A cellular senescence phenotype is associated with frailty in men with HIV.

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Background:
Antiretroviral therapy has improved the lifespan of people living with HIV (PLWH), but has increased the burden of comorbidities, including frailty. Immunosenescence may contribute to frailty pathogenesis, but evidence remains limited in the context of HIV. The aim of this study was to examine cellular senescence and frailty in men with HIV.

Methods:
One hundred people with HIV aged 50 years and older were recruited from The Alfred Hospital in 2015, and 83 men with available stored samples were classified as non-frail (n=65) or frail (n=18) based on the Frailty Index. Peripheral blood mononuclear cells were immunophenotyped using a panel targeting key lymphoid and monocyte populations to assess cellular senescence (p16) and senescence-associated β-galactosidase (SA-β-gal) activity. Hierarchical cluster analysis was performed using Euclidean distance and Ward's D2 linkage method.

Results:
Cellular senescence as assessed by SA-β-gal median fluorescent intensity (MFI) was 1.3- to 1.6-fold higher in lymphocytes (B cells, T cells, NK cells) and monocytes (classical and intermediate subsets) in frail participants compared to non-frail participants (all $p<0.05$) and remained significant upon age-adjusted logistic regression. Similarly, age-adjusted logistic regression showed elevated MFI levels of cell cycle arrest marker p16 in frail participants for all cell types except classical and intermediate monocytes (all $p<0.05$). Soluble IL-6 levels were positively correlated with all cellular senescence markers on all measured cell types (rho range: 0.238-0.404, all $p<0.05$). Hierarchical cluster analysis separated participants into two groups based on cellular senescence profiles, with frail individuals significantly more likely in the senescence-enriched cluster 1 (OR = 7.88, 95% CI: 2.45–23.50).

Conclusion:
We have shown that cellular senescence broadly impacts the innate and adaptive immune systems and is enriched in frail men with HIV. Cellular senescence may contribute to frailty pathogenesis and represents a novel therapeutic target to improve healthy ageing in PLWH.

Disclosure of Interest Statement:

None.