Habitual resistance exercise and endothelial ischemia–reperfusion injury in young adults

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A B S T R A C T

Resistance exercise involves muscular contractions that can render downstream tissues ischemic and may precondition the vasculature against ischemia–reperfusion (IR) injury, but it is unknown if habitual resistance exercise protects against IR injury in humans. We determined the magnitude and recovery from endothelial IR injury induced by forearm occlusion in 22 healthy young sedentary and resistance-trained adults. After IR injury, brachial artery flow-mediated dilation (FMD) significantly decreased by 36% in sedentary, but not resistance-trained subjects and fully recovered within 45 min. Though HDL-cholesterol, handgrip strength and systolic blood pressure were significantly associated with FMD 15 min after IR injury, the change in FMD from before to 15 min after IR injury was not associated with any subject characteristics. These results are consistent with the notion that habitual resistance exercise may protect against endothelial IR injury in young adults, presumably through effects analogous to ischemic preconditioning.

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1. Introduction

Cardiovascular disease is the leading cause of death in the United States and over half of cardiovascular-related deaths are attributable to coronary artery disease. Coronary artery disease significantly increases the risk for myocardial infarction, a condition characterized by blood flow restriction to the heart and downstream blood vessels, producing tissue hypoxia and damage. This form of injury, known as ischemia–reperfusion (IR) injury, also occurs during certain surgical treatments including coronary angioplasty and thrombolytic therapy [1].

Regular exercise, in addition to pharmacotherapy and alternative therapies, is currently being investigated for its possible role in preventing and/or attenuating IR injury in the cardiovascular system. Resistance exercise may be a promising modality as it involves muscular contractions that can render downstream tissues ischemic and may precondition the vasculature against subsequent IR injury, but this hypothesis has not yet been examined. Accordingly, we determined the magnitude of IR injury and rate of recovery of conduit artery endothelial function in sedentary or resistance-trained men and women. Brachial artery flow-mediated dilation (FMD) was chosen as a surrogate model of the coronary arteries because this measure is strongly associated with gold-standard measures of coronary artery function [2].

2. Materials and methods

Eleven resistance-trained subjects (10 men and one woman; four Hispanic and seven non-Hispanic; three Asian, seven white and one of more than one race; mean ± SEM; 25 ± 2 years of age) who had lifted weights targeting all major muscle groups >2 times per week for >1 year and 11 sedentary subjects (nine men and two women; three Hispanic and eight non-Hispanic; three Asian and eight white; 26 ± 2 years of age) who reported either none or <2 h of formal exercise per week for the past year were recruited from The University of Texas at Austin and surrounding community (Table 1). All subjects were free of overt cardiovascular or other chronic diseases, were not taking any cardiovascular-acting medications as assessed by a medical history questionnaire, were not performing any endurance exercise training, non-smoking and...
were not currently taking any herbal supplements or refrained from taking herbal supplements for the two weeks prior to vascular testing. Self-reported exercise training status was verified in a subgroup of subjects by handgrip strength (eight resistance-trained men = 56 ± 2 kg; six sedentary men = 38 ± 1 kg; p < 0.01) measured by a hydraulic hand dynamometer (JAMAR 5030J1, Sammons Preston Rolyan, Bolingbrook, Illinois) in the dominant hand with the elbow at 90°. Body composition was measured by dual energy X-ray absorptiometry (Lunar DPX, General Electric Medical Systems, Fairfield, Connecticut). The Human Research Committee reviewed and approved all procedures and written informed consents were obtained from all subjects.

Subjects reported to the laboratory in the morning after fasting >10 h, not taking any medications for >24 h, abstaining from moderate to high intensity exercise >24 h and for women, during the early follicular phase of their menstrual cycle [2]. Brachial blood pressure was measured by the oscillometric technique (STBP-780, Colin Medical, San Antonio, Texas). Blood samples were obtained from the left antecubital vein using a closed intravenous catheter system (Saf-T-Intima, BD Medical, Sandy, Utah) and immediately analyzed for serum total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides (Table 1) using a multianalyte chemistry analyzer certified by the Centers for Disease Control’s Cholesterol Reference Method Laboratory Network (Cholestech LDX System, Cholestech Corporation, Hayward, California). Endothelial-dependent vasodilation of the right brachial artery was assessed by FMD using an ultrasound machine (IE33, Philips Medical, Bothell, Washington) equipped with a high-resolution linear-array transducer before and 15, 30 and 45 min after 20 min of lower-arm cuff occlusion. At each time point, longitudinal images of baseline brachial artery end-diastolic diameters (47 ± 4 cardiac cycles) were recorded proximal to the forearm cuff prior to a 5 min forearm occlusion with a rapid cuff inflator (E20 Inflator, Hokanson, Bellevue, Washington) set to >100 mmHg suprasystolic pressure. Ultrasound images were transferred to digital viewing software (Brachial Analyzer, Vascular Tools, Version 5, Medical Imaging Applications, Coralville, Iowa) where all diameters were analyzed by the same investigator (AED) who was not blinded to subject group assignment. An average of the three highest consecutive end-diastolic diameters after cuff release was calculated as the maximal diameter. One-way ANOVA and ANOVA with repeated measures and LSD adjustments were used to determine changes in FMD within and between groups over time (p < 0.05). One-tailed bivariate correlation and multiple linear regression of significantly correlated variables were used to determine relations between subject characteristics and the FMD response to IR injury (p < 0.05).

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Sedentary</th>
<th>Resistance-trained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>9/2</td>
<td>10/1</td>
</tr>
<tr>
<td>Age (year)</td>
<td>26 ± 2</td>
<td>25 ± 2</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>66 ± 3</td>
<td>79 ± 3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23 ± 1</td>
<td>26 ± 1</td>
</tr>
<tr>
<td>Total body lean mass (kg)</td>
<td>48 ± 2</td>
<td>62 ± 3</td>
</tr>
<tr>
<td>Right arm lean mass (kg)</td>
<td>2.9 ± 0.1</td>
<td>4.5 ± 0.3</td>
</tr>
<tr>
<td>Total body fat (%)</td>
<td>23 ± 4</td>
<td>18 ± 2</td>
</tr>
<tr>
<td>Heart rate at rest (bpm)</td>
<td>56 ± 2</td>
<td>56 ± 3</td>
</tr>
<tr>
<td>Systolic BP at rest (mmHg)</td>
<td>109 ± 2</td>
<td>116 ± 1</td>
</tr>
<tr>
<td>Diastolic BP at rest (mmHg)</td>
<td>63 ± 2</td>
<td>62 ± 1</td>
</tr>
<tr>
<td>Pulse pressure at rest (mmHg)</td>
<td>46 ± 1</td>
<td>54 ± 2</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>143 ± 10</td>
<td>183 ± 12</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>89 ± 9</td>
<td>116 ± 11</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>36 ± 2</td>
<td>42 ± 2</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>88 ± 14</td>
<td>115 ± 9</td>
</tr>
</tbody>
</table>

Values are mean ± SEM; BP, blood pressure. * p < 0.05 vs. sedentary.

### 2.1 Experimental results

All subjects were non-obese, normotensive and normolipidemic except for HDL-cholesterol in the young sedentary group (Table 1). As expected, resistance-trained subjects had higher levels of total lean body mass and right arm lean mass than their sedentary counterparts, but lean mass and reported physical activity were not associated with FMD at any time point. Before IR injury, FMD was not different between groups (Fig. 1). Fifteen minutes after ischemic injury, FMD significantly decreased by 36% in sedentary subjects (p = 0.04), but not in the resistance-trained group. One-tailed bivariate correlation revealed that HDL-cholesterol (r = 0.55, p < 0.01), handgrip strength (r = 0.60, p = 0.01) and systolic blood pressure (r = 0.37, p = 0.05) were significantly associated with, but in regression analyses did not significantly predict, FMD at 15 min after ischemia. No other subject characteristics were correlated with the change in FMD from baseline to 15 min after ischemia (15 min post FMD–before FMD). Both groups were fully recovered by 45 min after injury.

### 3. Discussion

The primary finding of this study is that habitual resistance exercise is associated with protection from endothelial IR injury in young adults. The present results are consistent with the notion that resistance exercise training may precondition the vasculature against IR injury. To the best of our knowledge, this is the first study to address this issue.

Repeated brief periods of controlled ischemia followed by brief periods of recovery, a phenomenon called “ischemic conditioning”, has been shown to attenuate tissue damage from subsequent IR injury in both animals and humans [1]. When remote ischemic conditioning is applied before (preconditioning) or after (postconditioning) IR injury in humans, vascular injury is attenuated in coronary and conduit arteries [3,4]. Resistance exercise is strikingly similar to remote ischemic conditioning. During resistance exercise, blood flow through the contracting muscle is briefly disrupted, causing temporary ischemia in downstream tissues when exercise intensities exceed 30% of maximal voluntary contraction [5]. When muscle contraction ends, reactive hyperemia is induced and blood flow is restored to the tissues. These repeated bouts of IR during daily resistance exercise sessions may exert conditioning effects on the vasculature. In this context, recent studies have found...
that brachial artery FMD was unaffected or improved after an acute bout of resistance exercise in strength-trained adults, but blunted in sedentary adults [6,7], suggesting that habitual resistance exercise may protect the endothelium against “stressors”.

Alternatively, increases in nitric oxide bioavailability from chronic resistance training may also preserve endothelial function after IR injury by decreasing free radical production and/or increasing antioxidant capacity [8,9]. Indeed, chronic resistance training may induce adaptations that lower circulating markers of oxidative stress and raise antioxidant levels [10,11]. However, unlike the beneficial effects of endurance exercise training on endothelial function, the effects of resistance training on endothelial function and FMD remain controversial. In young adults, 13 weeks of whole body resistance training did not alter brachial FMD [12] whereas six weeks of resistance training increased forearm perfusion [13]. Additionally, an 18-week resistance training intervention study with older post-menopausal women produced no changes in brachial FMD [14]. In the present study, resistance-trained subjects and sedentary subjects had similar FMD values before IR injury, which is likely a result of all subjects being young and healthy. The health and age of our population in addition to the method of measuring endothelial function (FMD versus plethysmography) may also explain why subjects in the present study were fully recovered from IR injury within 30 min unlike previous studies in healthy young and middle-aged, but not resistance-trained, adults [8,15].

Future studies should determine if the beneficial effects of habitual resistance exercise on endothelial IR injury in younger adults persists in studies involving a greater number of subjects and if these findings can be extended to aging and/or diseased populations. Moreover, the results of the present study must be confirmed in resistance exercise intervention studies.

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Conflict of interest

The authors declare that there is no conflict of interest.

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