CMV IgG is Associated with Muscle Function but not Quality or Mass in People with HIV

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KM Erlandson[1], T Umbleja[2], ET Overton[3], T Burdo[4], JM Flynn[4], MT Lu[5], J Taron[5,6], SR Schnittman[5], E Fulda[5], CJ Fichtenbaum[7], C Malvestutto[8], HJ Ribaudo[2], PS Douglas[9], SK Grinspoon[5], TT Brown[10]

[1]University of Colorado-Anschutz Medical Campus, Aurora, CO, U.S.A; [2]Harvard T.H. Chan School of Public Health, Boston, MA, U.S.A; [3]University of Alabama at Birmingham School of Medicine, Birmingham, AL, U.S.A.; [4]Lewis Katz School of Medicine at Temple University, Philadelphia, PA; [5]Massachusetts General Hospital and Harvard Medical School, Boston, MA, U.S.A.; [6]University of Freiburg, Frieberg, GERMANY; ;[7]University of Cincinnati College of Medicine, Cincinnati, OH, U.S.A.; [8]Ohio State University Medical Center, Columbus, OH, U.S.A.; [10]Duke University School of Medicine, Durham, NC, U.S.A;[13]Johns Hopkins University School of Medicine, Baltimore, MD, U.S.A.

BACKGROUND

- Cytomegalovirus (CMV) infection is associated with poor outcomes, including physical function impairment, in people without HIV.
- We examined associations of CMV IgG antibody titers with physical function and muscle quality/quantity in virologically suppressed middle-aged people with HIV (PWH), leveraging REPRIEVE baseline data.

METHODS

- REPRIEVE is a double-blind randomized trial evaluating pitavastatin for primary prevention of CVD in PWH.
- This cross-sectional analysis focused on participants enrolled in a substudy with additional biomarker testing and imaging at study entry.
- CMV IgG was measured in duplicate using the human CMV IgG enzyme immunoassay by Genway Biotech.
- Paraspinal muscle area (MA) and density (MD) were assessed on non-contrast CT.
- Physical function and frailty were obtained by a modified version of the Short Physical Performance Battery (mSPPB), and the Fried Frailty Phenotype, respectively. Physical function was standardized by maximum performance.
- Associations between CMV IgG (risk factor) and outcomes were evaluated using partial Spearman correlation, and linear and log-binomial regression models.

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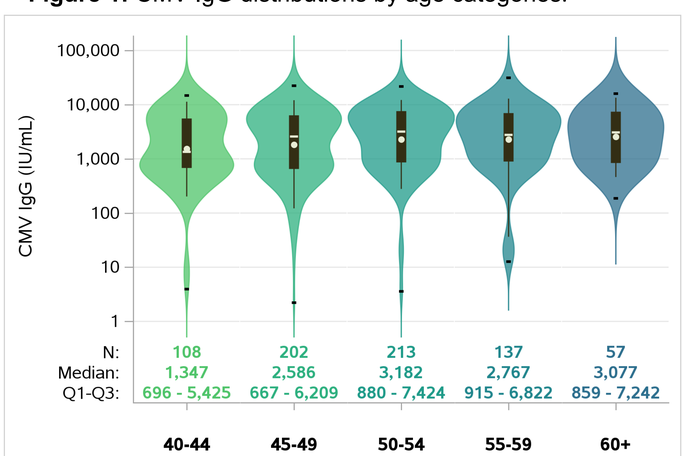
Higher CMV IgG was associated with poorer physical function and frailty among PWH, even after accounting for age, sex, BMI, nadir CD4 and hsCRP.

RESULTS

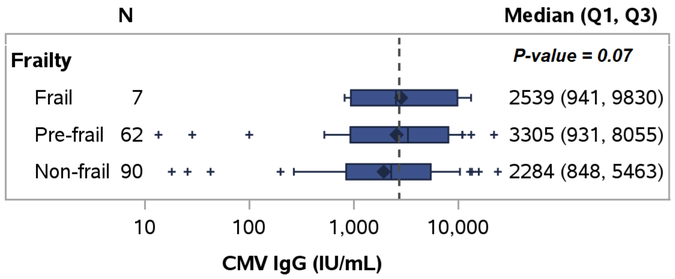
- Among 717 participants with CMV IgG measurements, the median age was 51 (Q1, Q3: 46, 55) years.
- 18% were natal female, 51% White, 37% Black, and 25% Hispanic.
- Median BMI was 27 (24, 31) kg/m^2.
- 93% had HIV-1 RNA <50 copies/mL, and 50% nadir CD4<200.
- All participants had detectable CMV IgG.
- Median CMV IgG was 2716 (807, 6672) IU/mL, with higher concentrations with increasing age (Figure 1).
- There was no evidence of association between CMV IgG and muscle density or area among n=631 with CT-based measures, controlling for age, sex and BMI (r=-0.03, p>0.5).

Figure 1: CMV IgG distributions by age categories.



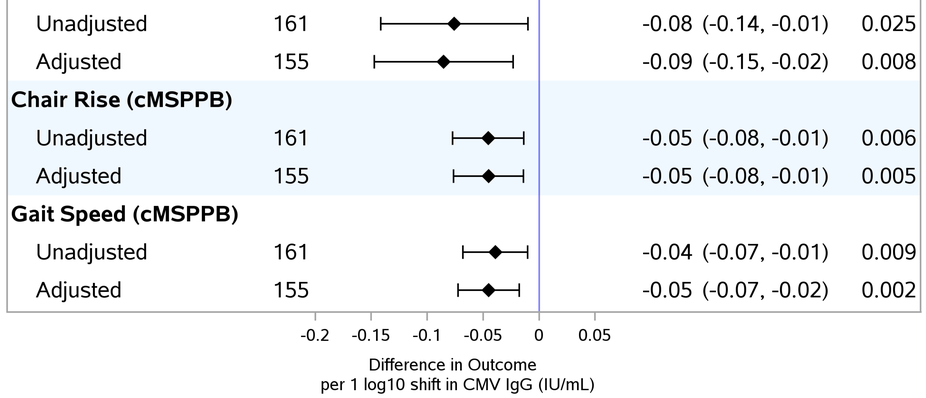
RESULTS

Figure 2: Association between CMV IgG and frailty.



- While the number of frail participants was limited (n=7), trends were consistent for associations with pre-frailty and frailty (p=0.07; **Figure 2**).

Figure 3: Associations between CMV IgG and physical function.



Estimates are from linear regression models with CMV IgG as risk factor and physical function measures as outcomes, unadjusted and adjusted for age, sex, BMI, nadir CD4 and hsCRP.

- Among participants with physical function data (N=161), higher CMV IgG was associated with poorer physical function (mSPPB), largely driven by chair rise and gait speed components (**Figure 3**).
- Higher CMV IgG was associated with impairment on SPPB (score≤10) (relative risk=1.74 per 1 $\log_{10}$ shift, 95% CI: 1.13, 2.69). The effect sizes were similar after adjusting for CD4 nadir and hsCRP.

SUMMARY

- The known association between CMV IgG and physical function or frailty is replicated in PWH and does not appear to be explained by changes in muscle quantity or quality, nadir CD4 or inflammation.
- Further mechanistic studies are needed to understand this association and whether CMV eradication or CMV-specific therapy can impact physical function in PWH.