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Longitudinal associations of the endocrine environment on fat partitioning in postmenopausal women

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Abstract

Among postmenopausal women, declining estrogen may facilitate fat partitioning from the periphery to the intra-abdominal space. Furthermore, it has been suggested that excess androgens contribute to a central fat distribution pattern in women. The objective of this longitudinal study was to identify independent associations of the hormone milieu with fat distribution in postmenopausal women. 53 healthy postmenopausal women, either using or not using hormone replacement therapy (HRT), were evaluated at baseline and 2 years. The main outcomes were intra-abdominal adipose tissue (IAAT), subcutaneous abdominal adipose tissue (SAAT), and total thigh fat analyzed by computed tomography (CT) scanning and leg fat and total body fat mass measured by dual energy X-ray absorptiometry (DXA). Serum estradiol, estrone, estrone sulfate, total testosterone, free testosterone, androstenedione, DHEA-S, SHBG, and cortisol were assessed. On average in all women combined, IAAT increased by 10% (10.5 cm^2) over two years ($P<0.05$). Among HRT users, estradiol was inversely associated with, and estrone was positively associated with, 2-yr gain in IAAT. Among HRT non-users, free testosterone was inversely associated with, and SHBG was positively associated with, 2-yr gain in IAAT. These results suggest that in postmenopausal women using HRT, greater circulating estradiol may play an integral role in limiting lipid deposition to the intra-abdominal cavity, a depot associated with metabolically detrimental attributes. However, a high proportion of weak estrogens may promote fat partitioning to the intra-abdominal cavity over time. Further, among postmenopausal women not using HRT, greater circulating free testosterone may limit IAAT accrual.

Introduction

With age, women experience a gain in intra-abdominal adipose tissue (IAAT) and a loss of fat in the hip-thigh area, both of which increase risk for chronic metabolic diseases such as type 2 diabetes and cardiovascular disease [1, 2]. Understanding the factors that regulate body composition and fat distribution in older women is critical for preventing undesirable changes in IAAT and for preventing decline in metabolic health.

Changes in fat distribution may be due to age-related changes in the endocrine environment. Circulating concentrations of estrogens, androgens, and growth factors decline with age and the shift in fat distribution from the hip/thigh region to the abdominal/upper body region

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with age in women has been attributed to the changes in the reproductive hormonal milieu[3, 4]. In an observational study of perimenopausal women, an increase in follicle stimulating hormone (FSH) was associated with an increase in waist circumference[5]. Interventional studies involving administration of exogenous hormones suggest that estrogen promotes deposition of fat in the hip/thigh area[6, 7]. However, associations between endogenous estrogens and fat distribution among postmenopausal women have not been investigated.

Age-related changes in fat distribution may also be attributed to changes in the androgenic environment. However, conflicting evidence exists as to the precise relationship between total and free testosterone and IAAT accrual in women. It was been widely speculated that an androgenic profile is related to increased central adiposity in women, specifically in women with polycystic ovary syndrome[8]. Other studies have demonstrated an inverse relationship between IAAT and total testosterone in women [9], and furthermore studies in males also suggest testosterone limits IAAT accrual [10, 11]. To date, no longitudinal studies have been conducted to examine the relationship among changes in IAAT and total and free testosterone in postmenopausal women.

The use of oral conjugated equine estrogens results in pharmacological increases in circulating concentrations of weak estrogens (e.g., estrone), and increases in estradiol that are in the low-normal range for premenopausal women[12–14]. Further, orally administered estrogen stimulates hepatic production of sex hormone binding globulin (SHBG), the major binding protein for circulating testosterone[15]. Thus, an increase in SHBG to supra-physiological levels may result in a reduction in circulating free testosterone. Oral estrogen also increases circulating cortisol due to stimulation of hepatic production of cortisol binding globulin[15]. Cortisol promotes energy partitioning toward fat, particularly central fat [16], at the expense of lean mass. It is not clear if elevated cortisol among oral HRT users has implications for adiposity and fat distribution. Therefore use of exogenous hormones may alter the endocrine environment in such a way that influences body composition and fat distribution.

The purpose of this 2-year observational, longitudinal study was to examine associations between the hormone milieu and body fat distribution in healthy postmenopausal women. We hypothesized that androgen concentrations would be positively associated with IAAT; estrogen concentrations would be positively associated with leg/thigh fat and inversely associated with IAAT; and cortisol concentration would be positively associated with IAAT. In addition to measuring circulating levels of sex steroid hormones, we analyzed the relationship between their metabolites and potential precursors (estrone sulfate, DHEA-S) and fat distribution. We included both women using hormone replacement therapy (HRT) and women not using HRT to determine if the use of exogenous hormones affected the nature of the relationship of the endocrine environment with fat distribution.

Methods and Procedures

Participants and Protocol

Metabolic testing and body composition assessment took place at baseline and at a 2-yr follow up evaluation under controlled conditions during an in-patient visit to the Department of Nutrition Sciences and the General Clinical Research Center (GCRC) at the University of Alabama at Birmingham (UAB). Subjects were 53 postmenopausal women aged 45–55 years. Only women who experienced a natural menopause, with the time of menopause known to occur at least 6 months prior to contact, were recruited. Both women using HRT and women not using HRT were recruited. Among hormone users (n=35), subjects predominantly used conjugated equine estrogens, 0.625 mg/day, and medroxyprogesterone

acetate, 2.5 mg/day. The estrogens in this preparation of hormone replacement are a combination of estrogens with relatively strong (estradiol) and weak (estrone, >50%; equilin, 15–25%; and equilenin) activity. Two women used unopposed oral estrogen (conjugated equine estrogens), and one used a transdermal estradiol patch in combination with an oral progestin. In cases where usage was cyclic, testing was conducted during the combined (estrogen + progestin) portion of the cycle. No HRT use (n=18) was defined as no current use, and no use within the past 6 months. Over the 2 year observation period, several women in the HRT group changed their hormone use: three women changed dosage of the same preparation; two women switched to a different formulation of the same hormone (e.g., from Provera to Prometrium); three women altered their hormone use (e.g., from estrogen only to estrogen plus progestin); and two women discontinued HRT. One woman in the non-user group started using HRT (Premarin vaginal cream) during the course of the study. Among the women recruited, 10% were African American (n=5) and 90% European American (n=48). Two of the African American women were HRT users. None of the women smoked. The protocol was approved by the Institutional Review Board for Human Use at UAB, and all subjects signed an informed consent prior to testing.

Body Composition and Fat Distribution

Total and regional body composition were measured by DXA using a Lunar DPX-L densitometer (LUNAR Radiation Corp., Madison, WI). Subjects were scanned in light clothing while lying flat on their backs with arms at their sides. DXA scans were performed and analyzed with adult software version 1.5g.

IAAT and subcutaneous abdominal adipose tissue (SAAT) were analyzed by computed tomography (CT) scanning with a HiLight/Advantage Scanner (General Electric, Milwaukee) as previously described [17, 18]. A scout scan was first performed to locate the L4–L5 inter-vertebral space. Subsequently, a 5mm scan of this abdominal site was taken. Thigh adipose tissue area was determined using a one slice mid-thigh (between the superior border of the patella and the inferior anterior iliac crest) CT scan. Due to poor mid-thigh scan quality, 15 follow-up scans were deemed unusable and excluded from analyses. Scans were analyzed for cross-sectional area (cm^2) of adipose tissue using the density contour program with Hounsfield units for adipose tissue set at −190 to −30. We have shown the test-retest reliability for IAAT to be 1.7 percent [19].

Hormone Assay

Serum was collected after a 12 h fast. All hormone concentrations were determined by RIA or IRMA in the Core Laboratory of UAB's Nutrition Obesity Research Center, General Clinical Research Center, and Diabetes Research and Training Center. Kit vendor, assay sensitivity, and intra-/inter-assay cvs are listed for each hormone measured. Estradiol: Diagnostic Products, Siemens, Los Angeles, CA; 15.42 pmol/L, 5.3%/6.0%. Estrone: Diagnostic Systems Laboratories, Inc., Beckman-Coulter, Webster, TX; 8.99 pg/ml, 6.68%/7.43%. Estrone sulfate: Diagnostic Systems Laboratories, Inc., Beckman-Coulter; 0.04 ng/ml, 5.68%/8.86%. Total testosterone: Diagnostic Products, Siemens; 0.409 ng/dL, 7.7%/8.2%. Androstenedione: Diagnostic Systems Laboratories, Inc., Beckman-Coulter; 0.09 ng/ml, 7.97%/9.83%. DHEA-S: Diagnostic Products, Siemens; 4.96 ug/dl, 6.15%/4.32%. SHBG: Diagnostic Systems Laboratories, Inc., Beckman-Coulter; 5 ng/mL, 8.2%/8.2%. Cortisol: Diagnostic Products, Siemens; 0.52 ug/dl, 5.63%/3.55%. Free testosterone (pmol/L)was calculated from serum concentrations of total testosterone and SHBG using the method of Sodergard et al[20]. This method is based on the concentration of albumin, the binding capacity of SHBG, and the association constants of testosterone for SHBG and albumin, as determined in a sample of normal men and women.

Statistical methods

Descriptive statistics were computed for all study variables of interest. Variables known to deviate from a normal distribution, such as hormone measurements, were log 10 transformed prior to statistical analysis. All statistical tests were two-sided and were performed using a type I error rate of 0.05. Statistical analyses were performed using SAS (version 9.1; SAS Institute, Inc., Cary, NC). Two-way repeated measures analysis of variance was used to examine the effects of time (baseline to 2-year follow-up) and group (HRT users and non-users) on measures of fat distribution and hormone concentrations.

Exploratory analyses were conducted using multiple linear regression to determine potential associations among baseline hormone variables (estradiol, estrone, estrone sulfate, androstenedione, total testosterone, free testosterone, DHEA-S, SHBG, cortisol) and 2-yr fat distribution variables (SAAT, IAAT, leg fat, thigh fat)among all women combined. Further subgroup analysis was conducted in HRT users and non-users separately examining differential group contributions to hormonal associations with 2-yr change in IAAT. Due to sample size limitations in the non-user group, further multiple linear regression analyses were performed only in the HRT users to identify potential independent associations among baseline hormone concentrations and change in IAAT, with 2-yr IAAT as the dependent variable adjusted for baseline IAAT and 2-yr total body fat.

Results

Demographic variables are shown in Table 1, by HRT use status. No significant differences were observed between groups at baseline in regards to age, BMI, and time since menopause. Women who changed HRT preparations during the course of the study remained in the longitudinal analyses as the results did not differ with the exclusion of these subjects; however, women who discontinued hormone use during the course of the study were not included in longitudinal analyses. Baseline and follow up measures of fat distribution are shown in Table 2.A. Significant group effects were observed for total fat and IAAT such that HRT users had less than non-users. Significant time effects were observed for IAAT, such that IAAT increased over 2 years.

Hormone concentrations at baseline and follow up are reported in Table 2.B. Significant group effects were observed for estrone, estradiol, estrone sulfate, cortisol, and SHBG (all higher in HRT users), and for free testosterone and FSH (lower in HRT users). Significant time effects were observed for estrone sulfate, cortisol, and SHBG (increased over 2 years), and for androstenedione (decreased over 2 years).

Associations among all baseline hormone concentrations and 2-yr changes in fat distribution variables are shown in Table 3 for all women combined. Estrone, estrone sulfate, estrone/estradiol ratio, free testosterone, and SHBG were significantly associated with 2-yr change in IAAT. Subgroup analysis indicating associations between baseline hormone concentrations and 2-yr change in IAAT are reported in Table 4. Estrone, estrone sulfate, and estrone/estradiol ratio were significantly associated with 2-yr change in IAAT among HRT users. Free testosterone and SHBG were significantly associated with 2-yr change in IAAT among HRT non-users. Independent associations of baseline hormone concentrations with 2-yr changes in IAAT among HRT users are shown in Tables 5. Multiple linear regression analysis in only the HRT users (Table 5) for dependent variable 2-yr IAAT indicated a significant positive association with estrone, and a significant inverse association with estradiol, after adjustment for covariates.

Discussion

The goal of this study was to identify associations of the endocrine environment with fat distribution in healthy postmenopausal women. We tested the specific hypotheses that circulating concentrations of androgens would be positively associated with IAAT, and that circulating concentrations of estrogens would be inversely associated with IAAT and positively associated with leg fat. We also examined other hormones (SHBG, cortisol) possibly involved in body fat distribution for their contribution to outcomes of interest. We conducted this study both in women who were using postmenopausal HRT and in women who were not using HRT in order to determine if HRT use per se affected the association of the endocrine environment with fat distribution. We examined longitudinal (2-yr) changes in fat distribution for potential associations with the endocrine environment.

We hypothesized an inverse association between estrogen concentrations and IAAT. Longitudinal data indicated a significant positive association between baseline estrone and 2-yr change in IAAT and a significant inverse association between baseline estradiol and 2-yr change in IAAT among the HRT users, independent of total fat mass. Thus, the longitudinal data support the hypothesis that estradiol limits IAAT accrual, but implicate the weaker estrogen estrone in promoting visceral adiposity among postmenopausal women using HRT. Although the mechanism for these contrasting effects is not clear, it is possible this phenomenon is the result of either the greater variability in estrone or the non-physiological concentrations of circulating estrone produced by HRT use. Binding of the estrogen receptor by this weaker estrogen may have limited or blocked the activity of estradiol. This is the first longitudinal study to identify this positive relationship of estrone with IAAT accrual and a contrasting inverse relationship with estradiol and IAAT accrual over 2 years among HRT users. Further research is needed to determine whether, in postmenopausal women using HRT, the nature of the estrogen profile plays a role in fat distribution.

Conflicting evidence exists as to the relationship between circulating testosterone and IAAT. In a cross-sectional study, Armellini et al observed total testosterone to be inversely associated with IAAT in obese premenopausal women[9]. Similarly in males, studies have demonstrated free and total testosterone to be inversely associated with IAAT [10, 11]. However, others have speculated that a relatively androgenic hormone profile is associated with greater visceral adiposity in women [8, 21]. Discrepancies among studies may be due to the cross-sectional study design and potential for confounding, or differences in subject population. Results may differ depending on whether men, or pre-, peri-, or postmenopausal women are examined. Our longitudinal data in HRT non-users indicated an independent, inverse, association between baseline free testosterone and 2-yr gain in IAAT, which supports the hypothesis that testosterone inhibits accumulation of IAAT. It has been suggested that exogenous testosterone plays a role in regulating IAAT accrual by inhibiting lipoprotein lipase activity to a greater degree in visceral adipose tissue than in femoral adipose tissue[22, 23]. These observations suggest that testosterone may act similarly in women and men to limit IAAT accrual.

Associations between testosterone and IAAT may be confounded by SHBG, which may be independently associated with IAAT [21, 24, 25]. While SHBG binds testosterone in the circulation limiting its bioavailability, synthesis of SHBG is also suppressed by testosterone. Thus, low concentrations of SHBG may reflect elevated testosterone, and would increase the concentration of bioavailable testosterone. Cross-sectional studies have shown an independent inverse relationship between SHBG and IAAT in women [26, 27]. Our longitudinal study is the first to examine the association of SHBG with change in IAAT over 2 years in postmenopausal women. Our data suggest that women not using HRT with higher

circulating SHBG at baseline gained more IAAT over the 2 year study period. While the mechanism for the independent effect of SHBG on IAAT is not clear, this positive relationship between SHBG and IAAT is compatible with the inverse association identified between free testosterone and IAAT in our HRT non-users. Further studies are needed to determine the precise relationships among testosterone, SHBG, and IAAT accrual in postmenopausal women.

We hypothesized that cortisol would be positively associated with IAAT. In our population, cortisol was higher among HRT users vs non-users, and increased significantly from baseline to follow up in all women combined. Higher total cortisol among users of oral estrogen has been attributed to the stimulation of hepatic production of CBG[15] and the resultant reduction in free cortisol, which engages feedback processes that promote cortisol synthesis. We did not observe an association between cortisol concentration and 2-yr gain in IAAT in either group or all women combined. It is possible that bioavailable cortisol concentrations were below that required for an effect on IAAT, and that in this population of postmenopausal women, estrogen status, free testosterone, and SHBG played the predominant role in regulating fat distribution.

This study has several strengths. Measures of fat distribution were obtained using DXA and computed tomography scanning. To our knowledge, this is the only study comparing relationships of hormone concentrations with fat distribution longitudinally in postmenopausal women. Limitations to the study include the observational study design, relatively small number of subjects especially in the non-HRT group, not accounting for history of hyperandrogenicity, and the change in hormone status of several participants over the course of the study. This study may not have had sufficient power to detect significant interaction effects in longitudinal changes over time, or determine if ethnicity affected the nature of the relationships between hormones concentrations and body fat distribution outcomes.

In conclusion, results suggested that in postmenopausal women using HRT, greater circulating estradiol may play an integral role in limiting lipid deposition to the intra-abdominal cavity, a depot associated with metabolically detrimental attributes. However, a high proportion of weak estrogens may promote fat partitioning to the intra-abdominal cavity over time. In addition, among postmenopausal women not using HRT, greater circulating free testosterone may limit accrual of IAAT. Further studies are needed to elucidate the precise mechanisms by which the estrogen/androgen profile regulates IAAT accrual in postmenopausal women, and the extent to which use of exogenous hormones affects these relationships.

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Reference List

1. Despres JP, Moorjani S, Lupien PJ, Tremblay A, Nadeau A, Bouchard C. Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. Arteriosclerosis. 1990; 10(4):497–511. [PubMed: 2196040]
2. Despres JP. Health consequences of visceral obesity. Ann Med. 2001; 33(8):534–541. [PubMed: 11730160]

3. Gower BA, Munoz J, Desmond R, Hilario-Hailey T, Jiao X. Changes in intra-abdominal fat in early postmenopausal women: effects of hormone use. Obesity (Silver Spring). 2006; 14(6):1046–1055. [PubMed: 16861610]
4. Munoz J, Derstine A, Gower BA. Fat distribution and insulin sensitivity in postmenopausal women: influence of hormone replacement. Obes Res. 2002; 10(6):424–431. [PubMed: 12055317]
5. Sowers M, Zheng H, Tomey K, et al. Changes in body composition in women over six years at midlife: ovarian and chronological aging. J Clin Endocrinol Metab. 2007; 92(3):895–901. [PubMed: 17192296]
6. Elbers JM, Asscheman H, Seidell JC, Gooren LJ. Effects of sex steroid hormones on regional fat depots as assessed by magnetic resonance imaging in transsexuals. Am J Physiol. 1999; 276(2 Pt 1):E317–E325. [PubMed: 9950792]
7. Gambacciani M, Ciaponi M, Cappagli B, De SL, Orlandi R, Genazzani AR. Prospective evaluation of body weight and body fat distribution in early postmenopausal women with and without hormonal replacement therapy. Maturitas. 2001; 39(2):125–132. [PubMed: 11514111]
8. Pasquali R, Casimirri F, Cantobelli S, et al. Insulin and androgen relationships with abdominal body fat distribution in women with and without hyperandrogenism. Horm Res. 1993; 39(5–6):179–187. [PubMed: 8314200]
9. Armellini F, Zamboni M, Castelli S, et al. Interrelationships between intraabdominal fat and total serum testosterone levels in obese women. Metabolism. 1994; 43(3):390–395. [PubMed: 8139490]
10. Marin P, Holmang S, Jonsson L, et al. The effects of testosterone treatment on body composition and metabolism in middle-aged obese men. Int J Obes Relat Metab Disord. 1992; 16(12):991–997. [PubMed: 1335979]
11. Seidell JC, Bjorntorp P, Sjostrom L, Kvist H, Sannerstedt R. Visceral fat accumulation in men is positively associated with insulin, glucose, and C-peptide levels, but negatively with testosterone levels. Metabolism. 1990; 39(9):897–901. [PubMed: 2202881]
12. Rothman MS, Carlson NE, Xu M, et al. Reexamination of testosterone, dihydrotestosterone, estradiol and estrone levels across the menstrual cycle and in postmenopausal women measured by liquid chromatography-tandem mass spectrometry. Steroids. 2011; 76(1–2):177–182. [PubMed: 21070796]
13. Dorr MB, Nelson AL, Mayer PR, et al. Plasma estrogen concentrations after oral and vaginal estrogen administration in women with atrophic vaginitis. Fertil Steril. 2010; 94(6):2365–2368. [PubMed: 20466363]
14. Stricker R, Eberhart R, Chevailler MC, Quinn FA, Bischof P, Stricker R. Establishment of detailed reference values for luteinizing hormone, follicle stimulating hormone, estradiol, and progesterone during different phases of the menstrual cycle on the Abbott ARCHITECT analyzer. Clin Chem Lab Med. 2006; 44(7):883–887. [PubMed: 16776638]
15. Shifren JL, Desindes S, McIlwain M, Doros G, Mazer NA. A randomized, open-label, crossover study comparing the effects of oral versus transdermal estrogen therapy on serum androgens, thyroid hormones, and adrenal hormones in naturally menopausal women. Menopause. 2007; 14(6):985–994. [PubMed: 17507833]
16. Rockall AG, Sohaib SA, Evans D, et al. Computed tomography assessment of fat distribution in male and female patients with Cushing's syndrome. European Journal of Endocrinology. 2003; 149:561–567. [PubMed: 14640998]
17. Kekes-Szabo T, Hunter GR, Nyikos I, Nicholson C, Snyder S, Berland L. Development and validation of computed tomography derived anthropometric regression equations for estimating abdominal adipose tissue distribution. Obesity Res. 1994; 2:450–457.
18. Smith SR, Lovejoy JC, Greenway F, et al. Contributions of total body fat, abdominal subcutaneous adipose tissue compartments, and visceral adipose tissue to the metabolic complications of obesity. Metabolism. 2001; 50:425–435. [PubMed: 11288037]
19. Goran M, Kaskoun MC, Shuman WP. Intra-abdominal adipose tissue in young children. Int J Obesity. 1995; 19:279–283.
20. Sodergard R, Backstrom T, Shanbhag V, Carstensen H. Calculation of free and bound fractions of testosterone and estradiol-17 beta to human plasma proteins at body temperature. J Steroid Biochem. 1982; 16(6):801–810. [PubMed: 7202083]

21. Evans DJ, Hoffmann RG, Kalkhoff RK, Kissebah AH. Relationship of androgenic activity to body fat topography, fat cell morphology, and metabolic aberrations in premenopausal women. J Clin Endocrinol Metab. 1983; 57(2):304–310. [PubMed: 6345569]

22. Marin P, Oden B, Bjorntorp P. Assimilation and mobilization of triglycerides in subcutaneous abdominal and femoral adipose tissue in vivo in men: effects of androgens. J Clin Endocrinol Metab. 1995; 80(1):239–243. [PubMed: 7829619]

23. Rebuffe-Scrive M, Marin P, Bjorntorp P. Effect of testosterone on abdominal adipose tissue in men. Int J Obes. 1991; 15(11):791–795. [PubMed: 1778664]

24. Haffner SM, Katz MS, Stern MP, Dunn JF. Relationship of sex hormone binding globulin to overall adiposity and body fat distribution in a biethnic population. Int J Obes. 1989; 13(1):1–9. [PubMed: 2703288]

25. Raison J, Bonithon-Kopp C, Egloff M, Ducimetiere P, Guy-Grand B. Hormonal influences on the relationships between body fatness, body fat distribution, lipids, lipoproteins, glucose and blood pressure in French working women. Atherosclerosis. 1990; 85(2–3):185–192. [PubMed: 2102082]

26. Haffner SM, Katz MS, Dunn JF. Increased upper body and overall adiposity is associated with decreased sex hormone binding globulin in postmenopausal women. Int J Obes. 1991; 15(7):471–478. [PubMed: 1894424]

27. Tchernof A, Toth MJ, Poehlman ET. Sex hormone-binding globulin levels in middle-aged premenopausal women. Associations with visceral obesity and metabolic profile. Diabetes Care. 1999; 22(11):1875–1881. [PubMed: 10546023]

Table 1

Baseline participant characteristics by HRT use status.

Variable	HRT users (n=35)	HRT non-users (n=18)
Age (yr)	50.3± 2.4	51.2± 2.8
BMI (kg/m^2)	24.9± 3.5	25.6± 3.9
Time since menopause (yr)	2.8± 1.5	2.8± 1.6
HRT use (yr)	3.0 ± 2.6	0

Mean ± standard deviation.

BMI, body mass index; HRT, hormone replacement therapy

Table 2

Body composition outcomes at baseline and 2-yr follow-up

Variable	HRT status	Baseline (mean ± SD)	2-yr follow-up (mean ± SD)	Time $P^{\dagger}$	Group $P^{\dagger}$	Group*time $P^{\dagger}$
Weight (kg)	User	67.5 ± 3.3	67.9 ± 9.9	0.07	0.82	0.22
	Non-user	67.7 ± 10.7	70.0 ± 10.6			
Total Fat (kg)	User	24.5 ± 8.0	24.9 ±8.3	0.40	0.04	0.91
	Non-user	27.3 ± 8.3	27.8 ± 7.8			
IAAT (cm^2)	User	88.2 ± 32.9	96.9 ± 36.2	0.02	<0.01	0.52
	Non-user	115.2 ± 41.9	127.4 ± 52.4			
SAAT (cm^2)	User	294.2 ± 119.2	286.43 ± 119.0	0.96	0.62	0.52
	Non-user	302.1 ± 110.8	313.0 ± 102.0			
Thigh Fat (cm^2)	User	284.4 ± 101.0	289.0 ± 99.0	0.55	0.58	0.82
	Non-user	257.1 ± 80.1	261.8 ± 85.5			
Leg fat (kg)	User	10.6 ± 3.4	11.0 ± 3.6	0.30	0.31	0.37
	Non-user	11.0 ± 3.5	11.1 ± 3.1			
Total Lean (kg)	User	39.4± 3.4	39.5± 3.4	0.06	0.77	0.13
	Non-user	38.1 ± 4.1	38.9 ± 3.4			

P, p-value; IAAT, intra-abdominal adipose tissue; SAAT, subcutaneous abdominal adipose tissue

$p^{\dagger}$, P-value for 2-way ANOVA

Table 3

Hormone outcomes at baseline and 2-yr follow-up

Variable	HRT status	Baseline (mean ± SD)	2-yr follow up (mean ± SD)	Time $P^{\dagger}$	Group $P^{\dagger}$	Group*Time $P^{\dagger}$
Estradiol (pg/ml)	User	36.1 ± 19.9	38.9 ± 25.3	0.42	<0.001	0.75
	Non-user	9.1 ± 6.3	13.6 ± 18.8			
Estrone (pg/ml)	User	176.8 ± 119.1	165.0 ± 116.2	0.84	<0.001	0.27
	Non-user	39.5 ± 35.8	48.1 ± 68.2			
Estrone Sulfate (ng/ml)	User	7.8 ± 5.0	10.6 ± 8.1	<.001	<0.01	0.82
	Non-user	1.8 ± 2.0	3.8 ± 5.6			
Free testosterone (pmol/L)	User	3.6 ± 1.7	4.1 ±2.7	0.88	<0.001	0.57
	Non-user	6.9 ± 3.4	7.3 ± 4.9			
Total testosterone (ng/dl)	User	17.5 ± 6.1	20.1 ± 6.9	0.44	0.59	0.34
	Non-user	21.1 ± 11.2	21.1 ± 6.8			
Androstenedione (ng/ml)	User	1.2 ± 0.6	0.7 ± 0.3	<0.001	0.66	0.43
	Non-user	1.2 ± 0.6	0.9 ± 0.4			
DHEA-S (μg/dl)	User	61.7 ± 34.9	64.1 ± 31.5	0.95	0.08	0.57
	Non-user	84.1 ± 47.1	82.3 ± 42.4			
SHBG (ng/ml)	User	174.3 ± 68.4	217.4 ± 113.2	0.02	<.001	0.09
	Non-user	89.8 ± 32.7	97.6 ± 58.8			
Cortisol (μg/dl)	User	15.1 ± 7.5	17.5 ± 5.6	0.02	0.03	0.22
	Non-user	11.7 ± 3.4	13.1 ± 4.0			
FSH (mIU/ml)	User	30.2 ± 15.7	34.9 ± 17.2	0.08	<0.001	0.93
	Non-user	62.5 ± 20.0	67.2 ± 21.0			

P, p-value; DHEA-S, dehydroepiandrosterone sulfate; FSH, follicle stimulating hormone; SHBG, sex hormone binding globulin.

$p^{\dagger}$, P-value for 2-way ANOVA

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Table 4

Prediction of 2-yr change in fat distribution outcomes by baseline hormone concentrations among all women combined

	IAAT	SAAT	Leg fat	Thigh fat
Estradiol	0.15	−0.07	0.05	−0.01
Estrone	**0.29** **	−0.03	0.04	0.02
Estrone/estradiol ratio	**0.19** *	0.03	0.00	0.08
Estrone sulfate	**0.25** *	−0.06	0.00	−0.04
Total testosterone	−0.07	−0.07	0.02	0.07
Free testosterone	**−0.20** *	−0.06	−0.02	0.02
Androstenedione	0.05	0.02	0.03	0.05
DHEAS	0.05	−0.03	0.03	0.02
SHBG	**0.22** *	0.00	0.06	0.07
Cortisol	0.04	0.03	−0.03	0.02

Standardized regression coefficients reported.

Multiple linear regression analysis of 2-yr IAAT, SAAT, leg fat, thigh fat, adjusted for dependent variable's baseline value, 2-yr total body fat, and HRT use.

* p-value <0.05

** p-value <0.01

Table 5

Prediction of 2-yrchange in IAAT by baseline hormone concentrations in HRT users and non-users

	HRT users	HRT non-users
Estradiol	0.14	0.29
Estrone	0.26**	0.14
Estrone sulfate	0.21*	0.02
Estrone/estradiol ratio	0.24**	−0.04
Total testosterone	0.01	−0.33
Free testosterone	−0.02	−0.50**
Androstenedione	0.08	0.10
DHEAS	0.09	−0.21
SHBG	0.02	0.55**
Cortisol	0.11	−0.04

Standardized regression coefficients reported.

Multiple linear regression analysis of 2-yr IAAT, adjusted for baseline IAAT and 2-yr total body fat.

* p-value <0.05

** p-value <0.01

Table 6

Prediction of 2-yr IAAT by baseline hormone concentrations in HRT users only

Independent variable	Variable estimate ± SEE	Standardized β	*P*
Estrone	0.52 ± 0.11	0.43	<.0001
Estradiol	−0.34 ± 0.15	−0.23	0.02

Linear regression model adjusted for baseline IAAT and 2-yr total body fat