Glycemic Status and Physical Function Among Men With and Without HIV

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MULTICENTER AIDS COHORT STUDY

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Background

- Gait speed and grip strength are key measures of physical function and are core determinants of frailty.
- Persons living with HIV (PLWH) exhibit accelerated declines in gait speed and grip strength.
- Abnormal glucose metabolism has been associated with impaired physical function in cross-sectional studies of PLWH.
- The goal of this study was to evaluate longitudinal relationships between hyperglycemia and objective measures of physical function in men with and without HIV.

Methods

Study Participants

- The Multicenter AIDS Cohort Study (MACS) a large ongoing prospective observational cohort study of men living with HIV (MLWH) and demographically similar HIV-uninfected men who have sex with men.
- All MACS participants undergo semi-annual assessments of glycemic status and physical function.
- 2,575 MACS participants with at least 2 measurements of gait speed or grip strength anytime between 2006 and 2018 were included in this analysis.

Evaluations and Definitions

- Gait speed was assessed as time to complete a 4-meter walk.
- Dominant hand grip strength was calculated as the average of three trials using a hand-held dynamometer.
- Glycemic status categories:
  - Normal: fasting blood glucose (FBG) <100 mg/dl
  - Impaired fasting glucose (IFG): FBG between 100-125 mg/dl
  - Diabetes mellitus (DM): self-reported DM as a medical condition, use of anti-diabetic medications, or FBG ≥ 126 mg/dl on least two consecutive study visits. Persons with DM were further dichotomized as having controlled (hemoglobin A1C [HbA1C] <7.5%) or uncontrolled DM (HbA1C ≥7.5%).

Data Analysis

- Linear mixed models with random intercept were used to assess associations between glycemic status category, gait speed and grip strength between 2006-2018.
- Subgroup analysis was also performed among MLWH using the same linear mixed model format from the initial model with addition of HIV specific risk factors.

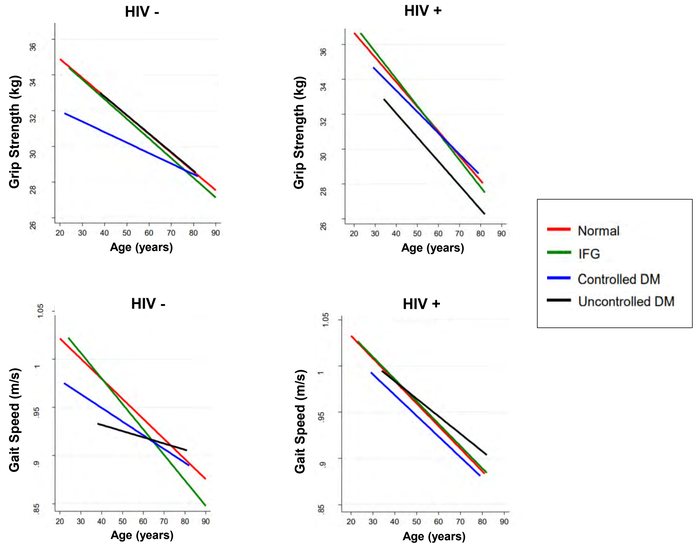
Results

Table 1. Participant Characteristics at Study Baseline by HIV Serostatus

	HIV – N=1227	HIV + N=1348	p-value
Age in years	49.2 (11.9)	45.0 (10.3)	<.01
Glycemic status			
Normal	59.5%	63.1%	0.01
IFG	33.2%	28.6%	
Controlled DM	4.7%	7.0%	
Uncontrolled DM	2.7%	1.3%	
Grip strength (kg)	39.7 (9.0)	39.9 (9.5)	0.71
Gait speed (m/s)	1.20 (0.2)	1.17 (0.2)	<.01
Undetectable HIV viral load	-	69.6%	-
CD4 nadir <200	-	26.7%	-
Years of ART	-	5.2 (4.6)	-

Presented as number (%) or mean (SD)

Figure 1. Physical Function Over Time by Glycemic Status and HIV Serostatus



No significant interactions between physical function, HIV serostatus, and glycemic status over time were noted.

Table 2. Association Between Glycemic Status and Physical Function in All Participants: Multivariable Models

	Grip Strength β (95% CI)	p-value	Gait speed β (95% CI)	p-value
Age in years	*-0.13 (-0.17, -0.09)*	*<0.01*	*-0.003 (-0.003, -0.002)*	*<0.01*
Glycemic status				
Normal	Ref		Ref	
IFG	-0.14 (-0.43, 0.14)	0.32	-0.004 (-0.012, 0.003)	0.23
Controlled DM	*-0.56 (-1.10, -0.02)*	*0.04*	*-0.018 (-0.032, -0.005)*	*0.01*
Uncontrolled DM	*-0.94 (-1.68, -0.19)*	*0.01*	-0.007 (-0.026, 0.011)	0.44
HIV infection	0.48 (-0.27, 1.24)	0.21	-0.002 (-0.016, 0.012)	0.77

Other variables included in the model: BMI, race, education, MACS study site, cohort, smoking status, history of cocaine use, history of marijuana use, alcohol use status, liver disease, kidney disease, hypertension, arthritis, depression (Center for Epidemiologic Studies Depression Scale score ≥16), self-reported testosterone use, chronic hepatitis B infection, chronic hepatitis C infection.

Both controlled and uncontrolled DM were associated with grip strength decline.

Controlled DM was associated with decline in gait speed.

Table 3. Association Between Glycemic Status and Physical Function in MLWH Only: Multivariable Models

	Grip strength β (95% CI)	p-value	Gait speed β (95% CI)	p-value
Age in years	*-0.21 (-0.27, -0.14)*	*<0.01*	*-0.003 (-0.004, -0.002)*	*<0.01*
Glycemic status				
Normal	Ref		Ref	
IFG	-0.01 (-0.42, 0.39)	0.95	0.004 (-0.006, 0.015)	0.41
Controlled DM	-0.19 (-0.92, 0.53)	0.60	-0.012 (-0.031, 0.006)	0.19
Uncontrolled DM	*-1.87 (-2.92, -0.82)*	*<0.01*	0.006 (-0.020, 0.032)	0.65
Years of ART	*0.18 (0.07, 0.29)*	*<0.01*	0.002 (0.000, 0.004)	0.08
Years of Specific ARV				
AZT	-0.10 (-0.22, 0.03)	0.12	*-0.005 (-0.007, -0.002)*	*<0.01*
DDI	*-0.23 (-0.45, -0.01)*	*0.04*	-0.002 (-0.006, 0.002)	0.40

Abbreviations: AZT, zidovudine; D4T, stavudine; DDI, didanosine; EFV, efavirenz; PI, protease inhibitor. All variables listed in Table 2 were included in this model. CD4 nadir, viral load, and use of stavudine, efavirenz or any protease inhibitor were also included in this model but were not found to be significant.

Uncontrolled DM and DDI use were associated with grip strength decline.

Longer duration of ART use was associated with improved grip strength.

AZT use was strongly associated with decline in gait speed.

Conclusions

- Abnormal glucose metabolism was associated with declines in gait speed and grip strength regardless of HIV serostatus.
- Uncontrolled DM exerted a greater effect on grip strength decline among MLWH compared to all MACS participants.
- Improved glucose control, independent of virologic suppression, is an intervenable target to prevent progression of physical function limitations among MLWH.

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