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Original Article

Initial Drop of Blood Pressure during Head-up Tilt in Patients with Cerebrovascular Accidents

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Abstract

***Objective*: To investigate cardiovascular responses to orthostatic stress in patients with cerebrovascular accidents (CVA).**

***Methods*: Twelve male patients with CVA, 11 healthy elderly and 12 healthy young males participated in the present study. The CVA patients had suffered stroke with hemiplegia at least 11 months prior to the study, their medical conditions were stable, and no subjects were taking medications affecting the cardiovascular system. Heart rate (HR) was determined using RR intervals from the ECG. Stroke volume (SV) was estimated by an impedance method, and cardiac output (CO) was calculated by multiplying SV by HR. Blood pressure (BP) was determined by the auscultatory method. SV, HR, CO and BP were measured every 2 min before and during 7 min of 60-degree head-up tilt (HUT).**

***Results*: SV decreased and HR increased immediately after starting HUT in all groups. CO in healthy elderly and young subjects immediately decreased during HUT also, and the decrease was sustained throughout the head-up period. However, CO in CVA patients remained constant throughout the experiment. HUT immediately decreased SBP in all groups and the magnitude of initial SBP reduction in CVA patients was greater than that in the other groups.**

***Conclusions*: We identified an initial reduction of BP during HUT in CVA patients and the recovery of BP by 3 min of head-up tilt. We emphasize that adjustment to orthostatic stress in CVA patients should be practiced by HUT, as our findings showed that CVA patients maintained physiological orthostatic tolerance except for the initial fall in BP.**

Key words: blood pressure, cardiac output, orthostatic stress, cerebrovascular accident, rehabilitation

Introduction

The human cardiovascular system is well adjusted to orthostatic stress (1, 2). Orthostatic stress induces blood shift from the thoracic vessels to the dependent veins of the legs, and decreases venous return and stroke volume (SV). Decreased SV reduces cardiac output (CO) and simultaneously activates cardiopulmonary receptors. Reduction of CO decreases arterial blood pressure (BP) and stimulates baroreceptors in the aortic arch and carotid sinus. Information from cardiopulmonary receptors and baroreceptors is integrated in the medullary cardiovascular center that regulates parasympathetic and sympathetic nerves to increase heart rate (HR) and vascular resistance. These mechanisms do not involve supratentorial structures, and therefore cardiovascular responses during head-up tilt should not be impaired in patients with cerebrovascular accidents (CVA).

However, CVA patients are well known to have autonomic dysfunctions, such as reflex sympathetic dystrophy (3–5) and supraventricular tachycardia (6–10). Recently, Mizushima et al. (11) measured the postganglionic sympathetic nerve activities (muscle sympathetic nerve activity, MSNA) in CVA patients and reported that MSNA in CVA patients was activated during supine rest and that the increase of MSNA was attenuated during the cold pressor test. Based on these findings, it was speculated that supratentorial lesions in CVA patients could alter cardiovascular responses during orthostatic stress.

Standing up is a basic requirement for CVA patients to

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partake in physical, mental and social activities in their daily living (12, 13). Bed rest is well known to be associated with impaired orthostatic tolerance and circulatory, respiratory, metabolic and mental dysfunctions (14, 15). Orthostatic stress counteracts most of the dysfunctions induced by bed rest (16, 17). Thus, we believe that standing up and walking activities in chronic CVA patients should be highly recommended to prevent these dysfunctions. However, there have been no reports of cardiovascular responses during orthostatic stress in CVA patients.

The purpose of the present study was to investigate the cardiovascular responses to orthostatic stress in CVA patients. SV, HR, CO and BP were measured before and during 60-degree head-up tilt in 12 CVA patients who had sustained subcortical or cortical lesions more than 11 months prior to enrollment in the present study. We compared their cardiovascular responses during head-up tilt to those of healthy elderly and young subjects.

Methods

Subjects

Twelve male patients with CVA, 11 healthy elderly males and 12 healthy young males participated in the experiment. The mean age, height, weight and body mass index (BMI) in each group are shown in Table 1. The age and BMI of CVA patients was similar to that of elderly subjects. The CVA patients had suffered stroke with hemiplegia at least 11 months prior to the present study (33.8±8.4 [SEM] months). Their medical conditions were stable, and no subjects were taking any medication affecting the cardiovascular system. The stroke lesion was confirmed by CT scan, and the Barthel index (18) and modified Rankin Scale (19) were used to assess disability. The CVA patients had returned to their own home after staying in acute care hospitals to receive necessary medical treatment and rehabilitation. Then, they participated in day care programs for rehabilitation at a geriatric facility 2 days a week. The program included physical therapy and occupational therapy to improve their daily activity level and ambulatory ability. The CVA patient characteristics and types of CVA are shown in Table 2. CVA patients, elderly and young subjects were free of diabetes mellitus and neurological and cardiovascular disorders with the exception of CVA. The elderly subjects were retired active inividuals who participated in sports activities and/or social events 3 days a week. The young subjects were college students. All subjects received physical examinations including blood pressure and electrocardiogram (ECG).

Table 1 Anthropometric data

	n	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)
CVA	12	68±11	159.4±8.4	55.5±10.6	21.7±2.6
Elderly	11	67±5	167.7±4.8	60.5±8.7	21.4±2.4
Young	12	19±1	173.5±6.5	61.3±7.7	20.3±1.8

Data are mean±SEM. BMI: body mass index.

Each subject gave signed informed consent before participation, and the experimental protocol was approved by the Ethics Committee of Aomori University of Health and Welfare, Aomori, Japan.

Study protocol

Each subject reported to the laboratory at 1000 am after a light meal at 0800 am on the experimental day. The ambient temperature was 24 to 26°C in the experimental room and all subjects wore T-shirts and long pants. They were outfitted with electrodes for ECG and impedance cardiography, and a blood pressure cuff was attached to the CVA patients' unaffected arm and healthy subjects' left arm. After a resting period for at least 20 minutes in the supine position on a tilt table, SV, HR and BP were measured as the basal recordings (supine period). The tilt table was then raised to 60 degrees, which took less than 3 seconds, and maintained in the head-up tilt position for 7 minutes (head-up period), and SV, HR and BP were measured at 1, 3, 5 and 7 min during the head-up period.

Cardiovascular measurements

HR was determined using five consecutive RR intervals from the ECG (PC-630G, Nihonkohden Co. Ltd., Tokyo, Japan). SV was estimated by an impedance cardiograph (AI-601G, Nihonkohden Co. Ltd., Tokyo, Japan), using the standard four-band electrode arrangement (20). A pair of disposable, self-adhesive tape electrodes was wound around the neck and base of the thorax at the level of the xiphisternum. By applying a small amount of high frequency current (100 kHz; 300 μA) between the outer electrodes, a signal whose voltage was proportional to the impedance of the intra-thoracic tissues was

Table 2 Patient characteristics and type of cerebrovascular lesion

No.	Age	Type of Lesion	Location of Lesion	Hemiplegia	Months from onset	Barthel Index	Rankin
1	81	Infarction	cortical branches	Left	96	100	3
2	74	Infarction	penetrating branches	Left	93	60	4
3	58	Bleeding	putamen	Left	20	55	4
4	83	Infarction	penetrating branches	Right	24	100	3
5	67	Infarction	penetrating branches	Left	13	55	4
6	84	Bleeding	subcortical	Right	27	80	4
7	52	Bleeding	putamen	Left	22	100	3
8	50	Bleeding	thalamus	Right	22	95	3
9	68	Bleeding	thalamus	Left	11	60	4
10	67	Infarction	penetrating branches	Right	39	100	3
11	72	Bleeding	putamen	Left	21	80	4
12	64	Bleeding	putamen	Right	18	50	4

obtained through the inner electrodes. The resultant waveforms were recorded at a paper speed of 50 mm/s to ensure adequate separation of the various components of the waves (RTA-1100M, Nihonkohden Co. Ltd., Tokyo, Japan). The SV was computed based on the following equation described by Kubicek et al. (21):

$$SV=\rho(L/Z_0)^2\cdot T\cdot(dZ/dt)_{min}$$

where ρ is a constant (150 Ω·cm) representing blood resistivity at 100 kHz, L is the mean distance between the inner pair of electrodes (cm), Z_0 is the basal thoracic impedance (Ω), $(dZ/dt)_{min}$ is the minimal rate of change of impedance (Ω/s), and T is the ventricular ejection time (s) obtained from the dZ/dt wave form. The CO was calculated by multiplying SV by HR. BP was determined by the auscultatory method using a sphygmomanometer (TM-2543R, A and D Co. Ltd., Tokyo, Japan) with both arms still and rested at heart level on the shelves of the tilt table during the head-up period.

Statistical analysis

During the supine resting period, basal SV, HR, CO and DBP were significantly different among CVA patients, elderly and young subjects (Table 3). In addition, SV and CO estimated by the impedance method were suitable for intra-individual comparison, but not for inter-individual comparison. Therefore, for analysis of the responses to head-up tilt among CVA patients, elderly and young subjects, all data during the head-up period were expressed as percentage change from the corresponding values of the supine period. All results were expressed as means±SEM. Differences among CVA patients, elderly and young subjects at 1, 3, 5 and 7 min during the head-up period, and those between the supine period and each time point in each group were evaluated by the analysis of variance (ANOVA) and repeated-measures ANOVA, respectively. Multiple comparisons were made using Fisher's protected least significant difference analysis (22). A value of $p<0.05$ was considered significant.

Results

All cardiovascular measurements at the supine position and during head-up tilt in CVA patients, elderly and young subjects are shown in Table 3. Head-up tilt rapidly resulted in a decreased SV in all subjects, and there were significant differences in the decrease among the groups ($p<0.05$) at 7 min of head-up tilt (Fig. 1). HR immediately increased during head-up tilt in all groups and the magnitude of tachycardia in the young group was significantly greater than that in the other groups throughout the head-up period (Fig. 2). There were no differences in HR change between CVA patients and elderly subjects during the head-up period. CO in elderly and young subjects decreased immediately after the head-up tilt, and the decrease was sus-

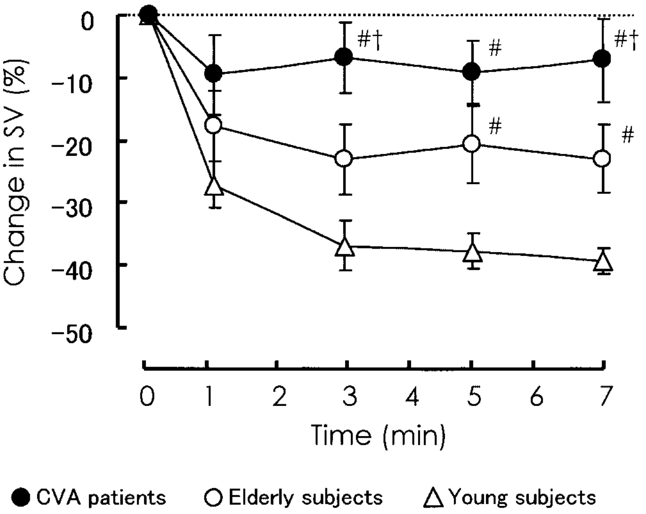

Fig. 1 Percentage change in stroke volume (SV) in patients with cerebrovascular accidents (CVA), elderly and young subjects during the head-up period. Data represent mean±SEM. Closed circles: CVA patients, open circles: elderly subjects, triangles: young subjects. # $p<0.05$ *vs.* Young; † $p<0.05$ *vs.* Elderly.

Table 3 Cardiovascular parameters measured at supine position and during head-up tilt in subjects of the three groups

		supine	head-up tilt			
		0	1 min	3 min	5 min	7 min
Stroke volume (ml)	CVA	56.1±6.1	48.3±4.4*	49.2±3.4*	48.1±3.4*	48.5±3.2*
	Elderly	78.9±3.8	63.0±2.1*	59.0±3.1*	60.6±2.7*	59.0±2.5*
	Young	89.6±5.6	64.7±4.2*	56.6±5.5*	55.6±4.2*	54.5±4.1*
Heart rate (bpm)	CVA	70.7±4.0	74.9±4.3*	75.2±3.7*	76.0±3.8*	77.8±3.7*
	Elderly	62.4±2.2	69.3±3.4*	69.3±2.6*	68.2±2.4*	69.0±2.6*
	Young	62.3±2.5	77.6±2.5*	82.9±4.0*	81.3±3.8*	81.0±3.9*
Cardiac output (l/min)	CVA	3.9±0.4	3.6±0.3	3.7±0.3	3.6±0.2	3.7±0.2
	Elderly	4.9±0.3	4.2±0.2*	4.1±0.2*	4.2±0.2*	4.1±0.2*
	Young	5.6±0.4	4.8±0.3*	4.6±0.4*	4.4±0.3*	4.2±0.3*
Systolic BP (mmHg)	CVA	122.6±5.0	106.0±5.2*	112.6±6.0*	114.4±4.9*	113.5±5.1*
	Elderly	127.5±3.8	119.9±4.6*	118.6±4.6*	120.4±4.3*	117.6±4.5*
	Young	115.8±3.2	108.0±4.6*	106.2±4.2*	105.1±3.0*	107.8±3.7*
Diastolic BP (mmHg)	CVA	75.9±2.7	69.6±2.7*	72.3±3.4*	70.1±2.7*	73.1±2.5
	Elderly	82.6±1.9	79.6±3.2	78.8±3.5	78.2±3.7	76.3±3.1*
	Young	65.8±2.8	64.2±2.6	64.3±3.0	65.0±2.6	65.9±2.5

Data are mean±SEM. * $p<0.05$ compared with supine period in each group.

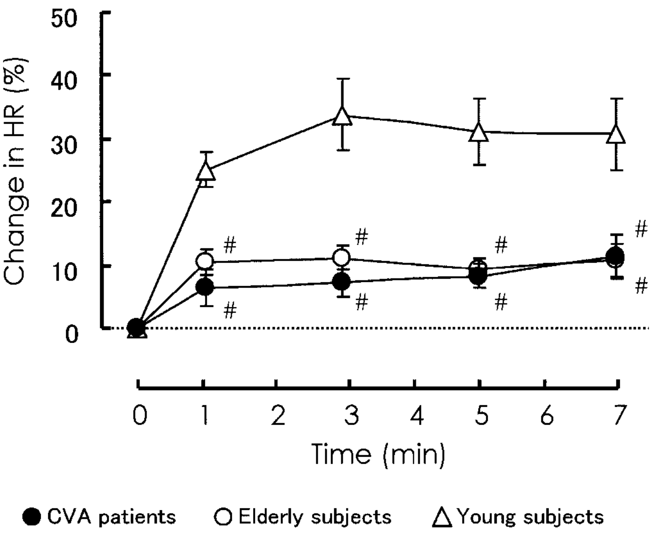

Fig. 2 Percentage change in heart rate (HR) in patients with cerebrovascular accidents (CVA), elderly and young subjects during the head-up period. Data represent mean±SEM. Closed circles: CVA patients, open circles: elderly subjects, triangles: young subjects. # $p<0.05$ *vs.* Young.

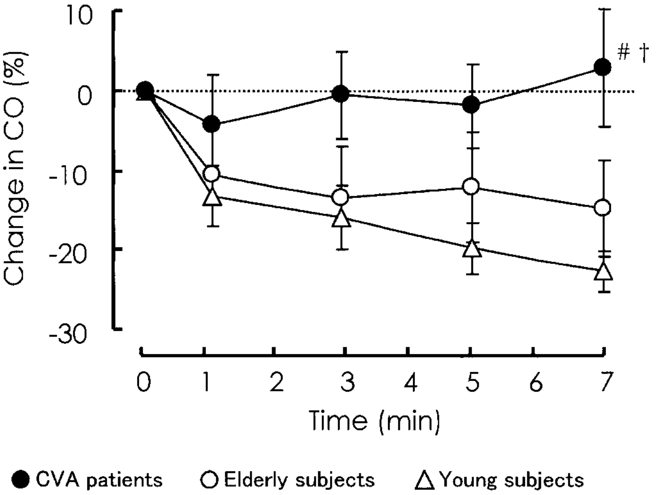

Fig. 3 Percentage change in cardiac output (CO) in patients with cerebrovascular accidents (CVA), elderly and young subjects during the head-up period. Data represent mean±SEM. Closed circles: CVA patients, open circles: elderly subjects, triangles: young subjects. # $p<0.05$ *vs.* Young; † $p<0.05$ *vs.* Elderly.

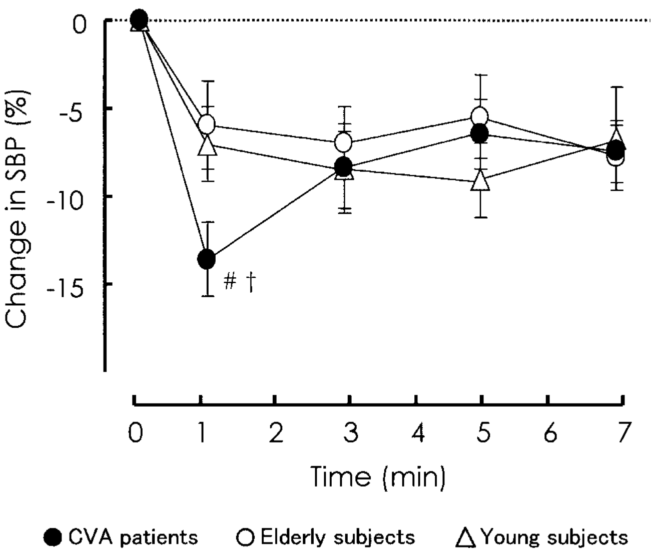

Fig. 4 Percentage change in systolic blood pressure (SBP) in patients with cerebrovascular accidents (CVA), elderly and young subjects during head-up tilt. Data represent mean±SEM. Closed circles: CVA patients, open circles: elderly subjects, triangles: young subjects. # $p<0.05$ *vs.* Young; † $p<0.05$ *vs.* Elderly.

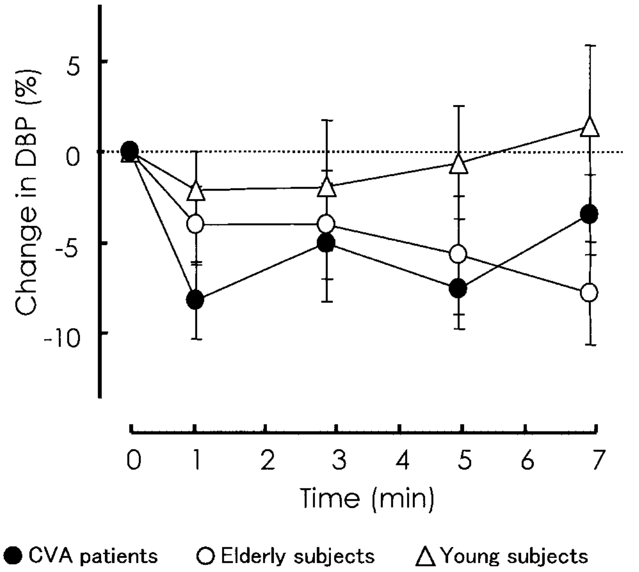

Fig. 5 Percentage change in diastolic blood pressure (DBP) in patients with cerebrovascular accidents (CVA), elderly and young subjects during head-up period. Data represent mean±SEM. Closed circles: CVA patients, open circles: elderly subjects, triangles: young subjects.

tained throughout the head-up period (Fig. 3). In contrast, CO in CVA patients remained almost constant throughout the experiment, and the falls in CO with head-up tilt in healthy elderly and young subjects were significantly greater than that in the CVA patients at 7 min of head-up tilt ($p<0.05$, respectively).

SBP in CVA patients exhibited extraordinary results. Head-up tilt resulted in immediate fall in SBP in all groups and the magnitude of the initial SBP reduction in CVA patients was greater than that in the healthy groups ($p<0.05$, Fig. 4). A significant decrease in SBP was sustained throughout the head-up period in all groups. Similarly, the fall in DBP in CVA patients was largest at 1 min of head-up tilt (Fig. 5), but recovered to the level of supine rest at 7 min of head-up tilt. In comparison, DBP in elderly subjects also decreased at the start of head-up tilt but gradually decreased further during the head-up period and was significantly lower by 7 min of head-up tilt compared to that in the control state. In contrast, DBP in young subjects remained constant throughout the test.

Discussion

The major findings of the present study were as follows: 1) the fall of SV in CVA patients was less than that in healthy subjects at 7 min of head-up tilt, however, the decrease in SBP and DBP was similar to that in healthy subjects at 7 min of head-up tilt; 2) a rapid increase of HR resulted in constant CO at 1 min of head-up tilt, however, SBP and DBP remained significantly decreased at 1 min of head-up tilt in CVA patients; 3) in CVA patients, the CO did not change from 1 min to 3 min of head-up tilt, however, the SBP recovered to the level in the healthy groups by 3 min of head-up tilt.

Orthostatic upright stress primarily results from the human body structure, which is composed of elastic cutaneous tissue and muscles covering the skeleton, like an elastic or distensible tube. When humans stand, gravitational forces cause a shift of blood from the thoracic cavity to the abdomen and lower extremities with a consequent fall in ventricular filling pressure and SV. Therefore, the immediate decrease in SV in all groups during head-up tilt in the present study was consistent with these physiological concepts (23–26) during orthostatic stress in humans. However, our finding of a small decrease of SV in CVA patients during head-up tilt suggested that the blood shift from the thoracic cavity in CVA patients was less than that in healthy subjects during the 7 min of head-up tilt. We assumed that the elasticity of the body cavity in CVA subjects might be reduced, that is, stiffer than that in young healthy subjects.

Normal cardiovascular responses to upright posture include, 1) increased HR, 2) preserved CO, 3) increased peripheral vascular resistance, and 4) maintenance of BP (1). The medullary vasomotor center receives pressure signals from both cardiopulmonary and arterial baroreceptors, consequently increasing HR through vagal suppression and activation of sympathetic nerves, and induces vasoconstriction of peripheral vessels by stimulating sympathetic nerve activity (27). The increase of HR and preservation of CO during head-up tilt in all groups indicated that these cardiovascular homeostatic systems were mostly intact in all groups. However, the responses of CO and SBP during head-up tilt in CVA patients were different from the other groups.

Numerous studies have compared cardiovascular responses to orthostatic stress in elderly and young subjects (28–33). A blunted HR response and a smaller increase in peripheral resistance are well documented in the elderly (29–31, 33). In the present study, the magnitude of tachycardia during head-up tilt in elderly subjects was attenuated compared with young subjects. However, it has been suggested that a small decrease in SV is the cause of attenuated tachycardia during head-up tilt. Therefore, the blunted HR response during head-up tilt in the elderly is probably not due to age-related attenuation of sensitivity in baroreceptors and cardiopulmonary receptors. Previous studies (34, 35) have reported a significantly attenuated SV response to orthostatic changes in elderly subjects compared with young subjects, and suggested that a decreased volume shift from the intrathoracic to the peripheral circulation in the elderly contributed to attenuation of the SV response. We also observed identically attenuated SV and blunted HR response during head-up tilt in the elderly. Furthermore, our present study demonstrated an attenuated SV decrease and blunted HR response during head-up tilt in CVA patients.

In the present study, we observed differences in the following parameters between CVA patients and age-matched normal elderly individuals: 1) SV, HR, and CO during supine rest, 2) SV and CO at 7 min of head-up tilt, and 3) initial reduction of SBP. The significant initial reduction of SBP induced by head-up tilt in CVA patients was particularly puzzling. The attenuated SV and slightly increased HR in CVA patients comparable to elderly control subjects were expected to produce equivalent decreases in SBP and DBP to both patients and controls. We, therefore, speculated that peripheral vasoconstriction inhibited the decrease of SBP and DBP in elderly control and young subjects. However, other mechanisms, such as blunted baroreceptors and cardiopulmonary receptors, disorder of the medullary cardiovascular center, and attenuated responses of peripheral sympathetic nerve activities might have contributed to the initial reduction of SBP and DBP in CVA patients. In this regard, Mizushima et al. (11) reported attenuated responses of muscle sympathetic nerve activities during the cold pressor test in CVA patients. Therefore, CVA *per se* might have attenuated muscle sympathetic nerve activity and induced the initial reduction of SBP and DBP in our present study.

The present CVA patients were well trained and lived in their own home. However, their daily activities and fitness were lower than those of age-matched healthy elderly subjects. The present study was performed to investigate the cardiovascular regulating system during head-up tilt in CVA patients, and this regulating system is modulated by age (32), thus, we used age-matched healthy subjects as a kind of control. Unfortunately, we did not recruit age-matched healthy controls with similar SV, CO and HR. Thus, we did not eliminate the possibility of floor effects of cardiovascular responses during orthostatic stress in CVA patients. Although floor effects might have contributed to constant CO during head-up tilt in CVA patients, the consistent CO did not maintain SBP during initial phase of head-up tilt. Nevertheless, weather our findings may have resulted from stroke in itself or a secondary impairment from attenuated daily activities caused by hemiplegia, an initial reduction of SBP to head-up tilt could be induced by the cardiovascular regulating system in chronic CVA patients. However, further studies considering the characteristics of control subjects will be needed.

In conclusion, the most important finding of the present study was the initial falls in SBP and DBP in CVA patients and the recovery of both parameters by 3 min of head-up tilt. We consider that standing up and walking activities should be basic physical programs in health management for chronic CVA patients. Clinically, the fluctuation of BP in CVA patients is undesirable, and therefore, physicians, nurses, physical therapists, and medical staff should consider this initial reduction of BP when CVA patients are exposed to orthostasis. In addition, we emphasize that orthostatic tolerance in humans is required for any daily activity and adjustment to orthostatic stress in CVA patients should be practiced by head-up tilt, as our findings showed that CVA patients maintained physiological orthostatic tolerance, except for the initial fall in blood pressure.

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