Lack of age-related decreases in basal whole leg blood flow in resistance-trained men

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Mean and diastolic blood pressures were higher (P < 0.05–0.001) in the middle-aged compared with the young men, but there were no significant differences between the sedentary and resistance-trained groups. In the sedentary group, basal whole leg blood flow (duplex Doppler ultrasound) and vascular conductance were lower (−30 and −38%, respectively; P < 0.01) in the middle-aged compared with the young men. There were no such age-related differences in the resistance-trained group. In the young men, basal whole leg blood flow and vascular conductance were not different between the two activity groups, but, in the middle-aged men, they were higher (−35 and −36%, respectively; P < 0.01) in the resistance-trained men than in the sedentary men. When blood flow and vascular conductance were expressed relative to the leg muscle mass, the results were essentially the same. We concluded that the age-related reduction in basal whole leg blood flow is absent in resistance-trained men. These results suggest that resistance training may favorably influence leg perfusion in aging humans, independent of its impact on leg muscle mass.

BASAL WHOLE LEG BLOOD FLOW decreases progressively with advancing age in healthy men and women (9, 10, 23), which is related to corresponding reductions in leg fat-free mass and estimated leg oxygen demand (10). Reduced peripheral blood flow has been suggested to be mechanistically involved in the metabolic syndrome, a cluster of disease states that include hyperinsulinemia, dyslipidemia, and hypertension (18). Additionally, older adults appear to be limited in their ability to vasodilate in response to functionally demanding tasks and/or states, including dynamic exercise, energy intake, and heat stress (16, 19, 31). Accordingly, the prevention and treatment of the age-related reductions in basal leg blood flow are of great clinical importance.

Regular physical activity is regarded as an important component of prevention and treatment of cardiovascular disease (24) and functional disability (11). It is reasonable to hypothesize that habitual aerobic exercise exerts beneficial influence on basal peripheral blood flow. However, habitual aerobic exercise does not appear to modulate the age-related reductions in basal leg blood flow in healthy men (10). The lack of influence of regular aerobic exercise is presumably due to the fact that the key determinants of leg blood flow, i.e., leg fat-free mass, decreased similarly with advancing age in both sedentary and endurance-trained healthy men (28). Resistance training is an important part of preventive and rehabilitative program for the age-related loss in muscle mass and function (i.e., sarcopenia). Given this, it is plausible to hypothesize that habitual resistance training attenuates the age-related reduction in basal whole leg blood flow through its impact on leg skeletal muscle mass. Accordingly, the primary aim of the present cross-sectional study was to determine the relation between resistance training, leg muscle mass, and basal leg blood flow. We hypothesized that resistance training is associated with elevated leg perfusion in aging humans through its impact on leg skeletal muscle mass.

METHODS

Subjects

A total of 104 healthy men aged 20–34 yr (“young”) and 35–65 yr (“middle aged”) participated in the present study (Table 1). The sedentary subjects were recruited through various forms of advertisements and had not participated in a regular exercise program for at least the previous 2 yr. The resistance-trained men were recruited from various fitness clubs and had been performing vigorous resistance training for >2 yr. All resistance-trained men have been performing moderate- to high-intensity “full-body” resistance exercise involving large muscle groups. To better isolate the effect of resistance exercise training, those who had been concurrently performing regular aerobic exercise (i.e., “cross-training”) were excluded. All subjects were normotensive (<140/90 mmHg), nonobese, and free of overt chronic diseases as assessed by medical history, physical examination, and complete blood chemistry and hematological evaluation. Men aged >40 yr were further evaluated by ECG at rest and, along with blood pressure, during incremental treadmill exercise performed to exhaustion. Candidates who smoked in the past 4 yr, were taking medications, had ever used anabolic steroids or other performance-enhancing drugs, or had significant femoral intima-media thickening (IMT < 1.1 mm), plaque formation, and/or other characteristics of atherosclerosis [ankle-brachial index (ABI) < 0.90] were excluded. All subjects gave their written, informed consent to participate. All procedures were reviewed and approved by the Human Research Committee of the National Institute of Health and Nutrition.
the day-to-day reproducibility of the measurements for common tor, who was blinded to the identity of the subject. In our laboratory, liters per minute. The data reported were time averages of 10 mea-

Measurements

Before they were tested, subjects abstained from caffeine and fasted for at least 4 h (a 12-h overnight fast was used for determination of metabolic risk factors). Subjects were studied 20–24 h after their last exercise training session to avoid the immediate (acute) effects of exercise, but they were still considered to be in their normal (i.e., habitually exercising) physiological state.

Femoral blood flow. A duplex ultrasound machine (model 180Plus, Sonosite) equipped with a high-resolution (5–10 MHz) linear-array transducer was used to measure vessel diameter and blood velocity on the right common femoral artery, as previously described (9, 10). Femoral arterial diameter was determined by a perpendicular measure-

Table 1. Selected subject characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Young</th>
<th>Middle aged</th>
<th>Resistance Trained</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>30</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>Age, yr</td>
<td>26±1</td>
<td>50±2*</td>
<td>27±1</td>
</tr>
<tr>
<td>Height, cm</td>
<td>174±1</td>
<td>172±1</td>
<td>177±1</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.93±0.03</td>
<td>0.95±0.02</td>
<td>0.90±0.02</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>4.64±0.22</td>
<td>5.01±0.19</td>
<td>4.35±0.20</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/l</td>
<td>1.47±0.07</td>
<td>1.48±0.11</td>
<td>1.57±0.14</td>
</tr>
<tr>
<td>Plasma glucose, mmol/l</td>
<td>5.01±0.12</td>
<td>5.31±0.09*</td>
<td>4.90±0.11</td>
</tr>
<tr>
<td>Maximal heart rate, beats/min</td>
<td>193±2</td>
<td>177±3*</td>
<td>192±2</td>
</tr>
<tr>
<td>V˙O2max, l/min</td>
<td>3.0±0.1</td>
<td>2.9±0.1</td>
<td>3.7±0.1†</td>
</tr>
<tr>
<td>V˙O2max/body weight, ml·kg⁻¹·min⁻¹</td>
<td>42.3±1.6</td>
<td>36.9±1.4*</td>
<td>44.9±1.4</td>
</tr>
<tr>
<td>V˙O2max/LBM, ml·kg⁻¹·min⁻¹</td>
<td>51.4±1.7</td>
<td>50.2±1.6</td>
<td>53.6±1.4</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjects. V˙O2max, maximal oxygen consumption; LBM, lean body mass. *P < 0.05 vs. young. †P < 0.05 vs. sedentary of same age group.

Arterial blood pressure at rest. Chronic levels of arterial blood pressure at rest were measured with a semiautomated device (Form PWV/ABI, Colin Medical Technology) over the brachial and dorsalis pedis artery. Recordings were made in triplicate with subjects in the supine position. ABI was then calculated and was used as a measure of atherosclerosis in leg arteries.

Body composition. Body composition was determined by using dual-energy X-ray absorptiometry (DEXA; model DPX-IQ, Lunar Radiation) with subjects in the supine position. Leg tissue mass was determined using body landmark sites for the legs (i.e., from the femoral neck to the phalange tips). Leg skeletal muscle mass reported represents right leg lean soft tissue mass. The measurement of leg muscle and fat mass using DEXA has been well validated against other standards (12, 13). Waist circumference was measured at the narrowest part of the torso and was used as a surrogate measure of total abdominal fat.

Left ventricular function. Echocardiography was used to measure left ventricular (LV) function, according to established guidelines (7, 27). Stroke volume (SV) was measured from LV diastolic and end-systolic volumes calculated from LV internal dimensions (20). Cardiac output was derived as SV times heart rate. Total peripheral resistance was calculated by the following formula: brachial mean blood pressure/cardiac output.

Incremental exercise. To demonstrate that the subjects had been sedentary, we measured maximal oxygen consumption during an incremental cycle ergometer exercise (21). Oxygen consumption (CV = 4 ± 1%), heart rate, and ratings of perceived exertion were measured throughout the protocol (21).

Metabolic risk factors for coronary heart disease. To screen for the presence of coronary heart disease, fasting plasma concentrations of cholesterol and glucose were determined with enzymatic techniques (29).

Statistical Analyses

Data were analyzed by two-way ANOVA (age × physical activity status). In the case of a significant F value, a post hoc test using the Newman-Keuls method identified significant differences among mean values. Relations of interest were identified by univariate correlational and regresional analysis. All data are reported as means ± SE. Statistical significance was set a priori at P < 0.05 for all comparisons.

RESULTS

Selected subject characteristics are presented in Table 1. There was a >20-yr age difference between young and middle-aged subjects. There were no significant differences in height
among all four groups. Although all metabolic risk factors were well within clinically normal levels in all groups, total cholesterol and plasma glucose concentrations were higher ($P < 0.05$) in middle-aged compared with young groups. Average years of training were 4.2 ± 1.3 and 18.3 ± 2.4 yr ($P < 0.001$) in young and middle-aged resistance-trained men, respectively. There were no significant differences in training frequency (4.8 ± 0.4 and 4.6 ± 0.4 times/week) and duration (63 ± 12 and 52 ± 5 min/session) between young and middle-aged resistance-trained men.

As shown in Table 2, systolic blood pressure was similar among all groups. Mean and diastolic blood pressures were higher ($P < 0.05$) in the middle-aged compared with the young men; there were no significant differences between the sedentary and resistance-trained groups. Femoral arterial lumen diameter in the resistance-trained young and middle-aged men was larger ($P < 0.001$) than that in their sedentary peers. There were no significant differences in SV and cardiac output index among all four groups.

In the young men, basal whole leg blood flow, vascular conductance, and vascular resistance were not different between the two activity groups ($P = 0.08–0.09$). In the sedentary group, basal whole leg blood flow and vascular conductance were lower and vascular resistance was higher (all $P < 0.01$) in the middle-aged compared with the young men (Fig. 1). Moreover, basal whole leg blood flow and blood flow relative to the leg muscle mass were negatively related with age ($r = −0.39$ and $−0.30, P < 0.001$; Fig. 2, left). However, in the resistance-trained group, there were no age-related differences in basal whole leg blood flow and vascular conductance. Additionally, there were no relations between age and femoral blood flow in resistance-trained men ($r = −0.15$ and 0.05, not significant (NS); Fig. 2, right). Furthermore, basal whole leg blood flow and vascular conductance were higher and vascular resistance was lower ($P < 0.01$) in the resistance-trained middle-aged men compared with the sedentary middle-aged men. When basal blood flow, vascular conductance, and vascular resistance were expressed relative to the leg muscle mass, these results were essentially unchanged (Fig. 3).

Whole body mass and lean body mass were higher ($P < 0.01$) in resistance-trained men compared with their age-matched sedentary peers (Table 3). In the middle-aged men, body fat and waist-to-hip ratio of the resistance-trained group were smaller ($P < 0.01$) than those of the sedentary group. There were no significant differences in absolute right leg muscle mass between young and middle-aged men. As expected, leg muscle mass in the resistance-trained men was

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**Table 2. Cardiovascular measures**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sedentary</th>
<th>Resistance Trained</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young (Young)</td>
<td>Middle aged</td>
</tr>
<tr>
<td>Brachial systolic BP, mmHg</td>
<td>115 ± 2</td>
<td>119 ± 3*</td>
</tr>
<tr>
<td>Brachial mean BP, mmHg</td>
<td>83 ± 1</td>
<td>90 ± 2*</td>
</tr>
<tr>
<td>Brachial diastolic BP, mmHg</td>
<td>65 ± 1</td>
<td>74 ± 2*</td>
</tr>
<tr>
<td>Ankle-brachial index, units</td>
<td>1.12 ± 0.01</td>
<td>1.18 ± 0.02*</td>
</tr>
<tr>
<td>Femoral artery diameter, mm</td>
<td>9.0 ± 0.2</td>
<td>8.9 ± 0.2</td>
</tr>
<tr>
<td>Femoral artery IMT, mm</td>
<td>0.46 ± 0.01</td>
<td>0.53 ± 0.02**</td>
</tr>
<tr>
<td>Femoral artery MBV, cm/s</td>
<td>8.3 ± 0.5</td>
<td>6.7 ± 0.4*</td>
</tr>
<tr>
<td>Stroke volume, ml</td>
<td>89 ± 6</td>
<td>99 ± 4</td>
</tr>
<tr>
<td>Stroke volume index, ml/kg</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>5.2 ± 0.2</td>
<td>5.0 ± 0.3</td>
</tr>
<tr>
<td>Cardiac output index, ml/min⁻¹·kg⁻¹</td>
<td>74 ± 3</td>
<td>67 ± 3</td>
</tr>
<tr>
<td>TPR, mmHg·m⁻¹·kg⁻¹</td>
<td>16.1 ± 0.5</td>
<td>19.0 ± 1.1*</td>
</tr>
</tbody>
</table>

Values are means ± SE. BP, blood pressure; IMT, intima-media thickness; MBV, mean blood velocity; TPR, total peripheral resistance. *$P < 0.05$ vs. young. †$P < 0.05$ vs. sedentary of same age group.
significantly higher than that in their sedentary peers (P < 0.001).

In the pooled population, absolute leg muscle mass was significantly associated with whole leg basal blood flow (Fig. 4; r = 0.41, P < 0.001). Whole leg basal blood flow was not significantly related to cardiac output at rest (r = 0.19, NS).

DISCUSSION

The salient findings of the present study were as follows. First, basal whole leg blood flow in the resistance-trained middle-aged men was ~35% higher than in their sedentary healthy controls. Second, because the blood flow was not significantly different between sedentary and resistance-trained young men, the age-related decrease in the basal whole leg blood flow was greater in the sedentary men compared with the resistance-trained men. Third, when basal blood flow was expressed relative to the leg tissue mass and leg muscle mass, the results were essentially the same. These findings suggest that the age-related reduction in basal whole leg blood flow is absent in resistance-trained men independent of leg muscle mass.

Resistance training has become an integral component of exercise training programs for health and disease prevention (1, 2, 25, 30, 32). Because of the clinical and functional importance associated with basal leg blood flow, we initiated our effort to address the impact of resistance training on leg blood flow. As an initial approach to address this question, we used a cross-sectional study design. Because of the well-recognized limitations associated with this design (8), we attempted to isolate the influence of resistance training and aging as much as possible. To do so, resistance-trained men were carefully matched for age, height, brachial blood pressure, and metabolic risk factors compared with their sedentary counterparts. Additionally, in an attempt to isolate the effect of chronic resistance training per se, we excluded those who had been concurrently performing endurance training or those taking anabolic steroids or other performance-enhancing drugs. Our present results indicate that chronic resistance training is associated with higher whole leg basal blood flow in healthy middle-aged men. Nevertheless, the results of the present cross-sectional study need to be confirmed prospectively with the exercise intervention study in the future.

Because there was no age-related differences in leg muscle mass, it may be argued that a lack of age-related reductions in basal whole leg blood flow in resistance-trained men may be due to the examination of less trained and less elite young vs. middle-aged resistance-trained men and that, if the young subjects were highly resistance trained, it is possible that an age-related difference in basal leg blood flow would be observed in the resistance-trained group. However, in the present study, the young and middle-aged resistance-trained men were carefully matched for current training volume (training frequency and duration/session). Additionally, we believe that the resistance-trained men were homogeneous with regard to relative competitiveness, as their bench press one-repetition maximum strength (102 ± 9 and 87 ± 9 kg in young and middle-aged men, respectively) was matched for age-adjusted Masters power-lifting records (4). Ideally, the present cross-
sectional findings should be confirmed with prospective studies. However, because the latter studies will be difficult to perform, our cross-sectional results will probably remain unique in that they will provide the only currently available information on effect of resistance training on age-related reduction in basal leg blood flow.

Physiological mechanisms underlying the preserved basal leg blood flow in resistance-trained men are not clear. On the basis of the well-known coupling between blood flow and metabolism, we initially hypothesized that resistance-trained men would demonstrate a greater basal leg blood flow because of the larger skeletal muscle mass and the greater metabolic demands because both leg oxygen consumption and fat-free mass are strongly associated with whole leg blood flow (10). Consistent with these concepts, in the pooled population, leg muscle mass was significantly related to whole leg basal blood flow ($r = 0.41$). These findings suggest that absence of age-related decreases in whole leg basal blood flow in resistance-trained men is, at least in part, associated in the larger leg muscle mass. In the present study, however, there were no obvious differences in leg muscle mass between young and middle-aged men, and the magnitude of age-related reductions in leg muscle mass was similar between sedentary and resistance-trained men. Interestingly, when blood flow was expressed relative to leg muscle mass, the results remained essentially the same as whole leg blood flow (Figs. 2 and 3). These results suggest that not only quantitative but also qualitative changes in skeletal muscle and/or alterations in non-skeletal muscle components induced by resistance training may be responsible for an absence of age-related reduction in basal leg blood flow in resistance-trained men. In this context, resistance training is known to be a strong stimulus to increase leg skeletal muscle turnover (syntheses and degradation) (14) and basal metabolic demands (3) in older subjects, which may have acted to preserve leg blood flow independent of leg muscle mass. Leg oxygen demand was not measured in the present study, because it requires a highly invasive procedure involving both arterial and venous catheterizations, and this is an important limitation in this study.

Additional possibility for explaining group differences in leg blood flow is that a reduction in local (leg) blood flow may be

Table 3. Whole body and whole leg body composition

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sedentary</th>
<th>Resistance Trained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole body mass, kg</td>
<td>71.8±2.0</td>
<td>82.0±2.4†</td>
</tr>
<tr>
<td>Whole body fat, %</td>
<td>18±1</td>
<td>17±1</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>59.2±1.4</td>
<td>68.3±1.6†</td>
</tr>
<tr>
<td>Right leg total tissue mass, kg</td>
<td>12.3±0.4</td>
<td>14.1±0.5†</td>
</tr>
<tr>
<td>Right leg muscle mass, kg</td>
<td>9.6±0.3</td>
<td>11.2±0.3†</td>
</tr>
<tr>
<td>Right leg fat mass, kg</td>
<td>2.8±0.2</td>
<td>2.8±0.3</td>
</tr>
<tr>
<td>Right leg fat, %</td>
<td>19±1</td>
<td>18±1†</td>
</tr>
</tbody>
</table>

Values are means ± SE. *$P < 0.05$ vs. young. †$P < 0.05$ vs. sedentary of same age group.
a simple reflection of changes in systemic (total) blood flow (17). However, there were no obvious group differences in the cardiac output and total peripheral resistance, and no significant relation was found between cardiac output and basal whole leg blood flow. Age-related reductions in basal whole leg blood flow are associated with tonically elevated muscular sympathetic nerve activity that would result in vasoconstriction (9). However, sympathetic nerve activity is reported to be higher, rather than lower, in resistance-trained older adults than in sedentary controls (26). Together, these findings do not support the hypothesis that changes in systemic blood flow and sympathetic nerve activity contributed to the preserved leg blood flow in resistance-trained men in the present study. Clearly, further studies are warranted to determine physiological mechanisms underlying effects of resistance exercise on arterial hemodynamics.

The present findings have potentially important clinical and physiological implications. It is widely accepted that resistance training in middle-aged and older adults increases power, reduces the difficulty of performing daily tasks, and promotes participation in spontaneous physical activity (6, 15). The present findings extend the beneficial influence of resistance training to vascular function in the aging human, contributing to the preservation of basal whole leg blood flow with age. The reduction in leg blood flow may limit peripheral glucose uptake and contribute to glucose intolerance and hyperinsulinemia in middle-aged and older adults (18). Additionally, it may also impair the clearance of atherogenic lipids and contribute to chronic dyslipidemia (5). Daily resistance training may contribute to the lower incidence of cardiovascular disease through its influence on basal leg blood flow.

Our laboratory has previously reported that the repeated increases in blood flow due to exercise training are associated with expansive arterial remodeling in the femoral artery (21). Our present results extend these previous reports in endurance-trained men to resistance training. In the present study, resistance-trained men had larger femoral arterial diameter compared with sedentary counterparts. Taken together, these results suggest that both aerobic and resistance exercise appear to increase arterial remodeling in the femoral artery (21). Clearly, further studies are warranted to determine physiological implications. It is widely accepted that resistance training in middle-aged and older adults increases power, reduces the difficulty of performing daily tasks, and promotes participation in spontaneous physical activity (6, 15). The present findings extend the beneficial influence of resistance training to vascular function in the aging human, contributing to the preservation of basal whole leg blood flow with age. The reduction in leg blood flow may limit peripheral glucose uptake and contribute to glucose intolerance and hyperinsulinemia in middle-aged and older adults (18). Additionally, it may also impair the clearance of atherogenic lipids and contribute to chronic dyslipidemia (5). Daily resistance training may contribute to the lower incidence of cardiovascular disease through its influence on basal leg blood flow.

As illustrated in the present study as well as in other studies, age is an important factor for determining leg blood flow and hemodynamics. However, it should be noted that age explains only 10–20% of variance associated with leg blood flow. Thus many more aspects need to be critically analyzed in the future studies.

In summary, the age-associated reduction in basal whole leg blood flow did not occur in resistance-trained men, suggesting that daily weight training may prevent decreases in basal whole leg blood flow with advancing age. Importantly, preserved blood flow in resistance-trained men was independent of muscle mass. These results suggest that habitual resistance exercise may favorably influence leg perfusion and hemodynamics in the aging human.

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