Hemodynamic and Thermal Responses to a 30-Minute Constant-Workload Aerobic Exercise in Middle- or Old-Aged Patients With Cardiovascular Diseases

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The aim of the present investigation was to compare the hemodynamic and thermal responses to a 30-min aerobic exercise between middle- or old-aged patients with normal left ventricular function and those with left ventricular dysfunction. Constant-load sitting ergometer exercise of approximately 90% of the subject's oxygen uptake ($\dot{V}O_2$) at the anaerobic threshold for 30 min was conducted in 21 patients with left ventricular dysfunction (61 ± 10 years, left ventricular ejection fraction (LVEF) $35 \pm 7\%$) and 24 patients with normal left ventricular function (59 ± 9 years, LVEF $71 \pm 7\%$). Heart rate (HR), blood pressure, deep temperatures in the forehead and thigh, and forearm skin blood flow (SkBF) were measured every minute, and cardiac output (CO) and stroke volume (SV) were determined every 10 min with the dye-dilution technique during the exercise. Patients of both groups exhibited a progressive elevation in each temperature and an increase in SkBF during the exercise. Although the $\dot{V}O_2$ and CO remained stable, almost the same magnitude of decrease in SV as increase in HR was seen after the 10th min of exercise in both groups. The magnitude of the decrease in SV was greater in old-aged than middle-aged patients with left ventricular dysfunction. Thus, the downward drift in SV during a 30-min constant-load aerobic exercise might not be influenced by left ventricular function, but intensified by aging in patients with left ventricular dysfunction. (*Jpn Circ J* 2000; 64: 370–376)

Key Words: Cardiovascular drift; Heat stress; Prolonged exercise

In short-duration exercise, oxygen uptake ($\dot{V}O_2$) increases exponentially to a steady state within 3 min for work rates below the anaerobic threshold (AT) in healthy subjects,¹ who may walk or run for about 1 h with a $\dot{V}O_2$ below the AT, maintaining their $\dot{V}O_2$, heart rate (HR), and cardiac output (CO) at approximately the same level as that attained after 5 min of exercise.² However, more prolonged (1–2 h) moderate- or severe-intensity exercise results in a downward drift in stroke volume (SV) and systemic arterial pressure, concomitant with a rise in HR, even in young healthy subjects.^{3–6}

It has been believed that exercise of intensity below the AT can be sustained for a prolonged duration without adverse complications even in patients with depressed left ventricular function, and hence low-level (ie, below the AT) exercise is thought to be more advantageous as an exercise training protocol for patients with cardiovascular diseases.^{7–9} Recently, Foster et al reported that SV was stable after the 10th min during a 30-min low-level exercise in healthy middle-aged subjects.¹⁰ However, there have been few reports concerning the hemodynamic response to prolonged (ie, 30 min), low-level (<AT) exercise in middle-

or old-aged patients with left ventricular dysfunction (LVD) despite the fact that these patients are the major participants in cardiac rehabilitation programs.

The possible mechanisms of the downward drift are decreased ventricular preload and/or depressed myocardial function.^{4,11,12} So, there is a possibility that the downward drift due to prolonged exercise is deleterious for patients with cardiovascular diseases, even if its intensity is below the AT. Furthermore, it has been pointed out that exercise training may have detrimental effects on left ventricular function and elicit remodeling in patients with previous myocardial infarction and LVD.^{13–15}

The aim of the present investigation was to compare the hemodynamic and thermal responses to a 30-min constant-workload exercise below the AT between middle- or old-aged patients with normal left ventricular (LV) function and those with LVD.

Methods

Study Group

We studied 45 male middle- (40–64 years) or old-aged (≥ 65 years) patients (mean age, 60 ± 9 years, range, 40–79) with cardiovascular diseases. The patients were divided into 2 groups: patients with LVD (LVD group, $n=21$), and patients with normal left ventricular systolic function (N group, $n=24$). LVD was considered present if the left ventricular ejection fraction (LVEF) at rest was less than 50% (2-dimensional echocardiography) or 45% (radionuclide ventriculography).

LVD Group The mean value of the LVEF of the LVD

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group was $35 \pm 7\%$ (range, 24–48%), as assessed by 2-dimensional echocardiography ($n=15$) or radionuclide ventriculography ($n=6$). The etiology of LVD was previous myocardial infarction in 13 patients and idiopathic dilated cardiomyopathy in 8. Ten patients were in class II and 11 patients were in class I of the New York Heart Association classification. Eight of 23 patients in the LVD group were on diuretic agents, 4 on digitalis, 10 on an angiotensin-converting enzyme inhibitor, 3 on amiodarone, 11 on a calcium channel blocker, 12 on long-acting nitrate and 1 on a β -blocker.

N Group The mean value of the LVEF of the N group was $71 \pm 7\%$ (range, 58–83%), as assessed by 2-dimensional echocardiography ($n=16$) or radionuclide ventriculography ($n=8$). The etiology of the cardiovascular disease was coronary artery disease (CAD) in 8 patients (3 patients with effort angina after a successful percutaneous transluminal coronary angioplasty and 5 patients with vasospastic angina and good control with medication), mild hypertension in 3, atypical chest pain in 8 and ECG abnormalities in 5. Both the patients with atypical chest pain and those with ECG abnormalities had normal left ventricular global and regional function as determined by echocardiography, and normal coronary perfusion as determined by exercise scintigraphy. Seventeen of the 24 patients in the N group were on a calcium channel blocker, 10 on long-acting nitrate, 2 on a β -blocker and 1 on an angiotensin-converting enzyme inhibitor.

Patients were excluded if they had had a myocardial infarction within 6 months prior to the experiment. Other exclusion criteria were the presence of hemodynamically-important valvular disease, exercise-induced angina pectoris, or exercise limitation by pulmonary, peripheral vascular, arthritic or neurological disease. All subjects provided informed consent prior to participation and both groups remained on medications during the study.

Exercise Testing

Within a time frame of 2 weeks, each of the patients performed 2 exercise tests on an electrically-braked ergometer (Lode model, Groningen, The Netherlands) while in the sitting position. In the first exercise test, a progressive incremental protocol was used for determination of the subject's peak oxygen uptake ($\dot{V}O_2$) and $\dot{V}O_2$ at the ventilatory threshold. The ventilatory threshold was identified using standard criteria, such as the ventilatory equivalent and V-slope methods.¹⁶ Peak $\dot{V}O_2$ was determined from data obtained during the final 30 s of exercise. The test procedure was described in detail in our previous study.¹⁷ Patients had previously performed at least one symptom-limited exercise test in order to be familiar with the procedure. In the second exercise test, which was performed within 1 week of the first exercise test, a 30-min submaximal constant-workload exercise, corresponding to approximately 90% of the $\dot{V}O_2$ at the subject's ventilatory threshold, was performed.

CO was measured with the dye-dilution technique using an ear-piece method and indocyanine-green as the indicator, and was calculated by a dye-dilution cardiac output calculator (Nippon Koden, Tokyo, Japan). Initially, CO was determined twice, while subjects were in a sitting position, and an averaged value was used for the control value. CO was measured again after the 10th, 20th and 30th min of the constant-workload exercise test. Injection of the dye was done by an experienced physician. Each dye-dilution

curve was confirmed by its figure to be appropriate. Arterial blood pressure (BP) was obtained by cuff sphygmomanometry. Total peripheral resistance (TPR) was calculated using the standard formula (ie, $CO/mean\ BP$).¹⁸ The total systemic arteriovenous oxygen difference ($cA\dot{V}O_2\ diff$) was calculated using Fick's equation as follows: $cA\dot{V}O_2\ diff = \dot{V}O_2/CO$.

Measurement of Skin Blood Flow Laser-Doppler flowmetry (ALF-2100, Advance Co, Ltd, Tokyo, Japan) was used to continuously monitor skin blood flow (SkBF). Flow changes were recorded on a Unicorder U228 (Nippon Denshi Kogaku Co, Ltd, Kyoto, Japan) at a chart speed of 30 mm/min. The basic theory of laser-Doppler flowmetry has been described elsewhere.^{19,20} The laser-Doppler flow probe was fixed to the skin of the median right forearm near the wrist with adhesive ring tape. Resting blood flow was recorded after 10 min of acclimatization.

Measurement of Temperature Deep temperatures of the forehead and thigh were measured during upright rest and during exercise by use of a deep body thermometer with deep probes (Coretemp CTM-205, Terumo Co, Tokyo, Japan), and used as central and peripheral temperatures, respectively. Skin temperatures of the forehead and thigh were measured similarly. Sequential temperatures were recorded during the exercise at 1-min intervals.

Plasma Norepinephrine Measurements Plasma norepinephrine (NE) concentrations in the forearm artery were determined at rest in the sitting position and every 10 min during exercise in 15 patients of the LVD group and 8 patients of the N group. The method for NE determination was described in our previous study.²¹

All exercise tests were conducted in a room maintained at $25 \pm 2^\circ C$. Patients were dressed in shorts and shoes.

Statistics

Data are the mean values $\pm$ SD except for Fig 1. Data were analyzed by the Wilcoxon signed rank test, chi-square test with Yates' correction, the paired t test, and Friedman test. A p value of <0.05 was considered significant. In order to evaluate whether a steady-state condition of a given parameter was maintained or not, we analyzed the measurement values of the 10th, the 20th, and the 30th min of exercise by the Friedman test.

Results

No significant differences were observed between the N group and the LVD group in age (58.7 ± 9.3 years, middle age in 15 and old age in 9 vs 60.8 ± 9.7 years, middle age in 12 and old age in 9), height (164.5 ± 5.8 vs 164.8 ± 6.6 cm), weight (62.3 ± 7.3 vs 65.1 ± 9.3 kg) or body surface area (1.70 ± 0.12 vs 1.73 ± 0.14 m²). Also, no significant differences in those parameters were found between the 11 patients with CAD or hypertension and the 13 subjects with atypical chest pain or ECG abnormalities of the N group.

Incremental Exercise Test

All patients stopped exercise because of either leg fatigue or dyspnea. No patients in either group were limited by angina, and none had electrocardiographic evidence of ischemia during exercise testing. The peak $\dot{V}O_2$ (ml·kg⁻¹·min⁻¹) was greater ($p<0.01$) in the N group patients (19.3 ± 2.8) than in the LVD group patients (15.0 ± 2.9). The $\dot{V}O_2$ at the ventilatory threshold (ml·kg⁻¹·min⁻¹) was also greater ($p<0.05$) in the N group patients (13.7 ± 2.3) than in

Fig 1. The magnitude of change from the 10th to the 30th min of exercise in the hemodynamic and thermal parameters in both groups. Data show the mean value and SE. The magnitude of change in each parameter is calculated as the value at the 30th min/that at the 10th min. HR, heart rate; SV, stroke volume; SkBF, skin blood flow; fDT, forehead deep temperature; tDT, thigh deep temperature; fST, forehead skin temperature; tST, thigh skin temperature.

the LVD group patients (11.7 ± 2.3). No significant difference in peak $\dot{V}O_2$ was found between the 13 patients with previous myocardial infarction (14.7 ± 3.3) and the 8 patients with dilated cardiomyopathy (15.5 ± 2.3) of the LVD group, or between the 11 patients with CAD or hypertension (19.4 ± 3.3) and the 13 subjects with atypical chest pain or ECG abnormalities (19.2 ± 3.4) of the N group.

Constant-Workload Exercise Test

All patients, except for 2 in the LVD group who stopped exercise at the 20th min, completed the 30-min exercise without any complications. The hemodynamic responses observed during the constant-workload exercise test are shown in Tables 1 and 2. Because no significant differences in each parameter were found between the 11 patients with CAD or hypertension and the 13 patients with atypical chest pain or ECG abnormalities of the N group, the results of the 2 subgroups are not shown independently.

The exercise workload of the LVD patients (34.3 ± 11.0 W) was lower ($p < 0.01$) than that of the patients of the N group (45.6 ± 5.0 W). Oxygen uptake remained essentially unchanged after the 10th min of exercise in both groups (Tables 1, 2). Oxygen uptake at the 30th min of exercise was $90.5 \pm 11.2\%$ (LVD group) and $87.8 \pm 7.9\%$ (N group) of the $\dot{V}O_2$ at each patient's ventilatory threshold (NS).

Cardiac output increased significantly ($p < 0.01$) from rest to the 10th min of exercise; however, there was no significant change in CO with continued exercise in either group. Beyond the 10th min, an increase in HR was demonstrated in the N group ($p < 0.01$, Table 2). Similarly, HR increased significantly from the 10th to the 30th min of exercise in the LVD group ($p < 0.01$, Table 1). The magnitude of increase in HR (HR at the 30th min/HR at the 10th min)

was not different between groups (Fig 1). Stroke volume (ml/min) increased significantly from rest to the 10th min of exercise in the N and LVD groups ($p < 0.01$, $p < 0.01$). Beyond the 10th min, the N group demonstrated an insignificant decrease in SV ($p = 0.23$, Table 2). Similarly, an insignificant decrease in SV was seen in the LVD group ($p = 0.06$, Table 1). The magnitude of decrease in SV was not different between groups (Fig 1). Mean blood pressure increased significantly ($p < 0.01$) from rest to the 10th min of exercise, then remained unchanged from the 10th min to the 30th min of exercise in both groups. There were no significant correlations between the magnitude of change in mean blood pressure (mean blood pressure at the 30th min/that at the 10th min) and the magnitude of increase in HR in both groups. The TPR decreased from rest to the 10th min of exercise ($p < 0.01$) and there was no further significant change in the TPR with continued exercise in either group. Similarly, the $c\dot{V}O_{2\text{diff}}$ was unchanged after the 10th min of exercise in both groups.

Skin temperatures in the forehead and in the thigh elevated progressively during the exercise in both groups (Tables 1, 2). The magnitude of elevation of skin temperature in the forehead as well as in the thigh was similar between the groups (Fig 1). The deep temperature in the thigh elevated progressively in both groups. The change in deep temperature in the forehead was minimal in both groups, but the increase after the 10th min was significant in both groups ($p < 0.01$, $p < 0.01$). Although the deep temperature in the forehead at baseline was lower in the LVD group than in the N group ($p < 0.05$), the magnitude of increase in the temperature during exercise was not significantly different between the groups (Fig 1). The magnitude of increase in the deep temperature in the thigh was also

Table 1 Serial Measurements (Mean±SD) of Constant-Workload Exercise Test in the Left Ventricular Dysfunction (LVD) Group

	Time (min)			
	Baseline	10	20	30
Oxygen uptake (L/min)	0.23±0.03	0.64±0.08*	0.65±0.10*	0.65±0.09*
Cardiac output (L/min)	6.3±1.4	10.6±1.9*	10.7±1.9*	10.6±2.0*
Heart rate (beats/min)	82.7±13.8	103.3±15.5*	105.2±15.4*	109.6±16.5**§
Stroke volume (ml/min)	79.2±25.7	105.9±26.4*	104.4±22.5*	99.4±22.8*
Mean BP (mmHg)	93.3±13.3	102.5±14.4*	100.8±14.0*	99.8±13.7*
TPR (dyne·s ⁻¹ ·cm ⁵)	1252.9±270.4	805.1±205.9*	779.8±179.2*	783.1±186.2*
cAVO ₂ diff (vol%)	3.7±0.9	6.2±1.4*	6.2±1.2*	6.3±1.1*
Temperature (°C)				
Forehead skin	34.4±0.9	34.6±0.8*	34.9±0.9*	35.0±0.9**§
Thigh skin	32.3±0.8	32.8±0.7*	33.7±0.8*	34.0±0.9**§
Forehead deep	36.6±0.4	36.7±0.4*	36.8±0.4*	36.9±0.4**§
Thigh deep	35.1±0.6	35.8±0.6*	36.5±0.5*	36.9±0.5**§
Forearm SkBF (ml·100g ⁻¹ ·min ⁻¹)	1.6±0.5	3.1±1.1*	3.4±1.1*	3.9±1.4**§
Norepinephrine (pg/ml)	622±187	906±252*	876±207*	889±237*

*p<0.01 vs baseline; **p<0.01 vs 10 min.

BP, blood pressure; TPR, total peripheral resistance; cAVO₂ diff, total systemic arteriovenous oxygen difference; SkBF, skin blood flow.**Table 2** Serial Measurements (Mean±SD) of Constant-Workload Exercise Test in the Normal LV Systolic Function (N) Group

	Time (min)			
	Baseline	10	20	30
Oxygen uptake (L/min)	0.23±0.03	0.76±0.11*	0.77±0.09*	0.78±0.10*
Cardiac output (L/min)	6.5±1.8	11.5±2.2*	12.1±2.2*	11.6±1.8*
Heart rate (beats/min)	75.5±11.0	96.5±12.2*	101.9±13.0*	103.9±13.9**§
Stroke volume (ml/min)	86.1±22.1	120.6±24.4*	120.8±25.6*	113.1±20.5*
Mean BP (mmHg)	97.3±13.3	109.3±12.1*	105.3±10.5*	107.0±11.7*
TPR (dyne·s ⁻¹ ·cm ⁵)	1273.7±316.8	782.2±163.2*	717.4±135.4*	748.6±111.8*
cAVO ₂ diff (vol%)	3.8±0.8	7.1±0.9*	6.7±1.6*	7.0±1.2*
Temperature (°C)				
Forehead skin	34.3±0.7	34.6±0.7*	35.0±0.8*	35.1±0.7**§
Forehead deep	36.9±0.4	36.9±0.4	37.0±0.3*	37.2±0.3**§
Thigh skin	32.3±0.8	32.8±0.9*	33.6±0.8*	33.9±0.8**§
Thigh deep	35.4±0.7	36.1±0.6*	36.9±0.5*	37.2±0.5**§
Forearm SkBF (ml·100g ⁻¹ ·min ⁻¹)	2.2±0.8	3.7±1.2*	4.5±1.9*	5.2±2.3**§
Norepinephrine (pg/ml)	533±111	881±348*	883±307*	864±262*

*p<0.01 vs baseline; §p<0.05, **p<0.01 vs 10 min. Abbreviations as in Table 1.

Fig 2. The relation between age and the magnitude of decrease in stroke volume (SV) in patients with left ventricular dysfunction. SV decrease, SV at the 30th min of exercise/that at the 10th min of exercise.

similar in both groups (Fig 1).

The SkBF in the forearm increased significantly ($p < 0.01$) even during the first 10 min of exercise, and then further increased with continued exercise in both groups (Tables 1, 2). The magnitude of increase in the SkBF from baseline to the 30th min of exercise was similar in both groups, and that from the 10th to the 30th min of exercise was not significantly different between the groups (Fig 1).

Plasma NE concentrations both at rest and during exercise were not significantly different between the 2 groups. Plasma NE concentration increased significantly ($p < 0.01$) from rest to the 10th min of exercise, but there was no significant change in either group with continued exercise (Tables 1, 2).

There were no significant correlations in either group between the magnitude of increase in HR and each parameter, including age, LVEF, peak $\dot{V}O_2$, $\dot{V}O_2$ at the ventilatory threshold, the magnitude of increase in deep and skin temperatures, and the magnitude of increase in SkBF. Also, there were no significant correlations between the magnitude of decrease in SV and the each of these parameters in the N group. There was a weak but significant correlation between the magnitude of decrease in SV and age in the LVD group ($r = 0.46$, $p < 0.05$, Fig 2), and the magnitude of decrease in SV was greater in old-aged than middle-aged patients in the LVD group (0.87 ± 0.14 vs 0.99 ± 0.10 , $p < 0.05$). Again, there was no significant correlation between the magnitude of decrease in SV and LVEF in the LVD group. There were no significant correlations between the magnitude of decrease in SV and the other parameters in the LVD group.

Discussion

Cardiovascular Adjustments to Prolonged Exercise

Previous studies noted progressive cardiovascular adjustments and responses, including steadily-falling central venous pressure, SV and mean arterial pressure, with a steadily-rising HR and little or no change in CO, to prolonged (1–2 h) moderate- or severe-intensity exercise in young healthy subjects.^{3–6}

In the present study, a small but significant increase in the HR after the 10th min of exercise was seen in the patients with cardiovascular diseases, regardless of left ventricular function. The magnitude of increase in HR in patients with cardiovascular diseases was almost identical to that of healthy subjects in other studies.^{22,23} However, it has been still debatable whether a decrease in the SV is induced by submaximal exercise or a 30-min exercise. Upton et al reported that the SV was stable after the 10th min of exercise in 9 young (20–32 years) healthy subjects during a 120-min submaximal exercise²⁴ but Fritzsche et al showed a significant decline in the SV after the 15th min of exercise in their 7 young (21–37 years) subjects during a 60-min submaximal (57% of $\dot{V}O_2$ peak) exercise²⁵ Grimby et al reported that the decrease in the SV after the 10th min of exercise was insignificant in 11 young healthy (22–39 years) subjects during a 30-min submaximal (mean 68% of $\dot{V}O_2$ max) exercise.²⁶

There have been few reports concerning the hemodynamic response to prolonged submaximal exercise in middle- or old-aged subjects. Åstrand reported that the HR, and therefore probably the SV, could be expected to remain constant during 1 h of exercise at a workload equivalent to approximately 50% of aerobic work capacity in middle-

aged or older (40–65 years) healthy female subjects.²⁷ Foster et al reported that the SV was stable after the 10th min of exercise in middle-aged (44.4 ± 5.4 years) healthy subjects during a 30-min submaximal exercise.¹⁰ In the present study, a decline in the SV after the 10th min of exercise was insignificant in the middle- or old-aged patients with LVD as well as in those with normal left ventricular function. An insignificant decrease in the SV seems to be explained by a minimal rise in central temperature (heat stress) after the 10th min of exercise in patients (Tables 1, 2).

Thermal and Cutaneous Circulatory Adjustments to Prolonged Exercise

Cardiovascular adjustments have been thought to be related to an increase in body temperature (heat stress) and subsequent redistribution of blood flow to the skin.⁵ Although Shellock et al pointed out that heart-failure patients had an unusual core-temperature decrease throughout short-term maximal exercise,²⁸ it is not the case in prolonged aerobic exercise, as the present investigation showed. The central temperature, measured as forehead deep temperature, steadily increased after the 10th min of exercise in the patients with cardiovascular diseases regardless of LV function, and the magnitude of the central temperature increase did not seem to be different between the patients with cardiovascular disease in the present study and the young healthy subjects reported by Saito et al.²²

During prolonged dynamic exercise, the SkBF must increase to transfer the excess heat from the body core to the skin surface. Johnson has reported that forearm skin blood flow increased slightly during the first 10 min and progressively increased during 10–40 min of prolonged leg exercise in young healthy subjects.²⁹ A continuous increase in the SkBF was also observed in the present investigation during 30-min constant-workload aerobic exercise in patients with cardiovascular diseases.

Mechanisms of the Cardiovascular Drift During Prolonged Exercise

It has been suggested that the central and peripheral thermoreceptor reflexes, responding to increased body temperature, evoke sympathetic nerve activity.³⁰ So, it is likely that a rise in HR is due to increased sympathetic nerve activity. Galbo et al have reported that in young healthy subjects plasma NE concentration increases together with HR during prolonged exercise and reflects the progressive increase in sympathetic nerve activity.³¹ In the present investigation, plasma NE concentration did not change after the 10th min of exercise in the patients of either group. So, evidence of sympathetic stimulation of HR increase after the 10th min of exercise could not be found. However, the lack of a significant increase in plasma NE concentration does not preclude a causal relation between the HR increase and increased sympathetic nerve activity, because the small increase in HR in the present study suggests a mild, if any, increase in sympathetic nerve activity. Although it has been reported that the plasma NE response to exercise is augmented in patients with congestive heart failure,³² the plasma NE concentrations during exercise were not different between the groups in the present study. The discrepancy of the studies may be explained by the difference in the severity of heart failure of the patients of the different studies. Baroreflex-induced increase in HR is also unlikely in the present study because

there was no correlation between the change in mean BP and the increase in HR in either group.

Recently, Foster et al reported that left ventricular end-diastolic volume decreases progressively during sustained submaximal exercise in middle-aged healthy subjects.¹⁰ However, they also reported that SV was stable due to the predominant effect of a continuous decrease in systemic vascular resistance. In the present study, the TPR was unchanged after the 10th min of exercise in the both groups. One of the mechanisms of decrease in SV in the patients with cardiovascular diseases might be decreased ventricular preload, probably caused by an increase in blood pooling in the peripheral tissue, and no decrease in systemic vascular resistance. Diuretics are likely to affect SV response through their action of accentuated decreased ventricular preload. Although 8 (38%) of the 21 patients with LVD group were on diuretic agents, but none of the N group patients ($p < 0.01$), the magnitude of decrease in SV was not different between the 2 groups. So, the effect of diuretics on the cardiovascular drift is unclear in the present investigation.

The present investigation showed that despite essentially stable $\dot{V}O_2$ and CO, almost the same magnitude of decrease in SV was seen between the 2 groups. So, the magnitude of the downward drift in SV during low-level prolonged exercise was unaffected by left ventricular function in these middle- or old-aged cardiovascular patients. Instead, it was influenced by age in the LVD group, but the reasons why age influenced to the downward drift in SV are beyond the scope of this paper. Beiser et al found that a reduction in right atrial pressure, but no change in atrial mean pressure (ie, a selective reduction in the activity of cardiopulmonary baroreceptors) caused a significant vasoconstriction in skin.³³ So, it is possible that the cardiopulmonary reflex has a role in correcting excessive cardiovascular drift during prolonged exercise. However, Cleroux et al showed that despite a similar decrease in central venous pressure, the increases in forearm vascular resistance by cardiopulmonary reflex during lower body negative pressure were smaller in elderly than in young subjects, and they suggested that an impaired cardiopulmonary reflex was due to an impaired ability of cardiac receptors to sense alterations in central blood volume because of an age-dependent reduction in cardiac compliance.³⁴ So, the impairment in cardiopulmonary reflex might be intensified by a combination of old age and left ventricular diastolic dysfunction.

Another possible mechanism of the downward drift of SV is deterioration of myocardial function. Further studies are needed to confirm whether this possibility is true or not.

Study Limitations

Although it might have been inappropriate to include subjects with atypical chest pain or ECG abnormalities who had no other cardiac functional abnormalities as did the patients with cardiovascular diseases, there were no significant differences in the results between those subjects and the other patients of the N group.

We used deep forehead temperature as an index of central temperature. Although it has been shown to be correlated with the temperature in the pulmonary artery at rest,³⁵ esophageal temperature measurements seem to be preferable. So, the possibility of underestimation of central temperature change cannot be ruled out.

We measured CO using the dye-dilution method, but

other methods, such as the acetylene-rebreathing technique, may be preferable. It has been reported that the dye-dilution method had a methodical error of $\pm 10\%$.³⁶

The other limitations are follows: (1) we did not evaluate left ventricular volumes and central venous pressure during exercise, and (2) the patients remained on medications during all studies, so it is possible that these drugs affected the results of the present investigation.

Conclusions

A similar magnitude of cardiovascular drift, including a decline in SV, and increase in heart rate was observed in middle- or old-aged cardiovascular patients regardless left ventricular function. The magnitude of decrease in SV was intensified by aging in patients with LVD.

Addendum

There was a strong correlation ($r = 0.879$) between the LVEF at rest as measured by echocardiography ($52.6 \pm 19.7\%$) and by radionuclide ventriculography ($46.4 \pm 17.9\%$) in the 11 patients whose LVEF was measured by these 2 methods. Also, there was a strong correlation ($r = 0.733$) between the CO at rest as measured by dye-dilution method (6.3 ± 1.7 L/min) and by Fick's method (4.8 ± 0.8 L/min) in the 9 patients whose CO was measured by these 2 methods.

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