Reduced leg blood flow during dynamic exercise in older endurance-trained men

DAVID N. PROCTOR, PETER H. SHEN, NIKI M. DIETZ, TAMARA J. EICKHOFF, LORI A. LAWLER, ETHAN J. EBERSOLD, DARRELL L. LOEFFLER, AND MICHAEL J. JOYNER

Department of Anesthesiology and General Clinical Research Center, Mayo Clinic, Rochester, Minnesota 55905

Proctor, David N., Peter H. Shen, Niki M. Dietz, Tamara J. Eickhoff, Lori A. Lawler, Ethan J. Ebersold, Darrell L. Loeffler, and Michael J. Joyner. Reduced leg blood flow during dynamic exercise in older endurance-trained men. J. Appl. Physiol. 85(1): 68–75, 1998.—It is currently unclear whether aging alters the perfusion of active muscles during large-muscle dynamic exercise in humans. To study this issue, direct measurements of leg blood flow (femoral vein thermodilution) and systemic arterial pressure during submaximal cycle ergometry (70, 140, and 210 W) were compared between six younger (Y: 22–30 yr) and six older (O: 55–68 yr) chronically endurance-trained men. Whole body O2 uptake, ventilation, and arterial and femoral venous blood-gas, catecholamine, and lactate determinations were also obtained. Training duration (min/day), estimated leg muscle mass (dual-energy X-ray absorptiometry; Y: 21.5 ± 1.2 vs. O: 19.9 ± 0.9 kg), and blood hemoglobin concentration (Y: 14.9 ± 0.4 vs. O: 14.7 ± 0.2 g/dl) did not significantly differ (P > 0.05) between groups. Leg blood flow, leg vascular conductance, and femoral venous O2 saturation were ~20–30% lower in the older men at each work rate (all P < 0.05), despite similar levels of whole body O2 uptake. At 210 W, leg norepinephrine spillover rates and femoral venous lactate concentrations were more than twofold higher in the older men. Pulmonary ventilation was also higher in the older men at 140 (+24%) and 210 (+39%) W. These results indicate that leg blood flow and vascular conductance during exercise are significantly lower in older endurance-trained men in comparison to their younger counterparts. The mechanisms responsible for this phenomenon and the extent to which they operate in other groups of older subjects deserve further attention.

EXERCISE PERFORMANCE declines with advancing age. Blood flow to active skeletal muscles is a potentially important factor in the decline in exercise performance associated with aging (8, 14–16, 18). During the performance of small-muscle-mass exercise such as handgripping, active muscle blood flow appears to be well preserved in healthy older humans (8). Similar findings have been reported in studies involving single-leg cycling (3) and unilateral or bilateral isolated knee extensions (14). However, in each case the size of the active muscle mass was substantially less than that recruited during conventional whole body exercise such as bicycling, walking, or running.

To our knowledge, only one investigation has examined the influence of age on active muscle blood flow during large-muscle-mass exercise in humans (34). In that study, Wahren et al. (34) reported that leg blood flow responses during upright leg cycling were 10–15% lower in older endurance-trained men compared with those reported in an earlier investigation of younger athletes (10). However, the cardiac output responses of older and younger endurance athletes at a given submaximal power output or whole body O2 uptake (VO2) appear to be similar (22, 28). This latter finding has often been interpreted to suggest that even during large-muscle-mass exercise, blood flow to exercising muscles should be well maintained with aging (31).

With this information as a background, the present study was designed to determine whether leg blood flow and vascular conductance during submaximal, large-muscle-mass exercise are reduced in older vs. younger humans. To do this, we made direct measurements of leg blood flow (femoral vein thermodilution) and systemic arterial pressure in younger (22–30 yr) and older (55–68 yr) chronically endurance-trained men during submaximal bouts of two leg cycle ergometry. Trained subjects were used rather than sedentary subjects to ensure that comparisons of leg hemodynamic and metabolic responses between the age groups would not be confounded by the normal age-related decline in physical activity or by differences in subject motivation and to ensure that the older subjects could be studied across a wide range of submaximal power outputs (i.e., at the same power outputs as the younger subjects). A secondary objective was to determine whether the relationships among leg VO2, power output, and whole body VO2 during dynamic exercise in older subjects are similar to those previously reported in younger subjects (6, 12, 19, 20). Our primary hypothesis was that leg blood flow and vascular conductance at a given power output would be lower in the older subjects as a result of augmented sympathetic restraint of vasodilation in the active (i.e., leg) muscles.

METHODS

Subject Screening

Six younger (22–30 yr) and six older (55–68 yr) chronically endurance-trained men volunteered to participate and completed the study. All were nonsmokers, and none were taking medications. Their exercise training histories were reviewed in detail by questionnaire and personal interview. Each of the subjects was chronically trained and successful in local and regional competitions, but none were elite-level competitors. The older men completed a graded treadmill test with 12-lead electrocardiograph (ECG) and blood pressure monitoring 1–2 wk before the invasive blood flow study to screen for occult cardiovascular disease. Overall, the subjects’ physical characteristics, training histories, and cycle ergometer peak VO2
Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Younger</th>
<th>Older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>27 ± 1</td>
<td>63 ± 2*</td>
</tr>
<tr>
<td>Height, cm</td>
<td>181 ± 2</td>
<td>179 ± 2</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>72.5 ± 3.6</td>
<td>78.5 ± 3.3</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>11.5 ± 1.3</td>
<td>21.0 ± 2.0*</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>64.3 ± 3.6</td>
<td>61.8 ± 2.2</td>
</tr>
<tr>
<td>Leg muscle, kg</td>
<td>21.5 ± 1.2</td>
<td>19.9 ± 0.9</td>
</tr>
<tr>
<td>VO2peak, l/min</td>
<td>4.28 ± 0.24</td>
<td>3.04 ± 0.13*</td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>14.9 ± 0.4</td>
<td>14.7 ± 0.2</td>
</tr>
<tr>
<td>Training yr</td>
<td>12 ± 2</td>
<td>18 ± 3</td>
</tr>
<tr>
<td>hr/wk</td>
<td>7 ± 1</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Mode</td>
<td>4 Runners</td>
<td>4 Runners</td>
</tr>
<tr>
<td></td>
<td>2 Cyclists</td>
<td>2 Cyclists</td>
</tr>
</tbody>
</table>

Values are means ± SE. Body composition variables were estimated by using dual-energy X-ray absorptiometry. Peak O2 uptake (VO2peak) was measured during upright cycle ergometry. Hemoglobin values are for venous blood measured at rest.

VO2peak levels (Table 1) are similar to those of younger and older male endurance athletes we recently studied (22). Five of the 12 subjects (3 older, 2 younger) had served as subjects in previous studies in our laboratory on related issues (22, 23). Subjects were informed of the risks of the study before giving written consent in accordance with the Mayo Clinic Institutional Review Board guidelines.

Subject Preparation

Subjects were instructed to eat a light breakfast (no caffeine) at least 3 h before arriving at the General Clinical Research Center on the morning of the leg blood flow studies. When the subject arrived, a venous blood sample was drawn to ensure that his hemoglobin concentration was adequate for repeated blood sampling (i.e., ≥12.9 g/dl). A dual-energy X-ray absorptiometry (DEXA) scan was also performed at this time to estimate the subject’s body fat percent and leg (i.e., entire lower extremity) muscle mass as described previously (23).

Catheterization of the femoral vein (for leg blood flow and venous blood sampling) and radial artery (arterial pressure and gases) was performed by using aseptic procedures and local anesthetic. After infiltration of 1% lidocaine into the right groin, an 18-gauge flexible single-lumen catheter (Cook royal flush II 4.0-French angiographic catheter) was inserted just below the inguinal ligament into the femoral vein and advanced ~10 cm distally. This infusion catheter was then opened and had 10 lateral side ports to facilitate mixing of the iced saline and femoral venous blood (20). A second 18-gauge catheter was then inserted 2–3 cm below the inguinal ligament and advanced ~5 cm proximally into the same femoral vein. A thermister (IT-18, Physitemp Instruments, Clifton, NJ) was subsequently introduced into this catheter. The catheter was then removed, leaving the thermister in the vein. The infusion catheter and the thermister were carefully secured into place with adhesive tape. Subsequently, a 20-gauge Teflon catheter (Arrow arterial catheterization set FA-04020) was inserted into the right radial artery under local anesthesia for arterial pressure measurements and blood sampling.

Measurements of Leg Blood Flow and Arterial Pressure

The constant infusion thermodilution technique (1, 20, 25) was used to measure leg blood flow. During exercise, iced saline (3–5°C) was infused for 10–15 s until femoral vein blood temperature had decreased to a stable level. The rate of saline infusion was adjusted with a roller-pump controller to achieve an ~1°C drop in femoral vein temperature at each workload. Thermister signals and saline bag weight changes (Grass displacement transducer FT10C) were displayed on personal computer-based WinDaq software, which enabled real-time observation of each measurement. Leg blood flow was calculated by using the thermal balance equation (20), which was doubled to give two-leg blood flow (l/min). Simultaneous recordings from the arterial pressure transducer (Baxter PX-MK99) were also displayed and recorded by using WinDaq. The arterial pressure transducer was zeroed at heart level for each subject. Mean arterial pressure (MAP) represents the true mean of the arterial waveform, and leg vascular conductance was calculated as leg blood flow/MAP.

Exercise Protocol

Before exercise, resting blood samples were collected with the subject supine and then 10–15 min after he was positioned on the bike seat. Exercise was performed on an electronically braked cycle ergometer (Lode Excalibur Sport) with toe clips, and the subject was not permitted to lean forward or stand. After a 5–10 min warm-up, subjects completed two continuous incremental exercise bouts (70, 140, and 210 W, 7–10 min at each power output). Approximately 15 min of light pedaling and rest separated the two incremental bouts. These three power outputs were chosen because preliminary studies indicated that these corresponded to “light” (~40% VO2peak), “moderate” (~65% VO2peak), and “very heavy” (~90% VO2peak) workloads in older endurance-trained men. These power outputs were also within the range of available reference values for younger male subjects (12, 13, 19, 20) and corresponded to “very light” (~30% VO2peak), “light” (~50% VO2peak), and “moderate” (~70% VO2peak) workloads in younger endurance-trained men. A large fan was placed in front of the subjects, and they were encouraged to drink water between bouts to ensure that they remained well hydrated.

Pulmonary gas exchange (VO2, CO2 production, minute ventilation (V̇E)) was monitored during the last 3–4 min of each submaximal power output by using an automated breath-by-breath system (21). Heart rates were measured with a five-lead ECG (CM-5) during the same time period. Blood flow and arterial pressure measurements (described in Measurements of Leg Blood Flow and Arterial Pressure) were obtained at least three times during each workload (at ~3, 5, and 7 min), and arterial and deep venous blood samples were obtained between the second and third flow measurement (at ~5–6 min).

Blood-Gas Measurements and Leg VO2 Calculations

The arterial and venous blood-gas samples (3 ml each) were collected anaerobically in heparinized plastic syringes, placed on ice, and analyzed within 15 min. Total hemoglobin, methemoglobin, and percent oxyhemoglobin saturation were measured by using an AV0X CO-oximeter (model 2000). Blood PO2, PCO2, and pH were analyzed by using an IL-1620 blood-gas analyzer. All blood-gas measurements were made at 37°C and corrected to the femoral vein blood temperature obtained immediately before blood sampling (12). Blood O2 content was calculated as [1.39 × corrected hemoglobin concentration x %O2 saturation] + [0.003 x blood PO2]. Leg arteriovenous O2 content difference was calculated as the difference between arterial and venous blood O2 content. Leg arteriovenous O2 content difference and leg blood flow (2 legs) were then multiplied to give leg VO2 (l/min).
Catecholamines and Lactate

Blood samples for arterial and venous plasma catecholamine concentrations (5 ml each) were measured by using high-performance liquid chromatography (4). Rate of norepinephrine spillover (net overflow) from the leg was calculated as described previously (29). Arterial and venous lactate concentrations (2 ml each) were also measured at each power output by using a standard enzymatic assay (catalog no. 735-10, Sigma Chemical). Approximately 200–250 ml of blood were collected from each subject over the course of the study.

Statistical Analysis

All data are presented as means ± SE. Leg blood flow and other primary-dependent variables (i.e., leg vascular conductance, plasma catecholamines) were reproducible across the two incremental exercise bouts (intraclass correlations > 0.98, P > 0.05). Therefore, it was decided to combine the data for the two incremental bouts before age-group comparisons were made. For most of the age-group comparisons, t-tests were conducted at each power output (70, 140, and 210 W) and where possible at baseline. Age-group comparisons at a given power output, rather than across power outputs (regression approach), were justified because whole body VO$_2$ at each of these power outputs was essentially identical in the two age groups (Table 2). The P ≤ 0.05 level was used for all statistical tests.

RESULTS

Systemic Responses

Table 2 shows the mean systemic responses to graded cycle ergometer exercise averaged across the two incremental bouts. At a given power output, whole body VO$_2$ was similar between age groups. Respiratory exchange ratio was similar in both groups except at 210 W, where it was higher in the older men. Pulmonary VE (l/min) was similar between groups at 70 W but was significantly higher at 140 (+24%) and 210 W (+39%) in the older men. The higher VE at 140 and 210 W in the older group resulted from their higher breathing frequency. No significant age differences were seen for heart rate or MAP.

Leg Blood Flow and Conductance Responses

Reproducibility. Leg blood flow measurements at a given power output (typically n = 3/subject) were highly reproducible, with coefficients of variation averaging between 5 and 7% for both age groups at each power output (i.e., 70, 140, and 210 W). Mean leg blood flow and MAP responses at a given power output were also reproducible across the two incremental exercise bouts in both age groups (i.e., intraclass correlations >0.98, P > 0.05). Therefore, it was decided to average the data for the two incremental bouts before age-group comparisons were made.

Age effects. At a given power output, absolute leg blood flow responses were ~20–30% lower in the older men (P < 0.05) during both trials (Fig. 1A). Values averaged 6.3, 10.2, and 13.2 l/min in the younger men but only 4.8, 7.5, and 10.2 l/min in the older men at 70, 140, and 210 W, respectively. Similarly, leg vascular conductances were reduced 26–30% in the older vs. younger men (Fig. 1B).

Blood Measurements (Table 3)

Blood gases. Arterial Po$_2$ along with O$_2$ saturation and content were maintained across all power outputs within normal levels in both age groups. By contrast, femoral vein O$_2$ saturation (Fig. 1C) and content at each power output were significantly lower in the older group. Consequently, leg arteriovenous O$_2$ content differences averaged ~2 ml/dl higher (P = 0.08–0.11) in the older group at these power outputs. Mean leg VO$_2$ responses tended to be lower in the older group (Table 3), but these differences did not reach statistical significance. Arterial PCO$_2$ was maintained at ~41 Torr during all three power outputs in the younger men but fell in the older men from an average of 37 Torr at 70 W to 33 Torr at 210 W.

Catecholamines and lactate. Baseline levels (i.e., seated rest before exercise; data not shown) of arterial and venous norepinephrine, epinephrine, and lactate concentrations were similar in the two groups. During exercise, norepinephrine spillover rates (Fig. 2A) and venous lactate concentrations (Fig. 2B) were not significantly different between the two age groups except at 210 W, where increases in both variables were larger in the older men.

DISCUSSION

The primary new finding of this study is that leg blood flow and vascular conductance during submaximal cycle ergometry are reduced substantially in fit older men relative to their younger counterparts. These results are not likely to be confounded by significant age differences in leg muscle mass, cycling experience, or arterial O$_2$-carrying capacity, because these variables were similar between these two groups of younger men.
and older men. Our findings are unique because they differ from those reported for exercise involving smaller muscle masses, where active muscle perfusion appears to be well preserved up to ~70 yr of age in healthy subjects (3, 8, 14–16).

Table 3. Blood measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Power Output, W</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial PO2, Torr</td>
<td>Younger</td>
<td>70   140 210</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>92  ±3 95  ±8</td>
</tr>
<tr>
<td>Arterial PCO2, Torr</td>
<td>Younger</td>
<td>41  ±2 41  ±2</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>37  ±1 33  ±1</td>
</tr>
<tr>
<td>Arterial O2 saturation, %</td>
<td>Younger</td>
<td>74  ±2 96  ±4</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>95  ±4 94  ±2</td>
</tr>
<tr>
<td>Arterial O2 content, ml/dl</td>
<td>Younger</td>
<td>20  ±0.5 21  ±0.5</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>20  ±0.5 20  ±0.5</td>
</tr>
<tr>
<td>Venous Po2, Torr</td>
<td>Younger</td>
<td>25  ±1 23  ±1</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>18  ±1 18  ±1</td>
</tr>
<tr>
<td>Venous PCO2, Torr</td>
<td>Younger</td>
<td>60  ±3 71  ±5</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>57  ±1 67  ±2</td>
</tr>
<tr>
<td>Venous O2 saturation, %</td>
<td>Younger</td>
<td>36  ±2.3 23  ±1.2</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>21  ±0.3 16  ±1.6</td>
</tr>
<tr>
<td>Venous O2 content, ml/dl</td>
<td>Younger</td>
<td>7.2  ±0.4 4.9  ±0.2</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>4.4  ±0.7 3.4  ±0.4</td>
</tr>
<tr>
<td>Arteriovenous O2 difference, ml/dl</td>
<td>Younger</td>
<td>13.4  ±0.8 15.2  ±0.9</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>15.8  ±0.7 17.4  ±0.7</td>
</tr>
<tr>
<td>Leg VO2, l/min</td>
<td>Younger</td>
<td>0.94  ±0.14 1.95  ±0.20</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>0.75  ±0.04 1.76  ±0.09</td>
</tr>
<tr>
<td>Leg O2 extraction, %</td>
<td>Younger</td>
<td>65.8  ±2.9 75.5  ±1.3</td>
</tr>
<tr>
<td></td>
<td>Older</td>
<td>78.1  ±3.4 83.8  ±1.8</td>
</tr>
</tbody>
</table>

Values are means ± SE for 4 younger and 6 older subjects except where indicated (*6 subjects) and represent steady-state responses averaged over 2 bouts for each workload. Arterial and venous measurements represent radial artery and femoral vein samples, respectively. All blood gases are corrected for venous blood temperature. Formulas used to compute leg VO2 and O2 extraction are given in the text. *Significant difference vs. younger group, P < 0.05.

Our results quite consistently indicate that the fit older men studied had ~25% lower leg blood flows at the three submaximal work rates assessed. Because of the cross-sectional design of this study, we cannot entirely rule out the possibility that these age-group comparisons might reflect genetically influenced adaptations to training in either of the two groups. Differences in skeletal muscle plasticity in response to exercise training at a given age are also a possibility because the older men were not continuously active in endurance sports throughout their adulthood (i.e., average age of commencing endurance training was ~45 yr; Table 1). However, we attempted to minimize these and other potential influences by recruiting nonelite younger and older subjects with similar endurance training habits over at least the past 5- to 10-yr period (e.g., training mode and hours per week, Table 1). Both groups of subjects also had similar results in age-group competitions that placed them in the “good” but not “elite” category. Five of the six older subjects also indicated involvement in high school and/or college sports. Thus the question of “nature or nurture” probably has limited relevance to the findings of this study.

Validity of Leg Blood Flow Results

We are confident that the blood flow differences detected between these two age groups are valid for the following reasons. First, before conducting this study we constructed a hydraulic model to validate our saline infusion system against volume displacement. Second, the present in vivo results are based on direct measure-
ments of leg blood flow that are highly reproducible in our laboratory (within-trial coefficient of variation 5–7%). Third, the magnitude of the age difference in this study is substantially larger than the reported technical variability (5–10%) of the technique (12, 13, 20). Fourth, the blunted leg blood flow response in the older men was observed during both incremental bouts, indicating that this is a reproducible difference. Fifth, blood flow to the legs at 140 W (whole body \( \dot{V}O_2 \) of 2.1 l/min) averaged, 10 l/min in the younger men, which is nearly identical to values previously reported (19, 32, 34). Finally, our calculated leg \( \dot{V}O_2 \) values (Table 3) are consistent with what is considered a physiologically valid range (i.e., 60–75% of whole body \( \dot{V}O_2 \); Refs. 19, 20) in the absence of an absolute "gold standard" for comparison. The leg \( \dot{V}O_2 \) values for our younger subjects are nearly identical to values previously reported (19, 20).

Normal aging is associated with changes in vascular compliance and possibly other physical properties of human blood vessels (33). However, we see nothing about aging per se that invalidates the assumptions of femoral vein thermodilution for assessing limb blood flow in healthy older humans. For example, the drop in blood temperature during the iced-saline infusion period occurs rapidly (5–10 s) and is primarily dependent on adequate mixing of saline with blood. In addition, there are no major age-dependent differences in viscosity (i.e., hematocrit; Ref. 5) or other physical properties of human blood that would be expected to alter the specific heat constant (0.92) used in the equation for calculating blood flow (1). The possibility that atherosclerotic vascular disease might somehow impact thermodilution measurements of leg blood flow is also remote considering that venous infusion and sampling were used and that the subject population we studied consisted of healthy and fit older subjects. Finally, it should also be noted that Magnusson et al. (14) used essentially the same technique and reported no age-associated differences in leg blood flow during small-muscle-mass exercise (isolated knee extensions).

Our findings are in general agreement with the study of Wahren et al. (34), who used a different (indocyanine green dilution) technique to measure leg blood flow during cycle ergometry in trained 52- to 59-yr-old men. Their reported age-associated differences in leg blood flow were 10–15% lower in comparison to younger historical controls (10). As in the present study, they found significantly larger exercise-induced increases in femoral arteriovenous \( O_2 \) difference in the older vs. younger subjects. This latter measurement provides an independent indication that leg blood flow is reduced during cycle ergometry in fit older men.

Potential Mechanisms

The lower absolute levels of leg blood flow in the older men did not appear to be attributable to a significant age-associated loss of total limb muscle mass, at least as estimated by using DEXA. However, it is possible that an age-related preferential atrophy or loss of fast-twitch (type II) muscle fibers might alter the quantity of active muscle or motor unit recruitment patterns during exercise in humans (2). However, even in the absence of any age differences in total muscle mass or insight into muscle recruitment patterns, it seems reasonable to speculate that the percentage of leg muscle mass recruited by the older men at a given work rate was at least the same or higher than it was in the younger men because of the differences in relative work intensity (i.e., higher \%\( \dot{V}O_2 \)peak in older men at a given work rate). Collectively, these observations argue against the possibility that quantity of active muscle during cycle ergometry is significantly less in fit older men, at least to the degree that it may explain the large (i.e., 25%) differences in leg blood flow compared with younger men having a similar training background.
It is also unlikely that the reduced leg blood flows seen in the older men of the present study can be attributed to age differences in systemic cardiac output. This is because we (22) and others (28) have shown that the cardiac output-VO$_2$ relationship during submaximal cycle ergometry is well maintained with age in endurance-trained subjects. Additionally, there is no evidence that maximal vasodilatory capacity of the leg muscles is reduced in endurance-trained older men. Martin et al. (15, 16) have reported that the magnitude of hyperemia after ischemic calf exercise (toe raises) is the same in endurance-trained younger and older men. We also observed this in a subset of subjects from the present study (unpublished observations). These findings are consistent with the observation that capillary density is similar in the leg muscles of younger and older endurance-trained men (24). Muscle blood flow is also reportedly similar in fit younger and older men during submaximal contractions with small-muscle groups (14). Finally, blood flow to the legs of the older men did not appear to be limited by arterial perfusion pressure because there were no significant age-group differences in systemic arterial pressure at any of the three work rates studied. Collectively, these observations indicate that the older subjects had sufficient muscle mass, cardiac output reserve, and peripheral vasodilatory capacity to achieve the blood flow values seen in the younger subjects but that blood flow was somehow limited in these older subjects during two-leg cycle ergometry.

The reduced blood flow in the older subjects was associated with a reduced vascular conductance. These age differences were roughly the same across the three workloads studied (all 20–30% lower in older men; Fig. 18). The blunted vasodilation in these older men could be due to either reduced vascular responsiveness to local vasodilator substances or less release of such substances at a given workload. We have no direct evidence for either of these possible mechanisms, but the fall in pH and rise in lactate were much higher in the older men at 210 W, suggesting an augmented vasodilatory stimulus at this workload. The increased norepinephrine spillover in the older subjects at 210 W raises the possibility that sympathetic restraint of active muscle blood flow (30) also contributed to the reduced vasodilation of these subjects at this "very heavy" workload.

Finally, it could be argued that the blood flow "deficit" seen in the older men is simply an appropriate hemodynamic response given the age difference in relative exercise intensity. During dynamic exercise, blood pressure and regional vascular resistance (each determinants of organ blood flow) are thought to be regulated according to the relative, rather than absolute, work intensity (26). In this regard it is interesting that the mean levels of MAP were nearly identical in the two groups when comparisons were made at a similar relative work intensity (i.e., 210 W for younger vs. 140 W for older; ~65–70% VO$_2$peak). However, the leg blood flow values averaged 13.2 l/min in the younger men at 210 W vs. only 7.5 l/min in the older subjects at 140 W. Where is the Extra Blood Flow Going?

As indicated in Potential Mechanisms, we and others have reported that the absolute level of cardiac output at a given submaximal VO$_2$ (≤70% of VO$_{2\text{peak}}$) during cycle ergometry is well maintained in the older endurance-trained subject. If so, then a significant amount of flow not reaching the exercising leg muscles must be distributed to other regional circulations. Saltin (28) originally raised this question and suggested that older trained athletes might shunt more blood to the skin. However, Kenney and co-workers (11) have recently demonstrated that older fit men actually shunt less blood flow to the skin during exercise and/or heat stress compared with younger subjects.

During exercise, visceral blood flow (i.e., renal and splanchnic circulations) decreases in an intensity-dependent manner because of increased sympathetic nervous activity to this region (26). Ho et al. (7) recently reported that fit older men shunt less blood flow away from their splanchnic and kidney circulations than younger control (i.e., untrained) subjects do during exercise and/or heat stress. This suggests that fit older men may experience less visceral vasoconstriction during exercise than younger men do (i.e., less blood is being shunted away from the visceral organs to the exercising leg muscles in the older men), even though venous plasma norepinephrine spillover rates at a given workload increase with age (17). This could account for some (perhaps 0.5–1.0 ml/min; Refs. 7, 11, 28), but not all, of the leg blood flow deficit.

The finding that pulmonary ventilation was significantly higher in the older men at the two highest work rates suggests that some of the "extra" blood flow may be directed to the respiratory muscles. The higher ventilations seen in the older men at 140 and 210 W probably result from an age-associated increase in the dead space-to-tidal volume ratio and increased ventilatory drive associated with greater acidosis at a given absolute power output. The reduced chest wall compliance of older subjects would also tend to increase their work of breathing at any given level of ventilation (e.g., 70 W) (9). The increased demand for respiratory muscle blood flow in exercising older humans may result in greater competition between respiratory and locomotor muscles for blood flow. In this context, the higher ventilation in the older men at 210 W would conservatively require 200 ml more O$_2$ per minute (see Fig. 5.8 of Ref. 9). This additional O$_2$ cost would require on the order of ~1–1.5 l/min more blood flow (assuming ~6 liters blood flow per liter VO$_2$). If anything, these calculations would probably underestimate the extra blood flow requirements of breathing in older subjects due to mechanical factors affecting their work of breathing (9).

The existence of such a respiratory muscle "steal" phenomenon during exercise has recently been demonstrated in younger male athletes with respiratory muscle loading and unloading. Harms et al. (6) reported that unloading the respiratory muscles at maximal exercise via proportional-assist ventilation in-
creased leg blood flow and reduced norepinephrine spillover in younger trained men, whereas respiratory muscle loading elicited the opposite responses. However, it is unclear what regulatory mechanism that governs sympathetic outflow to muscle would be engaged by these maneuvers.

The high ventilatory demands associated with large-muscle mass exercise could also explain why we observed an age-associated reduction in leg blood flow, whereas Magnusson et al. (14) did not. In that study, leg blood flow responses during knee-extensor exercise were the same in physically active older and younger men. However, it is likely that the demand for respiratory muscle blood flow is far less during the knee extension exercise model than it is during conventional cycle ergometer exercise. Taken together, a blunted skin blood flow response to exercise, reduced shunting from visceral organs (e.g., 0.5–1.0 l/min), and increased blood flow to respiratory muscles (e.g., 1–1.5 l/min) could theoretically account for a substantial amount of the leg blood flow deficit seen in the older men in the present study (i.e., 2–3 l/min).

Summary

The findings of this study demonstrate that perfusion of the leg muscles during conventional cycle ergometry is significantly lower in older chronically endurance-trained men in comparison to their younger counterparts. A variety of mechanisms that might be responsible for this observation have also been discussed. The potential mechanisms responsible for the age-associated differences in leg blood flow observed in fit older and younger men and their possible impact on muscle blood flow regulation and exercise tolerance in other groups of older subjects deserve further investigation.

We thank each subject for enthusiastic participation. We thank Drs. Peter Wagner, Russell Richardson, and Jerome Dempsey for their helpful recommendations during the process of setting up the femoral vein thermodilution technique. We also acknowledge Dr. John Halliwill for setting up the WinDaq data-acquisition system, Paul Odenbach for assisting with preparation of tables and figures, J anet Beckman for secretarial assistance, and Dr. Bruce Johnson for helpful advice. Finally, we appreciate the efforts of the Mayo Clinic General Clinical Research Center staff for the screening and follow-up care of our subjects and the General Clinical Research Center immunochemical core laboratory for performing the blood catecholamine and lactate assays. This study was supported by National Institutes of Health Grants HL-46493, NS-32352, RR-00585-25, and RR-00585-2452 and by the Glen L. and Lyra M. Ebling Cardiology Research Endowment. Address for reprint requests: D. N. Proctor, Anesthesia Research, Mayo Clinic, 200 First St. SW, Rochester, MN 55905 (E-mail: proctor.david@mayo.edu).

Received 5 November 1997; accepted in final form 10 March 1998.

REFERENCES


