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Attenuated Cardiovascular Reserve During Prolonged Submaximal Cycle Exercise in Healthy Older Subjects

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OBJECTIVES The goal of this study was to determine the effect of age on the hemodynamic response to prolonged submaximal aerobic exercise in healthy volunteers.

BACKGROUND Reductions in peak work rate, heart rate (HR), and left ventricular (LV) emptying but higher blood pressure (BP) and systemic vascular resistance occur in healthy older versus younger humans during short bursts of graded maximal aerobic exercise. However, the effect of aging on the cardiovascular response to prolonged exercise at submaximal work rates typical of daily aerobic activities remains unknown.

METHODS We evaluated cardiovascular performance throughout prolonged submaximal upright cycle ergometry in 40 carefully screened healthy untrained volunteers, 8 men and 12 women <50 years old, mean = 37 ± 8 years (younger), and 10 men and 10 women ≥50 years old, mean = 66 ± 9 years (older), during upright cycle exercise at 70% of peak cycle oxygen consumption (VO_2) to exhaustion or a maximum of 120 min. Cardiac volumes were acquired by gated blood pool scans with ^{99m}Tc at rest and every 10 min throughout exercise.

RESULTS Duration of exercise was similar in younger ([81 ± 28 min] versus older [71± 29 min] subjects, p = NS). At 10 min of exercise in the steady state, older subjects demonstrated lower VO_2 (1.1 ± 0.2 l/min vs. 1.3 ± 0.3 l/min) and lower HR (118 ± 17 vs. 135 ± 11 beats/min, $p < 0.001$) but larger end-diastolic (80 ± 11 ml/m^2 vs. 73 ± 8 ml/m^2, p = 0.03) and end-systolic volume index (ESVI) 20 ± 6 ml/m^2 vs. 17 ± 4 ml/m^2, $p < 0.05$) than younger ones. Between 10 min and exercise termination, with VO_2 held constant in both groups, increases in HR (14.0 ± 12.4 beats/min vs. 5.9 ± 11.5 beats/min, p = 0.04), cardiac index (1.6 ± 1.0 l/min/m^2 vs. 0.8 ± 1.1 l/min/m^2, p = 0.03), and LV ejection fraction (7.1 ± 4.0% vs. 2.9 ± 4.4%, p = 0.003) were greater in younger than older subjects, respectively, as was the reduction in ESVI (−5.1 ± 3.0 ml/m^2 vs. −1.8 ± 3.3 ml/m^2, p = 0.002), despite similar declines in systolic BP (−12.3 ± 6.3 mm Hg vs. −12.1 ± 15.0 mm Hg, p = NS).

CONCLUSIONS Thus, age-associated deficits in chronotropic and LV systolic reserve performance occur during prolonged submaximal upright cycle ergometry, analogous to those observed during graded maximal exercise. (J Am Coll Cardiol 2002;40:1290–7) © 2002 by the American College of Cardiology Foundation

Traditional laboratory assessment of cardiovascular exercise performance involves maximal graded exercise protocols of 8- to 12-min duration. Although such protocols provide useful insight into the maximum capacity of an individual to augment cardiac and peripheral vascular function and the mechanisms involved in this process, their relevance is not directly applicable to the usual aerobic activities of everyday living, which are typically submaximal but sustained for longer time periods. Indeed, classical endurance training regimens consist of ≥20 min of exercise at a work level between 50% and 70% of maximal oxygen consumption (VO_2max). It is noteworthy, however, that relatively little is known regarding the hemodynamic response to such routine bouts of sustained submaximal exercise, and the effect of age on this response.

Age dramatically affects the cardiovascular response to maximal aerobic exercise, with reduced exercise capacity, cardiac output, heart rate (HR), and ejection fraction (EF) and higher end-systolic and diastolic cardiac volumes, blood pressure (BP), and systemic vascular resistance typically observed in older versus younger subjects (1–5). These age-associated differences in cardiovascular performance involve, in part, a reduction in beta-adrenergic responsiveness (5,6). The greater increase in BP observed in older versus younger subjects during maximal exercise may also contribute to the blunted left ventricular (LV) emptying that occurs. In contrast, prolonged bouts of submaximal exercise are typically accompanied by a decline, rather than an increase, in BP (7–9). Whether age, per se, affects the cardiovascular response to prolonged submaximal exercise (PSE) similarly to its effect during graded maximal protocols is not known. This study was designed to evaluate the changes in cardiovascular performance induced by PSE, using radionuclide ventriculography, in carefully screened healthy, but untrained, younger versus older volunteers.

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Abbreviations and Acronyms

a-vO_2	= arteriovenous oxygen
BLSA	= Baltimore Longitudinal Study of Aging
BP	= blood pressure
CI	= cardiac index
CNTR	= contractility index
DBP	= diastolic blood pressure
EAI	= arterial elastance index
EDV	= end-diastolic volume
EDVI	= end-diastolic volume index
EF	= ejection fraction
ESV	= end-systolic volume
ESVI	= end-systolic volume index
HR	= heart rate
LV	= left ventricular
MBP	= mean blood pressure
PSE	= prolonged submaximal exercise
SBP	= systolic blood pressure
SV	= stroke volume
SVI	= stroke volume index
TSVR	= total systemic vascular resistance
VO_2	= oxygen consumption
VO_2max	= maximal oxygen consumption

METHODS

Study population. Healthy subjects were recruited from the Baltimore Longitudinal Study of Aging (BLSA), a community-dwelling panel of volunteers age 21 to 96 years (10). The inclusion criteria for this protocol were: 1) negative cardiovascular history and physical exam; 2) no use of cardiovascular medications; 3) normal resting electrocardiogram; 4) normal electrocardiographic response to maximal treadmill exercise, performed using a modified Balke protocol and interpreted according to Minnesota code criteria (11); 5) achievement of VO_2max as defined in the following text; and 6) normal exercise thallium scan in subjects age ≥40 years, using standard methodology (12). Individuals who engaged in vigorous aerobic exercise ≥20 min at least three times per week, combined with a VO_2max >1 SD above the age-adjusted mean for BLSA participants, were excluded.

Exercise protocol. The protocol was approved by the Joint Committee on Clinical Investigation of the Johns Hopkins Medical Institutions and by the BLSA Steering Committee. Initially, each subject underwent graded maximal treadmill exercise for determination of treadmill VO_2max. Criteria for achieving VO_2max included at least two of the following: 1) ≥90% of maximal HR predicted by age; 2) respiratory exchange ratio ≥1.10; and 3) an increase of oxygen consumption (VO_2) ≤2.0 ml/kg from the penultimate exercise stage. Two days later, after informed consent, upright cycle exercise was performed in the Nuclear Cardiology Laboratory of Johns Hopkins Hospital at a constant workload equivalent to 70% of the peak predicted cycle VO_2. The calculation of peak cycle VO_2 was based on the relation between treadmill VO_2max and peak cycle VO_2 previously derived from 40 men and 33 women from the BLSA. In men: cycle peak VO_2 ($ml/kg^{-1}min^{-1}$) = (treadmill VO_2max × 0.81) − 2.6; for women: cycle peak VO_2 ($ml/kg^{-1}min^{-1}$) = (treadmill VO_2max × 0.66) + 4.3. These relations are independent of age (4).

Upright cycle exercise on an electronically controlled cycle ergometer was begun at 25 W. Workload was increased by 12.5 W every 90 s until the measured cycle VO_2 reached 70% of predicted peak cycle VO_2. Steady-state VO_2 was uniformly achieved within 10 min and maintained throughout the duration of the test by minor adjustments of external work rate, if needed. With the feedback of a visible tachometer, subjects maintained a constant pedal speed of 60 rpm throughout exercise and pedaled until unable to continue, or until 120 min had elapsed. A 12-lead electrocardiogram and manual measurements of brachial arterial cuff pressure were performed at rest and every 5 min during exercise. Cardiac volumes were acquired by gated radionuclide ventriculography with ^{99m}Tc before exercise and every 10 min during exercise, all in the seated upright position. Expired O_2 and CO_2 concentrations were measured continuously and O_2 consumption, CO_2 production, and respiratory exchange ratio calculated every 30 s using a metabolic cart (Medgraphics CPX, St. Paul, Minnesota). In the final 10 subjects, peripheral venous hematocrit was measured both before exercise and 10 min into recovery.

Gated blood pool scans. After subjects gave informed consent, in vitro labeling of red blood cells was performed with ^{99m}Tc (12 mCi/m^2 body surface area), as previously described (13). The camera was placed in a position to best define the interventricular septum, usually the 40° left anterior oblique view. Gated cardiac images were acquired at seated rest and during the final 3 min of each 10 min of exercise, using a high-sensitivity parallel-hole collimator attached to a standard Anger camera interfaced with a commercial Nuclear Medicine computer system. Data were acquired on a magnetic disk (64 × 64 matrix, 1.9 zoom) for subsequent off-line analysis.

Measurement of LV volumes. Left ventricular volumes were determined using standard methods (13) by a single technician who was unaware of the study purpose. Briefly, end-diastolic count rate was obtained from a large manually drawn region of interest and corrected for background activity with the use of a separate region of interest drawn lateral and inferior to the left ventricle in the end-systolic frame. A blood sample was drawn at the end of exercise, counted with the same camera-collimator system used for the scintigraphic study, and corrected for time delay between the scintigram and the blood sample counting. Left ventricular end-diastolic volume (EDV) was obtained from the ratio of attenuation-corrected end-diastolic count rate from the gated study to the count rate per milliliter from the sample of venous blood drawn 5 to 10 min after the completion of exercise. Ejection fraction was calculated by a semiautomated algorithm after background subtraction. End-systolic volume (ESV) and stroke volume (SV) were

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calculated from the measured EF and EDV. Left ventricular volumes were normalized per m^2 of body surface area.

Statistical analysis. The effect of age on the hemodynamic response to PSE was examined by stratifying the sample into subsets older versus younger than the median age. The following cardiovascular variables were examined: total body oxygen consumption (VO_2 in l/min); arteriovenous oxygen difference (a-vO_2) defined as (VO_2 in ml/min ÷ cardiac output in ml/min) × 100; HR in beats/min; systolic blood pressure (SBP) and diastolic blood pressures (DBP) in mm Hg; mean blood pressure (MBP), calculated as (SBP + 2 DBP) ÷ 3; cardiac index (CI), stroke volume index (SVI), end-diastolic volume index (EDVI), and end-systolic volume index (ESVI), defined respectively as cardiac output, SV, EDV, and ESV ÷ body surface area in m^2; EF, contractility index (CNTR) (defined as SBP/ESVI), total systemic vascular resistance (TSVR), calculated from MBP in mm Hg ÷ cardiac output in l/min; and arterial elastance index (EAI), an index of arterial load defined by the ratio of end-systolic pressure (estimated by [{2 SBP + DBP}] ÷ 3) ÷ SVI (14). Two-way repeated measures analysis of variance (i.e., age group and exercise time point) was used to compare VO_2 and cardiovascular parameters every 10 min during exercise, once a steady-state VO_2 was achieved. In addition, Student unpaired *t* test was used to compare baseline characteristics, seated hemodynamics, and cardiovascular responses between 10 min of exercise and exhaustion in older versus younger subgroups. Within group changes between these points were assessed by paired *t* test. Simple linear regression analysis was utilized to assess correlations between continuous variables. Values are expressed as means ± SD unless otherwise noted. For all analyses a two-tailed $p \leq 0.05$ indicates statistical significance.

RESULTS

Baseline characteristics and seated hemodynamics. The study population consisted of 40 healthy volunteers, 18 men and 22 women, age 27 to 84 years (mean, 52 ± 17 years). The 8 men and 12 women below age 50 years (mean, 37.5 ± 8.3 years) included 5 subjects in their twenties, 8 in the thirties, and 7 in the forties. The older subset (mean, 66.2 ± 8.8 years) consisted of 10 men and 10 women, including 4 subjects in their fifties, 8 in the sixties, 7 in the seventies, and 1 in the eighties. Mean body mass (72.6 ± 12.4 kg vs. 72.3 ± 10.0 kg), body mass index (25.0 ± 3.4 kg/m^2 vs. 25.2 ± 3.8 kg/m^2), and body surface area (1.84 ± 0.19 m^2 vs. 1.83 ± 0.17 m^2) were nearly identical in younger and older groups, respectively. Treadmill VO_2max, however, was higher in the younger group, as anticipated (33.0 ± 5.7 ml/kg/min vs. 28.0 ± 6.0 ml/kg/min, $p < 0.01$). Self-reported higher intensity physical activity levels (≥6 metabolic equivalents) were similar in younger and older subsets (169 ± 185 metabolic equivalent-min/day vs. 230 ± 475 metabolic equivalent-min/day, respectively, p = NS).

Hemodynamic comparison of older versus younger subjects in the seated position before exercise revealed no significant differences in BP, SVI, CI, or TSVR. The older subset, however, demonstrated lower seated HR (68 ± 10 beats/min vs. 76 ± 10 beats/min, $p < 0.02$), EF (65 ± 6 vs. 70 ± 6; $p < 0.02$), and SBP/ESVI (5.1 ± 1.4 mm Hg/ml/m^2 vs. 6.2 ± 1.5 mm Hg/ml/m^2, $p < 0.03$) and larger EDVI (77 ± 7 ml/m^2 vs. 69 ± 9 ml/m^2, $p < 0.003$) and ESVI (27 ± 5 ml/m^2 vs. 21 ± 6 ml/m^2, $p < 0.002$) than the younger subset.

Hemodynamic changes from rest to steady-state exercise at 70% of peak cycle VO_2. During the initial 10 min of exercise, in the overall sample there was a 109% increase in CI, from 3.5 ± 0.5 l/min/m^2 to 7.3 ± 1.3 l/min/m^2, mediated by a 70% increase in HR from 72 ± 11 beats/min to 126 ± 17 beats/min and a 22% increase in SVI from 49 ± 7 ml/m^2 to 58 ± 8 ml/m^2. The latter was achieved by a 6% increase in EDVI (from 73 ± 9 ml/m^2 to 77 ± 10 ml/m^2) and 24% decrease in ESVI (from 24 ± 6 ml/m^2 to 18 ± 5 ml/m^2), reflecting both utilization of the Frank-Starling mechanism and enhancement of LV systolic performance. The subset younger than 50 years demonstrated larger increases in VO_2 (1.04 ± 0.27 l/min vs. 0.83 ± 0.21 l/min, $p < 0.01$), and a-vO_2 difference (5.2 ± 1.0 ml/100 ml blood vs. 4.3 ± 1.0 ml/100 ml blood, $p < 0.02$) from rest to 10 min of exercise, reflecting their higher absolute work rates. The increase in HR was also greater in younger subjects (60 ± 14 beats/min vs. 49 ± 19 beats/min, $p < 0.05$); however, no significant age differences were observed in the changes of any other hemodynamic variables between rest and 10 min of exercise.

Hemodynamic changes during PSE. The mean exercise duration for the overall sample was 76 ± 29 min (range, 25 to 120 min). Eight subjects (five young and three older, three men and five women) exercised for the entire 120 min, whereas 32 stopped earlier due to exhaustion (n = 28) or orthopedic reasons (n = 4). No significant relation was observed between submaximal exercise duration and treadmill VO_2max (r = 0.18, p = NS). The median level of perceived exertion was 15, that is, hard, as measured by the Borg scale, and did not differ by age group or gender. Mean cycle VO_2 at exercise termination was 1.18 ± 0.2 l/min (16.7 ± 3.2 ml/kg/min), corresponding to 72% of estimated cycle peak VO_2 or approximately 55% of treadmill VO_2max. Respiratory gas exchange ratio decreased significantly across exercise, from 1.00 ± 0.09 at 10 min of exercise to 0.91 ± 0.05 at exercise termination, $p < 0.001$, representing metabolic adaptation to the constant work rate. No ischemic electrocardiographic changes, significant arrhythmias, or other complications occurred in these carefully screened subjects.

Despite a constant VO_2 throughout PSE, there was an 11% increase of CI from 7.3 ± 1.3 l/min/m^2 at 10 min of exercise to 8.1 ± 1.5 l/min/m^2 at exercise termination, $p < 0.001$, whereas a-vO_2 difference decreased reciprocally ($p < 0.001$). The augmentation in CI from 10 min to end-

Table 1. Hemodynamic Changes Between 10 Min and Exercise Termination in Younger Versus Older Subjects

	Younger (n = 20)	Older (n = 20)	p Value
VO_2 (1/min)	0.029 ± 0.22	0.00 ± 0.08	NS
a-vO_2 diff (ml/100 ml)	−1.4 ± 1.3*	−1.1 ± 1.2*	NS
CI (l/min/m^2)	1.55 ± 0.95*	0.84 ± 1.08*	0.03
HR (beats/min)	14.0 ± 12.4*	5.9 ± 11.5*	0.04
SVI (ml/m^2)	5.1 ± 5.8*	3.7 ± 7.5*	NS
EDVI (ml/m^2)	−0.02 ± 6.0	2.0 ± 6.9	NS
ESVI (ml/m^2)	−5.1 ± 3.0*	−1.8 ± 3.3*	0.002
EF (%)	7.1 ± 4.0*	2.9 ± 4.4*	0.003
CNTR (mm Hg/ml/m^2)	4.0 ± 4.7*	0.4 ± 2.5	0.008
SBP (mm Hg)	−12.3 ± 16.3*	−12.1 ± 15.0*	NS
DBP (mm Hg)	−10.8 ± 9.5*	−7.7 ± 7.9*	NS
TSVR (mm Hg/l/min)	−2.1 ± 1.1*	−1.4 ± 1.2*	0.08
EAI (mm Hg/ml/m^2)	−0.23 ± 0.21*	−0.16 ± 0.18*	NS

*Indicates significant change within age group.

a-vO_2 diff = arteriovenous oxygen difference; CI = cardiac index; CTNR = contractility index, defined as SBP ÷ ESVI; DBP = diastolic blood pressure; EAI = arterial elastance index; EDVI = end-diastolic volume index; EF = ejection fraction; ESVI = end-systolic volume index; HR = heart rate; SBP = systolic blood pressure; SVI = stroke volume index; TSVR = total systemic vascular resistance; VO_2 = oxygen consumption.

exercise was achieved by a 3% increase in HR and a 6.3% increase in SVI ($p < 0.001$ for both). The SVI increase was achieved by a 14.7% decrease in ESVI ($p < 0.001$), whereas EDVI remained unchanged throughout exercise. Significant increases in EF (5.4%) and SBP/ESVI (11.7%) occurred between 10 min and termination of exercise, each $p < 0.001$, indicating an enhancement of systolic LV performance. No significant correlation was observed between any of the hemodynamic variables and exercise duration. In addition, SBP and DBP decreased significantly (7.4% and 12.2%, respectively, each $p < 0.001$), resulting in a 20% reduction in calculated TSVR and a 12.4% decline in EAI.

Effect of age on exercise response. The effects of age on the response to PSE between 10 min of exercise and exhaustion are shown in Table 1 and Figures 1 to 3. Whereas Table 1 compares the absolute change in each variable between 10 min and exhaustion, the p value in Figures 1 to 3 is derived from a repeated measures analysis of variance from 10 min through 40 min of exercise. Concordance between these analyses was very high. Because VO_2 was held constant between these two points, any associated hemodynamics changes should be minimally influenced by age-associated differences in absolute work rates or VO_2. Exercise duration was similar in younger versus older subjects (80.6 ± 27.8 min vs. 71.0 ± 29.3 min, respectively, $p = 0.29$). Furthermore, VO_2 remained unchanged throughout exercise in both groups by study design. As shown in Table 1 and Figure 1, a smaller increase in CI occurred between 10 min and end-exercise in older subjects, mediated by a lesser acceleration of HR. However, SVI increased similarly in both age groups. An age-associated deficit in pump function between these points was manifested by lesser augmentation of EF and CNTR and a smaller reduction of ESVI in older versus younger subjects (Fig. 2). Similar results were obtained when the hemodynamic changes from 10 min to exercise termination were regressed on age as a continuous variable. Specifically, increases in HR ($p = 0.09$), EF ($p = 0.04$), and CNTR ($p = 0.01$), and the decline in ESVI ($p = 0.03$) between these time points varied inversely with age. Although no significant age group difference in EDVI response was evident between 10 min of exercise and exhaustion (Table 1), repeated measures analysis of variance between 10 min and 40 min revealed consistently larger EDVI in older than younger subjects across these time points (Fig. 2A). These age differences in hemodynamics were not explicable by differences in BP responses or derived indexes of ventricular afterload (Fig. 3), which declined similarly in both groups over time. Between 10 min of exercise and exhaustion and across exercise time points between 10 and 40 min, no gender difference in VO_2, a-vO_2 difference, or any hemodynamic variable was detected.

Effect of exercise-induced hemoconcentration on cardiac volume calculations. Prolonged exercise can produce hemoconcentration, which could affect estimates of cardiac volumes derived from a hematocrit measured after exercise. Thus, in the final 10 subjects, peripheral venous hematocrit was measured both before exercise and at exhaustion to assess the magnitude of hemoconcentration that occurred. The hematocrit increased minimally and nonsignificantly between these time points, from 39.4 ± 3.4% to 40.0 ± 3.7%, $p = 0.46$; this lack of change was observed in both younger and older subjects.

DISCUSSION

Major findings. This study examined the effect of age on the hemodynamic changes accompanying prolonged submaximal upright exercise in healthy, nonendurance trained adults. The primary focus was to compare those changes that occurred between 10 min of exercise, when a steady-state VO_2 had been achieved, and exercise termination in older versus younger individuals. In the overall sample, significant increases in LV performance and CI were observed between these points, with reciprocal declines in afterload and a-vO_2 difference. The significant rise in CI across PSE was probably necessitated to support an augmented blood flow to skin blood vessels to dissipate the heat generated by exercise (7). This preferential distribution of blood flow to skin rather than exercising muscle with progressive exercise would also explain the observed decline in a-vO_2 difference. The 11% increase in CI between 10 min and exercise cessation was achieved by increases in both HR and SVI, the latter mediated by a reduction of ESVI, while EDVI remained unchanged. Both EF and the ratio of SBP/ESVI increased during exercise, indicating an augmentation of LV systolic performance. However, the increases in HR, CI, EF, and SBP/ESVI between 10 min and end-exercise were reduced in older versus younger subjects.

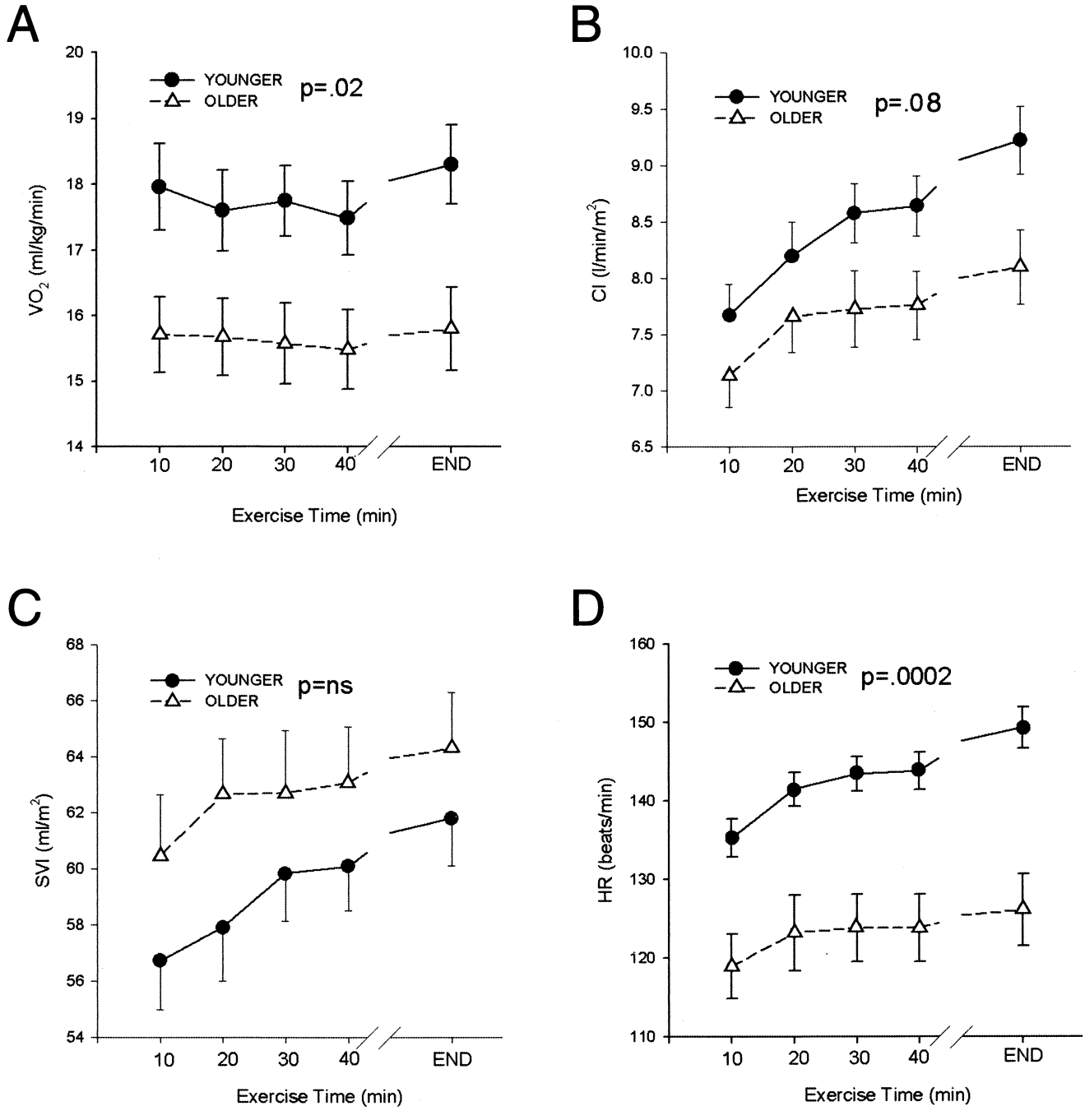

Figure 1. Oxygen consumption (VO_2), cardiac output, and its components. On this and subsequent figures, mean values ± SEM of individual cardiac parameters are shown before exercise, every 10 min during exercise through 40 min, and at end-exercise for subjects younger versus those older than the median age of 50 years. The p value shown is derived from repeated measures analysis of variance comparing all time points between 10 min and 40 min of exercise, achieved by 19 of 20 younger subjects and 17 of 20 from the older group. Oxygen consumption remained constant in both age groups across time but was higher in younger subjects **(A).** An increase in cardiac index (CI) **(B)** occurred in each group, with a trend toward a larger increase in younger subjects. Stroke volume index (SVI) **(C)** increased modestly and to a similar extent in both groups between 10 and 40 min; heart rate (HR) **(D)** was consistently higher in the young.

Prior radionuclide evaluations of LV performance during PSE. Few prior studies have employed radionuclide ventriculography to examine LV performance during PSE. Upton et al. (15) measured LV volumes by the first pass technique at 10 and 60 min of a 110-min bout of upright cycle ergometry at 70% of maximal work rate in nine well-conditioned men age 20 to 32 years. Their major findings generally paralleled our own. Cardiac output increased 10% between 10 and 60 min of exercise, due to a 7% increase in HR and a 3% rise in SV. Ejection fraction rose from 79% to 83% between these points, while EDV remained essentially constant. Another ventriculogram ob-

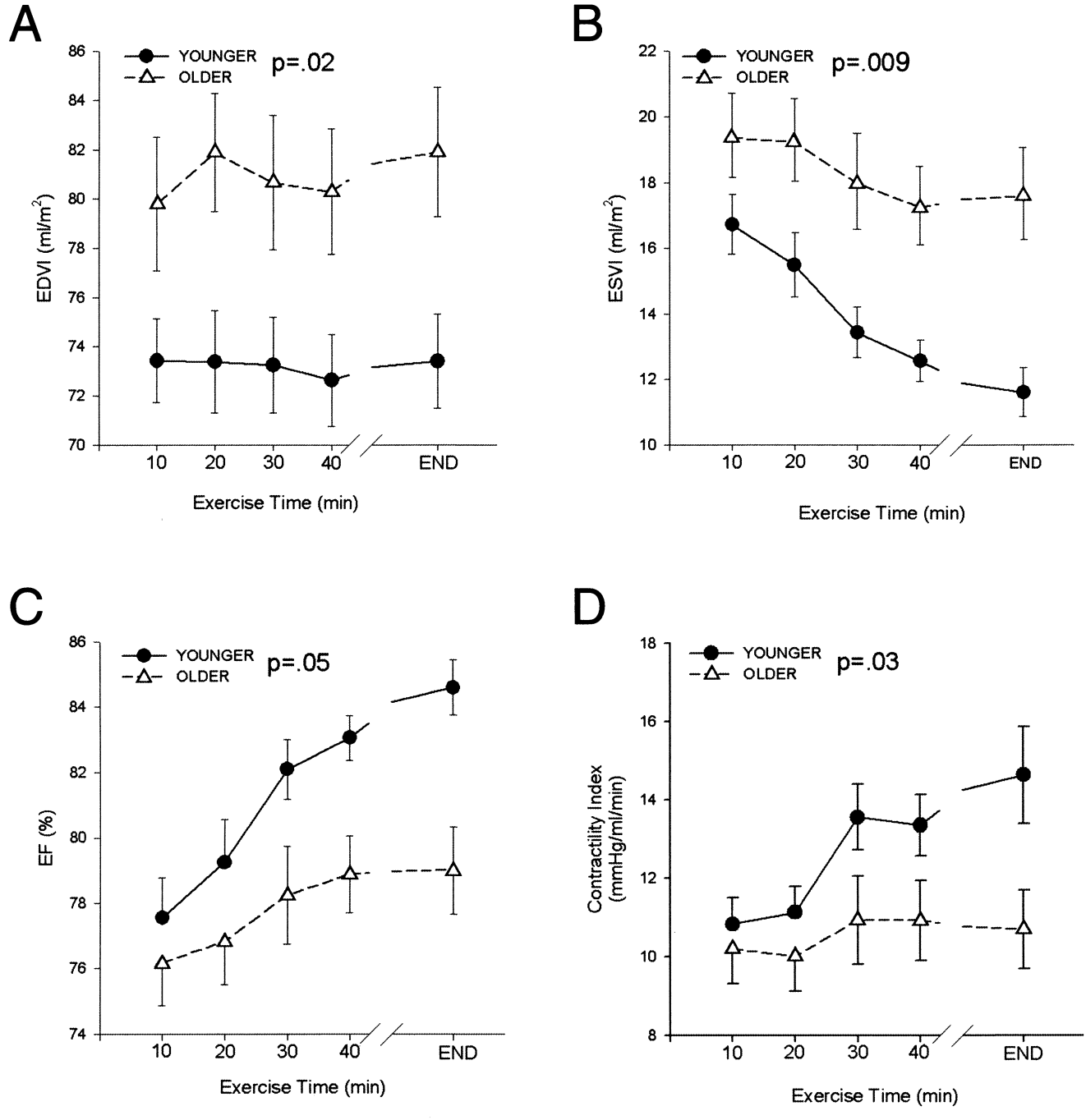

Figure 2. Left ventricular volumes and pump function. End-diastolic volume index (EDVI) **(A)** remained relatively constant throughout exercise in both groups but was consistently higher in older subjects. End-systolic volume index (ESVI) **(B)** declined between 10 and 40 min in both groups, though to a greater extent in younger subjects. Conversely, ejection fraction (EF) **(C)** increased in both groups but to a lesser extent in the older group. Contractility index, defined as systolic blood pressure/ESVI **(D)**, increased in the young but did not change significantly in the older group.

tained at 120 min, after 10 min of near maximal effort, demonstrated a further 21% rise in cardiac output from the 60-min value. However, VO_2 was not monitored during exercise, and cardiac function data was not obtained during the final 50 min of submaximal exercise. Furthermore, the youth and excellent conditioning status of their subjects limit the generalizability of these findings to sedentary older individuals and to women. Similarly, in 10 young men, Foster et al. (16) reported that EF during steady-state upright cycling at approximately 75% of VO_2max increased from 73% to 79% between 10 and 30 min of exercise, paralleling an 11 beats/min rise in HR. In a subsequent study by these authors using the same exercise protocol, no significant change in EF was observed between these time points in patients with coronary heart disease (17).

Reduced cardiovascular reserve with age during both PSE and graded maximal exercise. The salient finding of the present study was a blunted increase in HR, CI, EF, and

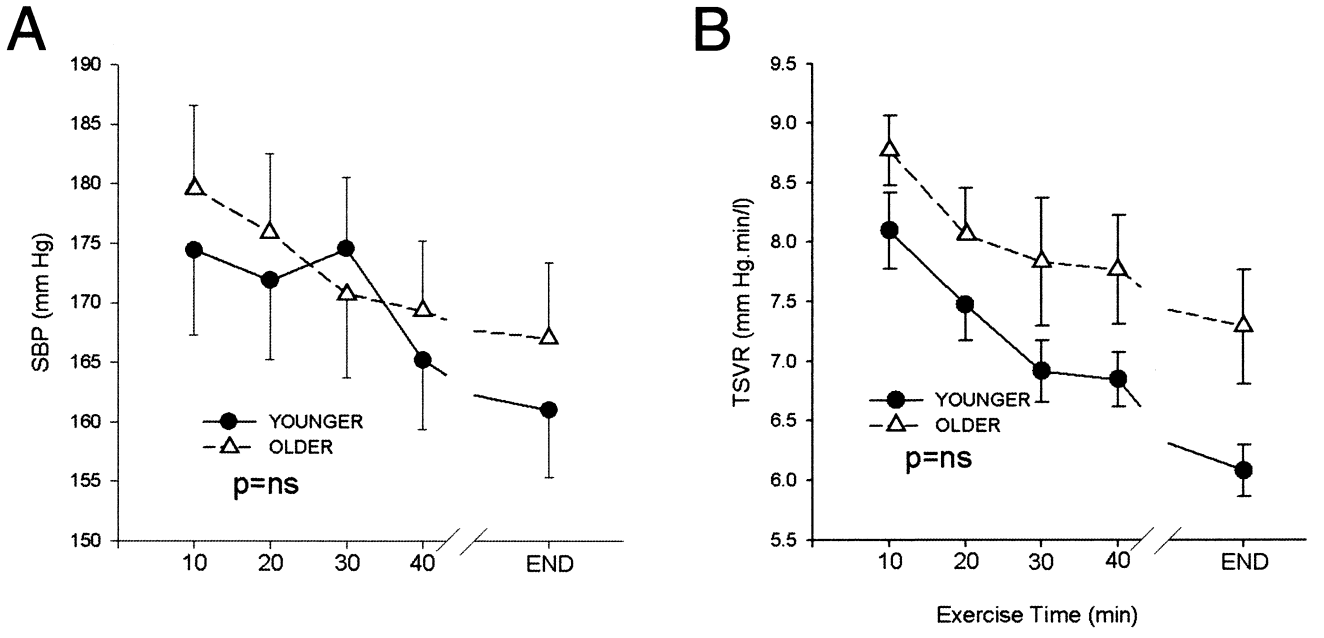

Figure 3. Left ventricular afterload. There were similar significant declines in systolic blood pressure (SBP) **(A)** and total systemic vascular resistance (TSVR) **(B)**, as well as in diastolic blood pressure and arterial elastance index (not shown), in both age groups between 10 and 40 min of exercise.

SBP/ESVI between 10 min and exercise termination in older versus younger subjects. In addition, EDVI remained higher in older than younger subjects throughout exercise, analogous to the LV response to graded maximal cycle ergometry (1–5). Because no change in exercise intensity occurred in either group between these time points, this age difference in hemodynamic response is not explicable by the higher absolute work rate in younger subjects. It is noteworthy that the same variables demonstrating age-associated deficits during graded maximal exercise, that is, HR, CI, and LV pump performance (1–4), also showed blunted responses to PSE. Because both younger and older groups exercised at an identical percent of their treadmill VO_2max by study design, the blunted hemodynamic response in the latter group is not explicable by a lesser relative effort or a saturation of reserve capacity. Given that a similar decline in BP, TSVR, and EAI occurred between 10 min and end-exercise in the two age groups, it is unlikely that the blunted LV emptying in older subjects was secondary to a lesser decline in afterload. Thus, the present study extends the concept of an age-associated reduction in cardiac performance reserve to PSE typical of everyday aerobic activities.

Study limitations. Certain limitations of the present study should be recognized. Exercise in a thermoneutral laboratory setting may not reproduce the hemodynamic effects of prolonged exercise in extreme heat or cold or high humidity. Such extreme conditions may elicit deterioration of SVI, CI, and LV systolic performance not observed in the present study. Although correction for the nonsignificant increase in hematocrit that occurred between rest and exhaustion would slightly attenuate the increases in SVI and CI between these points, calculations of EF would not be affected. Left ventricular afterload was approximated by TSVR and EAI. A better assessment of afterload would be provided by aortic characteristic impedance (18), which did not change significantly during incremental exercise in young beagle dogs but increased markedly in older ones; SV rose progressively in young dogs but increased minimally in older animals (18). If a similar age-associated differential change in impedance occurred during exercise in the present study, this could help to explain the blunted LV systolic emptying in older subjects; however, it would not explain their attenuated cardioacceleratory response. Finally, our failure to monitor plasma catecholamines during exercise does not allow us to determine whether the blunted HR and LV systolic performance in older adults is mediated by a reduced responsiveness to endogenous cathecholamines, as seen during graded maximal aerobic exercise (6), or to an attenuated rise in plasma norepinephrine during PSE, as observed by others (8,9,19,20).

Conclusions. In summary, prolonged submaximal cycle exercise up to 2 h in a thermoneutral environment elicited progressive increases in cardiac performance throughout exercise in healthy volunteers. However, older subjects demonstrated lesser augmentation of HR and systolic LV performance between 10 min and exercise termination than younger ones, analogous to findings during traditional graded maximal exercise protocols.

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