Poster # 0703

Glycemic Control and Cognition Are Independently Associated with Gait Speed Decline

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The A5322 (HAILO) Study

Background

- Slow gait speed is an established predictor of functional impairment and mortality in older adults.
- Persons with HIV (PWH) exhibit accelerated decline in physical function and high rates of frailty.
- A5322 or HAILO (HIV Infection, Aging, and Immune Function Long-term Observational Study) is a longitudinal, observational study of 1035 PWH who were over the age of 40 at the time of enrollment.
- The goal of this study was to identity characteristics associated with development of impaired gait speed in older HIV-infected adult HAILO participants.

Methods

Study Participants

- 929 PHW ≥40 years with gait speed and neurocognitive evaluations
- Received initial ART regimen through an ACTG randomized, interventional clinical trial

Evaluations and Definitions

- Gait speed was ascertained by the average of 2 readings on a 4-meter walk: men ≤173 cm and women ≤159 cm in height who required ≥6.22 seconds or men >173 cm and women >159 cm who required ≥5.33 seconds to complete the walk met the criterion for slowness.
- Diabetes was defined as a hemoglobin A1C (HbA1C) level ≥6.5% or prior diagnosis of diabetes.
- Neurocognitive impairment (NCI) was assessed using the A5001 Neuroscreen which includes normalized, demographic-adjusted scores on the Trailmaking tests A and B and the Wechsler Adult Intelligence Scale-Revised Digit Symbol tests.
- NCI was defined by at least 1 z- score that was at least 2 standard deviations (SDs) below the mean or multiple z-scores that were at least 1 SD below the mean on separate tests.

Data Analysis

- Participants were categorized into 4 groups based on their gait speed over time. PWH who developed slow gait were compared to those who retained normal gait speed. Participants who entered the study with slow gait speed and improved to normal speed were compared to those who remained slow.
- Associations were examined using logistic regression models; covariates with category-specific p-value <0.10 were retained in the final multivariable model.

Results

Table 1. Participant Characteristics at HAILO Entry by Gait Speed Status

	Persistently normal gait N=813	Development of slow gait N=52	Resolution of slow gait N=38	Persistently slow gait N=26	P-Value
Age	50 (46-56)	51 (44-57)	52 (47-55)	56 (52-61)	0.01
Female	140 (17%)	19 (37%)	8 (21%)	10 (38%)	<.001
White	423 (52%)	13 (25%)	14 (37%)	7 (27%)	<.001
Black	224 (28%)	28 (54%)	18 (47%)	15 (58%)	
Hispanic	166 (20%)	11 (21%)	6 (16%)	4 (15%)	
Education <12 yrs	111 (14%)	12 (23%)	7 (18%)	5 (19%)	0.21
HbA1C%	5.50 (5.20-5.80)	5.60 (5.20-6.00)	5.60 (5.40-6.10)	6.00 (5.40-6.40)	0.01
NCI at Entry	108 (13%)	16 (31%)	12 (32%)	8 (31%)	<.001
AIDS-defining condition	165 (20%)	9 (17%)	9 (24%)	4 (15%)	0.82
Nadir CD4 <200 cells/mm^3	409 (50%)	31 (60%)	20 (53%)	10 (38%)	0.66
CD4 cells/mm^3	620 (463-838)	678 (420-828)	648 (419-906)	677 (511-837)	0.85
HIV-1 RNA copies/mL	39 (20-40)	39 (20-40)	21 (20-40)	40 (20-40)	0.64

Presented as number (%) or median (interquartile range)

Gait Speed Status Over 3 Years of Follow-up in HAILO Participants

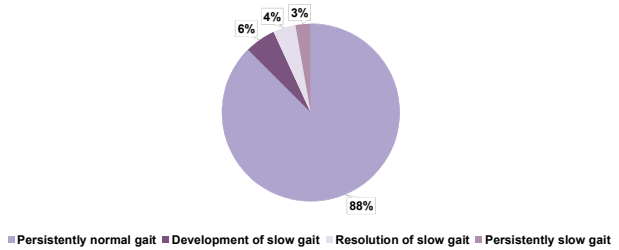

Table 2. Factors Associated with Gait Speed Change in Multivariable Models

Characteristic at HAILO Entry	Development of slow gait (OR, 95% CI)	Resolution of slow gait (OR, 95% CI)
NCI vs. no NCI	*3.38 (1.53, 7.46) p=0.003*	
Age (years)	1.02 (0.98, 1.06) p=0.40	*0.92 (0.86, 0.98) p=0.01*
Heavy Alcohol Drinker vs. Abstainer	0.72 (0.27, 1.88) p=0.50	
Light Alcohol Drinker vs. Abstainer	0.55 (0.25, 1.19) p=0.13	
Moderate Alcohol Drinker vs. Abstainer	0.68 (0.15, 3.15) p=0.62	
BMI (kg/m^2)	1.00 (0.93, 1.07) p=0.99	0.94 (0.84, 1.04) p=0.22
Education (≥ 12 yrs vs. <12 yrs)	0.68 (0.28, 1.64) p=0.39	
HbA1C (per 1% increase)	*1.40 (1.06, 1.85) p=0.010*	
Waist Circumference (high vs. normal)	1.65 (0.66, 4.14) p=0.28	0.61 (0.16, 2.41) p=0.48
Black vs. White Race	*2.34 (1.03, 5.29) p=0.04*	
Hispanic vs. White Race	1.04 (0.36, 2.98) p=0.95	
Female vs. Male Sex	1.12 (0.48, 2.58) p=0.80	

All characteristics were measured at baseline with the exception of gait speed. Other variables investigated but not included in multivariable analyses: self-reported physical activity, substance use, anxiolytic or antidepressant medication, history of a comorbidity (hypertension, stroke, kidney disease, history of cancer in the last 5 years, liver disease, stroke, hepatitis C), nadir CD4, or history of AIDS defining illness.

Higher hemoglobin A1C level, NCI, and black race were strongly associated with development of slow gait

Older age was associated with less likelihood of improvement in slow gait speed

Conclusions

- Increased levels of hemoglobin A1C, NCI, and black race are associated with gait speed decline among PWH; persons with these characteristics may benefit from early gait speed screening and intervention.
- Glycemic control may be an intervenable target to prevent functional decline in PWH.
- Although mechanisms accounting for the links between slow gait, impaired cognition, and glycemic control cannot be determined from this analysis, previous studies have shown that cerebral white matter disease is common to these three characteristics. Furthermore, both gait and cognition are vulnerable to impaired communication between brain regions in long white matter tracts.
- Additional analysis as the HAILO cohort continues to age will help further characterize these relationships.

Acknowledgements

- We thank the study participants and site staff for their ongoing dedication.
- The study was supported by the NIH: NIA K32 63008845 to KME, NIDDK T32 DK007169 to MCM, NIAID K24 120834 to TTB, NIAID UM1 AI068636 (ACTG) and UM1 AI068634 (SDAC)