIV enrolled in the Pharmacokinetic and clinical Observations in PeoPle over fiftY (POPPY) study to better understand inflammation-related cardiovascular risk.

METHODS

STUDY POPULATION

The POPPY study collects data on sociodemographic, lifestyle and clinical characteristics from three groups: 699 people with HIV aged ≥50 years, 374 people with HIV aged <50 years, and 304 people without HIV aged ≥50 years [3].

CVD BURDEN Z-SCORES

A cardiovascular disease (CVD) pattern was identified in participants with HIV using principal component analysis (PCA) at baseline (April 2013-January 2016).

Comorbidities (PCA loading) correlated with this pattern included coronary artery bypass grafting/percutaneous transluminal coronary angioplasty (0.68), heart failure (0.62), hypertension (0.70), ischaemic heart disease (0.72), myocardial infarction (0.69), peripheral vascular disease (0.46), renal problems (0.40) and dyslipidemia (0.34).

Participant burden z-scores were calculated using PCA loadings and information on the presence/absence of these comorbidities, and standardised (baseline mean and standard deviation). CVD burden z-scores >0 indicated higher CVD burden relative to the cohort mean.

INFLAMMATORY BIOMARKERS

Five biomarkers previously linked to CVD (IL-6, IL-10, TNF-α, CCL2/MCP-1, CXCL1) were measured using the OLINK platform and reported as normalised protein expression (NPX; log2 scale).

PREDICTED CVD RISK

Ten-year CVD risk was estimated in POPPY participants with HIV aged ≥40 years without prior myocardial infarction or stroke using SCORE2.

STATISTICAL ANALYSIS

Linear regression assessed associations between biomarker NPX values and both baseline CVD burden z-scores and SCORE2.

Models adjusted for age, sex, ethnicity, body mass index (BMI), smoking, nadir CD4+, years since HIV diagnosis and prior AIDS event.

IL-6 and IL-10 were differentially associated with PCA-derived CVD burden and 10-year CVD risk, with stronger links to predicted risk, highlighting their potential value to identify individuals at elevated cardiovascular risk.

RESULTS

- Analyses included 682 adults with HIV (median [IQR] age 53 [49-60] years; 87% male; 88% White) (Table 1).

- At baseline, the median [IQR] CVD burden z-score and SCORE2 were -0.62 (-0.62, 0.56) and 4.07 (2.45, 5.84), respectively.

- Median [IQR] biomarker NPX values: IL-6 -0.01 [-0.47, 0.62]; IL-10 0.00 [-0.35, 0.50]; TNF-α 0.00 [-0.28, 0.36]; CCL2/MCP-1 0.01 [-0.29, 0.34]; CXCL1 0.07 [-0.77, 0.73].

- After adjustment, higher IL-6 was associated with greater CVD burden (β= 0.07 [0.01, 0.14]) and SCORE2 (β= 0.68 [0.42, 0.94]). IL-10 was inversely associated with SCORE2 (β= -0.37 [-0.60, -0.13]).

- CCL2/MCP-1 and CXCL1 showed no clear associations with CVD outcomes after adjustment.

Table 1. Baseline characteristics of study participants

Characteristic	Total
n (%) or median (IQR)	(n=682)
Age (years)	53 (49 - 60)
Gender	
Male	594 (87.1)
Female	88 (12.9)
Ethnicity	
Black-African	83 (12.2)
White	599 (87.8)
BMI (kg/m²)	25.6 (23.3 - 28.1)
Smoking status	
Never	272 (39.9)
Past	242 (35.5)
Current	168 (24.6)
Alcohol use	
Never	50 (7.3)
Past	81 (11.9)
Current	551 (80.8)
CVD burden z-score	-0.62 (-0.62 - 0.56)
Predicted 10-year risk (SCORE2)	4.07 (2.45 - 5.84)
HIV-specific clinical factors	
Years since HIV diagnosis	14.5 (8.8 - 20.8)
On ART	673 (98.7)
Current CD4+ count (cells/ml)	631 (477 - 810)
Nadir CD4+ count (cells/ml)	197 (100 - 289)
Prior AIDS event	209 (30.7)

Figure 1. Associations of log-transformed normalised biomarker values with CVD burden z-scores and 10-year SCORE2 risk scores among POPPY participants with HIV (n=682). Crude and adjusted beta estimates with 95% confidence intervals are shown.
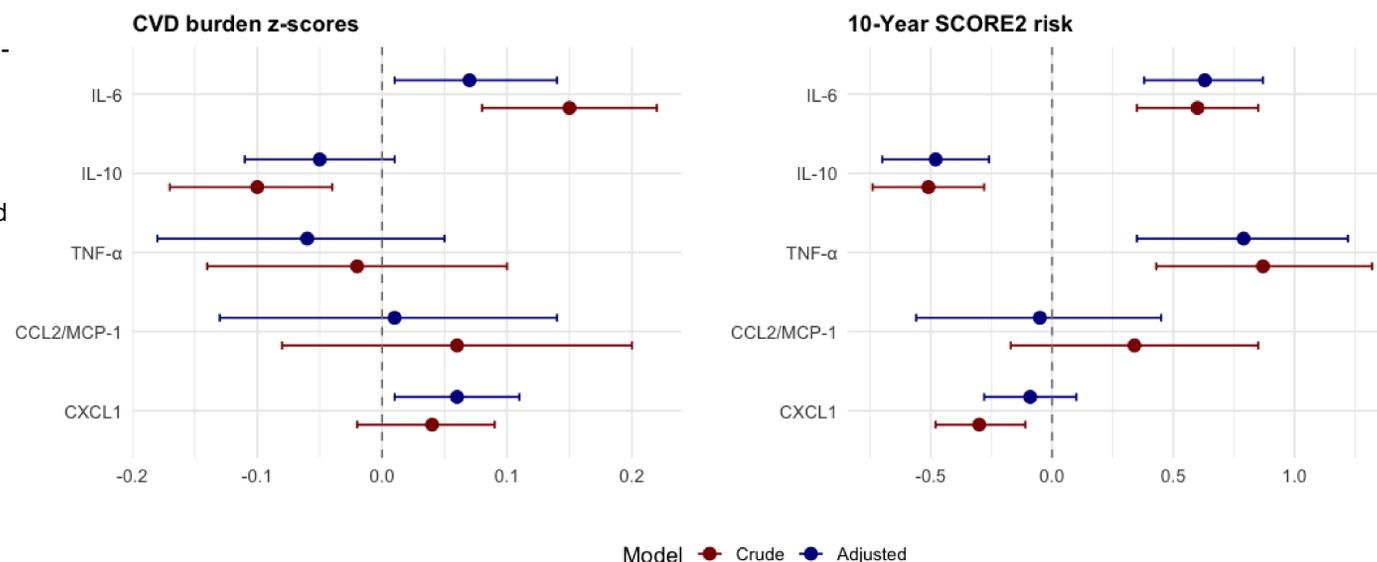
The CVD burden models were adjusted for age, sex, ethnicity, BMI, smoking status, nadir CD4+, years since HIV diagnosis, and prior AIDS event. CVD risk models were adjusted for all covariates except age, sex and smoking status, which are already incorporated in the risk score calculation.

CONCLUSIONS

- PCA-derived **CVD burden z-scores provided a nuanced measure of CVD morbidity,** capturing correlated cardiovascular events beyond simple counts.

- Inflammatory biomarkers showed differential associations, with **stronger associations observed for predicted 10-year CVD risk than current CVD burden,** partly reflecting age, smoking and other lifestyle factors.

- Higher **IL-6 was linked to both baseline CVD burden and predicted 10-year risk**; IL-10 was inversely associated with predicted risk.

- **Future studies should explore IL-6 and IL-10 levels over time** to improve CVD prediction and test whether targeting these pathways can reduce cardiovascular morbidity in people with HIV.

REFERENCES

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PLAIN LANGUAGE SUMMARY

People with HIV have a higher risk of heart disease, partly due to ongoing inflammation. This study found that several inflammation-related proteins, including TNF-α, IL-6, IL-10, were linked differently to existing heart problems or risk factors versus future cardiovascular risk, suggesting these proteins could help predict individuals who may develop heart-related conditions over the next 10 years.