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Elevated Insulin Resistance and Sex-Based Differences in Body Composition in Older PWH

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Background: Insulin resistance and increased visceral adiposity, especially relative to subcutaneous adiposity, are multifactorial and prevalent in older PWH. Females experience hormone shifts after menopause that may alter metabolism and body composition. We hypothesized that females would have greater insulin resistance and differential adipose distribution than men within our cohort of older PWH.

Methods: We conducted a single-center cross-sectional study of 115 PWH age 55+ including waist and hip circumference measurement, fasting insulin and glucose levels, a survey including self-report of historical D-drug use, and bioelectric impedance analysis (BIA). A subset of participants without pre-existing vascular stents (N= 89) completed a non-contrast CT scan to assess for coronary artery calcium and had visceral and subcutaneous adipose tissue area measured at the level of L4. Clinical data from the electronic medical record included diabetes diagnosis and diabetes medication use. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated for participants not using insulin therapy. Differences in waist:hip ratio (WHR), HOMA-IR, and VAT:SAT by sex were assessed with the Wilcoxon rank-sum test. The association between WHR and VAT:SAT was assessed with Spearman correlation. A linear regression model with VAT:SAT as the outcome was used to model the relationship with age, sex, HOMA-IR and prior D-drug use.

Results: Overall, of 115 participants the median age was 65 years (IQR: 61-70) and 42 (37%) were female. The median HOMA-IR was 3.23 [2.26-4.88]

in 99 participants with samples available who did not use insulin, consistent with moderate-high insulin resistance. Median WHR was significantly higher in males 0.99 [IQR: 0.95-1.04] as compared to females 0.93 [IQR: 0.89- 0.99], and there was no difference in HOMA-IR level by sex ($p=0.7$). Males had greater median visceral adipose area (196 cm² [IQR:114-249]) as compared to females (119 cm² [IQR:65-163]). Females had higher median subcutaneous adipose area (327cm² [IQR:234-392]) as compared to males (187 cm² [IQR:108-254]). The median VAT:SAT was 0.89 [IQR: 0.61-1.42] in males, and 0.39 [IQR: 0.24-0.52] in females which differed significantly ($p<0.001$). VAT:SAT was associated with WHR ($\rho=0.33$, $p=0.001$) by Spearman correlation. In a linear regression model with VAT:SAT as the outcome variable, only female sex (Beta -0.79 [95%CI: -1.12, -0.46]) was related to lower VAT:SAT, and there was no significant relationship with age (Beta -0.004 [-0.031, 0.022] $p=0.07$), HOMA-IR (Beta 0.008 [-0.052, 0.067] $p=0.8$), or prior D-drug use (Beta -0.051 [-0.043, 0.302] $p=0.8$). BIA showed that females had higher fat mass index ($p<0.001$) and lower skeletal muscle index ($p<0.001$) compared to males by Wilcoxon rank-sum.

Conclusions: There was a high prevalence of insulin resistance as measured by HOMA-IR, that did not differ significantly by sex or age, in our single-center study of older PWH. CT-based measurement at the level of L4 showed higher visceral adipose tissue in males, and higher subcutaneous adipose tissue in females, resulting in a higher VAT:SAT ratio in males. VAT:SAT was related to WHR. Females had significantly lower skeletal muscle, scaled for height, compared to males. Further research is needed to relate aging and insulin resistance to metabolic outcomes.

