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Higher plasma D-dimer, a marker of inflammation and coagulation, is linked to distal sensory polyneuropathy in people with HIV

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Objective

- Determine whether inflammation and coagulation abnormalities contribute to persistent distal sensory polyneuropathy in people with HIV

Background & Significance

- Elevated plasma D-dimer is a marker of abnormalities in coagulation and inflammation, both of which may be associated with sensory polyneuropathy in a variety of disorders such as diabetes mellitus, but this has not been examined in HIV-associated distal sensory polyneuropathy (DSP). We therefore assessed the cross-sectional correlation between plasma D-dimer levels and HIV DSP

Methods

- Participants in the prospective, observational CNS HIV AntiRetroviral Therapy Effects Research (CHARTER) cohort underwent standardized evaluations for clinical examination findings of distal sensory polyneuropathy (DSP) and distal neuropathic pain
- D-dimer measured by immunoassay. Values $\log_{10}$ transformed to improve their distribution for parametric analysis
- mitochondrial (mt)DNA by ddPCR
- Pearson correlations and multivariable regressions including age and other relevant covariates

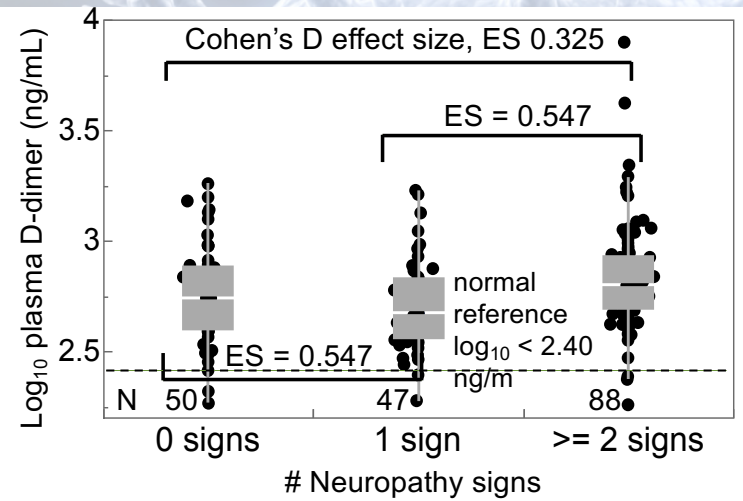


Figure. Box plots of Log_{10} plasm D-dimer levels were higher in participants with 2 or more signs of neuropathy compared to those with none or one sign. Cohen's D effect size, ES.

Results

- Participants were 183 PWH evaluated between 2016-2020, mean (SD) age 56.2 (8.10), 19.7% women, 56.4% non-white, median nadir and current CD4 lymphocytes 107 (IQR 20, 210) and 567 (348, 817), undetectable plasma HIV RNA 79.9%

Results, continued

- **Log_{10} plasma D-dimer levels (normal reference $\log_{10} < 2.40$ ng/mL) were highest in those with ≥ 2 neuropathy signs, Wilcoxon p=0.0027 (see Figure)**
- Older age also associated with increasing number of neuropathy signs (p <0.0001)
- In a multivariable regression, both age (p = 9.75e-8) and D-dimer (p = 0.0045) independently associated with ≥ DSP 2 signs
- Females had higher D-dimer and more neuropathy signs than males (ps 0.0213, 0.0348), use of estrogens and progestins was not associated with D-Dimer levels. Ethnicity not related to D-dimer or neuropathy signs
- More neuropathy signs also associated with higher D-dimer in those with undetectable plasma viral load (Wilcoxon p=0.041)
- Neuropathy signs not related to diabetes, nadir CD4, plasma HIV RNA or past neurotoxic d-drug exposure (ps > 0.20)
- Higher mtDNA copies per well modestly correlated with higher D-dimer (r=0.186, p=0.0373), but no with neuropathy signs
- Neuropathy symptoms (pain, paresthesias), not related to D-dimer levels

Conclusions

- **Chronic coagulation abnormalities and inflammation in PWH despite viral suppression may contribute to neuropathy, raising the possibility that treatments to normalize coagulation and inflammation may reduce susceptibility to neuropathy**

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