Rigshospitalet
Heart Centre

COPENHAGEN CO-MORBIDITY IN HIV INFECTION STUDY

UNIVERSITY OF COPENHAGEN

REGION

Cytomegalovirus antibodies and coronary artery disease in people with HIV

Moises A. SUAREZ-ZDUNEK[a]; Andreas D. KNUDSEN[a,b]; Andreas FUCHS[b]; Nikolai S. KIRKBY[c]; Thomas BENFIELD[d,e]; Jan GERSTOFT[a,e]; Marius TRØSEID[f]; Sisse R. OSTROWSKI[g,e]; Lars V. KØBER[b,e]; Klaus F. KOFOED[b,e]; Susanne D. NIELSEN[a,e].

[a]Department of Infectious Diseases, Copenhagen University Hospital – Rigshospitalet, Denmark; [b]Department of Cardiology, Copenhagen University Hospital – Rigshospitalet, Denmark; [c]Department of Clinical Microbiology, Copenhagen University Hospital – Rigshospitalet, Denmark; [d]Department of Infectious Diseases, Copenhagen University Hospital – Amager and Hvidovre, Denmark; [e]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark; [f]Research Institute of Internal Medicine and Section of Clinical Immunology and Infectious Diseases, Oslo University Hospital, Rikshospitalet, Norway; [g]Department of Clinical Immunology, Copenhagen University Hospital – Rigshospitalet, Denmark.

BACKGROUND

People with HIV (PWH) have twice the risk of myocardial infarction compared to the general population, possibly due to increased inflammation[1].

Latent cytomegalovirus (CMV) infection is associated with sustained inflammation and immune activation[2].

CMV is associated with 30% higher risk of cardiovascular disease in the general population but may disproportionately affect PWH by a synergistic effect on inflammation[3].

MATERIALS AND METHODS

Study design: Cross-sectional study from baseline of the prospective Copenhagen Comorbidity in HIV Infection Study.

Study population: Adult out-patient PWH, regardless of CVD risk.

CMV IgG antibodies: Concentrations using Diasorin LIAISON CMV IgG II immunoassay.

Cardiac CT angiography:

- Any atherosclerosis: Any stenosis ≥1%
- Obstructive CAD: Any stenosis ≥50%
- Extensive CAD: Any stenosis in >5 segments
- Plaque volume: Measured in µL and subdivided in plaque phenotypes.

KNOWLEDGE GAP

The role of CMV serostatus and CMV IgG concentrations on coronary artery disease (CAD) are unknown in non-selected PWH.

AIMS

To determine if positive CMV serostatus and higher CMV IgG concentrations are associated with CAD in PWH.

TABLE 1 Baseline characteristics (*N* = 620)

Demographics	
Age, median years (IQR)	50.1 (42.8-57.1)
Male sex, n (%)	553 (89.2%)
Cardiovascular disease risk factors	
Hypertension, n (%)	177 (41.3%)
Diabetes mellitus, n (%)	17 (2.7%)
Current smoking, n (%)	177 (28.5%)
Dyslipidaemia, n (%)	118 (19.0%)
Infection-related characteristics	
Positive CMV IgG serostatus	586 (94.5%)
Use of ART at baseline, n (%)	612 (98.7%)
HIV RNA ≥50 copies/mL, n (%)	29 (4.7%)
CD4 count <350 cells/µL, n (%)	40 (6.5%)

ART: Antiretroviral therapy. **IQR**: Inter-quartile range.

TABLE 2 CMV IgG serostatus and CAD

Variables	CMV IgG +ve	CMV IgG -ve
Coronary artery disease, n (%)		
Any atherosclerosis	261 (44.5%)	16 (47.1%)
Obstructive CAD	73 (11.5%)	4 (11.8%)
Extensive CAD	55 (9.4%)	3 (8.8%)
Plaque volume[a], µL, median (IQR)		
Total plaque volume	180 (88-393)	126 (67-278)
Calcified plaque volume	14 (2-54)	9 (2-37)
Fibrotic plaque volume	133 (66-254)	108 (50-201)
Inflamed plaque volume	32 (14-58)	18 (9-42)

[a]Among those with any atherosclerosis. **CAD**: Coronary artery disease. **CMV**: Cytomegalovirus. **+ve**: Positive. **-ve**: Negative.

RESULTS

Participant characteristics are presented in **Tables 1 and 2**.

CMV IgG serostatus was not associated with any measures of CAD (see **Figure 1 and Table 2**).

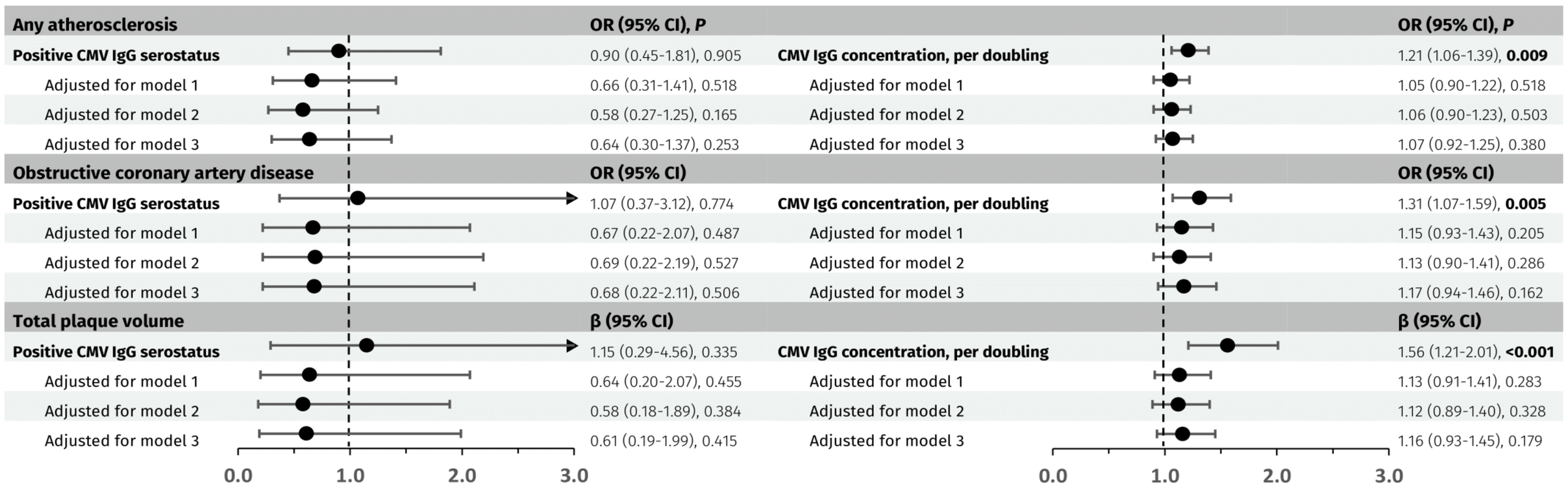
Higher CMV IgG concentrations were associated with all measures of CAD (see **Figure 1**), irrespective of plaque phenotype (data not shown).

- This was not significant after adjustment for traditional CVD risk factors
- Age accounted for 69% (P <0.01) of the effect of CMV IgG concentrations on total plaque volume adjusted for sex and smoking.

DISCUSSION

In contrast with a recent CCTA study of PWH at low-moderate CVD risk[4], we found an association of CMV IgG concentrations and CAD. However, this was, at least in part, explained by traditional CVD risk factors.

FIGURE 1 Associations of cytomegalovirus antibodies with coronary artery disease



CMV, cytomegalovirus. Model 1, age, sex, smoking. Model 2, age, sex, smoking, diabetes mellitus, and dyslipidaemia. Model 3, age, sex, smoking, and current CD4+ T cell count. OR, odds ratio. CI, confidence interval. β, regression coefficient to be interpreted as fold increase in total plaque volume.

SOURCE OF FUNDING

This work was supported by the Rigshospitalet Research Council, Novo Nordisk Foundation, Gilead Sciences, Aase and Ejnar Danielsen's Foundation, Independent Research Fund Denmark, and Capital Region of Denmark.

REFERENCES

[1]Shah et al. Circulation 2018;138:1100–12. [2]Talepoor et al. Front Immunol 2022;13:945016. [3]Wang et al. J Am Heart Assoc 2017;6:e005025 & Schnittman et al. Curr Opin HIV AIDS 2021;16:168-76. [4]Schnittman et al. Clin Infect Dis 2023;10:ofad106.

CONCLUSION

Higher CMV IgG concentrations were associated with CAD. However, this association was not significant after adjustment for traditional CVD risk factors. **This indicates that the association, in part, is explained by confounders, most importantly higher age.**