Original Article

Age-Related Reduction of Systemic Arterial Compliance Induces Excessive Myocardial Oxygen Consumption during Sub-Maximal Exercise

Takeshi OTSUKI¹⁾, Seiji MAEDA^{1),2)}, Yumiko KESSEN³⁾, Noriko YOKOYAMA²⁾, Takumi TANABE¹⁾, Jun SUGAWARA⁴⁾, Takashi MIYAUCHI^{1),5)}, Shinya KUNO²⁾, Ryuichi AJISAKA²⁾, and Mitsuo MATSUDA¹⁾

Reduction of systemic arterial compliance (SAC) with aging increases left ventricular afterload. The present study was designed to examine whether age-related reduction of SAC is related to excessive myocardial oxygen consumption during sub-maximal aerobic exercise. We studied elderly (60–69 years; $n=25$) and senior (70–82 years; $n=25$) subjects. We measured SAC immediately before the start of the ramp-fashion exercise (*i.e.*, at the end of the 20 W warm-up exercise) and the double product (DP: systolic blood pressure $\times$ heart rate) during the ramp-fashion exercise (20–50 W). SAC was significantly lower in senior subjects (0.76 ± 0.25 ml mmHg⁻¹ m⁻²) compared with elderly subjects (0.95 ± 0.22 ml mmHg⁻¹ m⁻²). DP was higher in senior subjects (20 W: 14.3 ± 3.1 ; 30 W: 15.9 ± 4.2 ; 40 W: 17.7 ± 4.9 ; 50 W: 20.6 ± 5.6 [$\times 10^3$ mmHg bpm]) than in elderly subjects (12.8 ± 3.0 , 14.0 ± 3.5 , 15.1 ± 4.0 , 17.1 ± 4.3 [$\times 10^3$ mmHg bpm]). In total subjects, SAC correlated significantly with DP ($r=-0.64$, $r=-0.64$, $r=-0.64$, $r=-0.64$). In senior subjects, SAC was related significantly to DP ($r=-0.83$, $r=-0.78$, $r=-0.76$, $r=-0.74$). In elderly subjects, SAC tended to correlate with DP although its relationships were not statistically significant ($r=-0.34$, $r=-0.36$, $r=-0.33$, $r=-0.31$). Correlation coefficients at each respective exercise intensity were significantly higher in senior subjects compared with elderly subjects. These results suggest that the age-related reduction of SAC is related to excessive myocardial oxygen consumption during sub-maximal aerobic exercise in older humans, but this relation does not become significant until the SAC reduction becomes pronounced. (*Hypertens Res* 2006; 29: 65–73)

Key Words: aging, double product, left ventricular afterload

Introduction

The central arteries, which consist of the aorta and the ramified large arteries, are distensible. Consequently, they are able to buffer the pulsatile systolic output of the ventricle (*I*).

Their buffering function is usually described in terms of compliance (*I*), *e.g.*, total arterial compliance or systemic arterial compliance (SAC) (2–4). Reduction of SAC increases cardiac and vascular load. For that reason, reduction of SAC may cause excessive myocardial oxygen demand. In contrast, increased SAC may reduce the myocardial oxygen consump-

From the ¹⁾Center for Tsukuba Advanced Research Alliance (TARA), ²⁾Institute of Health and Sport Sciences, and ³⁾Cardiovascular Division, Institute of Clinical Medicine, University of Tsukuba, Tsukuba, Japan; ³⁾Iwaki School for Disabled Children, Iwaki, Japan; and ⁴⁾Institute for Human Science and Biomedical Engineering, National Institute of Advanced Industrial Science and Technology, Tsukuba, Japan.

This work was supported by Grants-in-Aid for Scientific Research (14380008, 17700486) and special coordination Funds of the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Address for Reprints: Mitsuo Matsuda, M.D., Ph.D., Center for Tsukuba Advanced Research Alliance (TARA), University of Tsukuba, Tsukuba 305–8577, Japan. E-mail: m-matsuda@tara.tsukuba.ac.jp

Received April 5, 2005; Accepted in revised form December 6, 2005.

Table 1. Subject Characteristics

	Elderly (<i>n</i> =25; men/women: 6/19)		Senior (<i>n</i> =25; men/women: 6/19)		
	Mean±SD	Min–Max	Mean±SD	Min–Max	
Age (years)	64.6±2.7	60–69	73.5±3.1	70–82	
Height (cm)	153±8	139–173	151±6	138–164	n.s.
Weight (kg)	55.3±7.3	43.2–68.8	51.9±6.5	40.9–69.3	n.s.
Body mass index (kg m ⁻²)	23.6±2.7	19.3–29.5	22.7±2.6	18.7–27.1	n.s.
Systolic blood pressure (mmHg)	124±16	99–159	130±15	95–158	n.s.
Diastolic blood pressure (mmHg)	76±7	60–88	76±9	57–95	n.s.
Heart rate (beat min ⁻¹)	62±10	45–82	63±7	49–85	n.s.
Serum total cholesterol (mg dl ⁻¹)	216±25	145–249	205±36	129–248	n.s.
Serum HDL cholesterol (mg dl ⁻¹)	59±16	46–108	62±21	34–114	n.s.
Serum triglycerides (mg dl ⁻¹)	94±32	47–163	94±40	46–190	n.s.
Plasma glucose (mg dl ⁻¹)	98±8	83–112	95±16	55–121	n.s.

HDL, high-density lipoprotein; n.s., not significant.

tion, and consequently maintain left ventricular performance at lower energetic cost (5).

Increase in blood pressure and double product (DP: systolic blood pressure [SBP] × heart rate [HR]; an index of myocardial oxygen consumption) as evaluated by 24-h Cardiotens monitoring are demonstrably important determinants of ST-segment depression in hypertensive older humans (6). Myocardial oxygen consumption increases during exercise because cardiac output and blood pressure increase. Because SAC is reduced by aging (7–10), it is important to study whether SAC affects myocardial oxygen consumption during exercise in older humans. A prior study (3) has reported that SAC does not correlate with myocardial oxygen consumption, which was evaluated by the DP, during maximal exercise in older humans. However, maximal exercise intensity in older humans is determined by several factors other than cardiorespiratory function, *e.g.*, lower-body strength, motivation, physical condition and so on. Moreover, most physical activities of daily living in older humans are done at the sub-maximal exercise levels. For this reason, it would be preferable to examine the relationship between SAC and myocardial oxygen consumption in older humans at the sub-maximal exercise intensity of an aerobic exercise.

The present study was designed to examine whether age-related reduction of SAC is related to excessive myocardial oxygen consumption during sub-maximal aerobic exercise. We hypothesized that the contribution of SAC to myocardial oxygen consumption during sub-maximal aerobic exercise would be positive in older humans. To test this hypothesis, we measured SAC and DP as an index of myocardial oxygen consumption (11) at several sub-maximal exercise levels in older humans, and examined the relationships between these indexes. Since the reduction of SAC may advance with aging even in older humans, data analyses were performed not only in all older subjects, but also in two subgroups defined by age, *i.e.*, elderly subjects (60–69 years) and senior subjects (70–82 years). Our working hypothesis was that the relationship

between SAC and DP would be more pronounced in the senior subjects.

Methods

Subjects

We studied 50 normal subjects (aged 60–82 years) who were sedentary or recreationally active and who were recruited through advertisements. None were involved in strenuous exercise training. Candidates who smoked regularly or took regular medication for hypertension, hyperlipidemia or hyperglycemia were excluded. Subjects were grouped into elderly (*n*=25; age 60–69 years) and senior (*n*=25; 70–82 years) subjects (Table 1).

The Ethical Committee of the Institute of Health and Sport Sciences of the University of Tsukuba approved this study. This study conforms to the principles outlined in the Helsinki Declaration. All subjects gave their written informed consent before participation in the study.

Exercise Tolerance Test and Measurements

Subjects were examined after a 20-min rest in a quiet, temperature-controlled room during the experimental sessions. After resting, subjects moved onto an electromagnetically braked cycle ergometer and performed an exercise tolerance test. The cycle ergometer work rate protocol consisted of three phases: 2 min rest, then 4 min at 20 W, followed by a ramp work rate (20–50 W, 3 min).

A beat-to-beat analogue waveform of finger arterial pressure was recorded using the volume clamp method (Portapres; TNO BMI, Amsterdam, the Netherlands) (12, 13). The antialiasing filter in the Portapres has its –3 dB point at 100 Hz. After the antialiasing process, the analogue waveform was converted to a 200 Hz digital file (14). We further converted the 200 Hz digital file to a 100 Hz digital file using

Fig. 1. Comparison of age-related differences in a: systemic arterial compliance (SAC) and b: total peripheral resistance (TPR). * $p < 0.05$. Data are expressed as the mean $\pm$ SD.

analysis software (Beatscope; TNO BMI). Brachial arterial SBP and HR were also measured every 20 s using an automated monitor (DPBP measurement system; Kyokko Bussan, Tokyo, Japan). This system uses the R wave of an ECG as a trigger to detect Korotkoff sounds using a microphone placed over the brachial artery. HR was calculated from the R–R interval of the ECG.

Data Analysis

SAC can be calculated from the central arterial pressure waveform and stroke volume (SV) using the area method as (4):

$$\text{SAC} = \text{SV} \times \{(A_s + A_d) \times A_d^{-1}\}^{-1} \times (P_s - P_d)^{-1},$$

where A_s is the area under the arterial waveform during systole, A_d is that during diastole, P_s is the end-systolic pressure, and P_d is the end-diastolic pressure. In the previous study of Cameron and Dart (2), a carotid arterial waveform recorded with tonometry was used as the central arterial waveform to estimate SAC non-invasively. Cameron and Dart have reported that the carotid arterial waveform was in good agreement with the intra-aortic waveform (2). In the present study, a finger arterial waveform was transformed to a brachial arterial waveform using analysis software (Beatscope; TNO BMI) (12, 13); the transformed arterial waveform was used to calculate the SAC instead of the carotid arterial waveform (15, 16). In our previous study, the ratio of the area under the brachial arterial waveform during a cardiac cycle to that during diastole was highly correlated with the ratio calculated from the carotid arterial waveform ($r=0.89$), and the bias and error examined using the method of Bland and Altman (17) were small (95% confidence interval for the bias: 0.07 ± 0.06) during exercise in older subjects (16). We estimated SV using the Modelflow method from the arterial waveform transformed using the software (Beatscope; TNO BMI) (18–20). The previous study has reported that the difference in resting blood flow between the Modelflow and thermodilution meth-

ods was within -0.50 and $+0.65$ l/min (18). During exercise, blood flow measured using the Modelflow method was highly related to blood flow measured using Doppler echocardiography (older subjects, $r=0.89$; young subjects, $r=0.87$) in our previous studies (19, 20). We calculated SAC at each heartbeat from the arterial waveform for 15 s immediately before the start of the ramp-fashion exercise (*i.e.*, at the end of the 20-W warm-up exercise); a mean value for 15 s was obtained. Total peripheral resistance (TPR) was calculated from mean blood pressure and cardiac output ($\text{SV} \times \text{HR}$) as:

$$\text{TPR} = \text{mean blood pressure} \times \text{cardiac output}^{-1}.$$

Because physical size may affect SV, SAC and TPR were normalized for body surface area (21). The body surface area was calculated from height and weight as (22):

$$\text{Body surface area} = \text{height}^{0.725} \times \text{weight}^{0.425} \times 0.00718.$$

DP was calculated from SBP and HR during the exercise tolerance test as (11):

$$\text{DP} = \text{SBP} \times \text{HR}.$$

DP was highly correlated with the myocardial oxygen consumption measured using catheters during exercise ($r=0.90$) (11).

Statistics

Data are expressed as the mean $\pm$ SD. An unpaired *t*-test was used to assess age effects. A log-linear regression analysis was used to determine whether SAC correlated with DP at 20 W exercise (*i.e.*, immediately before the start of the ramp-fashion exercise; $\text{DP}_{20\text{W}}$), at 30 W exercise ($\text{DP}_{30\text{W}}$), at 40 W exercise ($\text{DP}_{40\text{W}}$), and at 50 W exercise ($\text{DP}_{50\text{W}}$), because these relationships appeared to be nonlinear. These regression analyses were performed for total subjects as well as for subjects in the elderly and senior age groups. The difference of correlation coefficients was evaluated by Fisher's *z* transformation. Total subjects were divided into 6 groups by the value of

Fig. 2. Comparison of a: double product (DP), b: systolic blood pressure (SBP) and c: heart rate (HR). * $p < 0.05$. Data are expressed as the mean $\pm$ SD.

SAC, and DP was compared by one way analysis of variance followed by Fisher's protected least significant difference test for multiple comparisons. Values of $p < 0.05$ were considered to indicate statistical significance.

Results

Figure 1 shows the age-related changes in SAC and TPR. We

Fig. 3. Comparison of exercise-induced increase in a: double product (DP), b: systolic blood pressure (SBP) and c: heart rate (HR). Δ DP, the increase in DP; Δ SBP, the increase in SBP; Δ HR, the increase in HR. * $p < 0.05$. Data are expressed as the mean $\pm$ SD.

found significant age-related change in SAC but not in TPR (Fig. 1). Figure 2 shows DP, SBP and HR during exercise. DP and SBP increased significantly with age, but HR did not (Fig. 2). The increases in DP, SBP and HR during exercise are shown in Fig. 3. The exercise-induced acute increase in DP was significantly higher in senior subjects compared with eld-

Fig. 4. Relationships between systemic arterial compliance (SAC) and double product (DP) in total subjects. DP_{20W}, DP at 20 W exercise (a); DP_{30W}, DP at 30 W exercise (b); DP_{40W}, DP at 40 W exercise (c); DP_{50W}, DP at 50 W exercise (d).

erly subjects at 50 W exercise (Fig. 3a).

Figure 4 shows the relationships between SAC and DP in total subjects. Since these relationships appeared to be nonlinear, they were analyzed using a log-linear model. In total subjects, SAC correlated significantly with DP at exercise of respective intensity (Fig. 4). Subjects were then divided into six groups according to the value of SAC as follows: group 1, -0.60 ml mmHg⁻¹ m⁻² ($n=7$); group 2, 0.61 – 0.70 ml mmHg⁻¹ m⁻² ($n=8$); group 3, 0.71 – 0.80 ml mmHg⁻¹ m⁻² ($n=8$); group 4, 0.81 – 0.90 ml mmHg⁻¹ m⁻² ($n=9$); group 5, 0.91 – 1.00 ml mmHg⁻¹ m⁻² ($n=8$); and group 6, 1.01 –ml mmHg⁻¹ m⁻² ($n=10$). The DP values were compared among these groups (Table 2). At all exercise levels, the DP values in groups 1 and 2 were significantly higher than those in groups 4–6 (Table 2). The DP in group 1 was significantly higher than those in groups 2 and 3 (Table 2).

The relationships between SAC and DP in the different age groups are demonstrated in Fig. 5a–h. In senior subjects, SAC was related significantly to DP at all exercise intensities (Fig. 5b, d, f, h). In elderly subjects, SAC tended to correlate with DP (Fig. 5a, c, e, g). The correlation coefficients between SAC and DP at each respective exercise intensity were signif-

icantly higher in senior subjects compared with elderly subjects.

Discussion

In this study, we measured SAC in a group of 50 older subjects. We then examined the relationship between SAC and DP at the sub-maximal intensity of an aerobic exercise to test whether SAC is related to myocardial oxygen consumption during exercise in older humans, and to determine whether the contribution of SAC to myocardial oxygen consumption during exercise is different between elderly (60–69 years) and senior (70–82 years) individuals. SAC correlated negatively with DP in all subjects, but the relationships appeared to be nonlinear, *i.e.*, only a marked reduction of SAC facilitated an increase in myocardial oxygen consumption during sub-maximal aerobic exercise. In the respective age groups, SAC values were significantly related to DP only in senior subjects, not in elderly subjects. The correlation coefficients between SAC and DP during exercise were significantly higher in senior subjects than in elderly subjects. These results appear to support our hypothesis. The contribution of SAC to myo-

Fig. 5. Relationships between systemic arterial compliance (SAC) and double product (DP) in the respective age groups. DP_{20W} , DP at 20 W exercise (a, b); DP_{30W} , DP at 30 W exercise (c, d); DP_{40W} , DP at 40 W exercise (e, f); DP_{50W} , DP at 50 W exercise (g, h). Left panels (a, c, e, g): elderly subjects; right panels (b, d, f, h): senior subjects.

Table 2. Comparison of Double Product among Groups Divided by the Value of Systemic Arterial Compliance

	Systemic arterial compliance (ml mmHg ⁻¹ m ⁻²)					
	-0.60 (n=7)	0.61–0.70 (n=8)	0.71–0.80 (n=8)	0.81–0.90 (n=9)	0.91–1.00 (n=8)	1.01– (n=10)
DP _{20W} (× 10 ³ mmHg bpm)	17.9±2.9	15.0±1.8*	13.6±2.2*	12.0±2.0*,†	12.3±3.0*	11.7±2.4*,†
DP _{30W} (× 10 ³ mmHg bpm)	20.2±3.6	17.1±3.1	15.2±3.5*	13.2±2.4*,†	12.8±3.5*,†	12.6±2.5*,†
DP _{40W} (× 10 ³ mmHg bpm)	22.6±4.3	18.7±4.5*	16.7±4.2*	14.4±2.0*,†	14.1±4.3*,†	13.7±2.8*,†
DP _{50W} (× 10 ³ mmHg bpm)	24.7±4.6	22.7±5.1	19.2±5.1*	16.7±2.3*,†	16.1±4.5*,†	15.3±3.2*,†

Values are mean±SD. DP, double product; DP_{20W}, DP at 20 W exercise; DP_{30W}, DP at 30 W exercise; DP_{40W}, DP at 40 W exercise; DP_{50W}, DP at 50 W exercise. * $p < 0.05$ vs. -0.60; † $p < 0.05$ vs. 0.61–0.70.

cardial oxygen consumption during sub-maximal aerobic exercise was positive in all subjects, but was more pronounced in senior subjects, whose SAC was significantly lower than that of the elderly subjects.

Next, we divided subjects into six groups according to the value of SAC, and compared DP during exercise among the groups. There were no statistically significant differences in DP among the highest SAC groups (groups 4–6). Compared with these groups, the DP in group 3 tended to be higher, and the DP values in the lowest SAC groups (groups 1 and 2) were significantly higher than those in groups 4–6. Thus, it is considered that a marked reduction of SAC, but not a mild reduction, may significantly contribute to excessive myocardial oxygen consumption during sub-maximal exercise. We propose that the contribution of SAC to excessive myocardial oxygen consumption during sub-maximal aerobic exercise would be pronounced when the SAC reduction reaches a very high level (e.g., $SAC < 0.70$ ml mmHg⁻¹ m⁻²).

Resting myocardial oxygen consumption has been reported to be about 8.0 ml (100 g left ventricle [LV])⁻¹ min⁻¹ in dogs (23). It has been demonstrated that myocardial oxygen consumption is 2.0 ml (100 g LV)⁻¹ min⁻¹ at complete arrest induced by vagal stimulation, and 3.4 ml (100 g LV)⁻¹ min⁻¹ in an empty but beating heart (23). Therefore, we can infer that most myocardial oxygen consumption depends on left ventricular hydraulic load (*i.e.*, afterload). Indeed, external cardiac work increases with increasing left ventricular afterload (5), and its increase is related closely to myocardial oxygen consumption per beat (24). Since SAC is a determinant of left ventricular afterload and the reduction of SAC leads to increased external cardiac work (5), reduced SAC increases myocardial oxygen consumption. Indeed, SAC has been reported to be significantly correlated with resting myocardial oxygen consumption (3). However, a study by Cameron *et al.* (3) showed that SAC does not correlate with myocardial oxygen consumption during maximal exercise in older humans. Thus, the effect of SAC on myocardial oxygen consumption during sub-maximal exercise has been unclear. In the present study, SAC was significantly related to DP at the sub-maximal intensity of an aerobic exercise in the total subject group. Those relationships, however, appeared to be nonlinear, and when the subjects were grouped by age, SAC correlated sig-

nificantly with DP only in senior subjects, but not in elderly subjects. Therefore, we infer that the age-related reduction of SAC is related to excessive myocardial oxygen consumption during sub-maximal aerobic exercise, but this relation does not become significant until the SAC reduction becomes pronounced.

Myocardial oxygen consumption per minute is affected by left ventricular afterload (SBP) and contractile frequency (HR) (11). Neither the absolute nor the increased values of HR during exercise were significantly affected by age in this study. The absolute values of SBP during exercise were significantly higher in senior subjects compared with elderly subjects, although the effect of age on the increase in SBP during exercise was not statistically significant. In DP, the absolute values and the increased values during exercise were significantly higher in senior subjects than elderly subjects. Thus, we considered that the contribution of left ventricular afterload to the increase in myocardial oxygen consumption with aging is higher than that of contractile frequency.

In general, SAC may make a relatively small contribution to the left ventricular afterload, since it has been reported that the ratio of pulsatile to total (steady + pulsatile) external work is 10% on average (25). Nevertheless, arterial distensibility decreases with age (26–33), and the contribution of SAC to the left ventricular afterload could be increased up to 50% with the decrease in distensibility (25). In this study, SAC may have made a greater contribution than TPR to the age related-increase in afterload, because age-related change of SAC was statistically significant but that of TPR was not. The present study showed that SAC correlated significantly with DP during sub-maximal exercise only in senior subjects who had a markedly increased DP and decreased SAC, but not in elderly subjects, and that the relationships between SAC and DP were significantly higher in senior subjects than in elderly subjects. These results suggest that the contribution of SAC to myocardial oxygen consumption during sub-maximal aerobic exercise would be pronounced in senior humans because the age-related reduction of SAC may enhance the contribution of SAC.

A previous study has reported that ST-segment depressions occurred when DP increased from 10,900 (24-h mean) to 14,500 mmHg bpm (during ST-depression) in hypertensive

patients (6). In the present study, the number of subjects, whose SAC was equal to or over 14,500 mmHg bpm, appears to have increased with increasing exercise work rate (Fig. 4). Moreover, the corresponding SAC value to its DP value was also increased with increasing exercise work rate (Fig. 4). As shown in Fig. 4, if we define DP at the critical value of 14,500 mmHg bpm, the corresponding SAC values are increased from 0.7 (20 W) to 0.9 (30 W), 1.0 (40 W), and 1.2 (50 W) ml mmHg⁻¹ m⁻². The number of subjects who showed an SAC lower than those values or a DP higher than the critical value was increased with increasing exercise work rate, and was larger in the senior subjects (20 W, *n*=14; 30 W, *n*=19; 40 W, *n*=22; 50 W, *n*=24) than in the elderly subjects (*n*=3; *n*=10; *n*=16; *n*=20; respectively) (Fig. 5). Thus, an age-associated decrease of SAC should not be treated lightly, but rather should be considered serious in subjects with heart disease.

The typical decrease in aerobic capacity and accompanying risk for myocardial ischemia could be improved if such a reduction of SAC with aging could be suppressed and myocardial oxygen consumption during sub-maximal aerobic exercise could be reduced. Arterial distensibility and SAC are increased by relatively short-term aerobic exercise training even in older humans (8, 10, 34–36). We have previously shown an increase in nitric oxide (NO) production (37) and a decrease in endothelin-1 (ET-1) production (38) in older humans, and an increase in endothelial NO synthase production (39) in the aorta of older rats with aerobic exercise training. Based on these findings, we proposed that short-term aerobic training could improve arterial distensibility or SAC in association with an improvement of endothelial function even in older humans. Attenuating the age-related reduction of SAC by exercise training would thus improve the quality of life enjoyed by older individuals.

Several potential limitations to this study should be mentioned. First, the finger arterial waveform was used to calculate the area ratio and SV for the estimation of SAC by transforming to the brachial arterial waveform. The difference in arterial waveform between the central artery and peripheral artery is relatively small in aged humans (40), and this transformed waveform closely resembles the actual intra-arterially measured waveform in shape and pressure level (12, 13). Furthermore, the area ratio under the transformed waveform obtained with Portapres, which is used in the calculation of SAC, is highly correlated with the value of the carotid arterial waveform (*r*=0.89) during exercise in old humans (16). The bias and error estimated by Bland-Altman's analysis (17) were small (95% confidence interval of the error: -0.12–0.26; 95% confidence interval for the bias: 0.01–0.13), and the error and bias of SAC by the error of the area ratio could be estimated as -0.09–0.05 and -0.05–0.00 ml mmHg⁻¹ m⁻², respectively. The blood flow estimated using the arterial waveform has been reported to be in good agreement with the value estimated using thermodilution in elderly subjects (the error: -0.62–0.80 l min⁻¹; the bias: 0.01–0.17 l min⁻¹) (18),

and the error and bias of SAC by the error of SV could be estimated as -0.09–0.09 and -0.01–0.01 ml mmHg⁻¹ m⁻², respectively. Various and rather rigid premises are needed to calculate SAC. Second, the number of subjects in the present study may have been insufficient. The correlation coefficients between SAC and DP in elderly subjects might become statistically significant if more subjects could be added in this study. Finally, certain assumptions were made when calculating SAC using the area method. For example, the offset pressure was assumed to be zero. However, the offset pressure is actually not zero, and might change during even a 20 W exercise. When the offset pressure during a light exercise is assumed to be 8.5 mmHg, *i.e.*, the right atrial pressure during an exercise at 35 W (41), the error and the bias of SAC by Bland-Altman's analysis are 0.010–0.050 and 0.027–0.033 ml mmHg⁻¹ m⁻², respectively.

In conclusion, SAC was correlated negatively with DP at sub-maximal intensities of an aerobic exercise in older humans. However, significant relationships between SAC and DP were observed only in senior subjects (70–82 years), and not in elderly subjects (60–69 years). These results suggest that the age-related reduction of SAC is related to excessive myocardial oxygen consumption during sub-maximal aerobic exercise in older humans, but this relation does not become significant until the SAC reduction becomes pronounced.

References

1. Safar ME, Levy BI, Laurent S, London GM: Hypertension and the arterial system: clinical and therapeutic aspects. *J Hypertens Suppl* 1990; **8**: S113–S119.
2. Cameron JD, Dart AM: Exercise training increases total systemic arterial compliance in humans. *Am J Physiol* 1994; **266**: H693–H701.
3. Cameron JD, Rajkumar C, Kingwell BA, Jennings GL, Dart AM: Higher systemic arterial compliance is associated with greater exercise time and lower blood pressure in a young older population. *J Am Geriatr Soc* 1999; **47**: 653–656.
4. Liu Z, Brin KP, Yin FC: Estimation of total arterial compliance: an improved method and evaluation of current methods. *Am J Physiol* 1986; **251**: H588–H600.
5. Kolh P, D'Orio V, Lambermont B, *et al*: Increased aortic compliance maintains left ventricular performance at lower energetic cost. *Eur J Cardiothorac Surg* 2000; **17**: 272–278.
6. Uen S, Baulmann J, Dusing R, *et al*: ST-segment depression in hypertensive patients is linked to elevations in blood pressure, pulse pressure and double product by 24-h Cardio-tens monitoring. *J Hypertens* 2003; **21**: 977–983.
7. McVeigh GE, Bratteli CW, Morgan DJ, *et al*: Age-related abnormalities in arterial compliance identified by pressure pulse contour analysis: aging and arterial compliance. *Hypertension* 1999; **33**: 1392–1398.
8. Tanaka H, Dinunno FA, Monahan KD, *et al*: Aging, habitual exercise, and dynamic arterial compliance. *Circulation* 2000; **102**: 1270–1275.
9. Mohiaddin RH, Underwood SR, Bogren HG, *et al*: Regional aortic compliance studied by magnetic resonance

- imaging: the effects of age, training, and coronary artery disease. *Br Heart J* 1989; **62**: 90–96.
10. Moreau KL, Donato AJ, Seals DR, DeSouza CA, Tanaka H: Regular exercise, hormone replacement therapy and the age-related decline in carotid arterial compliance in healthy women. *Cardiovasc Res* 2003; **57**: 861–868.
 11. Kitamura K, Jorgensen CR, Gobel FL, Taylor HL, Wang Y: Hemodynamic correlates of myocardial oxygen consumption during upright exercise. *J Appl Physiol* 1972; **32**: 516–522.
 12. Bos WJ, van Goudoever J, van Montfrans GA, van den Meiracker AH, Wesseling KH: Reconstruction of brachial artery pressure from noninvasive finger pressure measurements. *Circulation* 1996; **94**: 1870–1875.
 13. Gizdulich P, Prentza A, Wesseling KH: Models of brachial to finger pulse wave distortion and pressure decrement. *Cardiovasc Res* 1997; **33**: 698–705.
 14. Imholz BP, Langewouters GJ, van Montfrans GA, et al: Feasibility of ambulatory, continuous 24-hour finger arterial pressure recording. *Hypertension* 1993; **21**: 65–73.
 15. Otsuki T, Sugawara J, Tanabe T, et al: Simple and noninvasive estimate of systemic arterial compliance by using peripheral arterial blood pressure waveform in elderly people. *Int J Sport Health Sci* 2003; **1**: 136–141.
 16. Otsuki T, Sugawara J, Tanabe T, et al: Noninvasive estimate of systemic arterial compliance by using peripheral arterial blood pressure waveform during light exercise in elderly people. *Int J Sport Health Sci* 2003; **1**: 142–147.
 17. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307–310.
 18. Wesseling KH, Jansen JR, Settels JJ, Schreuder JJ: Computation of aortic flow from pressure in humans using a nonlinear, three-element model. *J Appl Physiol* 1993; **74**: 2566–2573.
 19. Sugawara J, Tanabe T, Miyachi M, et al: Non-invasive assessment of cardiac output during exercise in healthy young humans: comparison between Modelflow method and Doppler echocardiography method. *Acta Physiol Scand* 2003; **179**: 361–366.
 20. Sugawara J, Otsuki T, Iemitsu M, et al: Reliability of Modelflow method for cardiac output measurement during exercise in elderly people. *J Jpn Soc Clin Sports Med* 2004; **12**: 516–520.
 21. Chemla D, Antony I, Lecarpentier Y, Nitenberg A: Contribution of systemic vascular resistance and total arterial compliance to effective arterial elastance in humans. *Am J Physiol Heart Circ Physiol* 2003; **285**: H614–H620.
 22. Du Bois D, Du Bois EF: A formula to estimate the approximate surface area if height and weight be known. *Nutrition* 1989; **5**: 303–313.
 23. McKeever WP, Gregg DE, Canney PC: Oxygen uptake of the nonworking left ventricle. *Circ Res* 1958; **6**: 612–623.
 24. Suga H, Hisano R, Goto Y, Yamada O, Igarashi Y: Effect of positive inotropic agents on the relation between oxygen consumption and systolic pressure volume area in canine left ventricle. *Circ Res* 1983; **53**: 306–318.
 25. O'Rourke MF: Steady and pulsatile energy losses in the systemic circulation under normal conditions and in simulated arterial disease. *Cardiovasc Res* 1967; **1**: 313–326.
 26. Avolio AP, Chen SG, Wang RP, et al: Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community. *Circulation* 1983; **68**: 50–58.
 27. Avolio AP, Deng FQ, Li WQ, et al: Effects of aging on arterial distensibility in populations with high and low prevalence of hypertension: comparison between urban and rural communities in China. *Circulation* 1985; **71**: 202–210.
 28. Vaitkevicius PV, Fleg JL, Engel JH, et al: Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation* 1993; **88**: 1456–1462.
 29. Tanaka H, DeSouza CA, Seals DR: Absence of age-related increase in central arterial stiffness in physically active women. *Arterioscler Thromb Vasc Biol* 1998; **18**: 127–132.
 30. Kakiyama T, Matsuda M, Koseki S: Effect of physical activity on the distensibility of the aortic wall in healthy males. *Angiology* 1998; **49**: 749–757.
 31. Tomiyama H, Arai T, Koji Y, et al: The age-related increase in arterial stiffness is augmented in phases according to the severity of hypertension. *Hypertens Res* 2004; **27**: 465–470.
 32. Kohara K, Tabara Y, Tachibana R, Nakura J, Miki T: Microalbuminuria and arterial stiffness in a general population: the Shimanami Health Promoting Program (J-SHIP) study. *Hypertens Res* 2004; **27**: 471–477.
 33. Kurihara T, Tomiyama H, Hashimoto H, et al: Excessive alcohol intake increases the risk of arterial stiffening in men with normal blood pressure. *Hypertens Res* 2004; **27**: 669–673.
 34. Kakiyama T, Yokoyama N, Maeda S, et al: Effects of low-intensity exercise training for 6 months on arterial distensibility in middle-aged and elderly women. *J Jpn Soc Clin Sports Med* 2001; **9**: 226–233.
 35. Otsuki T, Sugawara J, Tanabe T, et al: Effects of systemic arterial compliance on cardiorespiratory fitness in elderly women—cross-sectional and longitudinal study—. *J Jpn Soc Clin Sports Med* 2003; **11**: 543–551.
 36. Sugawara J, Inoue H, Hayashi K, Yokoi T, Kono I: Effect of low-intensity aerobic exercise training on arterial compliance in postmenopausal women. *Hypertens Res* 2004; **27**: 897–901.
 37. Maeda S, Tanabe T, Otsuki T, et al: Moderate regular exercise increases basal production of nitric oxide in elderly women. *Hypertens Res* 2004; **27**: 947–953.
 38. Maeda S, Tanabe T, Miyauchi T, et al: Aerobic exercise training reduces plasma endothelin-1 concentration in older women. *J Appl Physiol* 2003; **95**: 336–341.
 39. Tanabe T, Maeda S, Miyauchi T, et al: Exercise training improves ageing-induced decrease in eNOS expression of the aorta. *Acta Physiol Scand* 2003; **178**: 3–10.
 40. Nichols W, O'Rourke M: McDonald's Blood Flow in Arteries, Theoretical, Experimental, and Clinical Principles, 4th ed. London, Arnold, 1998, pp 87–93.
 41. Raine AE, Erne P, Burgisser E, et al: Atrial natriuretic peptide and atrial pressure in patients with congestive heart failure. *N Engl J Med* 1986; **315**: 533–537.