Muscular markers for early identification of sarcopenia and frailty states in older people with HIV: the IMAGING study (Over50 cohort)

875

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BACKGROUND

Considering the critical need to identify the risk of frailty and sarcopenia at early stages in people with HIV (PWH), here we present the results of the Functional substudy of the IMAGING study. This is a study aimed at identifying image aging markers by whole-body magnetic resonance imaging (WB-RMI) in 50 PWH aged 50 years or older and 25 matched controls.

METHODS

The Functional substudy is an exploratory study that evaluates WB-MRI muscle markers (intramuscular fat content in glutes, psoas, iliac, and total muscle) and specific muscular (irisin and myostatin) and mitochondrial (coenzyme Q10) plasma biomarkers for diagnosing pre-frailty/frailty or sarcopenia in PWH. Imaging and muscle biomarkers were compared between PWH and controls and correlated with functional evaluations (Barber, Barthel, Lawton, Fried phenotype, SPPB and grip strength) and DXA scan. Statistical analyses were performed using R software. The protocol was approved by the Ethics Committee [Reference no. PI-20-035].

RESULTS

- Median duration of HIV infection was 29 years; all participants had undetectable viral loads at the time of recruitment. PWH had more comorbidities (median 5 vs. 3); and 50% of PWH and 28% of controls had over 5 comorbidities (**Table 1**). Malnutrition risk was higher in PWH (31% vs. 13.6%).
- A higher prevalence of dependency, prefrailty/frailty, and low bone mineral density (BMD) were observed among PWH (**Table 2**).
- Higher plasma levels of myostatin and lower levels of irisin were observed among PWH (**Table 3**). Higher coenzyme Q10 levels were associated with poorer health (dependency, frailty, osteopenia/osteoporosis); higher irisin levels with frailty and dependency; and lower myostatin levels with poorer health, though some contradictory data were noted.
- Lower intramuscular fat fractions were observed in malnutrition and less so in conditions like dependency. Associations were found between higher intramuscular fat content and time of infection, time on antiretroviral therapy and time until therapy; while a better immunological status was associated with lower fat content.

Overall, PWH were more dependent and frailer than controls. Unfavorable accompanying ***Irisin*** and ***Coenzyme Q10*** plasma markers, suggest these might be potential **diagnostic markers for dependency and frailty.**

Table 1. Demographic and clinical characteristics of participants

	Controls N = 25	**PWH** N = 50
Age, mean (SD)	64.1 (5.9)	61.2 (5.8)
Male, n (%)	20 (80%)	36 (72%)
Number of comorbidities, n (%)		
0-1	6 (24%)	5 (10%)
2-4	12 (48%)	20 (40%)
5+	7 (28%)	25 (50%)
Number of comorbidities, median [IQR]	3 [2; 5.75]	5 [3; 6]
HIV variables, median [IQR]		
Time with HIV (years)	-	29 [24; 33]
CD4 T-cell count (absolute)	-	672 [505; 886]
CD8 T-cell count (absolute)	-	695 [472; 904]
Ratio CD4/CD8	-	1.02 [0.65, 1.31]
Undetectable viral load, n (%)	-	50 (100%)

Table 2. Descriptive table of subjects' functional tests

	Control N = 25	**PWH** N = 50
Dependency (Barthel), n (%)		
Mild or moderate dependency	0 (0%)	9 (18.4%)
Total or severe dependency	0 (0%)	0 (0%)
Lawton, n (%)		
Altered	0 (0%)	1 (2%)
Barber, n (%)		
Altered (1+)	6 (25%)	25 (50%)
Fried criteria, n (%)		
Pre-frailty	7 (28%)	23 (46%)
Frailty	0 (0%)	7 (14%)
SPBB, n (%)		
Altered (<10)	1 (4%)	5 (10%)
Sarcopenia, n (%)		
Probable sarcopenia	2 (8%)	4 (8%)
Sarcopenia	0 (0%)	1 (2%)
Osteoporosis	4 (16%)	11 (22.5%)
Malnutrition (MNA), n (%)		
Risk of malnutrition	3 (13.6%)	13 (28.3%)
Malnutrition	0 (0%)	1 (2.2%)

Table 3. Plasma biomarkers and imaging muscle markers

	Control N = 25	**PWH** N = 50
Muscle biomarkers, median [25%,75]		
Myostatin (pg/ml)	2,811.94 [2,424.66; 3,311.88]	3,007.49 [2,441.34; 3,841.38]
Irisin (ng/ml)	33.66 [20.48; 42.33]	26.14 [14.72; 46.23]
Coenzyme Q (ng/ml)	1,903.00 [1,545.16; 2,085.22]	1,964.48 [1,727.34; 2,315.77]
Imaging markers, median [25%,75]		
Mean fat fraction (Gluti)	17.06 [13.82; 19.63]	16.74 [13.71; 20.61]
Mean fat fraction (Psoas)	16.64 [15.23; 18.94]	17.88 [15.67; 21.48]
Mean fat fraction (Iliac)	15.51 [11.61; 16.23]	15.46 [13.36; 17.29]
Mean total fat fraction (All)	16.36 [13.49; 18.61]	16.50 [13.83; 19.89]

CONCLUSIONS

In summary, PWH showed overall more dependency and frailty compared to controls, with more unfavorable accompanying plasma markers. Thus, specifically irisin and coenzyme Q10, might be potential diagnostic markers for dependency and frailty if larger studies support their clinical utility potential. These results encourage us to continue assessing these markers for their predictive and diagnostic potential.