INFLAMMATORY MARKERS AND FRAILTY, COGNITIVE IMPAIRMENT, CLINICAL OUTCOMES, AND MORTALITY IN PWH

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BACKGROUND

- Frailty is associated with increased risks of comorbidities and mortality in people with HIV[1].
- The associations between inflammatory markers and prevalent or incident frailty, cognitive impairment, clinical events and mortality in older people with HIV are poorly understood.

METHODS

- Participants ≥50 years in a longitudinal cohort study (**HAILO**, the Human Immunodeficiency Virus [HIV] Infection, Aging, Immune Function Long-Term Observational Study) were included.
- ❑ **Frailty** was evaluated using the *Fried Frailty phenotype* including 4-meter walk speed, grip strength, and unintentional weight loss, exhaustion, and low activity.
- ❑ **Cognitive impairment** was assessed with the *A5001 Neuroscreen* including Trail Making A, Trail Making B, and Digit Symbol tests.
- ❑ **Major clinical events** included a composite of non-AIDS defining cancers, cardiovascular disease events, diabetes mellitus, liver and kidney diseases.
- ❑ **Non-accidental mortality** was defined as mortality from all causes except external causes such as accidents, suicide, and homicide.

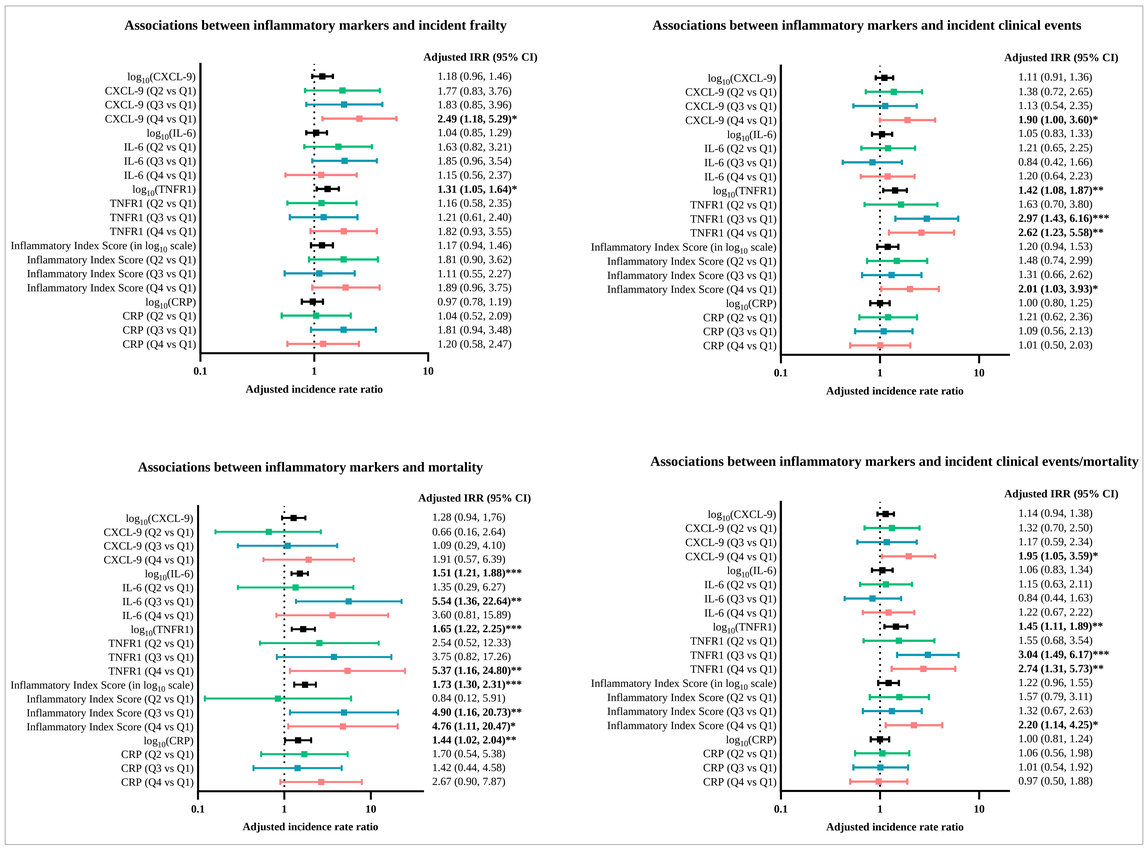
- **Baseline inflammatory markers** evaluated were *hsCRP, TFNR1, IL-6, CXCL-9 and inflammatory index score (1/3log(IL-6) + 2/3 log(TNFR1)).*
- Multivariable logistic regression and Poisson regression were used to examine associations between inflammatory markers and prevalence and incidence of frailty, CI, clinical events and non-accidental mortality, respectively. We used 10-fold cross validation to examine whether **addition of inflammatory markers to frailty** improve ability to predict incident clinical events and/or mortality.

Among older adults with HIV in HAILO cohort, increased inflammation such as CXCL-9, TNFR1 and IIS is associated with frailty, and clinical events. All inflammatory markers evaluated—except CXCL-9—such as hsCRP, IL-6, TNFR1 and IIS are also linked to a higher risk of mortality.

RESULTS

- Among 484 participants with inflammatory markers evaluated, 83 (17%) women, 121 (25%) Black and 98 (20%) Hispanic; median age was 56 years. Median BMI was 27 kg/m^2, median CD4 and nadir CD4 were 627 and 189 cells/μL, respectively and 95% had HIV RNA <200 copies/mL.

Figure. Associations between inflammatory markers and incident frailty, cognitive impairment, clinical events and mortality



RESULTS

Prevalent outcomes

- 7.8% (38/484), 32% (144/453) and 43% (210/484) participants had frailty, CI and major clinical events at baseline, respectively.
- IL-6, TNFR1, CXCL-9 and inflammatory index score were associated with increased risk of prevalent frailty and clinical events at baseline, but not CI.

Incident outcomes

- Incidence rates (95%CI) of frailty, CI, clinical events and mortality were 3.72(2.93-4.64), 9.58(7.93-11.5), 7.01(5.60-8.65) and 1.10 (0.73-1.58) per 100 person-years.
- In adjusted analyses, CXCL-9, inflammatory index score and TNFR1 were associated with an increased risk of incident frailty and clinical events. Higher inflammatory marker levels were also associated with an increased risk of mortality (***Figure***).
- No inflammatory markers were associated with cognitive impairment.
- TNFR1 and frailty together modestly improved a model's ability to predict incident clinical events and mortality relative to a model with frailty alone.

CONCLUSIONS

- Increased inflammation was associated with evaluated risks of prevalent and incident frailty and major clinical events/mortality, but not CI.
- Addition of inflammatory markers to frailty only modestly increased a model's ability to predict clinical events and mortality.

ACKNOWLEDEGMENTS

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Reference
1. Kelly SG, et. l. *Clin Infect Dis*. 2019;69(8):1370-1376. doi:10.1093/cid/ciy1101