Arterial Stiffness and Hormone Replacement Use in Healthy Postmenopausal Women

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Background. Arterial stiffness has been shown to be positively related to cardiovascular disease risk. Little, however, is known about the influence of hormone replacement use on arterial stiffness in females.

Methods. Arterial pulse wave velocity (PWV) and carotid augmentation index (AI, applanation tonometry) were measured in 34 healthy postmenopausal women, including users (n = 18) and nonusers (n = 16) of hormone replacement.

Results. There were no significant group differences in any of the physical characteristics including resting blood pressure. None of the measures of arterial stiffness differed between users and nonusers of hormone replacement.

Conclusions. The present cross-sectional study indicates that reduced arterial stiffness does not appear to be a likely mechanism contributing to the lower incidence of cardiovascular disease in postmenopausal women taking hormone replacement.

Hormone (estrogen) replacement therapy (HRT) is associated with reduced cardiovascular disease (CVD) risk in postmenopausal women (1). Although mechanisms including a favorable plasma lipid and lipoprotein profile have been suggested (1), as much as 50% of this beneficial effect remains unexplained. Arterial stiffness recently has been shown to be positively related to CVD risk (2). Females appear to have lower central arterial stiffness than males until menopause (3), an effect thought to be related to the presence of ovarian hormones. Therefore, it is possible that HRT is associated with lower arterial stiffness. However, little data are available on arterial stiffness in postmenopausal women chronically receiving HRT as compared with nonusers. Accordingly, the aim of the present investigation was to determine if central and peripheral arterial stiffness is lower in postmenopausal women on HRT compared with those who are not.

METHODS

Subjects
A total of 34 healthy postmenopausal women were studied. All subjects were free of overt cardiovascular disease as assessed by medical history questionnaire, physical examination, and maximal exercise electrocardiograms. None of the subjects smoked or took medications (other than hormone replacement). All women were at least 2 years postmenopausal. The majority (13 of 18) of the HRT users were taking combined conjugated estrogen (Premarin, 0.4-1.0 mg/d) and medroxyprogesterone acetate (Provera, 1-5 mg/d), and the remaining users were taking either Premarin (n = 3) or Provera (n = 2) only. All subjects gave their written informed consent to participate. This study was reviewed and approved by the Human Research Committee at the University of Colorado at Boulder.

Measurements
Body fat percentage was estimated from the hydrostatic weighing technique (4). Body mass index was calculated from the formula of body mass (kg)/height (m 2). Waist circumference was measured at the narrowest part of the torso, and hip circumference was measured at the maximal extension of the buttocks. Estimated daily energy expenditure was assessed by the Stanford Physical Activity Questionnaire (5).

Measurement of arterial stiffness was conducted after an overnight fast, a 12-hour abstinence from caffeine and alcohol, and a 24-hour period with no strenuous physical activity. Each subject rested supine for at least 15 minutes in a quiet, temperature-controlled room. Blood pressure was measured by ausculation according to American Heart Association guidelines.

Arterial applanation tonometry.—The pressure waveform and amplitude were obtained from the right common carotid artery with a pencil-type probe incorporating a high-fidelity strain-gauge transducer (Millar Instruments, Houston, TX; 6). The pressure waveform consists of both a “forward” or “incident” wave, and a “reflected” wave that is returning from a peripheral site. The reflected wave is superimposed on the incident wave such that the pulse and systolic pressures are increased. This increase is defined as an augmentation index (AI), and it is calculated as pressure wave above its systolic shoulder divided by pulse pressure (6). The shoulder was defined as the first concavity on the upstroke of the wave. The carotid AI has been proposed as
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an indicator of the magnitude of wave reflections, which is linked to arterial stiffness (6). Carotid AI was used as a measure of the stiffness of the central arteries.

**Pulse wave velocity.**—Pulse wave velocity (PWV) was measured from the “foot” (i.e., the commencement of the sharp systolic upstroke) of pressure waves recorded at two points along the path of the arterial pulse wave. PWV is calculated from the measurement of the distance traveled (cm) divided by pulse transit time (sec) between two arterial recording sites. Two Doppler flowmeters (Parks Medical, Aloha, OR) were used to obtain the pulse wave: (a) between the aortic arch and the femoral artery (aortic PWV); (b) between the femoral and posterior tibial artery (leg PWV); and (c) between the brachial and radial artery (arm PWV) (7). Distance traveled by the pulse wave was assessed in duplicate with a random zero length measurement over the surface of the body. Aortic PWV was used as a measure of the stiffness of the central arteries, whereas leg and arm PWV were used as measures of peripheral arterial stiffness.

**Statistical Analyses**

The differences between users and nonusers of HRT were assessed with a one-way analysis of variance. All data are reported as the mean ± SE. Statistical significance was set at \( p < .05 \).

**RESULTS**

There were no significant group differences in any of the physical characteristics, including resting blood pressure (Table 1). As shown in Figure 1, none of the measures of arterial stiffness differed between users and nonusers of hormone replacement (\( p = .22 - .96 \)).

**DISCUSSION**

The purpose of the study was to determine whether central and peripheral arterial stiffness is lower in postmenopausal women taking hormone replacement versus those who are not. In order to isolate the influence of HRT per se as much as possible, we carefully matched two groups of postmenopausal women for age, adiposity, arterial blood pressure, habitual physical activity, and years after menopause. The primary finding from the present study is that there are no obvious differences in central and peripheral arterial stiffness in postmenopausal women.

**Table 1. Physical Characteristics of Postmenopausal Women Grouped by the Use of Hormone Replacement**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nonusers (n = 16)</th>
<th>Users (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>61 ± 1</td>
<td>58 ± 2</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65 ± 0.02</td>
<td>1.63 ± 0.02</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>62.8 ± 2.6</td>
<td>64.6 ± 2.8</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>42.9 ± 1.1</td>
<td>42.6 ± 1.1</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.1 ± 1.1</td>
<td>24.4 ± 1.0</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>29 ± 3</td>
<td>33 ± 2</td>
</tr>
<tr>
<td>Waist/Hip ratio</td>
<td>0.78 ± 0.02</td>
<td>0.79 ± 0.02</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>118 ± 3</td>
<td>118 ± 2</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>77 ± 1</td>
<td>75 ± 1</td>
</tr>
<tr>
<td>Energy expenditure (kcal/kg/day)</td>
<td>38 ± 1</td>
<td>40 ± 2</td>
</tr>
<tr>
<td>Years after menopause</td>
<td>10 ± 2</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>Hormone replacement use (yr)</td>
<td>na</td>
<td>6.8 ± 0.9</td>
</tr>
</tbody>
</table>

![Figure 1. Pulse wave velocities (PWV) and carotid augmentation index (AI) of users and nonusers of hormone replacement. There were no obvious differences in central and peripheral arterial stiffness in postmenopausal women receiving hormone replacement compared with those not receiving it.](https://academic.oup.com/biomedgerontology/article-abstract/53A/5/M344/588265)
Females appear to have lower central arterial stiffness than males until menopause (3), an effect thought to be related to the presence of ovarian hormones. As such, we reasoned that central and peripheral arterial stiffness would be lower in postmenopausal women who take estrogen supplements than those who do not. Our results fail to support this idea. Rather, our data support and extend the findings of a recent report showing no difference in aortic PWV between postmenopausal women receiving Tibolone versus nonusers (8). Thus, data from the present study considered together with an earlier report (8) suggest that reduced arterial stiffness is not a likely mechanism contributing to the lower incidence of CVD in postmenopausal women taking HRT.

During the preparation of this article, Rajkumar et al. (9) reported that aortic PWV was lower and total systemic arterial compliance was higher in postmenopausal women taking hormone replacement compared with those who were not. The reason(s) for the difference in their results and those of the present study and Lehmann et al. (8) is not clear. As with all cross-sectional investigations, it is possible that constitutional makeup may have influenced the findings independent of HRT. Further investigation using a prospective, placebo-controlled randomized trial is warranted.

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