The effect of lifelong exercise dose on cardiovascular function during exercise

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Submitted 20 March 2013; accepted in final form 18 January 2014

The effect of lifelong exercise dose on cardiovascular function during exercise. J Appl Physiol 116: 736–745, 2014. First published January 23, 2014; doi:10.1152/japplphysiol.00342.2013.—An increased “dose” of endurance exercise training is associated with a greater maximal oxygen uptake ($V\dot{O}_{2\text{max}}$), a larger left ventricular (LV) mass, and improved heart rate and blood pressure control. However, the effect of lifelong exercise dose on metabolic and hemodynamic response during exercise has not been previously examined. We performed a cross-sectional study on 101 (69 men) seniors (60 yr and older) focusing on lifelong exercise frequency as an index of exercise dose. These included 27 who had performed ≤2 exercise sessions/wk (sedentary), 25 who performed 2–3 sessions/wk (casual), 24 who performed 4–5 sessions/wk (committed) and 25 who performed ≥6 sessions/wk plus regular competitions (Masters athletes) over at least the last 25 yr. Oxygen uptake and hemodynamics [cardiac output, stroke volume (SV)] were collected at rest, two levels of steady-state submaximal exercise, and maximal exercise. Doppler ultrasound measures of LV diastolic filling were assessed at rest and during LV loading (saline infusion) to simulate increased LV filling. Body composition, total blood volume, and heart rate recovery after maximal exercise were also examined. $V\dot{O}_{2\text{max}}$ increased in a dose-dependent manner ($P < 0.05$). At maximal exercise, cardiac output and SV were largest in committed exercisers and Masters athletes ($P < 0.05$), while arteriovenous oxygen difference was greater in all trained groups ($P < 0.05$). At maximal exercise, effective arterial elastance, an index of ventricular-arterial coupling, was lower in committed exercisers and Masters athletes ($P < 0.05$). Doppler measures of LV filling were not enhanced at any condition, irrespective of lifelong exercise frequency. These data suggest that performing four or more weekly endurance exercise sessions over a lifetime results in significant gains in $V\dot{O}_{2\text{max}}$, SV, and heart rate regulation during exercise; however, improved SV regulation during exercise is not coupled with favorable effects on LV filling, even when the heart is fully loaded.

aging; lifelong exercise; maximal exercise capacity; stroke volume; diastole

HEALTHY AGING IS CHARACTERIZED BY a progressive decline in maximal oxygen uptake ($V\dot{O}_{2\text{max}}$) (2, 20), which increases functional disability and risk of all-cause mortality (6). In longitudinal and cross-sectional studies, a smaller maximal cardiac output (Qt) and arteriovenous oxygen difference [(a-v)D02] contribute to the decline in $V\dot{O}_{2\text{max}}$ with senescence (4, 9, 28, 36).

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The “dose” of exercise consists of a number of factors, including intensity (how hard), duration (how long), and frequency (how often). A greater frequency of exercise is associated with a greater $V\dot{O}_{2\text{max}}$ (23), a larger left ventricular (LV) mass (23, 56), and improved heart rate and blood pressure regulation (37, 51). To date, no studies have examined the effect of lifelong exercise dose on physical fitness and exercise cardiovascular function. A greater depth of knowledge describing the metabolic and hemodynamic adaptations to different doses of lifelong exercise would be beneficial to determining the optimal exercise dose for minimizing the reduction in physical performance with aging.

The augmentation of stroke volume (SV) with endurance exercise training is primarily attributed to a larger end-diastolic volume (26, 46). In combination with LV compliance, rapid active relaxation and vigorous diastolic suction would enhance end-diastolic volume, while minimizing increases in filling pressure during exercise. However, compelling evidence of enhanced LV filling properties, including active relaxation and diastolic suction, are still lacking in endurance-trained individuals, even in those who perform near daily exercise (3, 8, 11, 31, 41). The apparent absence of a training effect may be related to methodological issues, including small sample size, heterogeneous exercise histories, or, importantly, an inability to comprehensively assess differences in LV loading conditions between trained and untrained participants.

Therefore, the purpose of this study was to examine the relationship between lifelong (>25 yr) exercise dose as tracked by exercise frequency and 1) metabolic and hemodynamic variables at rest and during exercise; 2) dynamic LV diastolic filling parameters at rest and during LV volume loading to simulate increased LV filling during exercise; and 3) postexercise heart rate recovery (HRR). We hypothesized that $V\dot{O}_{2\text{max}}$, exercise SV, dynamic LV diastolic filling properties, and HRR would be improved in a dose-dependent manner.

METHODS

Participant Recruitment

Participants were recruited primarily from the Cooper Center Longitudinal Study (58), a cohort of over 80,000 individuals in whom physical activity and cardiovascular risk factors have been quantified and followed for greater than 40 yr. The Masters athlete population was enriched through recruitment of top performers at regional and national endurance events. Participants were grouped based on lifelong exercise frequency [exercise session(s)/wk], with exercise being defined as periods of aerobic activity lasting at least 30 min. Sedentary participants exercised no more than once per week; “casual” exercisers engaged in 2–3 sessions per week; “committed” exercisers per-
formed 4–5 sessions per week; and Masters athletes trained 6–7 times per week and participated in regular competitions. All participants were nonsmokers, were not taking any cardiovascular medications, had a 24-h ambulatory blood pressure <140/90 mmHg, body mass index ≤ 30 kg/m², and a normal ECG and exercise stress echocardiogram. All participants were informed of the purpose and procedures used in the study and gave their written, informed consent to a protocol approved by the Institutional Review Boards of the University of Texas Southwestern Medical Center in Dallas and Texas Health Presbyterian Hospital Dallas.

Measurement of Resting and Exercise Metabolic and Hemodynamic Variables

Oxygen uptake (V\textsubscript{O2}) (Douglas bag technique), hemodynamics, and blood pressures were determined at the following treadmill conditions: 1) quiet rest, 2) low-intensity (=30–45% of V\textsubscript{O2max}) steady-state submaximal exercise, 3) moderate-intensity (=60–75% of V\textsubscript{O2max}) steady-state submaximal exercise, and 4) maximal exercise. A small number of participants (n = 4) were tested on an upright cycle at the same conditions because of orthopedic concerns or participant request. Gas fractions were analyzed by mass spectrometry and ventilatory volumes by a Tissot spirometer, as previously reported (1). V\textsubscript{O2max} was defined as the highest V\textsubscript{O2} measured from at least a 30-s Douglas bag. Q\textsubscript{c} was measured with the acetylene rebreathing method, which has been previously validated in this laboratory (29).

Heart rate was measured via a 12-lead ECG, and SV was calculated as Q\textsubscript{c}heart rate, while (a-v)D\textsubscript{O2} was calculated from the Fick equation. As differences in body size and composition may influence cardiovascular variables (9), SV was scaled relative to body surface area (BSA) (stroke index) and fat-free mass (FFM).

Body density and composition were determined by underwater weighing. Systemic vascular resistance (SVR) was calculated using the following formula: mean arterial pressure (MAP)/Q\textsubscript{c} × 80, where 80 is a conversion factor to dyn s cm\textsuperscript{-5}. Effective arterial elastance (Ea), an index of ventricular-arterial coupling, was estimated as ESP/SV, in which ESP represents end-systolic blood pressure, by multiplying brachial systolic blood pressure by 0.9 (12). Ea was scaled relative to BSA, as previously reported (43).

Measurement of HRR after Maximal Exercise

Immediately after the cessation of maximal exercise, participants recovered in an upright seated position. Heart rate was continuously recorded, and HRR was analyzed at 1-min periods from 1–5 min of recovery. HRR is presented as beats per minute and R-R interval, which was calculated from the following formula: 60/heart rate × 1,000.

Measurement of Body Composition

Body density and composition were determined by underwater weighing with correction for residual lung volume (59). Each subject performed at least three adequate measurements defined as a definitive plateau in underwater weight, and the mean value was calculated.

Assessment of Dynamic LV Diastolic Filling

LV function was assessed using previously described techniques (1, 41). Briefly, a 6 Fr balloon-tipped fluid-filled catheter (Edwards Lifesciences) was placed using fluoroscopic guidance to measure pulmonary capillary wedge pressure (PCWP). PCWP was determined from three measurements obtained at end expiration, as previously described (1, 41). PCWP, Q\textsubscript{c}, and Doppler measures of dynamic LV diastolic filling measurements were obtained after at least 20 min of supine rest. LV filling was increased through a rapid infusion of warm (37°C) isotonic saline solution at 200 ml/min via an antecubital intravenous line to achieve total volume infusion of 10–15 ml/kg (NS15). In this cohort, there was a positive association between SV at NS15 and during moderate intensity submaximal exercise (R = 0.69, P < 0.05) and maximal exercise (R = 0.58, P < 0.05) using the acetylene rebreathing method.

Echocardiographic images were digitally acquired using an iE33 (Philips,) and ATL HDI5000 (Advanced Technology Laboratories) and were measured offline in Xcelera cardiovascular image management system (Philips). LV end-diastolic volume was determined using a modified Simpson’s method, as previously described (1), and then scaled relative to BSA (left ventricular end-diastolic volume index).

Mitral inflow. A 2-mm sample volume placed at the tips of the mitral valve leaflets to determine peak early and late mitral inflow velocities, and the corresponding early-to-late ratio was calculated.

Tissue Doppler imaging. In the apical four-chamber view, a 2-mm sample volume was placed at the septal and lateral side of the mitral annulus. A mean value of septal and lateral values of the peak early (mean Em) mitral annular velocity was calculated (41).

Propagation velocity of early mitral inflow. A color M-mode image of LV inflow was obtained with the sampling area positioned to extend from mid-atrium to the apex, directly through the mitral valve orifice. The scale was reduced to produce a clear aliasing within the early portion of the mitral inflow. The slope of first aliasing velocity from the mitral plane to 4 cm into the ventricle was used to measure propagation velocity of early mitral inflow. Using a five-chamber apical view with a 4-mm sample volume, the interval between aortic valve closing and mitral valve opening [isosvolumic relaxation time (IVRT)] was determined.

Measurement of Total Blood Volume

Total blood volume (TBV) was measured using a carbon monoxide rebreathing method modified from that described by Burge and Skinner (7) and has been described in detail elsewhere (25). Typical error of measurement expressed as a coefficient of variation (%) for test-retest reproducibility for V\textsubscript{O2max} and maximal Q\textsubscript{c}, SV, and heart rate for 86 participants in the current cohort is 4.4% (2.15 ± 0.64 vs. 2.19 ± 0.64 l/min), 11.1% (15.9 ± 4.6 vs. 15.2 ± 4.8 l/min), 11.9% (99 ± 30 vs. 93 ± 30 ml), and 3.5% (163 ± 12 vs. 161 ± 12 beats/min), respectively.

Resting and exercise blood pressures were measured on the left arm by ECG gated electrophysymomanometry (Tango; SunTech Medical). Mitral inflow. A 2-mm sample volume placed at the tips of the mitral valve leaflets to determine peak early and late mitral inflow velocities, and the corresponding early-to-late ratio was calculated.

Statistical Analysis

One-factor ANOVA and repeated-measures ANOVAs were used to determine the effect of lifelong exercise frequency on subject characteristics, exercise metabolic and hemodynamics variables, Doppler measures of LV dynamic diastolic filling, and HRR. Tukey adjustments were used to control for multiple comparisons. Nonparametric data were analyzed via Kruskal-Wallis ANOVA on ranks. Pearson’s correlations were used to establish the relationship between TBV and V\textsubscript{O2max}. All statistical analysis was performed using SigmaStat (Systat Software). P < 0.05 was considered statistically significant. Data are presented as means ± SD in Tables 1–4 and means ± SE in Figs. 1–4.

RESULTS

Participants Characteristics

The LV pressure-volume curves and MRI measurements of cardiac morphology in this cohort have been reported (4a). The Masters athletes were lighter, had a smaller BSA, and were leaner, but were similar in terms of FFM (Table 1). TBV scaled relative to total body mass (ml/kg) and LV mass index were larger in Masters athletes and committed exercisers compared with sedentary exercisers (P < 0.05) (Table 1).
Table 1. Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sedentary</th>
<th>Casual</th>
<th>Committed</th>
<th>Masters Athletes</th>
<th>ANOVA P Value</th>
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<tbody>
<tr>
<td>n</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>No. men (%)</td>
<td>15 (56)</td>
<td>18 (72)</td>
<td>19 (79)</td>
<td>17 (68)</td>
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<td>Age, yr</td>
<td>57 ± 3∗</td>
<td>56 ± 3</td>
<td>57 ± 3</td>
<td>56 ± 3</td>
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<tr>
<td>Weight, kg</td>
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<td>76 ± 6</td>
<td>73 ± 7</td>
<td>69 ± 6</td>
<td>0.015</td>
</tr>
<tr>
<td>Height, cm</td>
<td>169 ± 10</td>
<td>174 ± 10</td>
<td>173 ± 8</td>
<td>171 ± 10</td>
<td>0.336</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.87 ± 0.19</td>
<td>1.91 ± 0.23</td>
<td>1.88 ± 0.18</td>
<td>1.76 ± 0.21</td>
<td>0.058</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>32 ± 8</td>
<td>30 ± 7</td>
<td>29 ± 5</td>
<td>22 ± 7†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FFM, kg</td>
<td>51 ± 9</td>
<td>53 ± 10</td>
<td>52 ± 9</td>
<td>51 ± 8</td>
<td>0.699</td>
</tr>
<tr>
<td>Hgb concentration, g/dl</td>
<td>14 ± 1</td>
<td>13 ± 1</td>
<td>14 ± 1</td>
<td>14 ± 1</td>
<td>0.153</td>
</tr>
<tr>
<td>TBV, ml/kg</td>
<td>66 ± 11</td>
<td>69 ± 8</td>
<td>73 ± 8∗</td>
<td>83 ± 8†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVMI g/m²</td>
<td>50 ± 8</td>
<td>52 ± 8</td>
<td>62 ± 11†</td>
<td>67 ± 12‡</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. BSA, body surface area; FFM, fat-free mass; Hgb, hemoglobin; TBV, total blood volume; LVMI, left ventricular mass index. ∗P < 0.05 vs. sedentary. †P < 0.05 vs. casual.

Resting Metabolic and Hemodynamics Variables

Resting metabolic and hemodynamic variables are presented in Table 2. Stroke index was larger, while heart rate and Ea were lower in the Masters athletes compared with sedentary and casual exercisers (P < 0.05). MAP, SVR, and (a-v)Do2 were not different among groups.

Steady-State Submaximal and Maximal Exercise

Maximal exercise metabolic variables are presented in Table 3. Irrespective of unit, VO2max was greater in committed exercisers and Master athletes compared with sedentary and casual exercisers (P < 0.05).

Figures 1 and 2 depict the relationship between VO2 expressed relative to total body mass (ml·kg⁻¹·min⁻¹) and as a percentage of VO2max (%VO2max) (Fig. 3) vs. Qc, SV, and (a-v)Do2 at rest, both levels of submaximal exercise, and maximal exercise. Plots of Qc vs. VO2 were basically superimposable among the groups, with committed exercisers and Masters athletes achieving a greater maximal Qc compared with sedentary and casual exercise groups (Figs. 1A and 3A). Heart rate response during submaximal exercise was lower in committed exercisers and Masters athletes relative to any VO2 expressed relative to total body mass (rightward shift) (Fig. 1B), but the response was not different among groups when depicted as a percentage of VO2max (Fig. 3B). Absolute and scaled SV were larger (upward shift) in committed exercisers and Masters athletes during submaximal and maximal exercise, while the casual exercisers mirrored the sedentary group (Figs. 2, A–C). While the response of MAP during exercise varied among the groups, MAP was not different at any condition (Fig. 1D).

Plots of (a-v)Do2 vs. VO2 scaled to total body mass and as a percentage of VO2max show that systemic oxygen extraction was greater (upward shift) in all trained groups compared with the sedentary group during moderate-intensity submaximal and maximal exercise (P < 0.05) (Figs. 1C and 3D). Masters athletes had a lower SVR during moderate-intensity submaximal exercise (P < 0.05 vs. sedentary and casual) and at maximal exercise (P < 0.05 vs. casual exercisers) (Fig. 1E). Ea was lower in Masters athletes compared with the sedentary and casual groups during submaximal exercise (downward shift) and was lower in committed exercisers and Masters athletes compared with the other two groups at maximal exercise (P < 0.05) (Fig. 1F).

HRR after Maximal Exercise

As shown in Fig. 4, A and B, heart rate was lower, while R-R interval was longer at 3–5 min of recovery in

Table 2. Resting parameters

<table>
<thead>
<tr>
<th></th>
<th>Sedentary</th>
<th>Casual</th>
<th>Committed</th>
<th>Masters Athletes</th>
<th>ANOVA P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2 ml/min</td>
<td>229 ± 56</td>
<td>214 ± 48</td>
<td>244 ± 63</td>
<td>230 ± 48</td>
<td>0.726</td>
</tr>
<tr>
<td>VO2 ml·kg⁻¹·min⁻¹</td>
<td>3.0 ± 0.5</td>
<td>3.2 ± 0.4</td>
<td>3.3 ± 0.7</td>
<td>3.5 ± 0.7*</td>
<td>0.037</td>
</tr>
<tr>
<td>VO2 ml·kg·FFM⁻¹·min⁻¹</td>
<td>4.5 ± 0.8</td>
<td>4.6 ± 0.6</td>
<td>4.7 ± 1.0</td>
<td>4.6 ± 0.8</td>
<td>0.920</td>
</tr>
<tr>
<td>Qc l/min</td>
<td>4.2 ± 1.0</td>
<td>3.8 ± 0.8</td>
<td>3.9 ± 0.9</td>
<td>4.1 ± 1.2</td>
<td>0.619</td>
</tr>
<tr>
<td>QL l·m²⁻¹·min⁻¹</td>
<td>2.2 ± 0.5</td>
<td>2.0 ± 0.3</td>
<td>2.1 ± 0.4</td>
<td>2.3 ± 0.5</td>
<td>0.130</td>
</tr>
<tr>
<td>Qc ml·kg</td>
<td>82.6 ± 15.0</td>
<td>72.8 ± 14.5</td>
<td>75.3 ± 14.6</td>
<td>81.4 ± 17.1</td>
<td>0.070</td>
</tr>
<tr>
<td>Qc FFm⁻¹·min⁻¹</td>
<td>4.5 ± 0.8</td>
<td>4.6 ± 0.6</td>
<td>4.7 ± 1.0</td>
<td>4.6 ± 0.8</td>
<td>0.920</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>81 ± 10</td>
<td>77 ± 13</td>
<td>68 ± 9†</td>
<td>67 ± 9†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SV, ml</td>
<td>53 ± 13</td>
<td>51 ± 16</td>
<td>59 ± 18</td>
<td>63 ± 19</td>
<td>0.056</td>
</tr>
<tr>
<td>SI, ml·kg⁻¹·min⁻¹</td>
<td>28 ± 7</td>
<td>27 ± 6</td>
<td>31 ± 8</td>
<td>35 ± 9†</td>
<td>0.002</td>
</tr>
<tr>
<td>SV, ml·kg·FFM⁻¹·min⁻¹</td>
<td>1.0 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>1.1 ± 0.3</td>
<td>1.2 ± 0.3†</td>
<td>0.007</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>98 ± 13</td>
<td>93 ± 10</td>
<td>96 ± 10</td>
<td>100 ± 9</td>
<td>0.115</td>
</tr>
<tr>
<td>Ea, mmHg·ml⁻¹·m⁻²</td>
<td>4.4 ± 1.2</td>
<td>4.4 ± 1.3</td>
<td>3.8 ± 0.9</td>
<td>3.5 ± 0.8‡</td>
<td>0.009</td>
</tr>
<tr>
<td>SVR, dyn·s·cm⁻⁵</td>
<td>1.976 ± 547</td>
<td>2.051 ± 557</td>
<td>2.035 ± 505</td>
<td>2.067 ± 504</td>
<td>0.586</td>
</tr>
<tr>
<td>(a-v)Do2, ml·dl⁻¹</td>
<td>6 ± 2</td>
<td>6 ± 1</td>
<td>6 ± 2</td>
<td>6 ± 1</td>
<td>0.206</td>
</tr>
</tbody>
</table>

Values are means ± SD. VO2, oxygen uptake; Qc, cardiac output; QL, cardiac index; SV, stroke volume; SI, stroke index; MAP, mean arterial pressure; Ea, effective arterial elastance index; SVR, systemic vascular resistance; (a-v)Do2, arteriovenous oxygen difference. ∗P < 0.05 vs. sedentary. †P < 0.05 vs. casual.
the committed exercisers and Masters athletes compared with sedentary subjects. The relative recovery of heart rate from maximal heart rate was only longer after 2 min of recovery in committed exercisers and Masters athletes when HRR was expressed as an R-R interval \( P < 0.05 \) vs. sedentary.

LV Volumes, Filling Pressure, and Doppler Measures of LV Filling and Active Relaxation at Rest and During Volume Infusion

Doppler indexes of LV diastolic filling at supine rest and during LV loading are shown in Table 4. Left ventricular

![Diagram](http://jap.physiology.org/)
end-diastolic volume index was larger in Master athletes at supine rest and during saline infusion ($P < 0.05$). Except for a faster mean Em and a slower IVRT in the Masters athletes compared with casual exercisers ($P < 0.05$), there were no differences in Doppler measures at rest among the groups. These differences in mean Em and IVRT between casual exercisers and Masters athletes persisted during LV volume loading. Propagation velocity of early mitral inflow was slower in Masters athletes compared with the sedentary group ($P < 0.05$), which in part likely reflects a lower PCWP ($P < 0.05$ vs. sedentary) in this group at the same condition.

Fig. 2. Absolute stroke volume (SV; A), stroke index (SI; B), and SV scaled relative to fat-free mass (FFM; C) as a function of $\dot{V}O_2$ scaled relative to total body mass. Values are means $\pm$ SE. *$P < 0.05$ vs. sedentary. # $P < 0.05$ vs. casual. † $P < 0.05$ vs. committed. Only statistically significant results at maximal exercise are indicated. Please refer to text for further details.

Fig. 3. $Q_c$ (A), heart rate (B), absolute SV (C), and (a-v)DO$_2$ (D) as a function of $\dot{V}O_2$ as a percentage of maximum (%$\dot{V}O_2_{\text{max}}$). Values are means $\pm$ SE. bpm, Beats/min. * $P < 0.05$ vs. sedentary. # $P < 0.05$ vs. casual. † $P < 0.05$ vs. committed. Only statistically significant results at maximal exercise are indicated. Please refer to text for further details.
Blood Volume and $\dot{V}O_{2\text{max}}$

As depicted in Fig. 5A, there was a positive relationship between absolute levels of TBV and $\dot{V}O_{2\text{max}}$ in all participants ($R = 0.77, P < 0.001$). Plots (Fig. 5, B and C) show that the direction of this relationship remained intact when TBV and $\dot{V}O_{2\text{max}}$ were scaled relative to total body mass ($R = 0.69, P < 0.001$) or FFM ($R = 0.42, P < 0.001$).

**DISCUSSION**

The primary novel finding from this study is that four or more weekly endurance exercise sessions for at least 25 yr resulted in enhanced $O_2$ transport and utilization during max-imal exercise compared with lower frequencies of lifelong exercise. Higher frequencies of lifelong endurance exercise also resulted in favorable effects on SV regulation (ventricular-arterial coupling) and heart rate control during and after exercise. By collecting measures of LV mass, TBV, and Doppler measures of LV filling at rest and during saline infusion, the findings of this present study indicate that a larger SV during exercise is coupled with cardiac growth and TBV expansion, but not necessarily with beneficial effects on LV filling properties, even when the heart is fully loaded. Thus the current findings suggest that four or more weekly exercise sessions over a lifetime appears to be an effective strategy to preserving cardiovascular structure and function during exercise in se-niors.

The Effect of Lifelong Exercise Frequency on $\dot{V}O_{2\text{max}}$, Exercise Hemodynamics, and (a-v)Do$_2$

An important observation of this study was a strong relation-ship between $\dot{V}O_{2\text{max}}$ and lifelong exercise frequency, which is consistent with previous findings in men only (23). We extend these findings by showing that: 1) a low frequency of lifelong exercise (2–3 sessions/wk) exerts a modest effect on $\dot{V}O_{2\text{max}}$ expressed relative to total body mass (=8%), and 2) the addition of one to two exercise sessions above this level (4–5 sessions/wk) is sufficient stimulus to limit the reduction in $\dot{V}O_{2\text{max}}$ with aging. Our present findings complement a recent study in elite octogenarian athletes, who had performed at least 4 sessions/wk over 50 yr, resulting in an 80% greater $\dot{V}O_{2\text{max}}$ (38 ± 1 vs. 21 ± 1 ml·kg$^{-1}$·min$^{-1}$) compared with age- and sex-matched controls (57) and are comparable to values ob-served in healthy untrained adults 40–50 yr younger (10).

Consistent with previous cross-sectional studies in men and women, the present study demonstrated that a high level of lifelong endurance exercise training is associated with a larger $Q_e$ and SV during submaximal and maximal exercise (26, 33, 36, 46). However, the effect of endurance training

<table>
<thead>
<tr>
<th>Table 4. Left ventricular volumes, Doppler parameters, and PCWP at supine rest and saline volume infusion (NS15)</th>
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<tbody>
<tr>
<td><strong>Supine rest</strong></td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
</tr>
<tr>
<td>E/A ratio</td>
</tr>
<tr>
<td>Mean Em, cm/s</td>
</tr>
<tr>
<td>IVRT, ms</td>
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<tr>
<td>$V_p$, cm/s</td>
</tr>
<tr>
<td>PCWP, mmHg</td>
</tr>
<tr>
<td>LVEDVI, ml/m²</td>
</tr>
<tr>
<td><strong>NS15</strong></td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
</tr>
<tr>
<td>E/A ratio</td>
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<tr>
<td>Mean Em, cm/s</td>
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<td>IVRT, ms</td>
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<td>$V_p$, cm/s</td>
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<tr>
<td>PCWP, mmHg</td>
</tr>
<tr>
<td>LVEDVI, ml/m²</td>
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</table>

Values are means ±SD. E/A ratio, the ratio of peak early-to-late mitral inflow velocities; Mean Em, mean peak early mitral annular velocity; IVRT, isovolumic relaxation time; $V_p$, propagation velocity; PCWP, pulmonary capillary wedge pressure; LVEDVI, left ventricular end-diastolic volume index. *$P < 0.05$ vs. sedentary. †$P < 0.05$ vs. casual. ‡$P < 0.05$ vs. committed.
end-diastolic volume, resulting from a combination of LV remodeling with increased compliance, hypervolemia, and potentially faster diastolic filling rates (1, 24, 26). In this present study, a greater lifelong exercise frequency was associated with a larger TBV and LV mass. A similar observation for LV mass was reported in men aged 18–77 yr (23), suggesting that LV growth and hypervolemia are influenced by frequency of endurance exercise training.

Coupled with enhanced LV compliance (1, 4a, 30), rapid LV active relaxation and vigorous diastolic suction would maximize LV end-diastolic volume, while attenuating increases in filling pressure in highly trained individuals (55). Previous work, including from our laboratory, has examined the effect of lifelong exercise training on early diastolic filling properties, including active relaxation and diastolic suction at rest and during exercise in seniors, with the majority reporting only modest improvements (3, 8, 31, 40, 41). Similar finding have been reported in young athletes compared with age-matched controls (3, 8), suggesting that any potential training-related improvements in echocardiographic parameters are not diminished with age. The apparent lack of a training effect on Doppler measures of LV filling at any age may reflect small sample sizes, large variations in subject’s exercise histories, and notably an inability to comprehensively assess differences in LV loading conditions between trained and untrained individuals. The latter factor is particularly relevant issue given the load-dependency of Doppler measures of dynamic LV diastolic filling (19).

One previous study from our laboratory (41) collected invasive measures of LV filling conditions and reported minimal improvements in dynamic LV filling parameters in Masters athletes compared with sedentary controls. This present study in a much larger cohort shows that resting noninvasive measures of LV relaxation and suction are not improved at any frequency of lifelong training. Collectively, these findings seem to suggest that training-related improvements in SV during exercise are not coupled with significant enhancements in LV relaxation and diastolic suction at rest or during LV volume loading, a model analogous to increased preload during exercise. However, a key limitation to our findings includes that Doppler measures were collected while the subjects were supine, which may not reflect cardiac hemodynamics and LV filling response that occur during upright exercise (39), or 2) changes in LV contractility during exercise, which would facilitate the ventricle contracting below its equilibrium volume engaging diastolic suction (35). Supporting this contention is previous work in our laboratory that showed that early diastolic intraventricular pressure gradients, an index of diastolic suction, increased progressively with incremental exercise workloads in Masters athletes, but only initially increased with low-intensity exercise in healthy, age-matched controls (40). Therefore, future studies should assess intraventricular pressure gradients and ventricular twist mechanics during exercise in a large cohort of senior athletes and controls to clearly determine the effect of lifelong exercise training on LV diastolic filling.

Early studies in small cohorts (21, 45) reported that measures of systolic function (ejection fraction, end-systolic volume) are improved during exercise in trained seniors, although this is not a consistent finding (46). A reduction in aortic impedance via a reduction in aortic stiffness (51) and SVR, improved ventricular-arterial coupling (22, 50), and potentially

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**Fig. 5. Absolute (A) and total blood volume (TBV) scaled relative to total body mass (B) and FFM (C) as a function of absolute and scaled VO$_{2max}$. Triangles [sedentary, 15 subjects (9 men)]; semi-filled diamonds [casual exercisers, 25 subjects (18 men)]; circles [committed exercisers, 24 subjects (19 men)]; semi-filled squares [Masters athletes, 13 subjects (11 men)].**

on maximal SV when begun later in life (>60 yr) is less clear, with several (17, 22, 52, 53), but not all (4, 18), studies reporting improvements. The reason for the discrepancy in study findings is unclear, but may be due to methodological differences, including measurement techniques, the mode of training, the length and intensity of the training stimulus, and the overall health of study participants. Given this uncertainty, further research is needed to establish the role of exercise dose, including intensity, frequency, and duration on maximal SV when exercise training is started later in life.

Irrespective of age or sex, increases in exercise SV with endurance-type training are primarily attributed to a larger
enhanced cardiac β-adrenergic sensitivity (54) would effectively augment LV emptying during exercise in trained seniors. Unfortunately, systolic volumes were not collected in this present study; thus we can only speculate on the effect of systolic function on SV regulation in our trained participants. However, Ea, an index that characterizes the total arterial load imposed on the LV, was lower during submaximal and maximal exercise in committed exercisers and Masters athletes, pointing toward improved arterial compliance and ventricular-arterial coupling in trained seniors, which is consistent with a previous observation in young trained men (38) and after 1 yr of training in previously untrained seniors (22). Therefore, these results highlight that improved ventricular-arterial coupling is a notable training-related adaptation for enhancing SV regulation during exercise in seniors.

We also found that maximal (a-v)Do2 was significantly greater in trained seniors, which has been reported in a prior study (36). Interestingly, we observed that even a low frequency of lifelong exercise (2–3 sessions/wk) improved oxygen extraction by metabolically active tissue during maximal exercise. These findings are important, as maximal (a-v)Do2 is reported to decline with aging (4, 9, 36), which probably in part reflects physical deconditioning in addition to the aging process itself, as maximal (a-v)Do2 is normalized in seniors with several months of exercise training (4, 53). Several mechanisms appear to underlie this improved oxygen extraction in trained seniors, including the preservation of FFM, increased number of mitochondria and enzymes activity (14), increased vasodilator response (44), and enhanced blood flow redistribution to exercising muscle mass (4).

The Effect of Lifelong Exercise Frequency on Heart Rate Control During and Recovery From Exercise

An important observation in this present study is that the relationship between \( \dot{V}O_2 \) relative to maximum effort (i.e., at the same relative workload) and heart rate was superimposable between our groups during exercise (Fig. 3B). Our results suggest that heart rate is precisely regulated in response to changes in SV during exercise to maintain the linear relationship between \( Q_c \) and metabolic demand, as depicted in Fig. 1A. The current findings and previous data (36, 42) demonstrate that the slope of the relationship between blood flow and metabolic demand during exercise is not influenced by age, sex, or fitness in healthy individuals. In some conditions, such as postural orthostatic tachycardia syndrome, a compensatory heart rate response is demonstrated due to a smaller SV to "normalize" the slope relationship between \( Q_c \) and \( O_2 \) delivery during exercise (49); however, this compensation may not be sufficient to "normalize" this slope in populations with metabolic disease or heart failure, with or without preserved ejection fraction (5, 13, 32).

In contrast to the regulation of HR during exercise, HRR immediately after the cessation of exercise is exclusively due to restoration of vagal tone, while longer recovery durations reflect the balance between vagal tone restoration and sympathetic tone withdrawal (16). Because of its clear association with vagal activity, HRR may be used as a measure of "global cardiovascular health" in healthy individuals and patients with cardiovascular disease (15, 48). We observed that ≈97% of our participants achieved a HRR of >12 beats at 1 min (15) and >22 beats at 2 min (48), indicators of an appropriate HRR after maximal exercise.

Heart rate was slower, while R-R interval was longer at 3–5 min of recovery in highly trained seniors (Fig. 5, A and B). Cross-sectional (15, 48) and longitudinal training studies (49) have reported that a greater fitness level is associated with either a slower heart rate or a faster relative decline in heart rate at recovery periods ranging from 30 s to 5 min. Studies (37, 51) from our laboratory have reported that weekly exercise frequency influences heart rate and blood pressure regulation in younger adults and seniors over a 1-yr training period. Of particular note, improvements were noted after 3–6 mo of training, suggesting that exercise training-related improvements in autonomic function may be observed after a relatively short period of training. We were, therefore, surprised that we did not observe a more marked decay in the early phase (1 min) of HRR, a period highly influenced by vagal reactivation, in our trained seniors. It is possible that the beneficial effects of lifelong exercise frequency on heart rate "recovery" are more evident before our earliest postexercise assessment, or, more likely, that a "normal" HRR before 2 min is more difficult to improve at any dose of lifelong exercise training.

Study Limitations

First, factors other than those measured in this study (genetics, lifelong physical activity levels) may influence \( V\dot{O}_2\text{max} \) and central hemodynamics; therefore, we cannot exclude the possibility that the improved metabolic and hemodynamic responses in our trained subjects may be related in part to factors other than exercise training. Second, this present study used a simple approach to allocate participants into lifelong exercise groups. The usage of such an approach limits any conclusions based on other components of exercise training program, including intensity and duration or mode, all of which may have an important impact on the metabolic and hemodynamic response during exercise. Third, our trained cohort was predominantly men, because we could only find a limited number of women whose lifelong exercise volume met our criteria. Further studies in a larger cohort of women are required to confirm these present results, or alternatively to elucidate whether sex may influence exercise function in response to different frequencies of lifelong exercise. Finally, our senior subjects were nonobese and normotensive and were screened for occult cardiovascular disease; therefore, it is unclear whether the present findings are applicable to the larger population.

Perspectives

One of the debilitating effects of aging is a progressive reduction in functional capacity as assessed by \( V\dot{O}_2\text{max} \). While it has been clearly established that vigorous lifelong exercise training minimizes the reduction in physical function and exercise function in seniors, there is very limited information on the optimal "dose" of lifetime exercise to obtain such benefits. This current study examined one component of the overall exercise "dose" and demonstrated that performing four or more endurance exercise sessions weekly over a lifetime is associated with a greater \( V\dot{O}_2\text{max} \), oxygen delivery and extraction, and improved ventricular-arterial coupling and heart rate control during exercise. It is important to note that, while the
largest values of \( \dot{V}O_{2max} \) and exercise function were observed in Master athletes, their level of training and competition are likely beyond the feasibility of most individuals. Instead, seniors who had consistently performed 4–5 exercise sessions/wk, and therefore likely reflect the current recommendations for weekly physical activity (≈150 min/wk) (34), still exhibited significant improvements in \( \dot{V}O_{2max} \), exercise function, and cardiovascular control variables compared with healthy controls and, therefore, should be viewed as the minimum frequency of lifelong exercise to attenuate the loss of functional capacity and exercise function with aging. Our results showed that aging effects on resting Doppler measures of LV relaxation and diastolic suction are not prevented even when subjected to many decades of stimulus.

**Conclusion**

In summary, these present findings emphasize that lifelong exercise training frequency favorably influences \( \dot{V}O_{2max} \), SV, systemic oxygen extraction, and ventricular-arterial coupling during exercise in healthy seniors, with the most prominent effect observed when four or more weekly endurance exercise sessions are performed throughout a lifetime.

**GRANTS**

This project was supported by the National Institute on Aging (Grant RO1 AG-17479).

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

**AUTHOR CONTRIBUTIONS**


**REFERENCES**


