ASSOCIATION OF PHENOTYPIC AGING WITH COMORBIDITIES, FRAILTY, AND INFLAMMATORY MARKER

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BACKGROUND

- People with HIV (PWH) suffer higher age-related comorbidities including frailty, neurocognitive impairment (NCI), and cardiometabolic diseases than people without HIV.
- Aging among PWH occurs heterogeneously, however some prior studies suggest that the aging process among PWH is faster than people without HIV.
- We investigated phenotypic aging using a novel aging marker and evaluated the factors associated with phenotypic age acceleration.

METHODS

- A cross-sectional study was conducted among older PWH and age- and sex-matched HIV-negative controls to compare **phenotypic age** and **phenotypic age acceleration** (PAA) in older PWH and HIV-negative controls.
- Phenotypic age was calculated using chronological age and 9 biomarkers from complete blood counts, inflammatory, metabolic-, liver- and kidney-related parameters [1,2]. PAA was calculated as the difference between chronological age and phenotypic age.
- Multivariate logistic regression models were used to identify the factors associated with higher PAA, defined as having higher than the median value.
- We assessed aging-related comorbidities including the Veterans Aging Cohort Study (VACS) index, frailty, NCI and inflammation (hsCRP and IL-6). Area under the receiver operating characteristics curve (AROC) was used to assess model discrimination for frailty.

The novel phenotypic aging marker calculated using chronological age and biomarkers from complete blood counts, inflammatory, metabolic-, liver- and kidney-related parameters was significantly associated with systemic inflammation, frailty, and CVD risk factors in older PLHIV.

Table 1. Multivariable logistic regression model for high phenotypic age acceleration (defined by PAA value above the median)

All participants	Univariate			Multivariate		
	Odds ratio	95%CI	p-value	Odds ratio	95%CI	p-value
Male	2.33	1.57-3.47	<0.001	1.68	1.03,2.73	**0.039**
BMI≥25	1.35	0.90-2.02	0.143			
HIV status	1.43	0.91-2.23	0.12	1.18	0.68,2.04	0.56
waist circumference	1.03	1.01-1.05	0.006	1.00	0.97,1.02	0.70
Smoking						
Never/ ex-smoker	Ref					
current	2.85	1.54-5.27	0.001	2.74	1.30,5.79	0.008
Alcohol drinking						
Never/ ex-smoker	Ref					
current	1.29	0.69-2.40	0.423			
Diabetes mellitus	4.29	2.37-7.76	<0.001	2.97	1.48,5.99	**0.002**
Hypertension	2.26	1.52-3.36	<0.001	1.67	1.02,2.72	**0.040**
Statin use	1.50	0.99-2.28	0.055	1.04	0.62,1.73	0.88
HDL-cholesterol	0.98	0.97-0.99	0.018			
LDL-cholesterol≥130	0.86	0.58-1.25	0.423			
Triglycerides≥150	1.31	0.90-1.90	0.17			
ALT	1.01	1.00-1.02	0.035	1.01	1.00,1.02	0.10
Insulin	1.05	1.02-1.08	0.001			
IL-6	1.10	1.05-1.15	<0.001	1.09	1.04,1.15	**0.001**
Fragility status						
Normal	Ref			Ref		
Pre-frail	1.14	0.75-1.72	0.539	1.05	0.66,1.67	0.83
Frail	4.98	1.94-12.8	0.001	3.82	1.33,10.93	**0.012**

P-values in bold represent significant values.

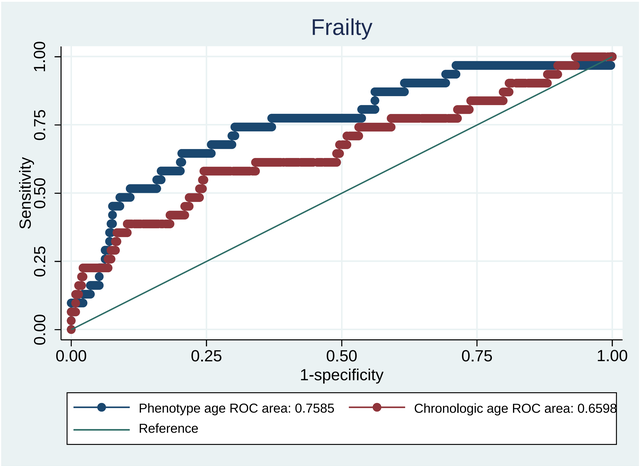

Figure 1. ROC curve comparing the predictability of phenotype age and chronological age for frailty

RESULTS

- Between 2017 and 2018, 333 PWH and 102 HIV-negative controls (38% female) with median chronological age of 54 (IQR 52-59) and 55 (53-58) years, respectively, were enrolled. Median phenotypic age (49.4 vs. 48.5 years, p=0.54) and PAA (-6.7 vs. -7.5, p=0.24) were higher in PWH than the controls, although not statistically significant.
  PWH with higher PAA had lower CD4/CD8 ratio (0.88 [0.63-1.22] vs. 1.00 [0.74-1.33], p=0.03) and higher VACS index (22.2 [I12-28] vs. 22.6 [18-34], p=0.01).

RESULTS II

- In a multivariable model including both PWH and negative controls, male sex (adjusted odds ratio=1.68 [95%CI=1.03-2.73]), current smoking (2.74, [1.30-5.79]), diabetes mellitus (2.97 [1.48-5.99]), hypertension (1.67 [1.02-2.72]), frailty (3.82 [1.33-10.93]), and higher IL-6 levels (1.09 [1.04-1.15]), but not hsCRP, HIV status and NCI, were independently associated with higher PAA (Table 1).
- Phenotypic age discriminated frailty better than chronological age alone (AROC 0.76 [0.66-0.85] vs. 0.66 [0.55-0.77], p=0.04) (Figure 1).

CONCLUSIONS

- While PWH did not appear to have accelerated aging in our cohort, the phenotypic aging marker was significantly associated with systemic inflammation, frailty, and cardiovascular disease risk factors. This simple aging marker could be useful to identify high-risk PWH within the similar chronological age group.

REFERENCES

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