Expanded blood volumes contribute to the increased cardiovascular performance of endurance-trained older men

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Expanded blood volumes contribute to the increased cardiovascular performance of endurance-trained older men. J. Appl. Physiol. 85(2): 484–489, 1998.—To determine whether expanded intravascular volumes contribute to the older athlete’s higher exercise stroke volume and maximal oxygen consumption (VO2max), we measured peak upright cycle ergometry cardiac volumes (99mTc ventriculography) and plasma (125I-labeled albumin) and red cell (NaCr51) volumes in 7 endurance-trained and 12 age-matched lean sedentary men. The athletes had ~40% higher VO2max values than did the sedentary men and larger relative plasma (46 vs. 38 ml/kg), red cell (30 vs. 26 ml/kg), and total blood volumes (76 vs. 64 ml/kg) (all P < 0.05). Athletes had larger peak cycle ergometer exercise stroke volume indexes (75 vs. 57 ml/m², P < 0.05) and 17% larger end-diastolic volume indexes. In the total group, VO2max correlated with plasma, red cell, and total blood volumes (r = 0.61–0.70, P < 0.01). Peak exercise stroke volume was correlated directly with the blood volume variables (r = 0.59–0.67, P < 0.01). Multiple regression analyses showed that fat-free mass and plasma or total blood volume, but not red cell volume, were independent determinants of VO2max and peak exercise stroke volume. Plasma and total blood volumes correlated with the stroke volume and end-diastolic volume changes from rest to peak exercise. This suggests that expanded intravascular volumes, particularly plasma and total blood volumes, contribute to the higher peak exercise left ventricular end-diastolic volume, stroke volume, and cardiac output and hence the higher VO2max in master athletes by eliciting both chronic volume overload and increased utilization of the Frank-Starling effect during exercise.

Plasma volume; red cell volume; total blood volume; body composition; stroke volume; cardiac output

MAXIMAL CARDIOVASCULAR (CV) performance decreases with age, as evidenced by the decline in maximal oxygen consumption (VO2max) of 8–10% per decade after the age of 25 yr (e.g., Refs. 8, 15, 28). However, numerous studies indicate that older endurance-trained athletes have substantially higher VO2max values than do their sedentary peers (7, 8, 16–19, 22, 23). Additional cross-sectional studies indicate that a larger maximal stroke volume and maximal cardiac output are responsible in part for the higher VO2max in endurance-trained older athletes (6, 7, 15, 17, 24, 26).

Considerable evidence (5, 6, 24) indicates that the increased maximal stroke volume evident with training in older men is the result of increased left ventricular end-diastolic volume (LVEDV) and hence preload. One mechanism by which endurance training may enhance venous return and left ventricular (LV) filling is via an increase in intravascular volumes. Coyle and co-workers (3) and Hopper and co-workers (9) showed that acute plasma volume expansion in young untrained individuals results in an increase in submaximal exercise stroke volume and VO2max and that the cessation of training in young individuals is accompanied by decreases in plasma volume, submaximal exercise stroke volume, and VO2max. Furthermore, endurance exercise training increases plasma volume in young people (2).

Plasma, red cell, and total blood volumes tend to be lower in older than in younger individuals matched for body composition and physical activity habits (4). Previous research examining the effects of exercise training on intravascular volumes in older persons was performed in mixed groups of men and women (1) or in women with different hormonal-replacement habits (27). In addition, neither of these studies evaluated the relationships between intravascular volumes and CV hemodynamics during maximal exercise.

The present study was designed to test the hypothesis that plasma, red cell, and total blood volumes differ between endurance-trained and sedentary older men and that these differences are directly related to the higher levels of peak CV performance in older athletes. Results consistent with this hypothesis would imply that expanded intravascular volumes contribute to the higher VO2max and maximal stroke volume that are evident in endurance-trained older men.

METHODS

Older men were recruited into master athlete and lean sedentary groups as defined in Initial screening. Subjects provided written informed consent to participate after the protocol and its risks were described to them. The study protocol was approved by the Institutional Review Boards of the Johns Hopkins University and the University of Maryland Schools of Medicine.

Initial screening. Subjects initially completed medical and physical activity history questionnaires. They underwent a
physical examination, screening blood chemistry, and maximal treadmill exercise test (13). Those with renal, hematologic or liver disease, diabetes, hyperlipidemia, or CV symptoms, hypotension, major arrhythmias, or \(\geq 0.1\) mV S-T segment depression on maximal exercise testing were excluded from the study.

The seven master athletes (age 51–67 yr) trained regularly and competed in local races; one was competitive at the national level. They were studied at the peak of their competitive season. None of the master athletes competed in middle- or long-distance running when they were young. Four of them had been involved in high school team sports. The remaining three had not been athletes in their youth. The master athletes had trained continuously for 9 ± 10 yr, with only one training continuously since his youth. At the time of the study they trained 5 ± 1 (SD) days/wk (range 4–7 days/wk). All master athletes ran as their primary form of training, averaging 53 ± 18 km/wk (range 40–81 km/wk). The three master athletes who were triathletes also trained by swimming 6 ± 2.5 km/wk (range 3–8 km/wk) and cycling 110 ± 12 km/wk (range 97–121 km/wk).

Twelve lean men of the same age range as the master athletes were also studied as a comparison group. They had not participated in regular endurance exercise training, defined as \(>15\) min of exercise three times per week at a continuously elevated heart rate, for at least 1 yr. All had \(<25\)% body fat as determined by hydrodensitometry (see Body composition assessment).

\(\dot{V}O_2\max\) assessment. Subjects underwent a progressive treadmill exercise test to measure their \(\dot{V}O_2\max\) (13). The master athletes and sedentary men were tested by using running and walking protocols we reported previously (7, 8). Oxygen consumption (\(\dot{V}O_2\)) was measured continuously during the test with a computerized system incorporating a mixing chamber, Applied Electrochemistry oxygen and carbon dioxide analyzers, and a Rayfield dry gasmeter. To ensure that a true \(\dot{V}O_2\max\) was achieved, three of the following criteria had to be achieved: \(<0.1\) l/min increase in \(\dot{V}O_2\) for the final change in work rate (leveling-off criterion), a maximal heart rate \(>95\)% of age-predicted maximal, a final respiratory exchange ratio \(>1.10\), and a predicted oxygen cost of the final work rate \(>\)measured \(\dot{V}O_2\). If these criteria were not met, additional \(\dot{V}O_2\max\) tests were performed.

Body composition assessment. Body composition was measured by underwater weighing (11) with use of a stainless steel tank and a load cell interfaced to a computerized system incorporating a high-sensitivity, parallel-hole collimator and a computer interfaced to a standard Anger camera interfaced with a customized software. Each subject underwent underwater weighing trials during a single session until greater than or equal to three values agreed to within 0.1 kg; these values were then averaged and used as the subject’s underwater weight. Underwater weight was corrected for residual volume, measured by helium equilibration (14), and percent body fat was calculated by using the Siri equation (25). Fat-free mass (FFM) was calculated by subtracting each subject’s fat mass from his total body mass.

Blood volume determinations. Subjects reported to the laboratory in the morning after an overnight fast. Subjects were instructed not to exercise for 24–36 h before these studies. Plasma volume was determined by measuring the dilution of intravenously injected \(^{125}\)I-labeled human serum albumin (10). Blood samples were drawn 10, 20, and 30 min after the injection. The net counts per minute of these samples were plotted on a semilogarithmic scale and extrapolated to time 0. This extrapolated time 0 count value was used to calculate plasma volume based on the relative dilution of the original injected label (26).

Table 1. Physical characteristics of the two groups of subjects

<table>
<thead>
<tr>
<th></th>
<th>Master Athletes (n = 7)</th>
<th>Older Lean Sedentary Men (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>56.0 ± 5.6</td>
<td>58.4 ± 3.6</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>70.5 ± 7.3</td>
<td>76.5 ± 6.6</td>
</tr>
<tr>
<td>%Body fat</td>
<td>15.9 ± 4.7</td>
<td>19.5 ± 4.9</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>59.3 ± 7.4</td>
<td>61.6 ± 5.4</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.86 ± 0.11</td>
<td>1.92 ± 0.11</td>
</tr>
<tr>
<td>(\dot{V}O_2\max, l/min)</td>
<td>3.60 ± 0.43*</td>
<td>2.60 ± 0.28</td>
</tr>
<tr>
<td>(\dot{V}O_2\max, ml·kg⁻¹·min⁻¹)</td>
<td>51.3 ± 5.1*</td>
<td>34.2 ± 4.3</td>
</tr>
<tr>
<td>(\dot{V}O_2\max, ml·kg⁻¹·FFM⁻¹·min⁻¹)</td>
<td>61.0 ± 6.2*</td>
<td>45.2 ± 5.4</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. \(\dot{V}O_2\max\), maximal O₂ consumption; FFM, fat-free mass. *Significantly different from older lean sedentary men, \(P < 0.01\).

To determine red cell volume, 10 ml of each subject’s blood was withdrawn into a syringe containing 2 ml acid citrate dextrose (ACD) solution. This blood was then added to 30 \(\mu Ci\) NaCr\(^{51}\). After 15 min of incubation of this solution, 50 mg ascorbic acid were added and the solution was again allowed to incubate at room temperature for 3 min. Another 10-ml sample of venous blood was then obtained for measurement of background radioactivity, and 5 ml of the ACD-blood-NaCr\(^{51}\) ascorbic acid solution were reinjected into the subject. Blood samples were drawn from the opposite arm 30, 60, and 90 min after the injection. Red cell volume was calculated on the basis of the dilution of the reinjected labeled red blood cells (10). Total blood volume was calculated as the sum of plasma volume and red cell volume. Plasma, red cell, and total blood volumes were expressed in absolute terms (liters) and after normalization for body weight (ml/kg) and for FFM (ml/kg FFM).

Exercise gated blood pool scans. All subjects underwent a progressive exercise protocol to exhaustion while seated upright on a cycle ergometer as previously described (21). Briefly, exercise began at a work rate of 25 W and increased by 25 W every 3 min until the subject was no longer able to maintain a pedal rate of 60 rpm. Gated blood pool scans were obtained at seated rest and during the last 2.5 min of each 3-min exercise stage in an \(40°\) left anterior oblique position after in vivo labeling of red blood cells with 25–30 mCi \(^{99m}\) Tc (21). The data reported are from upright seated rest and the highest (peak) work rate each subject achieved. Images were obtained by using a high-sensitivity, parallel-hole collimator attached to a standard Anger camera interfaced with a
commercial nuclear medicine computer system. All participants had normal regional LV wall motion throughout exercise. Calculation of LV volumes was performed with validated methods described in detail previously (12). Absolute LV volumes were computed based on the ratio of the attenuation-corrected count rate from the gated study to the count rate per milliliter of a sample of venous blood.

Statistics. All values are expressed as means ± SD. Significant differences between the endurance-trained and sedentary men were assessed by unpaired t-tests (20). Pearson product-moment correlation coefficients were determined to assess relationships between selected physiological variables. Multiple linear regression analyses were performed to determine the independent contributions of blood volumes and FFM to V˙O2max and stroke volume (20). A two-tailed P < 0.05 was accepted as statistically significant for all comparisons and relationships.

RESULTS

The master athletes and lean sedentary men were of similar age, weight, body fat, FFM, and body surface area (Table 1). V˙O2max normalized for body weight or expressed in absolute values or normalized for FFM was ~40% greater in the master athletes.

Both groups had similar hematocrits (Table 2). Plasma, red cell, and total blood volumes normalized for body weight were 15–20% larger in the master athletes compared with the lean sedentary men (all P < 0.05). When data were normalized for FFM, total blood volume was significantly greater in the athletes, and the plasma and red cell volume differences approached statistical significance. The master athletes had 5–10% larger plasma, red cell, and total blood volumes expressed in absolute terms, but these differences were not significant. Plasma volume normalized for body weight in the entire population of men correlated significantly with both red cell (r = 0.60, P = 0.006) and total blood volume (r = 0.96, P = 0.0001). Furthermore, red cell volume correlated significantly with total blood volume (r = 0.81, P = 0.0001).

V˙O2max normalized for body weight was correlated directly with total blood volume and each of its components, expressed per kilogram of body weight (Fig. 1). FFM also correlated positively with absolute plasma (r = 0.59), red cell (r = 0.61), and total blood volumes (r = 0.64) (all P < 0.01). In multiple regression analyses, FFM and plasma or total blood volumes were independent determinants of V˙O2max with red cell volume approaching significance (Table 3).

During upright seated rest before the cycle ergometer exercise test, the master athletes had a lower heart rate and a larger stroke volume index and LVEDV index than did the sedentary men (Table 4). Heart rate and blood pressures during peak cycle ergometer exercise did not differ between the groups (Table 4). However, stroke volume and cardiac indexes at peak exercise were both significantly larger in the master athletes than in the sedentary men. Furthermore, the increase in stroke volume from rest to peak exercise was significantly greater in the athletes.

There were strong positive relationships between peak cycle ergometer exercise stroke volume and each of the blood volumes (Fig. 2). In multiple regression analyses, stroke volume normalized for body weight was independently and significantly related to FFM and plasma or total blood volume but not to red cell volume (Table 5). Overall, these models accounted for 57–60% of the variance in peak exercise stroke volume. The change in stroke volume that occurred from rest to peak cycle ergometer exercise in the total group of subjects also correlated significantly with total blood volume (r = 0.64, P = 0.003), plasma volume (r = 0.60, P = 0.007), and red cell volume (r = 0.55, P = 0.01).

LVEDV index during peak cycle ergometer exercise was 17% higher in the master athletes, but this difference only approached statistical significance. In addition, LVEDV tended to increase and LV end-systolic stroke volume tended to decrease more from rest to peak exercise in the athletes compared with the sedentary men, although neither of these differences reached significance. In the total sample, LVEDV during peak

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Table 3. Multivariate regression determinants of V˙O2max (ml·kg⁻¹·min⁻¹)

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>Partial r²</th>
<th>Probability</th>
<th>Model r²</th>
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<tbody>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>Red cell volume</td>
<td>0.93</td>
<td>0.18</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Plasma volume</td>
<td>0.66</td>
<td>0.29</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Fat-free mass</td>
<td>-0.69</td>
<td>0.34</td>
<td>0.015</td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
<td></td>
<td>0.59</td>
</tr>
<tr>
<td>Total blood volume</td>
<td>0.74</td>
<td>0.60</td>
<td>0.0002</td>
<td></td>
</tr>
<tr>
<td>Fat-free mass</td>
<td>-0.70</td>
<td>0.35</td>
<td>0.01</td>
<td></td>
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</tbody>
</table>

Blood volumes are normalized for body weight; fat-free mass is expressed in kg. All values are adjusted for all other terms in the models.
cycle ergometer exercise correlated positively with plasma \( r = 0.53 \), \( P = 0.02 \) and total blood volumes \( r = 0.45 \), \( P = 0.05 \) but not with red cell volume \( r = 0.18 \), \( P = 0.47 \). The change in LVEDV from rest to peak cycle ergometer exercise was related to plasma volume normalized for body weight \( r = 0.51 \), \( P = 0.03 \), but was only marginally related to total blood volume \( r = 0.40 \), \( P = 0.09 \), and did not correlate with red cell volume \( r = 0.09 \), \( P = 0.72 \).

**DISCUSSION**

A number of studies indicate that older endurance-trained athletes have markedly higher \( VO_2_{max} \) values than do their sedentary peers \( (7, 8, 15–18, 22–24) \). An increase in maximal cardiac output is one mechanism responsible for the higher \( VO_2_{max} \) in older athletes \( (6, 15, 17, 24) \). Furthermore, this increased maximal cardiac output is solely the result of a larger maximal stroke volume, because maximal heart rate does not differ between older endurance-trained athletes and their sedentary peers \( (6, 24) \). The present results suggest that expanded intravascular volumes contribute to the greater \( VO_2_{max} \) and to the higher stroke volume and cardiac output during peak exercise in older endurance-trained athletes compared with their sedentary peers.

Several lines of evidence in this study suggest that expanded intravascular volumes contribute to the higher \( VO_2_{max} \) observed in older endurance-trained men. First, there were significant correlations between each of the component intravascular volumes and \( VO_2_{max} \) in the total sample. In multiple regression analyses, plasma or total blood volume was an independent predictor of \( VO_2_{max} \). Additional evidence is inferred from the underlying physiological principle that increased intravascular volumes may increase \( VO_2_{max} \) by augmenting maximal stroke volume and hence maximal cardiac output. In the present study, the master athletes had peak exercise cardiac and stroke volume indexes that were 25 and 31% higher, respectively, than those of the sedentary men. Furthermore, in multiple regression analyses, plasma volume or total blood volume contributed independently to the prediction of peak exercise stroke volume. Another major line of evidence supporting our conclusion is the significant relationships between intravascular volumes and the increases in LVEDV and stroke volume that occurred from rest to peak exercise in these subjects. Collectively, these results suggest that expanded intravascular volumes, particularly plasma and total blood vol-

![Fig. 2.](image_url)
enses, contribute significantly to the higher \( \dot{V}O_{2\text{max}} \) and to the increased stroke volume and cardiac output during peak upright exercise evident in older endurance-trained men.

Thus chronic volume overload LV hypertrophy may contribute to the differences in maximal exercise hemodynamics between master athletes and their sedentary peers. Although the master athletes had a 15% larger LVEDV index during upright seated rest and a 17% larger peak cycle ergometer exercise LVEDV index compared with the sedentary men, these differences only approached statistical significance because of the small sample. However, prior data from our laboratory and by others has shown 1) a significant LVEDV enlargement in older athletes relative to their sedentary peers (6, 8, 15, 21, 24), 2) increases in LVEDV with training in older men (5, 21), and 3) decreases in LVEDV with the cessation of training in master athletes (21). The direct correlations between plasma and total blood volumes and peak exercise LVEDV suggest that expanded intravascular volumes may have played a role in eliciting the chronic volume-overload LV hypertrophy and increased LVEDV in these older athletes.

Two recent studies suggest that expanded intravascular volumes contribute to the higher \( \dot{V}O_{2\text{max}} \) values in exercise-trained older persons (1, 27). Carroll and co-workers (1) reported that 26 wk of endurance exercise training in older men and women (average age 68 yr) increased \( \dot{V}O_{2\text{max}} \), plasma volume, and total blood volume by 11–13%. Stevenson and co-workers (27) reported that total, red blood cell, and plasma volumes, whether expressed in absolute terms or normalized for body weight or FFM, were 6–50% larger in older endurance-trained women (average age 55 yr) compared with sedentary age-matched controls. These women athletes had \( \dot{V}O_{2\text{max}} \) values that were 50–83% higher than those of the sedentary women. However, cardiac volumes were not measured in either of these studies; thus the role of expanded intravascular volumes in augmenting maximal exercise LVEDV, stroke volume, cardiac output, and \( \dot{V}O_{2} \) could not be assessed directly.

Several previous studies clearly demonstrate the importance of expanded blood volumes in maximizing stroke volume and \( \dot{V}O_{2\text{max}} \) during upright exercise in younger subjects (3, 9). Coyle and co-workers (3) found that the cessation of training in endurance-trained young men (average age 25 ± 2 yr) was associated with 10–12% decreases in blood and plasma volumes and submaximal exercise stroke volume and a 6% decline in \( \dot{V}O_{2\text{max}} \). When blood and plasma volumes were restored to trained levels by the infusion of dextran, exercise stroke volume and \( \dot{V}O_{2\text{max}} \) also returned to initial trained values. In a follow-up study from the same laboratory (9), plasma volume expansion in trained younger men had no effect on submaximal exercise stroke volume or \( \dot{V}O_{2\text{max}} \). However, expanding plasma volume by 400 ml in untrained young men, which resulted in plasma and blood volumes equal to those in the endurance-trained young men, increased submaximal upright exercise stroke volume by 11%. Further expansion of plasma and blood volume in the untrained young men by an additional 250 ml did not result in further increases in stroke volume during submaximal upright exercise.

Additional physiological factors may contribute to the higher peak exercise stroke volume, cardiac output, and \( \dot{V}O_{2\text{max}} \) evident in older endurance-trained individuals. Our previous studies demonstrated an increase in myocardial contractility, evidenced as a greater increase in stroke volume for a given increase in LVEDV as a result of endurance training in older individuals (21, 24). The trend for a greater reduction in end-systolic volume from rest to peak exercise in the athletes compared with sedentary men in the present study is consistent with these prior findings. We also showed that older endurance-trained athletes have lower arterial stiffness than do their sedentary peers, possibly contributing to their enhanced stroke volume by reducing LV afterload. Finally, recent cross-sectional and longitudinal training studies suggest that widening the arteriovenous difference during maximal exercise may account for a sizable portion of the increased \( \dot{V}O_{2\text{max}} \) associated with endurance exercise training in older people (5–7, 15, 24).

In summary, the present results show that older endurance-trained male athletes have expanded intravascular volumes compared with their sedentary peers. This suggests that increased intravascular volumes, particularly plasma volume, are a primary factor contributing to the higher \( \dot{V}O_{2\text{max}} \) and higher LVEDV, stroke volume, and cardiac output during peak exercise in endurance-trained older men. Thus maintenance or expansion of intravascular volumes may attenuate the decline in maximal cardiovascular performance observed with aging.

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REFERENCES


