Body Composition Changes Over The Menopausal Transition In Women With and At Risk For HIV

#00669

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Introduction

- Both overall and central adiposity increase during menopause.
- In healthy middle-aged women,this increase begins in the 5 years prior to the final menstrual period (FMP) (i.e. the late *peri*-menopausal phase).
- How HIV might affect adiposity changes during menopause is unknown.
- HIV has been associated with subcutaneous fat loss.
  - Thymidine analogs to treat HIV infection has been implicated as a factor
  - Studies report little recovery of fat after discontinuation of thymidine analogs.
- Central adiposity gains following ART initiation may represent a restoration of health.
- We hypothesized that body mass index (BMI) and waist circumference (WC), a marker of visceral obesity would increase over the menopausal transition and that HIV infection would blunt increases in BMI, and to a lesser extent WC.

Methods

Study Population

- WIHS is a multicenter prospective study established in 1994 to investigate the progression of HIV in women with and at risk for HIV via semiannual visits.
- 850 WIHS participants (632 HIV+ and 218 HIV-) who had serial measures of a marker of ovarian reserve and estrogen depletion Anti-Mullerian Hormone (AMH) were included based upon the following criteria: (1) Had at least one detectable AMH level prior to their undetectable AMH leve (<0.09ng/ml)l, (2) Had their last detectable AMH after the year 2000, (3) AMH became undetectable before 2014 but after 2000, and (4) Had available BMI data for at least 2.5 years after their undetectable AMH level.

Measurements

Primary Predictors

- Stages of menopausal transition as determined by years before or after AMH levels became undetectable. We categorized the menopausal transition as follows:
  - premenopause (>5 years before AMH became undetectable),
  - early perimenopause (1-5 years before),
  - late perimenopause (first visit with undetectable AMH to 5 years after),
  - early menopause (>5-10 years after),
  - late menopause (>10 years after).

Outcome

- Percentage change in BMI and WC per 5-years across the menopausal transition.

Statistical Analysis

- Multivariable linear mixed models were used to compare BMI and WC change for each peri- and post-menopause stage relative to premenopause, after adjustment for socio-demographics, lifestyle, viral hepatitis, depression, and CD4 count.
- All analyses were conducted using the SAS system, version 9.4 (SAS Institute, Inc., Cary, NC).

Results

During menopause, HIV infection *blunts* the trajectory of *increase in* ***total adiposity***, whereas the *increase in* ***central adiposity*** *is preserved*.

Table 1. Clinical Characteristics by HIV status at 1st visit of non-detectable AMH

N (%); Median (IQR)	HIV+ *(n=632)*	HIV- *(n=218)*	p-value*
Demographics			
Age at baseline visit (yrs)	36 (32, 39)	36 (32, 39)	0.74
Age at non-detectable AMH (yrs)	45 (43, 47)	45 (44, 47)	0.20
Race			
White	14%	10%	0.34
African American	57%	60%	
Hispanic	27%	26%	
Other‡	2.9%	4.1%	
Lifestyle			
Current Smoker	48%	61%	0.002
Drinking			
Abstainer	58%	49%	0.0002
>0-7 drinks/wk	33%	31%	
>7 drinks/wk	8%	19%	
Infection status			
HCV infection	24%	17%	0.14
HIV viral load, undetectable	53%	-	
CD4 (cells/mm^3)	415 (249, 621)	1014 (742, 1280)	<.0001
ART	70%	-	
Thyimidine analog use	29%		
INSTI use	4%		

‡Includes Asian, Pacific Islander, Native American, Alaskan and other study participants; Missing values were excluded when calculating frequencies/percentages; *P value from Pearson χ2 test, Wilcoxon rank-sum test or Fischer's exact test;

Figure 1. Compared to HIV- women, HIV+ had lower BMI and WC. For BMI, larger increases were seen in HIV- vs. HIV+, whereas both HIV- and HIV+ saw steady gains in WC

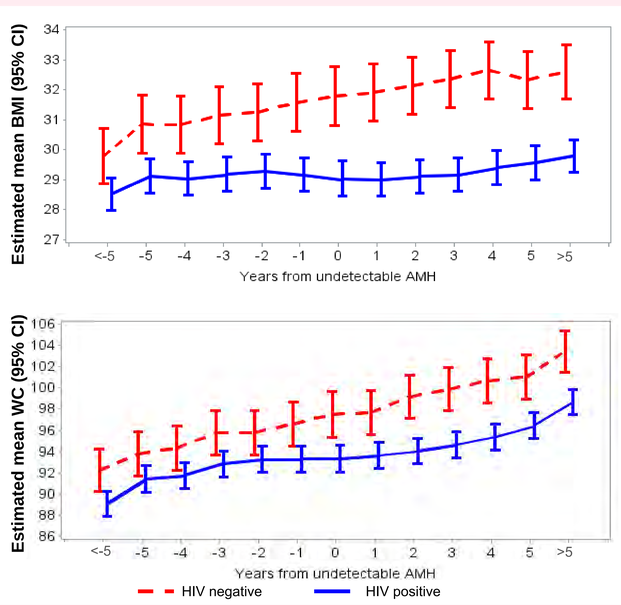
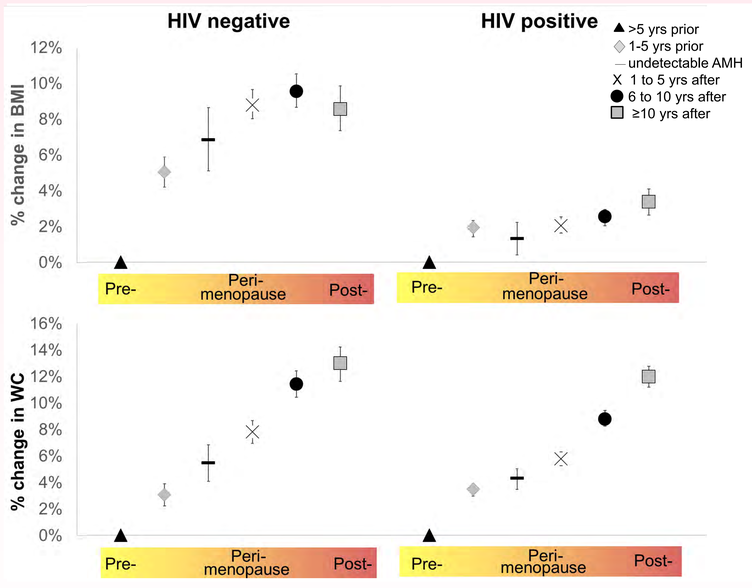


Figure 2. In HIV-, the expected increase in BMI beginning in perimenopause was observed; in HIV+, increase was much lower. By contrast, WC progressively increased over the menopausal transition, but in HIV+ the increase was blunted except in the early perimenopause phase



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Conclusions

- Our findings suggest that HIV infection blunts the expected trajectory of increase in BMI over the menopausal transition, whereas the expected trajectory of increase in WC is largely preserved.
- Additional study is needed to determine whether women with HIV in the menopausal transition are at greater risk for perturbations associated with visceral obesity (e.g. insulin resistance, fatty liver disease).
- Whether serial monitoring of AMH should be considered to determine optimal timing of preventative measures (e.g. diet, exercise) to reduce visceral obesity needs study.
- Longitudinal measurement of waist circumference may be more informative than BMI in women living with HIV.