MASH and the Progression of Cognitive Decline in Older People With HIV: A Prospective Study

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BACKGROUND

- People with HIV (PWH) are at increased risk of cognitive impairment. Cognitive decline in PWH is driven by multiple factors, including metabolic dysfunction.[1]
- Metabolic dysfunction-associated steatohepatitis (MASH) is common in PWH and linked to systemic inflammation.[2,3]
- We examined whether MASH predicts accelerated cognitive decline in older PWH.

METHODS

- Participants: data from HIV-NAT 006 and 207 cohorts
  - PWH aged ≥50 years
  - Baseline assessment: 2015-2017
  - Follow-up assessment: 2021-2024
- MASH definition
  - FibroScan-AST (FAST) score ≥0.67
  - FAST score is based on controlled attenuation parameter (CAP), liver stiffness measurement (LSM) and aspartate aminotransferase (AST) level
- Cognitive assessment
  - Montreal Cognitive Assessment (MoCA) score
  - Cognitive impairment defined as MoCA score <25
- Statistical analysis
  - Longitudinal MoCA score change between participants with and without baseline MASH
  - Multivariate linear mixed model
  - Adjusted for age, sex, body mass index, education, employment, smoking, alcohol use, diabetes, hypertension, HIV duration, and antiretroviral therapy regimen.

RESULTS

- Baseline characteristics: total 291 participants
  - Male 60.5%, median age 54.4 years(IQR: 51.8-59.1), median HIV duration 18.2 years(IQR: 15.0-20.9)
  - Baseline characteristics were comparable.
  - 60 participants (20.6%) met the criteria for MASH

Baseline MASH independently predicts accelerated cognitive decline in older PWH

RESULTS

- Cognitive performance
  - Participants with **MASH** showed **significantly greater cognitive decline** over time.

Parameter	**No MASH** (*n* = 231) *n (%)*	**MASH** (*n* = 60) *n (%)*	*P*-value
Baseline total MoCA score, median (IQR)	24.0 (21.0, 26.0)	24.0 (21.5, 26.0)	0.64
Cognitive impairment (MoCA score <25)	139 (60.2%)	35 (58.3%)	0.80
Mean change (95% CI)	-0.9 (-1.7, -0.1)	-3.5 (-5.3, -1.7)	0.006

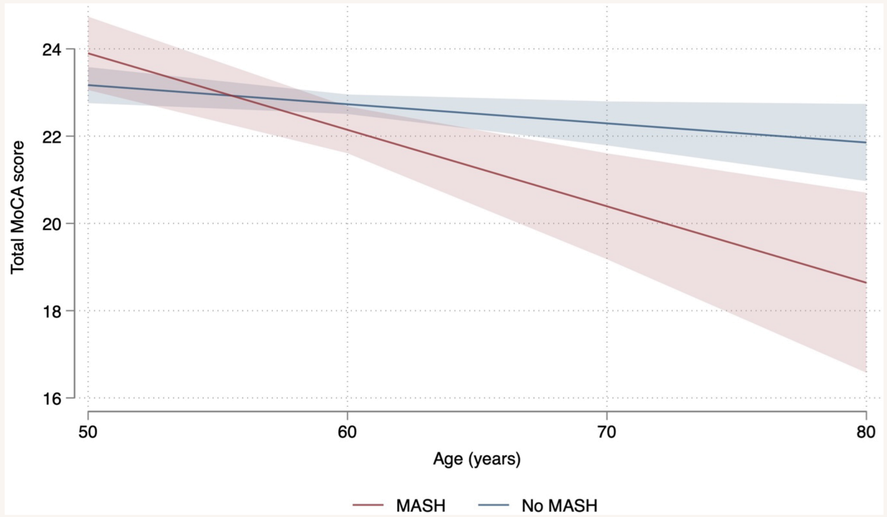


Figure: Modeled cognitive trajectories with 95% CI from age 50 to 80 years, comparing between PWH with and without MASH at baseline.

Adjusted for sex, body mass index, employment, education level, smoking, alcohol consumption, diabetes, hypertension, HIV duration, and baseline MoCA score

CONCLUSIONS

- MASH was independently associated with accelerated cognitive decline in older PWH over 6 years
- Early identification and management of MASH in PWH may help mitigate this risk.

LIMITATIONS AND FUTURE DIRECTIONS

1. MASH definition
   - MASH was defined using the non-invasive FAST score rather than biopsy-proven histology.
   - Future studies using biopsy-confirmed MASH are needed to validate these findings.
2. Cognitive assessment
   - Cognitive performance was assessed using MoCA alone.
   - Comprehensive neuropsychological battery tests are needed to evaluate domain-specific impairment.
3. Underlying mechanisms
   - Underlying mechanisms such as systemic inflammation, neuroinflammation, and liver fibrosis were not directly assessed.
   - Future studies incorporating imaging and biomarker-based approaches could provide deeper insight into these pathways.

REFERENCES

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PLAIN LANGUAGE SUMMARY

PWH who had MASH experienced faster cognitive decline compared with those without MASH.