Menstrual phase and the vascular response to acute resistance exercise

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Abstract
Introduction  Aerobic exercise has a favorable effect on systemic vascular function, reducing both central (large elastic artery) and peripheral (smaller muscular artery) stiffness. The effects of resistance exercise (RE) on arterial stiffness are more complex. Acute RE increases central artery stiffness while decreasing peripheral stiffness. To date, the majority of studies have been performed in predominantly male participants.

Purpose To examine the effect of acute RE on central and peripheral arterial stiffnesses in women, a secondary purpose was to explore the influence of cyclic changes in estrogen status across the menstrual cycle on the arterial response to acute RE.

Methods 18 healthy women [28 ± 7 years, body mass index (BMI) 22.6 ± 2.9 kg/m2] completed an acute RE bout during the early follicular and the early luteal phase of their menstrual cycle. Salivary 17β-Estradiol concentration was measured during each phase, using a passive drool technique. Pulse-wave velocity (PWV) was obtained from the carotid–femoral and carotid–radial pulse sites to measure central and peripheral stiffness, respectively, using applanation tonometry. PWV was measured at rest, immediately, 10, 20, and 30 min post-RE.

Results 17β-Estradiol concentration was significantly lower in the early follicular vs. the early luteal phase of the menstrual cycle (1.78 ± 0.51 vs. 2.40 ± 0.26 pg/ml, p = 0.01). Central PWV significantly increased (p < 0.05) and peripheral PWV significantly decreased (p < 0.05) post-RE in both the early follicular and early luteal phases. No phase-by-time interaction was detected for either vascular segment (p > 0.05).

Conclusion Women experience increases in central arterial stiffness and reductions in peripheral arterial stiffness following acute RE. Menstrual cycle phase may not influence changes in arterial stiffness in response to acute RE.

Keywords  Aortic stiffness · Resistance exercise · 17B-estradiol · Menstrual cycle

Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>ALx(75)</td>
<td>Augmentation index (@Heart Rate 75)</td>
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<td>AP</td>
<td>Augmented pressure</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
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<td>cMAP</td>
<td>Central mean arterial pressure</td>
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<td>CCA</td>
<td>Common carotid artery</td>
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<td>DBP</td>
<td>Diastolic blood pressure</td>
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<td>Pf</td>
<td>Forward wave pressure</td>
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<td>PP</td>
<td>Pulse pressure</td>
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<td>PWV</td>
<td>Pulse-wave velocity</td>
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<td>Pb</td>
<td>Reflected wave pressure</td>
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<td>RM</td>
<td>Repetition maximum</td>
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<td>RE</td>
<td>Resistance exercise</td>
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<td>SBP</td>
<td>Systolic blood pressure</td>
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<td>Tr</td>
<td>Time to reflection</td>
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<td>WSA</td>
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</table>

Introduction

Cardiovascular disease (CVD) is a leading cause of death in women in the United States (Heidenreich et al. 2011). Increased arterial stiffness is associated with increased risk of CVD and cardiovascular mortality (Vlachopoulos et al. 2010). Arterial stiffness increases with age and in the presence of disease and ultimately may lead to cardiac complications (i.e., stroke, myocardial infarction) (Townsend et al. 2018).
Regular physical activity improves arterial stiffness and prevents the risk and progression of CVD (Thompson et al. 2003; Seals et al. 2008). The benefits of aerobic exercise on arterial stiffness are well known (Seals et al. 2008); however, the effects of resistance exercise (RE) on arterial stiffness are less clear. Blood pressure during RE can be substantially higher than during aerobic exercise resulting in different cardiovascular recovery patterns (Heffernan et al. 2007a; Collier et al. 2010). Acute aerobic exercise reduces both central (large elastic artery) stiffness and peripheral (smaller muscular artery) stiffness. Conversely, acute RE increases central arterial stiffness while concomitantly decreasing peripheral arterial stiffness, with reductions in peripheral stiffness being related to improvements in endothelial function (DeVan et al. 2005; Heffernan et al. 2007a, b; Collier et al. 2010). Increases in arterial stiffness following acute RE may be related to increases in endothelin-1, activation of sympathetic nervous system, and subsequent increases in blood pressure (Otsuki et al. 2007). To date, the majority of studies exploring the acute vascular effects of resistance exercise have been performed in men (Kingsley et al. 2017; Okamoto et al. 2017; Heffernan et al. 2007b, a; Collier et al. 2010; DeVan et al. 2005). The effects of acute RE on systemic arterial stiffness are less clear in women.

Hormonal changes across the menstrual cycle can influence both central arterial stiffness and peripheral endothelial function (Adkisson et al. 2010; Williams et al. 2001). Estrogen is known to attenuate both the production of endothelin-1 (vasoconstrictor) and activation of SNS (Vongpatanasin et al. 2001). In addition, at rest, high levels of estrogen, a potent vasodilator, are associated with reductions in arterial stiffness and improvements in peripheral artery endothelial function while low levels of estrogen are associated with elevated arterial stiffness and reductions in peripheral artery endothelial function (Adkisson et al. 2010; Mendelsohn and Karas 2005). Women have been shown to be protected against detrimental vascular changes caused by such stressors as a high fat meal (Harris et al. 2012) and ischemia–reperfusion injury (Wang et al. 2005; Zhai et al. 2000) and this cardio-protection has been linked to estrogenic status (Wang et al. 2005; Zhai et al. 2000). High estrogen concentrations during the luteal phase might attenuate the increases in arterial stiffness observed after RE, because estrogen not only exhibits vasodilatory functions but also reduces both endothelin-1 production and SNS activity. Thus, cyclic hormonal changes may affect the systemic vascular response to acute RE in women.

Therefore, the aim of the present study was to examine the effect of acute RE on central and peripheral arterial stiffness in young healthy women. The second aim of this study was to compare the effects of acute RE on arterial stiffness in women during the early follicular phase (i.e., lower estrogen status) and the early luteal phase (i.e., higher estrogen status) of the menstrual cycle. It was hypothesized that following an acute bout of RE, there would be no change in central or peripheral arterial stiffness during the early follicular phase but there would be a decrease in both central and peripheral arterial stiffness following acute RE during the early luteal phase.

Methods

Study design

21 recreationally active women, ranging in age from 18 to 40 years, were recruited from the local University community for this study. Exclusion criteria included use of oral contraceptives, self-reported smoking, hypertension, diabetes mellitus, hyperlipidemia, pulmonary disease, renal disease, neurological disease or peripheral artery disease, irregular menstrual cycle (oligomenorrhea), amenorrhea (i.e., lack of menstrual cycle), and/or use of medications of any kind. From the sample of 21 women recruited, 3 women were excluded due to lack of adherence to study visits \( n = 1 \), nausea post-RE protocol \( n = 1 \) and current diagnosis of polycystic ovarian syndrome (PCOS, \( n = 1 \)). A sample of 18 women was used for study analysis. The Institutional Review Board of Syracuse University approved this study and all participants provided written informed consent prior to study initiation. This study adhered to the Declaration of Helsinki and all participants gave prior written consent.

Participants came to the laboratory on three different occasions. The first visit served as a screening visit in which participants filled out health history and physical activity questionnaires (IPAQ), discussed their menstrual cycle schedule, underwent exercise protocol familiarization and performed repetition maximum (RM) testing. Both the second and third visits occurred during the early follicular phase (days 1–7) and the early luteal phase/ovulation (dependent upon each individual cycle length, \( 14–19 \) days prior to start of menses). The early luteal phase was determined by a standard web-based ovulation calculator provided by American Pregnancy Association and confirmed by 17-\( \beta \) Estradiol concentrations, which were within the standard norms for early follicular and early luteal 17-\( \beta \) Estradiol Salivary concentrations. Height and weight were assessed via wall stadiometer and electronic scale, respectively, and body composition was estimated via air displacement plethysmography (BodPod; COSMED, Concord, CA). Body mass index (BMI) was calculated as weight (kg)/height \(^2 \) (m\(^2 \)). Waist circumference (cm) was measured using a tape measure at the level of the umbilicus.

For both the second and third visits, participants were instructed to fast for \( \geq 3 \) h, avoid vigorous exercise and to
not consume caffeine/alcohol ≥ 12 h before testing. Upon arrival, a saliva sample was collected for assessment of 17β-Estradiol. Participants then rested for 10 min in the supine position. This was followed by all vascular measures. Vascular testing was conducted in a quiet, dimly lit, temperature-controlled laboratory. Participants then performed upper body RE. The RE protocol consisted of five sets of five repetitions for bench press and five sets of ten repetitions for biceps curl, with each set being separated by 90 s of rest. Exercises were performed at 5-RM and 10 RM for bench press and biceps curl, respectively. This acute RE protocol has previously been shown to acutely increase arterial stiffness (Fahs et al. 2009). Post-testing vascular measures were made immediately post-RE (~2 min), 10, 20, and 30 min following acute RE based on the previous findings in men noting prominent changes in arterial stiffness to occur at these times (DeVan et al. 2005; Heffernan et al. 2007b; Fahs et al. 2009).

Exercise familiarization and RE protocol

The maximum amount of weight lifted with proper form through a full range of motion for five repetitions for the bench press and ten repetitions for the biceps curl was determined to be the participants’ 5-RM and 10-RM, respectively. This was determined using guidelines set forth by the National Strength and Conditioning Association (Baechle 2008). Biceps curl was performed using a two-arm E-Z curl bar. For both exercises, participants first completed a brief warm-up consisting of ten repetitions of a submaximal load. With the help of a prediction table that can estimate maximal work from submaximal loads (Baechle 2008), weight was added in 5–10 kg increments until participants could no longer successfully complete the five or ten repetitions (could not complete the concentric portion of the contraction without assistance). The heaviest weight lifted with proper form and no assistance for the five or ten repetitions was recorded as the subject’s 5-RM or 10-RM maximum weight, respectively. Participants were allowed 3–5 min of rest between sets to ensure that a maximal effort was exerted with each attempt. Maximal values were attained for all participants in less than five attempts. A spotter was present at all testing sessions to ensure the participant’s safety during testing. The RE bout consisted of a warm-up comprised of ten bench press repetitions of a submaximal weight. This was followed by five sets of the subject’s 5-RM on the bench press. After bench press, five sets of ten repetitions of the subject’s 10-RM for biceps curl was completed using a 2-arm E-Z curl bar. Cadence was set at an approximate 2-1-2 duty cycle (2 s concentric, 1 s pause, and 2 s eccentric). Exactly 90 s of rest was afforded between each set. The subject completed their 5-RM and 10-RM to its entirety. If the participant could not complete the allotted repetitions, a drop set was instigated whereby weight was taken off incrementally (5–10 kg) until the participant could complete a set of five or ten repetitions with proper form. A spotter was present during all exercise to ensure proper form and to assist the participant if fatigue occurred. No specific breathing techniques were instructed to the participants. This protocol has previously been used to successfully induce acute vascular changes (Fahs et al. 2009).

Pulse-wave velocity (PWV)

Applanation tonometry (AtCor Medical, SphygmoCor Technology, Sydney, Australia) was performed for measures of pulse-wave velocity (PWV). A single high fidelity pressure transducer was used to measure pressure waveforms over a 10 s period. The waveforms were measured between the: (1) left common carotid artery (CCA) and left radial artery (peripheral arterial stiffness) and (2) the left CCA and the left femoral artery (central arterial stiffness). The distances between measurement sites were measured with a tape measure. PWV was calculated using the difference in the distances between sites (Δ distance) and the measured time delay (Δ time) between proximal and distal waveforms. Simultaneous three-lead ECG was used to measure heart rate. The peak of the in-phase R-wave was used as a timing marker. For measures of carotid–radial and carotid–femoral PWV, distance from the sternal notch to the carotid pulse site was subtracted from the carotid–radial or carotid–femoral path length to account for the bi-directional nature of pressure propagation.

Central and peripheral blood pressure

Resting and post-RE peripheral systolic and diastolic blood pressure (SBP, DBP) was measured using an automated brachial cuff (Mobil-O-Graph, I.E.M.) (Weber et al. 2011). This validated method of estimating central blood pressure has been used in large studies (Weber et al. 2011, 2017). Peripheral blood pressure measurements were repeated until two values were obtained within 5 mmHg of each other. The average of the two values was used for pulse-wave analysis. In addition, using a generalized transfer function, the central blood pressure waveforms were derived from the radial pressure waveforms collected during the peripheral arterial stiffness measurements. Central and peripheral pulse pressure (PP) was calculated as cSBP–cDBP and SBP–DBP, respectively. Central MAP (cMAP) was calculated as area under the curve of the radial pressure waveform divided by the cardiac cycle period. Augmentation Index was calculated as the difference between the early and late systolic peaks of the pressure waveforms to the total PP expressed as a percentage: \((P2−P1)/(PP \times 100)\) and standardized to a heart rate of 75 beats per minute (AIX75). Augmented pressure...
(AP) was defined as the increase in blood pressure due to the arrival of the backward wave ($P_2 - P_1$), where $P_1$ corresponds to the peak blood pressure and $P_2$ corresponds to the point at which the backward wave meets the forward travelling waveform. Time to reflection (Tr) was defined as the time delay of the backward waveform from the onset of the ejected pulse to the arrival of the reflected waveform at the aorta. Wave separation analysis (WSA) was performed to gain further insight into pressure pulsatility following acute RE. Pressure waveforms were separated into forward (Pf) and backwards/reflected (Pb) components as previously described by Westerhof et al. (Westerhof et al. 2006). Reflection Index was calculated by dividing Pb by Pf as a measure of reflection magnitude (i.e., wave reflection relative to forward wave magnitude).

**Salivary 17β-estradiol**

17B-Estradiol was detected in saliva samples, using highly sensitive competitive binding immunoassay (Salimetric Assay, State College, PA). The samples of saliva were frozen at −80 °C and stored once collected. Once ready for analysis they were thawed, centrifuged, and pipetted into small wells on small assay plates. The hormones are detected on the plate and read by a spectrophotometer. The bound estradiol peroxidase was detected by the spectrophotometer at 450 nm and was inversely proportional to the amount of free estradiol present in the saliva samples. Inter- and intra-assay percentage coefficients of variation were 9.2 and 8.3%, respectively.

**Statistical analyses**

Normality of distribution for variables was assessed using histograms and Q–Q plots as well as quantitatively using the Shapiro–Wilkes test. An analysis of variance with repeated measures (two menstrual phases × five timepoints) was used to analyze main outcome variables. Post-hoc $t$ tests were used to investigate significant time effects within and between conditions. All data are reported as mean ± standard deviation and statistical significance was established as $p < 0.05$. Data were analyzed using the statistical software package SPSS (version 22.0, SPSS, Inc., Chicago, IL).

**Results**

Participant characteristics are presented in Table 1. Participants’ age and BMI, 5-RM bench and 10-RM biceps curl are displayed in Table 1. As expected 17β-Estradiol concentration was significantly higher in the early luteal phase when compared to the early follicular phase (Table 1; $p < 0.05$).
Wave reflections

Wave reflection measurements are displayed in Table 3. There were significant time effects across both menstrual phases in AIx and AIx75 ($p < 0.05$; Table 3). In the early follicular phase, AIx was increased immediately post-RE and remained elevated 10 min post-RE ($p < 0.05$; Table 3). In the early luteal phase, AIx was increased immediately post-RE and remained elevated 10 and 20 min post-RE ($p < 0.05$; Table 3). AIx75 was increased immediately post-RE and remained elevated across all timepoints compared to baseline in the early follicular phase ($p < 0.05$; Table 3). In the early follicular phase, AP (augmented pressure, $P1–P2$) was significantly increased immediately post-RE and remained significantly elevated 10 min post-RE ($p < 0.05$). In the early luteal phase, AP was significantly increased immediately post-RE and remained elevated 10 and 20 min post-RE ($p < 0.05$). $P1$ was significantly increased immediately post-RE and then returned to baseline ($p < 0.05$).
no change in \( T_r, P_2, P_f, \) and reflection index post-RE \((p > 0.05; \text{Table 3})\). There were no significant menstrual phase effects or phase-by-time interactions \((p > 0.05)\).

**Discussion**

The main finding of this study was that following an acute bout of RE, there was a significant increase in central arterial stiffness and significant decrease in peripheral stiffness in young healthy women during both the early follicular and early luteal phase of the menstrual cycle. Our findings, exclusively in women, are in accordance with the previous studies that have examined vascular responses to acute RE in men. Contrary to our hypothesis, the findings of the current study also suggest that despite significant differences in \(17\beta\)-Estradiol concentrations between luteal and follicular phases of the menstrual cycle in premenopausal women, and menstrual cycle phase may not influence changes in arterial stiffness during the immediate recovery period \(< 30 \text{ min}\) following acute RE.

**Peripheral arterial stiffness and acute RE**

The previous studies that have examined the effect of acute RE on arterial stiffness in men have found decreases in peripheral arterial stiffness in both the arm and leg (Heffernan et al. 2006, 2007b). Changes in peripheral stiffness appear to be related to the regional nature of the stimulus as acute whole body (predominantly upper body), RE does not impact peripheral stiffness (Heffernan et al. 2007a), while exclusively lower body acute RE reduces regional lower body peripheral stiffness (Heffernan et al. 2006). Our study found a significant decrease in peripheral arterial stiffness post-RE in both menstrual cycle phases in premenopausal women. The observed decrease in peripheral arterial stiffness may be largely related to increased vasodilation of the exercised limb muscle beds \(i.e.,\) arms (Kingwell et al. 1997; Tinken et al. 2010). Increased blood flow to the periphery may contribute to increased shear stress-induced release of nitric oxide \(NO\) from the endothelium and subsequent vasodilation of the peripheral microvasculature (Kingwell et al. 1997). Thus, decreases in peripheral arterial stiffness post-RE may be due to improvements in microvasculature/resistance vessel endothelial function (Joyner and Halliwill 2000).

Our finding of reductions in peripheral artery stiffness is not in agreement with findings from Franklin et al. who found reduced brachial artery vasodilatory capacity following acute RE in obese and sedentary women (Franklin et al. 2014). The vascular bed surveyed may explain discrepancies in our study findings and the previous studies. Whereas Franklin et al. examined peripheral vasodilatory capacity of the brachial artery, we examined peripheral artery stiffness of both the large brachial artery and smaller arteries of the forearm. Carotid–radial PWV encapsulates both the larger brachial artery and smaller arteries/arterioles that comprise the resistance microvasculature of the forearm. Structurally, these vascular beds differ in their proportions of smooth muscle, elastin, and collagen, which define their respective functions (Tinken et al. 2010; Phillips et al. 2011; Choi et al. 2016). Moreover, these distinct vascular beds have been

<table>
<thead>
<tr>
<th>Variables</th>
<th>Menstrual phase</th>
<th>Rest</th>
<th>Post-1</th>
<th>10 min</th>
<th>20 min</th>
<th>30 min</th>
<th>Time effect</th>
<th>Phase Effect</th>
<th>Interaction</th>
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<tbody>
<tr>
<td>( Alx (%) )</td>
<td>Follicular</td>
<td>8 ± 3</td>
<td>13 ± 2*</td>
<td>11 ± 2*</td>
<td>9 ± 2</td>
<td>11 ± 2</td>
<td>0.04</td>
<td>0.68</td>
<td>0.27</td>
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<td></td>
<td>Luteal</td>
<td>8 ± 3</td>
<td>15 ± 2*</td>
<td>12 ± 2*</td>
<td>13 ± 3*</td>
<td>8 ± 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( Alx75 (%) )</td>
<td>Follicular</td>
<td>0 ± 3</td>
<td>8 ± 1*</td>
<td>7 ± 2*</td>
<td>3 ± 2*</td>
<td>4 ± 2*</td>
<td>0.00</td>
<td>0.20</td>
<td>0.34</td>
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<td></td>
<td>Luteal</td>
<td>1 ± 2</td>
<td>9 ± 2*</td>
<td>7 ± 2*</td>
<td>9 ± 2*</td>
<td>5 ± 2*</td>
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<tr>
<td>Time to Reflection (Tr)</td>
<td>Follicular</td>
<td>158 ± 5</td>
<td>152 ± 4</td>
<td>161 ± 7</td>
<td>152 ± 4</td>
<td>153 ± 3</td>
<td>0.27</td>
<td>0.62</td>
<td>0.90</td>
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<tr>
<td></td>
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<td>154 ± 3</td>
<td>149 ± 5</td>
<td>174 ± 7</td>
<td>155 ± 6</td>
<td>150 ± 4</td>
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<td>Augmented Pressure (AP)</td>
<td>Follicular</td>
<td>3 ± 1</td>
<td>6 ± 1*</td>
<td>4 ± 1*</td>
<td>3 ± 1</td>
<td>4 ± 1</td>
<td>0.00</td>
<td>0.99</td>
<td>0.30</td>
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<tr>
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<td>6 ± 1*</td>
<td>4 ± 1*</td>
<td>5 ± 1*</td>
<td>3 ± 1</td>
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<td>Backward Wave Pressure (mmHg)</td>
<td>Follicular</td>
<td>15 ± 2</td>
<td>18 ± 3</td>
<td>15 ± 2</td>
<td>15 ± 1</td>
<td>15 ± 2</td>
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<td>18 ± 2</td>
<td>15 ± 1</td>
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<td>15 ± 1</td>
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<td>Forward Wave Pressure (mmHg)</td>
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<td>30 ± 1</td>
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<td>Reflection Index</td>
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<td>0.57 ± 0.03</td>
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</table>

*Significantly different than baseline, \(p < 0.05\); Mean ± standard error

\(Post-1\) immediately post-RE, \(Alx\) augmentation index, \(AP\) augmented pressure, \(Tr\) time to reflection, \(P_b\) backward wave pressure, \(P_f\) forward wave pressure
shown to respond differently to the acute stress of RE. While acute RE reduces brachial artery vasodilatory capacity, acute RE increases forearm microvascular vasodilatory capacity (Collier et al. 2010; Arce Esquivel and Welsch 2007; Fahs et al. 2009). Given that smaller downstream vessels comprise a larger net cross-sectional area, changes in resistance vessel function may offset changes in upstream vessel function resulting in a net decrease in PWV. In the current study regardless of the differences in 17β-Estradiol concentrations between early follicular and early luteal phases, we found a significant decrease in peripheral arterial stiffness post-RE in women.

Central arterial stiffness and acute RE

In the current study, we found a significant increase in central arterial stiffness following acute RE in women. Our finding is in accordance with the previous acute studies in men (DeVan et al. 2005; Miyachi et al. 2004) and training studies in premenopausal women (Cortez-Cooper et al. 2005) that suggest acute RE and RE training increases central arterial stiffness. Mechanisms responsible for increases in central arterial stiffness following acute RE are largely unknown. Increased arterial stiffness reported following acute RE might be due to increased plasma endothelin-1 (Otsuki et al. 2007). Vasoactive substances produced by endothelial cells have significant vasoconstrictive effects on the vasculature and blood pressure response to RE (Otsuki et al. 2007). These substances such as endothelin-1 may thus associated with increases in arterial stiffness following RE. The female reproductive hormones estrogen and progesterone are known to attenuate the production and subsequent release of endothelin-1 (Vongpatanasin et al. 2001). Likewise, estrogen is a known vasodilator as it is a co-factor for the production of nitric oxide (NO). Thus, because the concentration of these sex hormones fluctuates throughout the menstrual cycle, one could hypothesize that increases in estrogen during luteal phase may attenuate increases in arterial stiffness following RE, while decreases in estrogen during the follicular phase could have no effect on the changes in arterial stiffness following RE.

In addition, RE is known to stimulate sympathetic nervous system (SNS), which induces a vasoconstrictive effect and is associated with increases in arterial stiffness (Raastad et al. 2001). Estrogen and progesterone are known to inhibit and stimulate SNS, respectively (Vongpatanasin et al. 2001). Thus, it is hypothesized that high estrogen in the luteal phase might attenuate the increases in arterial stiffness observed after RE, because estrogen inhibits SNS activity. Even though progesterone also stimulates SNS activity, the effect of estrogen on vascular tone may be of a greater magnitude.

In the current study, increases in central arterial stiffness might be associated with acute intermittent elevations in blood pressure in the cardiothoracic region during RE (Miyachi et al. 2003). Artery wall stress is supported by compliant elastin fibers at low levels of blood pressure, while wall stress is supported by stiff collagen fibers at high levels of pressure (Townsend et al. 2015). The load bearing transition from elastin to collagen fibers occurs at a mean pressure of approximately 120 mmHg. During a bout of RE, mean pressure is known to increase as high as 270 mmHg (MacDougall et al. 1992). Although we hypothesized that estrogen, a potent vasodilator, may prevent increases in central stiffness in women during the early luteal phase, the mechanical blood pressure mechanisms responsible for increased arterial stiffness may override the potential vaso-dilatory effects of 17β-Estradiol.

A recent study from Okamoto et al. concluded that menstrual phase does influence increases in arterial stiffness following acute RE. This study reported that increases in arterial stiffness were attenuated during the luteal phase and markedly elevated during the follicular phase (Okamoto et al. 2017). Discrepancies between our findings and those of Okamoto et al. may be due to several factors: (1) sample size (n = 18 vs. n = 9); (2) timing of measurement (≤ 30 vs. ≥ 30 min); and (3) method of assessment (carotid–femoral PWV vs. brachial–ankle PWV). More research is needed to further elucidate the impact of menstrual phase on the vascular response to acute RE.

Wave reflections and acute RE

In the current study, we found a significant increase in central AIx75 following acute RE in both phases of the menstrual cycle. This finding is in accordance with the previous acute RE studies in men (Yoon et al. 2010; Lefferts et al. 2014) and in RE training studies in women (Cortez-Cooper et al. 2005). Our finding is novel, since no study has examined wave reflections following an acute bout of RE in women. Increases in central AIx75 following acute RE are typically ascribed to changes in wave reflection magnitude and/or timing. However, in the current study, there were no significant changes in aortic reflected wave pressure or time to reflection suggesting other potential moderators. Other factors that influence AIx include ventricular contraction/relaxation (dynamics) and LV suction (Fok et al. 2014; Hughes et al. 2013; Heffernan et al. 2010). Future studies need to examine AIx and other indices of wave reflections following acute RE in women to confirm and expand our findings.

Limitations and additional considerations

In the current study, we tested our participants during the early follicular phase (days 1–7 of the menstrual cycle) and the early luteal phase (approximately 2 weeks prior to start...
of next menses, ovulation) of the menstrual cycle. During the follicular phase, normal menses bleeding occurs; however, it is possible that some participants may have experienced bleeding or breakthrough bleeding that sometimes occurs during the ovulation phase, and thus, participants may falsely believe they have a menses cycle. Thus, this may influence our classification of phases for each participant. However, as expected 17B-estradiol levels were significantly higher in the early luteal phase compared to the early follicular phase.

In addition, we only chose to measure arterial stiffness and estrogen concentrations at two timepoints in the menstrual cycle and we did not measure throughout the cycle during three different phases. However, in our study, we aimed to isolate the effects of estrogen when estrogen levels are theoretically at their highest and the lowest. In addition, the lack of control of breathing techniques (i.e., Valsalva maneuvers) during the acute RE protocol in the current study may have influenced the magnitude of hemodynamic responses to acute RE. Thus, future studies should consider controlling for Valsalva maneuvers during acute RE. Finally, the participants’ training status might influence the effect of acute RE on arterial stiffness. In the current study, each of our participants filled out the IPAQ and from this, our participants on average were categorized as highly active engaging in over > 3000 MET minutes/week. However, in addition to physical activity data, knowledge of individuals that were RE trained compared to those who are endurance-trained vs. sedentary may give insight into responses to acute RE. Future studies should consider the influence of training status on arterial stiffness following to acute RE.

Applications and perspectives

The benefits of regular resistance training on physical fitness and overall health among premenopausal and postmenopausal women are well known (Thompson et al. 2003). However, acute exercise studies suggest that high-intensity RE may be associated with increases in arterial stiffness (Collier et al. 2010; DeVan et al. 2005; Heffernan et al. 2007a). Increased arterial stiffness is an independent risk factor for CVD (Vlachopoulos et al. 2010; Seals et al. 2008). It remains unknown whether increases in arterial stiffness associated with RE adversely impacts CVD. However, arterial stiffness increases with aging and menopause is a risk factor for increased arterial stiffness in older women (Zaydun et al. 2006). Thus, attenuating arterial stiffness may be essential in CVD prevention in younger premenopausal women.

The findings of the current study suggest that the menstrual phase does not modulate the effect of RE on arterial stiffness. Central PWV is significantly increased and peripheral PWV significantly decreased following RE during both the follicular and luteal phase of the menstrual cycle. Since the significant increase in central PWV was detected, perhaps, low-intensity RE rather than high-intensity RE should be implemented in women. Low-intensity RE has been demonstrated to provide similar benefits to CV health compared to high-intensity RE (Okamoto et al. 2015). Hence, low-intensity RE might be crucial for maintaining healthy vascular function in young women. However, future studies need to examine these relationships.

Conclusions

This is one of the first studies to examine the influence of the menstrual cycle on the arterial stiffness and central hemodynamic response to acute RE in women. The present study demonstrated that acute RE results in significant increases in central arterial stiffness and decreases in peripheral arterial stiffness. Even though 17B-Estradiol was significantly higher in the early luteal phase compared to the early follicular phase, the menstrual cycle phase did not influence changes in arterial stiffness in response to acute RE in young premenopausal women.

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Authors’ contributions

JAA data collection, statistical analyses, writing of manuscript, response, and management of reviewer comments and manuscript submission. KNN data collection and recruitment. KSH Assist with writing of manuscript and manuscript edits, supervisor.

Compliance with ethical standards

Conflict of interest

The authors have no conflicts of interest to disclose. The results of this study are presented clearly, honestly and without fabrication, or inappropriate data manipulation.

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