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Age attenuated response to aerobic conditioning in postmenopausal women

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Abstract

The decline in aerobic capacity does not appear to be linear across age. To explore this relationship, we examined the maximal cardiorespiratory response of 251 postmenopausal women to 6 months of exercise training: control (no exercise), or exercise at 4, 8, or 12 kcal/kg/week (KKW). Exercise intensity was set at a heart rate associated with 50% of peak $\text{VO}_{2\text{peak}}$ and women were stratified by age into three groups: <55 years, 55–59 years, >60 years. Differences in outcomes among groups were tested by ANOVA and the results were presented as adjusted least squares means with confidence intervals. At baseline participants who were >60 years had a lower $\text{VO}_{2\text{peak}}$ than those <55 years [mean (SD) 1.44 (0.24) vs. 1.20 (0.20) L/min, $P < 0.04$]. Following exercise training, we observed an attenuated training response due to age within the 8 and 12 KKW groups (both, P for trend 0.001). For the 8 KKW group, changes in $\text{VO}_{2\text{peak}}$ were [mean, (95% CI)]: <55 years [0.18 (0.12, 0.24) L/min], <55 years, 55–59 years [0.08 (0.02, 0.15) L/min], and >60 years [0.02 (–0.03, 0.08)]. For 12 KKW group, the changes were: <55 years [0.19 (0.15, 0.24) L/min], 55–59 years [0.13 (0.08, 0.18) L/min], and >60 years [0.05 (–0.01, 0.10)]. Our data show that despite similar exercise intensities, age plays a significant role in the maximal cardiorespiratory response to exercise training regardless of training volume in women who have completed menopause.

Keywords

Women; Fitness; Exercise; Individual response

Background

Menopause is marked by a number of changes that increase a woman's risk for cardiovascular disease (CVD), cancer, and other metabolic diseases (National Heart Lung and Blood Institute, National Institutes of Health (US) 2002). Cardiorespiratory exercise provides a critical means of reducing risk in women at all ages (Asikainen et al. 2004; Farrell et al. 2004; Sui et al. 2007b, c). However, the longitudinal rate of decline in peak oxygen consumption in healthy

adults is not constant across age and may therefore confound the applicability of exercise training as a prevention strategy (Fleg et al. 2005). Several studies have also shown little or no effect in response to exercise training in older participants. This lack of response may occur due to an insufficient training stimulus, gender related differences in the cardiorespiratory response to exercise, and the relative state of fitness at the start of an exercise training study, whereby those individuals with initially low fitness levels experience greater fitness gains than those with higher fitness levels (Hossack and Bruce 1982; Kohrt et al. 1991).

In the dose response to exercise in postmenopausal women (DREW) study, we reported that exercise training at 50, 100, and 150% of the National Institute of Health's (NIH) Consensus Development Panel recommendations for minimal physical activity improved the $\text{VO}_{2\text{peak}}$ of postmenopausal women in all treatment groups in a dose-dependent manner (Church et al. 2007). Like ours, studies of similar nature have reported a high degree of variability in the maximal cardiorespiratory response to exercise training (Church et al. 2007; Kohrt et al. 1991; Sisson et al. 2009; Wilmore et al. 2001). In an ancillary report from DREW examining the factors related to "non-response", we observed a 44.9, 23.8, and 19.3% non-response rate for the 4-, 8-, and 12-kcal/kg/week (KKW) treatment groups (Sisson et al. 2009), where 8 KKW represents the minimal dose of exercise associated with the Consensus Development Panel recommendation. Further, the lack of response was associated with the exercise treatment group (i.e., training volume), baseline $\text{VO}_{2\text{peak}}$, and ethnicity (i.e., Caucasian vs. African American). In essence, those who were younger, Caucasian, less fit, or exercised more during the DREW trial had greater odds of improving their fitness with training (Sisson et al. 2009).

Given the relationship between age, the accelerated decline in aerobic fitness beginning after the age of fourth decade of life (Fleg et al. 2005) and postmenopausal status, we herein further examine the effect of age on $\text{VO}_{2\text{peak}}$ responsiveness in the DREW cohort. An important contribution of the DREW study is that it directly examines the volume of exercise training surrounding the NIH guidelines in a homogenous sample of women and is important to future public health policy development (Haskell et al. 2007; Nelson et al. 2007).

Methods

Study design and participants

The primary outcomes from the DREW trial and a complete and detailed description of the design and rationale of the DREW study has been previously published (Church et al. 2007; Morss et al. 2004). In brief, DREW was a randomized, controlled trial examining the effects of incremental doses of cardiorespiratory endurance training of 464 sedentary postmenopausal women aged 45–75 years on aerobic fitness and blood pressure. Women recruited for participation were overweight or obese [body mass index (BMI) 25.0–43.0 kg/m²], postmenopausal, healthy and capable of engaging in the prescribed exercise training. All volunteers were sedentary (<35 kcal/kg/day in energy expenditure) and had elevated blood pressure (SBP 125.0–159.0 mmHg). Women were excluded if they had significant cardiovascular disease or other significant medical disorders, elevated low-density lipoproteins (≥ 3.36 mmol/L), or had lost 9.1 kg or more in the previous year (Morss et al. 2004).

The study was originally reviewed annually by The Cooper Institute and subsequently approved by the Pennington Biomedical Research Center IRB for continued analysis. Prior to participation, all volunteers signed a written informed consent document outlining the procedures involved in the DREW study. The current report is an ancillary analysis of the parent trial. For this report, we have excluded non-Caucasian participants for two compounding reasons: (1) in our previous work we show that African Americans have a greater prevalence of non-response than Caucasians and (2) there are not enough African American women within

our cohort to further stratify by ethnicity (Sisson et al. 2009). Thus, a high degree of statistical error would be introduced into our analysis that cannot be controlled.

Exercise testing

Exercise testing was conducted on a Lode Excalibur Sport cycle ergometer (Groningen, Netherlands), an electronic, rate-independent ergometer. Participants cycled at 30 W for 2 min, 50 W for 4 min, followed an increase of 20 W every 2 min until they could no longer maintain a pedal cadence of 50 rpm. Respiratory gases were measured using a Parvomedics True Max 2400 Metabolic Measurement Cart. Volume and gas calibrations were conducted before each test. Gas-exchange variables [VO_2 , CO_2 production, ventilation, and respiratory exchange ratio (RER)] were recorded every 15 s. Heart rate was measured directly from the ECG monitoring system. Ratings of perceived exertion (RPE) were obtained using the 20-point Borg scale. Two fitness tests were performed on separate days at baseline and follow-up. To determine $\text{VO}_{2\text{max}}$ had required to achieve two of the three following conditions: (1) a plateau or rise in VO_2 (L/min) < 100 mL, (2) RER > 1.1, and (3) a maximal heart rate within 10 beats/min of the participants age predicted maximum. If these criteria were not met, maximal aerobic capacity was described as $\text{VO}_{2\text{peak}}$. For consistency within our report we will use $\text{VO}_{2\text{peak}}$ to describe our data.

Exercise training

Following a pre-randomization run-in period, participants were randomized into one of the three exercise treatments or a non-exercise control group. Women in the control group were asked to maintain the regular habits of daily physical activity. We monitored the daily physical activity behavior of all women in the treatment and control groups using a pedometer (Accusplit Eagle, Japan) and the recording of daily steps. At the end of each month, the activity calendar with daily steps was returned to the study center. Women in the treatment groups removed the pedometer during their scheduled training so that only extracurricular physical activity was assessed.

The three exercise treatment groups were based on the NIH Consensus Development Panel Recommendation that adults should accumulate a minimum of 30 min of moderate-to-vigorous intensity physical activity most days of the week (NIH 1996). We calculated that 8 KKW is what a typical, overweight, sedentary, postmenopausal woman would expend when starting an exercise program based on the NIH recommendation and randomized women to this group (Morss et al. 2004). The remaining two exercise treatment groups were scaled to 50% above and 50% below the 8 KKW group (i.e., 12 and 4 KKW, respectively). The 4 KKW was utilized to examine if exercise in an amount less than the NIH Consensus Development Panel would still provide health and fitness benefits to this sedentary, overweight female population. The 12 KKW group was designed to examine if more exercise would translate into a proportionally greater increase in the health benefits of the population of interest. The primary outcome findings of this study have been published elsewhere (Church et al. 2007).

All treatment participants exercised for 6 months, 3–4 days/week at a heart rate associated with 50% baseline $\text{VO}_{2\text{peak}}$ under the supervision of trained technicians in an exercise laboratory. Participants exercised alternatively on a recumbent cycle ergometer and treadmill for a period long enough to reach their energy expenditure goal based on the treatment group (4, 8, or 12 KKW). After each session, the energy expended was recorded in a log and summed over the course of the training. A ramping protocol was used to get participants to their recommended exercise level. During the first week, each group expended 4 KKW. Those assigned to the 4 KKW group remained at this dose during the study while those assigned to the 8 and 12 KKW groups increased their energy expenditure by 1 KKW until their assigned exercise level was reached. In a previous report, we examined whether the potential for heart rate (HR) drift

influenced participant workloads during their exercise sessions and found this to be uninfluential (Mikus et al. 2008).

Clinical measures

Ethnicity, age, physical activity history, smoking, alcohol use, and dietary habits were self-reported by participants at baseline and post-training (Morss et al. 2004). Height was measured using a standard wall stadiometer and weight on an electronic scale (Siemens Medical Solutions, Malvern, PA). Body fat percent was estimated from skinfolds (bicep, triceps, mid-axillary, subscapular, abdominal, suprailiac, thigh, and calf) (Morss et al. 2004). The baseline and post-training $\text{VO}_{2\text{peak}}$ values were an average of two maximal exercise tests completed on separate days (Morss et al. 2004). The intraclass correlation for both baseline and follow-up of the two tests was 0.88 (Church et al. 2007). $\text{VO}_{2\text{peak}}$ testing was conducted on a Lode Excalibur Sport cycle ergometer (Groningen, The Netherlands), an electronic, rate-independent ergometer. Participants exercised at 30 W for 2 min, 50 W for 4 min, followed by 20 W increase every 2 min until volitional fatigue (Morss et al. 2004). Gas exchange variables (VO_2 , CO_2 production, ventilation, and RER) were measured using a pre-calibrated Parvomedics True Max 2400 Metabolic Measurement Cart.

Statistical analysis

Participants were categorized into one of the three age groups: <55 years, 55–59 years and ≥ 60 years. Descriptive statistics presented for the entire study population, across intervention and age groups are presented in Tables 1 and 2, respectively. Differences in outcomes among the groups were tested by ANOVA and the results are presented as adjusted least-squares means with confidence intervals. Age-group $\times$ randomization group interaction was assessed. As caloric expenditure during the exercise intervention was closely monitored for each participant, we regressed the change in fitness against total training caloric expenditure during the intervention and baseline fitness for each of the age groups. The regression coefficient for caloric expenditure during the intervention for each of the age groups was compared with one another. Based on the regression coefficients generated from the regression analysis and using the mean baseline fitness value for each age group, we graphed change in fitness against calories expended during the exercise intervention for the caloric range of 6,000–30,000. All reported P values are two-sided. All analyses were performed using SAS version 9.0 (Cary, NC).

Results

We have summarized the demographics and general health characteristics in Table 1. Overall, we started our analysis with 464 participants from our parent study and removed 165 individuals based on race. From the remaining 299 participants, 6 were lost to incomplete data on body mass, 30 were eliminated due to compliance issues (e.g., attended <85% of scheduled exercise sessions), and 12 were eliminated due to missing baseline and/or follow-up data. Our remaining cohort ($n = 251$) had a mean (SD) age of 58.3 (6.3) years and a mean BMI of 31.4 (3.9) kg/m^2 . Baseline systolic blood pressure showed that our participants had prehypertension or stage one hypertension [139.9 (13.1) mmHg] yet, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and glucose were within normal range. The same findings were also noted after stratifying our study participants by age (Table 2).

Exercise group $\text{VO}_{2\text{peak}}$ characteristics

We have presented the mean change data for $\text{VO}_{2\text{peak}}$ characteristics in Fig. 1a. The analysis of our maximal cardiorespiratory testing data demonstrates that our group achieved a mean (SD) respiratory exchange ratio of 1.15 (0.10) and a mean peak fitness level of 1.31 (0.20) L/

min and 15.9 (2.7) mL/kg/min for absolute and relative $\text{VO}_{2\text{peak}}$, respectively. Furthermore, no differences were noted between groups for baseline $\text{VO}_{2\text{peak}}$, maximal heart rate, or RER achieved during exercise testing. Overall, we observed a significant improvement in aerobic capacity for the 4, 8, and 12 KKW exercise groups (Fig. 1a). The control group decreased in maximal aerobic capacity by 1.6% (95% CI, -4.8, 1.0). We also observed that peak testing maximal heart rate was ~10% lower in women >60 years versus those who were younger than 55 years ($P < 0.0001$) and within the middle age group (55–59 years, $P < 0.005$).

Age stratified change in $\text{VO}_{2\text{peak}}$ data

We have presented the mean change data for our age-related sub-group stratification in Fig. 1b. At baseline, we observed that those in the >60-year-old age group exhibited at lower $\text{VO}_{2\text{peak}}$ than those participants in the <55-year-old age group ($P < 0.04$). In response to treatment, we observed a significant interaction for age group $\times$ intervention ($P < 0.0002$). The percent improvement in absolute $\text{VO}_{2\text{peak}}$ (L/min) for the <55-year-old groups were: control [-1.7% (95% CI -6.0, 2.7)], 4 KKW [1.9% (95% CI -2.2, 6.0)], 8 KKW [10.7% (95% CI 6.0, 15.4)], and 12 KKW [12.3% (95% CI 8.2, 16.3)]. For the 55–59-year-old age group, percent changes were: control [-0.3% (95% CI -5.0, 4.4)], 4 KKW [2.7% (95% CI -1.1, 6.6)], 8 KKW [9.6% (95% CI 4.3, 15.0)], and 12 KKW [9.5% (95% CI 5.2, 13.7)]. Finally, percent changes for >60-year-old age group were: control [-2.6% (95% CI -6.9, 1.8)], 4 KKW [5.6% (95% CI 2.2, 8.9)], 8 KKW [3.7% (95% CI -0.9, 8.2)] and 12 KKW [7.9% (95% CI 3.8, 12.0)].

Figure 2 depicts the change in $\text{VO}_{2\text{peak}}$ across total caloric expenditure during the exercise intervention within each age group for the caloric range of 6,000–30,000 kcal. The slope of the line of <55-year-old age group showing improvement was significantly steeper than the slope of >60 years group ($P < 0.05$); but, not different from the 55–59 years age group.

Discussion

The primary finding of our current analysis is that age plays a significant role in the responsiveness of maximal cardiorespiratory capacity to low-to-moderate levels of exercise intensity at fixed caloric energy expenditures (i.e., training volume). Our most notable finding is the observations that despite a significant improvement in peak VO_2 for the 4-, 8-, and 12-KKW groups as a whole, only those women under the age of 59 years showed significant improvements within the 8 and 12-KKW groups, while those above 60 years did not. These are important findings pertaining to the current and future NIH Consensus Panel Recommendations for exercise in women. Specifically, is low-moderate intensity sufficient to enhance maximal cardiorespiratory fitness in aging women? Moreover, recent findings from Fleg et al. (2005) examining the influence of age, gender, and physical activity on changes in peak VO_2 in a large cohort of women ($n = 375$) and men ($n = 435$) between the ages of 21–87 years show a longitudinal decline in peak VO_2 from 3–6% per 10 years in the 20s and 30s yet, >20% per 10 years after 70 years of age (Fleg et al. 2005). Recent data from our group support these findings (Jackson et al. 2009). In essence, the decline in maximal aerobic capacity with age is not linear, but curvilinear, whereby the rate of decline becomes more pronounced with age (Fleg et al. 2005; Jackson et al. 2009). Thus, the cardioresponsiveness to exercise training is an important issue for women as they age and must be accounted for accordingly when advising women to exercise.

Previous research examining the age-associated $\text{VO}_{2\text{max}}$ changes specifically in women is limited. Those studies addressing the topic typically involve mixed cohorts (i.e., men and women) using relatively small sample sizes. In addition, despite the recent findings of Fleg et al. and Jackson et al., there is still a gap in literature regarding the effectiveness of manipulating exercise training prescription parameters in an aging cohort; specifically, the frequency, time and intensity of exercise training regimens. In the DREW study, we addressed one aspect of

the training paradigm by holding the intensity of exercise constant while manipulating the time and ultimately the volume of training, in a dose-dependent manner. In our primary outcomes paper we demonstrated a clear dose response to exercise training when all age groups are combined (Church et al. 2007). In our current report we show a distinct attenuation in training response in Caucasian participants over the age of 60 years.

The mechanisms of action surrounding improvements in maximal cardiorespiratory exercise capacity following training are many and have been thoroughly reviewed elsewhere (Spina 1999). However, maximal oxygen consumption is a function of cardiac output (e.g., heart rate $\times$ stroke volume) $\times$ the arteriovenous oxygen difference. In accordance with this relationship, one major difference we observed in our current analysis was a lower maximum heart rate in women over 60 years compared to the younger groups. Though a lower baseline maximal heart rate does not dictate the responsiveness of women to exercise training, per se, an aging heart is hyporesponsive to sympathetic stimuli; hence, the exercise-induced increases in heart rate and myocardial contractility in older hearts is blunted (Ferrari et al. 2003). A blunted responsiveness of maximal heart rate may partially explain one aspect of the attenuated training response to exercise training we observed in older DREW participants. In addition, several gender differences detailed elsewhere are also worth noting as they pertain to cardiac output, stroke volume and arterial-venous oxygen differences (Spina 1999).

A classic example of cardioadaptive gender differences was demonstrated by Spina et al. (1993), who showed that though improvements during exercise training are similar between aging men and women (19% vs. 22%), the improvement in men is due to significant improvements in cardiac output, specifically, stroke volume, while the improvements in women were due to improvements in arterial-venous oxygen differences. However, stroke volume still influences maximal cardiorespiratory capacity in women as Wiebe et al. (1999) have shown a reduction in stroke volume with age in women. In their study, control women (20–29 years) were compared to three groups of aging women: 40–45, 49–54, and 58–63 years, showing corresponding reductions in stroke volumes of 12.8, 14.4, and 16.8%, respectively. Therefore, some of the cardiorespiratory response differences of the DREW cohort relative to training are the natural aging effects, heart rate, and stroke volume. Another candidate explanation for the lack of fitness response observed in our current study is the role of exercise intensity.

In a series of mixed gender studies, Hagberg et al. (1989a,b) examined the role of exercise intensity in older populations. In one study, 60–69-year-old participants with hypertension were examined after 9 months of low (53% $\text{VO}_{2\text{max}}$) or moderate-intensity (73% $\text{VO}_{2\text{max}}$) exercise training showing improvement only in the higher intensity group (Hagberg et al. 1989b). The low intensity group in DREW exercised at a similar intensity and similar length of time as those of Hagberg et al. In a similar study, Hagberg et al. (1989a) also showed a 22% improvement in $\text{VO}_{2\text{max}}$ in 70–79-year-old male and female participants following training at 75–85% $\text{VO}_{2\text{max}}$. Kohrt et al. (1991) have also demonstrated approximately 19% mean improvement in $\text{VO}_{2\text{max}}$ for 60–70-year-olds exercising at ~80% of maximal heart rate (~67% $\text{VO}_{2\text{max}}$) in 60–70 year olds (Londeree and Ames 1976). In one of the largest training studies to date, the HERITAGE Family Study showed 17.7 and 15.5% change in $\text{VO}_{2\text{max}}$ for women of 30–49 years ($n = 69$) and 50–65 years ($n = 44$), respectively, exercising at 55–75% of maximal cardiorespiratory capacity (Skinner et al. 2001). Despite the overall size of the HERITAGE trial, the age range reported in this trial was very broad and the sample size was much smaller than what we used in DREW.

Kraus et al. (2002) have examined the effects of moderate intensity and two doses of higher intensity exercise in a mixed gender cohort, showing significantly greater improvement in cardiorespiratory capacity in the two higher intensity training groups (16.7–17.8%). In contrast,

DiPietro et al. (2006) reported no response to 9 months of exercise training in women >60 years exercising at 50 ($n = 7$), 65 ($n = 9$) or 80% ($n = 9$) of their VO_{2peak} . It should also be noted that participants in the Kohrt study ranged in improvement from 0–58% (Kohrt et al. 1991). Thus, higher intensities (e.g., up to 80% VO_{2max}) are not a panacea for ensuring a training response; merely that intensity plays a vital role in improving aerobic capacity in an older population.

A major strength of the DREW study is that it is a well-controlled, dose response study performed in a laboratory setting. Accordingly, the primary aim of the study was to examine different doses of exercise relative to the minimal NIH Consensus Panel Recommendations. We have previously reported that participants in the DREW study were adherent to our exercise intervention (Church et al. 2007). Our current analysis is limited to the interpretation of sedentary, overweight, or obese, white postmenopausal women. Thus, we are not able to comment on men, younger women prior to menopause or black women following menopause. The second limitation is that because our study was a free-living population, we made no attempt to match or control for hormone replacement (HRT) usage during the course of the study. Given the size of our current sample, there is high likelihood that the distribution of HRT was evenly distributed across treatment groups. Unfortunately, we cannot adequately account for changes in HRT usage that may have occurred throughout the study and under the guidance of each participant's primary care physician.

The homogenous nature of the DREW study does allow us to provide notable insights into an aging female population who represent a significant proportion of the US population. For example, in our original report including all participants, we observed significant overall improvements in VO_{2peak} of 4.2, 6.0, and 8.2% for the 4-, 8-, and 12-KKW groups, respectively. In a follow-up report, we further observed that age, ethnicity, and baseline fitness were significant predictors of non-response (Sisson et al. 2009). In our current report, we only examined white women and the overall group VO_{2peak} response was higher for the 4 KKW (3.7%), 8 KKW (7.8%), and 12 KKW (9.9%) and much closer to our original projections of 7, 12 and 15%, respectively, used to statistically power the DREW study (Morss et al. 2004).

Conclusions

Overall, the current report is the largest exercise intervention to date specifically examining the fitness response of women past the age of menopause. Given our findings, strong consideration should be given to the relationship between menopause and CVD risk versus the normal decline in physiologic function associated with aging. Specifically, is the decline of cardiorespiratory fitness a function of menopause or merely a result of the aging process? As it pertains to other risk factors, Matthews et al. (2009) have recently shown that only total cholesterol, LDL-C, and apolipoprotein B demonstrated substantial increase within the 1-year interval following menopause, whereas other CVD risk factors such as glucose, insulin, blood pressure, fibrinogen, and C-reactive protein do not (Matthews et al. 2009). Regardless of the CVD risk associated with menopause and/or aging, cardiorespiratory fitness is positively associated with health at any age and should be continually recommended as a lifestyle intervention to affect better health (Sui et al. 2007a, d).

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Fig. 1.

a The change in peak VO_2 (L/min) for all 251 women in each exercise group. **b** The change in peak VO_2 (L/min) adjusted for baseline peak VO_2 in all 251 women stratified by age group. The data are mean values accompanied by 95% confidence interval error bars. *a* Significantly different versus the control group ($P < 0.05$). *b* Significantly different versus the < 55 years within the corresponding exercise group ($P < 0.001$). *c* Significantly different versus the < 55 –59 years within the corresponding exercise group ($P < 0.03$)

Fig. 2.

Data represent the slope of the change relationship for all 251 participants versus energy expenditure during the DREW study. ^a Significantly different versus the <55 years age group ($P < 0.05$)

Table 1

Baseline participant characteristics

	Exercise groups				
	All (n = 251)	Control (n = 57)	4 KKW (n = 80)	8 KKW (n = 48)	12 KKW (n = 66)
Age, mean (SD)	58.3 (6.3)	57.8 (6.0)	59.6 (6.4)	58.1 (6.1)	57.4 (6.5)
Anthropometry, mean (SD)					
Weight (kg)	83.4 (11.6)	85.7 (12.9)	82.7 (10.4)	84.7 (13.0)	81.2 (10.5)
Body mass index (kg/m ²)	31.4 (3.9)	32.2 (14.3)	31.1 (3.4)	32.0 (4.2)	30.7 (3.7)
Waist circumference (cm)	101.7 (11.7)	104.5 (12.5)	99.9 (10.2)	103.4 (10.5)	100.2 (13.1)
Clinical blood markers (mg/dL), mean (SD)					
Glucose	95.4 (8.1)	95.9 (9.0)	95.1 (8.0)	94.9 (7.3)	95.6 (8.3)
Triglycerides	143.8 (66.4)	144.4 (73.3)	141.1 (57.6)	140.4 (62.8)	149.0 (73.4)
LDL cholesterol	119.1 (27.0)	117.4 (27.4)	118.9 (26.7)	119.0 (27.7)	121.0 (27.0)
HDL cholesterol	57.4 (14.1)	57.6 (13.9)	58.3 (13.2)	58.1 (17.2)	55.8 (13.2)
Blood pressure (mmHg), mean (SD)					
Systolic	140.0 (13.1)	141.8 (12.1)	139.6 (12.0)	140.5 (15.2)	138.5 (13.6)
Diastolic	79.8 (8.7)	79.8 (8.1)	79.4 (9.8)	80.2 (8.3)	80.1 (8.2)
Exercise capacity, mean (SD)					
VO _{2peak} (absolute, L/min)	1.31 (0.2)	1.35 (0.3)	1.29 (0.2)	1.31 (0.2)	1.32 (0.2)
VO _{2peak} (relative, mL/kg/min)	15.9 (2.7)	15.9 (3.0)	15.7 (2.6)	15.5 (2.2)	16.3 (2.7)
Max HR (beats/min)	152 (16)	152 (15)	151 (17)	153 (15)	153 (16)
RER	1.15 (0.1)	1.14 (0.1)	1.15 (0.1)	1.13 (0.1)	1.16 (0.1)
Daily activity					
Steps per day	4,912 (1,752)	5,110 (1,721)	4,749 (1,873)	4,783 (1,624)	5,030 (1,731)
Medication use n (%)					
Hormone replacement	117 (47)	26 (46)	37 (46)	23 (48)	31 (47)
Blood pressure	193 (77)	48 (84)	63 (79)	35 (75)	47 (71)
Thyroid	201 (80)	45 (79)	68 (85)	37 (79)	51 (77)
Antidepressant	190 (76)	46 (80)	61 (76)	35 (75)	48 (73)
Cholesterol	208 (83)	48 (84)	63 (79)	40 (85)	57 (86)

SI conversions: to convert to SIU multiply LDL and HDL cholesterol by 0.0259; triglycerides by 0.0113, and fasting glucose by 0.0555

Table 2

Baseline participant characteristics by age

	<55 years (n = 82)	55-59 years (n = 76)	>60 years (n = 93)
Age, mean (SD)	51.7 (2.6)	57.5 (1.5)	64.9 (4.2)
Menopause age (SD)	45.6 (4.5)	47.9 (5.6)	48.7 (5.0)
Years since menopause at study entry (SD)	6.0 (3.8)	9.6 (5.8)	15.9 (7.7)
Anthropometry, mean (SD)			
Weight (kg)	85.6 (10.7)	83.0 (11.8)	81.8 (12)
Body mass index (kg/m ²)	31.8 (3.7)	31.4 (3.9)	31.1 (4.1)
Waist Circumference (cm)	101.2 (10.9)	101.0 (10.5)	102.8 (13.3)
Clinical blood markers (mg/dL), mean (SD)			
Glucose	95.3 (8.4)	95.1 (8.2)	95.7 (17.9)
Triglycerides	54.7 (13.6)	58.1 (15.5)	59.3 (13.2)
LDL cholesterol	117.5 (27.1)	119.3 (25.8)	120.5 (28)
HDL cholesterol	150.4 (66.6)	146.9 (68.8)	135.4 (64)
Blood pressure (mmHg), mean (SD)			
Systolic	138.9 (12.2)	138.7 (14.4)	141.9 (12.6)
Diastolic	82.8 (7.7)	80.0 (8.7)	77.0 (18.7)
Exercise capacity, mean (SD)			
VO _{2peak} (absolute, L/min)	1.44 (0.24)	1.32 (0.23)	1.20* (0.2)
VO _{2peak} (relative, mL/kg/min)	16.9 (2.5)	16.0 (2.6)	14.8* (2.4)
Max HR (beats/min)	158 (15)	154 (14)	146* (17)
RER	1.16 (0.06)	1.14 (0.07)	1.14 (0.07)
Daily activity			
Steps per day	5,450 (1,710)	4,972 (1,790)	4,390 (1,617)

SI Conversions: to convert to SIU multiply LDL and HDL cholesterol by 0.0259; triglycerides by 0.0113, and fasting glucose by 0.0555

* Significantly different than <55 ($P < 0.05$)