Moises Alberto Suarez-Zdunek[1], Alan Winston[2], Luxsena Sukumaran[3], Nikolai S. Kirkby[4], Susanne D. Nielsen[1,5], Caroline S. Sabin[3]

[1]Viroimmunology Research Unit, Dept. of Infectious Diseases, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark; [2]Dept. of Infectious Disease, Faculty of Medicine, Imperial College London, London, United Kingdom; [3]Institute of Global Health, Royal Free Campus, University College London, London, United Kingdom; [4]Dept. of Clinical Microbiology, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark; [5]Dept. of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

BACKGROUND

Latent cytomegalovirus (CMV) infection has been linked to cardiovascular disease (CVD), possibly through chronic inflammation[1]. However, the impact of CMV on traditional CVD risk factors is poorly understood[2]. HIV is also associated with chronic inflammation and CVD, but it is unknown if HIV and CMV act synergistically to influence CVD risk.

AIMS

1. Determine if CMV IgG serostatus/concentrations are associated with traditional CVD risk factors
2. Determine if the associations are modified by HIV status.

METHODS

Study design: Cross-sectional study from the prospective POPPY Study in the UK and Ireland[3].

Study population: Adult people with HIV aged ≥50 years and controls (people with HIV aged <50 and people without HIV aged ≥50 years).

Exposures: CMV IgG serostatus and concentrations measured on plasma at study entry (2013-2016).

Outcomes: *Estimated 10-year CVD risk*: SCORE2 based on age, sex, smoking, blood pressure and non-HDL concentrations. *Hypertension*: Blood pressure ≥140/90, use of antihypertensives and/or self-reported diagnosis. *LDL levels*: Measured in participants not using lipid-lowering drugs.

Statistics: (1) Logistic and linear regressions before and after progressive adjustment for **a)** HIV status **b)** age, sex, ethnicity **c)** smoking, body-mass index (BMI). (2) Interaction between CMV IgG and HIV status assessed in people aged ≥50.

CONTACT INFORMATION

Moises Alberto Suarez-Zdunek, MD
msua0003@regionh.dk

REFERENCES

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Both in people with and without HIV, CMV IgG serostatus and concentrations are associated with higher estimated CVD risk and lower LDL levels, but this association may be explained by confounding from demographic factors.

POPPY
Pharmacokinetic and clinical observations in people over 50

RESULTS

A total of 1017 people with HIV and 294 people without HIV were included (**Table 1**).

- **Estimated CVD risk** (Fig. 1): Associations between CMV IgG serostatus and concentrations and SCORE2 were attenuated after adjustment for sex, age, and ethnicity.
- **Hypertension** (Fig. 2): No association with CMV IgG serostatus and concentrations.
- **LDL levels** (Fig. 2): Associations between CMV IgG serostatus and concentrations and lower LDL levels was attenuated after adjustment for sex, age, and ethnicity.
- **HIV/CMV**: No interaction between CMV IgG concentrations and HIV status found (P_{int}=0.48).

Fig. 1. Associations of CMV IgG serostatus/concentrations and SCORE2. β indicates differences in SCORE2 before and after progressive adjustments for 1) HIV status 2) age, sex, ethnicity 3) smoking and BMI. [a]Per doubling.

SCORE2	β (95% CI), P		β (95% CI), P
Positive CMV serostatus	0.34 (-0.32, 1.01), 0.31	**CMV IgG concentrations**[a]	0.13 (0.03, 0.23), <0.01
+ HIV status	1.00 (0.28, 1.71), <0.01	+ HIV status	0.27 (0.16, 0.38), <0.001
+ age, sex, ethnicity	-0.14 (-0.60, 0.32), 0.56	+ age, sex, ethnicity	-0.02 (-0.09, 0.05), 0.53
+ smoking, BMI	-0.09 (-0.49, 0.31), 0.67	+ smoking, BMI	-0.03 (-0.09, 0.04), 0.40

Fig. 2. Associations of CMV IgG serostatus/concentrations, hypertension, and LDL levels among those not treated with lipid-lowering drugs. Estimates before and after progressive adjustment for 1) HIV status 2) age, sex, ethnicity 3) smoking, and BMI. [a]Per doubling.
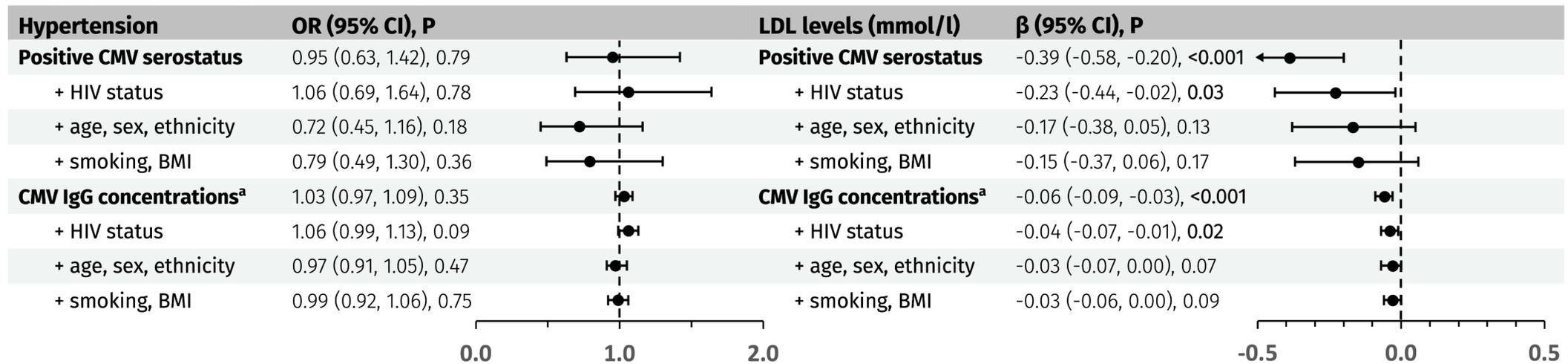

Hypertension	OR (95% CI), P	LDL levels (mmol/l)	β (95% CI), P
Positive CMV serostatus	0.95 (0.63, 1.42), 0.79	**Positive CMV serostatus**	-0.39 (-0.58, -0.20), <0.001
+ HIV status	1.06 (0.69, 1.64), 0.78	+ HIV status	-0.23 (-0.44, -0.02), 0.03
+ age, sex, ethnicity	0.72 (0.45, 1.16), 0.18	+ age, sex, ethnicity	-0.17 (-0.38, 0.05), 0.13
+ smoking, BMI	0.79 (0.49, 1.30), 0.36	+ smoking, BMI	-0.15 (-0.37, 0.06), 0.17
CMV IgG concentrations[a]	1.03 (0.97, 1.09), 0.35	**CMV IgG concentrations**[a]	-0.06 (-0.09, -0.03), <0.001
+ HIV status	1.06 (0.99, 1.13), 0.09	+ HIV status	-0.04 (-0.07, -0.01), 0.02
+ age, sex, ethnicity	0.97 (0.91, 1.05), 0.47	+ age, sex, ethnicity	-0.03 (-0.07, 0.00), 0.07
+ smoking, BMI	0.99 (0.92, 1.06), 0.75	+ smoking, BMI	-0.03 (-0.06, 0.00), 0.09

TABLE 1   Participant characteristics (N = 1311)

Variables N (%) or median (IQR)	People with HIV (N = 1017)	People without HIV (N = 294)
Age, years	52 (47–59)	58 (53–63)
Male sex	870 (85%)	188 (64%)
White ethnicity	857 (84%)	263 (89%)
Current smoking	256 (25%)	39 (13%)
BMI (kg/m²)	25.5 (23.2–28.2)	26.8 (24.2–29.5)
Positive CMV serostatus	990 (97%)	216 (73%)
Years on antiretrovirals	10.3 (5.2–16.7)	NA
Current CD4+ count/μL	630 (480–812)	NA
HIV RNA <50 copies/μL	920 (91%)	NA

CONCLUSIONS

CMV IgG serostatus and concentrations in people with and without HIV were not associated with higher estimated CVD risk, hypertension, and LDL levels after adjustment for sex, age, and ethnicity. This highlights the importance of demographic factors when interpreting the effect of CMV on CVD.

PLAIN LANGUAGE SUMMARY

Antibody levels against cytomegalovirus (CMV) were linked to higher estimated heart disease risk and lower cholesterol. However, these links were largely explained by differences in age, sex, and ethnicity. This shows that demographics matter when trying to understand if CMV infection increases heart disease risk.

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