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MITOCHONDRIAL DNA, COGNITIVE FUNCTION, AND FRAILTY IN OLDER ADULTS WITH HIV

Carrie Johnston MD[1] , Michelle Rice[1], Heather Derry PhD[1], Chelsie Burchett[1], Eugenia Siegler MD[1], Mary Choi MD[1], Marshall Glesby MD, PhD[1]
[1]Weill Cornell Medicine, New York, NY, USA

BACKGROUND

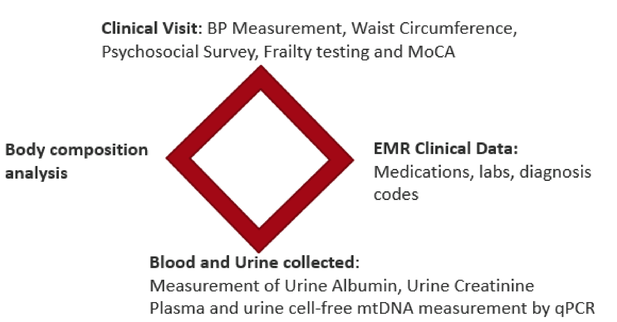
Advances in treatment of HIV with combination antiretroviral therapy have enabled people living with HIV (PLWH) to have life expectancies near those of their HIV-negative peers[1]

- Older PLWH experience a greater burden of comorbidities and geriatric syndromes, including neurocognitive impairment and frailty[2-3]
- Demographic Shift: The relative percentage of older adults with HIV is increasing[4]
- HIV may persist within and outside the CNS even after suppression of plasma viremia and is associated with inflammatory changes that may worsen cognitive and physical function[5]
- Mitochondrial DNA (mtDNA), which is released from dead and dying cells, is both a biomarker of inflammation and a mediator of immune activation[6]

We hypothesized that in older PLWH, plasma mtDNA is associated with cognitive impairment and frailty

METHODS

We analyzed cross-sectional data from PLWH over age 55 at a single urban medical center. Participants completed a psychosocial questionnaire, biomedical visit, Montreal Cognitive Assessment (MoCA), and frailty testing by Fried criteria. Plasma and urine cell-free mtDNA were measured by qPCR detection of mitochondrial NADH dehydrogenase-1.



PARTICIPANT DEMOGRAPHICS:

Measure	Result (N=164)
Age	61 (SD:6)
Female Sex	55 (34%)
Racial Identity: Black White Other	78 (48%) 47 (29%) 37 (23%)
Years with HIV	25 (IQR: 22-29)
HIV-1 Viral Load <200cp/ul	152 (93%)

Higher levels of plasma cell-free mitochondrial DNA were associated with cognitive impairment and some components of frailty (exhaustion and slow walk), suggesting mtDNA may have a role as a novel biomarker of geriatric-related syndromes in older people living with HIV

RESULTS

Plasma and Urine mtDNA:

- Geometric mean mtDNA level in plasma was 221 copies/µl (geometric SD: 2). Geometric mean urine mtDNA level was 2.4x10^{8}copies/gram of urine creatinine (geometric SD: 4).
- There was no relationship between levels of plasma and urine mitochondrial DNA (Spearman correlation rho=0.05, p=0.54)

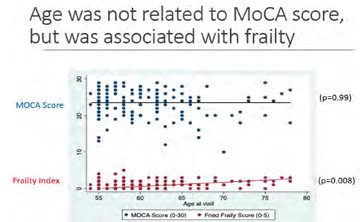
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Cognitive function and Frailty:

- Over 1/3 had a MoCA score below 23 consistent with cognitive impairment
- Approximately 2/3 met criteria for pre-frail or frail state

Fried Frailty Phenotype[7]:
- ❖Slowness (timed walk)
- ❖Weakness (grip strength)
- ❖Weight Loss
- ❖Low Activity
- ❖Exhaustion

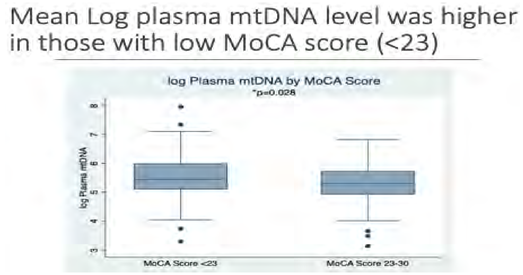
Score	State	N(%)
0	Non-Frail	49 (30%)
1-2	Pre-Frail	95 (58%)
3+	Frail	20 (12%)



RESULTS:

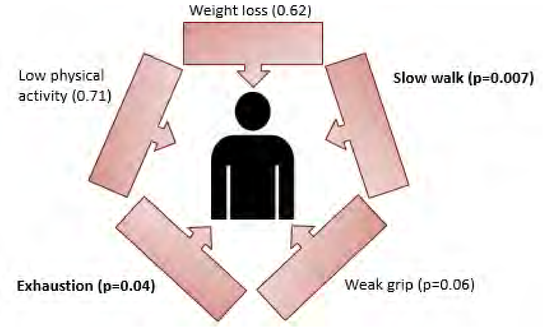
Relationships between mtDNA and MoCA score:

- Mean log plasma mtDNA level was higher in those with low MoCA score (p=0.028) by t-test



Relationships between mtDNA and Frailty:

Log Plasma mtDNA levels were associated with exhaustion (p=0.04) and slow walk (p=0.007).



CONCLUSIONS

- In this cross-sectional analysis we show a relationship between elevated levels of plasma mtDNA and lower performance on the MoCA, greater exhaustion, and slower walk.
- These data suggest mtDNA may have a role as a novel biomarker in assessing pathogenic inflammation associated with cognitive dysfunction and key components of frailty in older PLWH.

ADDITIONAL INFORMATION

Author Contact: **Carrie Johnston, MD** cmd9008@med.cornell.edu

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