Orthostatic Hypotension in Elderly Persons During Passive Standing: A Comparison With Young Persons

Takayasu Kawaguchi, Osamu Uyama, Miwako Konishi, Tadahiro Nishiyama, and Takeo Iida

1College of Nursing Art and Science Hyogo, Akashi, Japan.
2College of Science and Engineering, Ritsumeikan University, Kusatsu, Japan.

Background. The present study was aimed at clarifying the mechanism of orthostatic hypotension (OH) that occurs in elderly persons and at investigating assisting methods to prevent OH by evaluating changes in autonomic nervous system (ANS) activity and cerebral circulation of elderly persons when engaged in passive standing.

Methods. Eight elderly volunteers and 9 young volunteers gave informed consent to participate in the study. Two experimental conditions were established: (i) “active standing,” in which the subjects stood on their own with guidance from an assistant, and (ii) “passive standing,” in which the subjects were placed in a standing position completely by an assistant. ANS was determined before and after standing by measuring the heart rate variability. The reaction of the ANS was evaluated on the basis of low-frequency power (LF: 0.05–0.15 Hz) and high-frequency power (HF: 0.15–0.4 Hz), which were separated from the R-R interval data by power spectral analysis using the fast Fourier transformation. Cerebral perfusion was measured over the right frontal region using a near-infrared spectroscopy cerebral oxygen monitor.

Results. The main findings were: (i) Transient decreases in blood pressure occurred immediately after standing in both the young and elderly subjects. (ii) The LF:HF ratio increased significantly (p < .05) immediately after active standing in the young subjects, whereas this ratio increased in the elderly subjects after some delay. (iii) The LF:HF ratio increased significantly (p < .01) immediately after passive standing in the young subjects, whereas this ratio decreased significantly (p < .05) in the elderly subjects. (iv) In the elderly subjects, the total hemoglobin (HbT) and oxyhemoglobin showed the greatest decrease during the 15-second period after standing. The maximum changes in the HbT with passive standing differed significantly (p < .01) from those observed during active standing.

Conclusions. Our findings emphasize the need to devise bioengineered means that allow elderly persons to exert themselves, to maintain or improve muscle contractility and ANS function, while providing minimum assistance for standing.

The increase in the elderly population has been accompanied by a rising number of injuries and accidents due to physical disabilities associated with aging. This includes the problem of orthostatic hypotension (OH), which, until recently, has been almost exclusively associated with cerebrovascular diseases. However, an epidemiologic survey conducted by Robbins and colleagues (1) revealed that approximately 20% of elderly persons aged 65 and older, including those without cerebrovascular disease, show a propensity to develop OH. Similarly, in a survey conducted by Ooi and colleagues (2), more than 50% of elderly residents of retirement and nursing homes reported OH. Thus, OH appears to be a common finding even in elderly persons without apparent organic disabilities.

OH develops from hydrostatic pressure differences that occur during standing, during which time blood pools in the lower body, and the circulating blood volume decreases. This results in decreased blood pressure due to a reduction in cardiac output and diminished intra-arterial blood volume. Symptoms of OH, such as dizziness, lightheadedness, weakness, blurred vision, impaired concentration, and even loss of consciousness, may occur when cerebral perfusion is markedly impaired (3). Blood pressure regulatory reactions that prevent these symptoms when standing appear typically as (i) the increase of heart rate variability due to an activated sympathetic nervous system and (ii) the prevention of concentrated blood flow to the lower body due to the contractility of the lower limbs’ skeletal muscle (maintenance of venous return). For patients who have been fatigued or bedridden for a long time and for persons who have recently recovered from an illness, blood pressure regulatory reaction is made difficult because the contracting function of skeletal muscle and the reaction of the sympathetic nervous system have weakened. Therefore, when the patients’ postures are to be passively changed, to prevent OH it is necessary to ask for their positive participation in the move or to make them aware that they are to be moved (4,5).

Several studies on OH caused by passively changed posture have been conducted in connection with autonomic nervous system (ANS) activity (6–8). However, past studies have not examined how the passive change of posture changes cerebral circulation or if the passive change of posture relates to OH. Moreover, few studies have clarified what effects are given to the maintenance of cerebral circulation by the contractility of the lower limbs’ skeletal muscle or ANS activity, both of which have are caused by the movements required for active standing. Therefore, the present study was aimed at obtaining guidelines for prevent-
ing OH in elderly persons when they are assisted with passive standing. We evaluated cerebral circulation and ANS activity during passive standing (standing with complete assistance, mentally and physically) and compared this evaluation with the data taken during active standing (standing without assistance).

**METHODS**

**Subjects**
Two groups of healthy volunteers, an elderly group (4 women and 4 men; median age, 68.2 years; range, 64–79 years) and a younger group (5 women and 4 men; median age, 23.5 years; range, 21–32 years) were enrolled in the study. All subjects were screened by taking an accurate history, physical examination, routine laboratory tests, and resting 12-lead ECG to ensure that they were in good health and showed no evidence of acute illness, clinically apparent cardiovascular disease, diabetes mellitus, or neurological disorders. None of the subjects smoked cigarettes or were currently taking any medication. The research protocol was approved by the institutional review board, and each subject gave informed consent.

**Experimental Protocol**
Each subject performed a series of motions to assume or be placed into a standing position from a sitting position in a chair (height of seat surface, 33 cm). The subjects were all trained to stand in a uniform manner consisting of initial forward flexion of the back and neck followed by extension of the body. Two experimental conditions were established: (i) “active standing,” with guidance from an assistant, and (ii) “passive standing,” in which the subjects remained passive while an assistant placed them in a standing position. The active standing procedure began with the assistant holding the subject by both hands. The subject remained with their knees in flexion until given a verbal cue, after which the subject assumed a standing position with guidance from the assistant. The passive standing procedure began with the assistant placing a knee between both legs of the subject, positioning the subject’s arms at their side, and putting both hands of the subject around the neck of the assistant. While maintaining the center of gravity downward, the assistant positioned the subject in a standing position. To maximize the cooperation of the subjects during the study, a female nurse served as the assistant for female subjects, and a male nurse served as the assistant for male subjects.

After sitting at rest for 5 minutes, each subject performed active standing, remained standing for 5 minutes, and then sat down again. After the subject sat at rest for another 5 minutes, the passive standing procedure was performed, and the subject again remained standing for 5 minutes. The time required to complete active standing and passive standing was constant at 3 seconds. ECG monitoring and continuous monitoring and recording of cerebral circulation using a near-infrared cerebral oxygen monitor were performed during these procedures. In addition, an automated blood pressure monitor (Jentow-7700, Nihon Colin, Japan) was used to measure pre- and post-standing blood pressure. Blood pressure was measured at three time points: 2 minutes before standing, immediately after standing, and 3 minutes after standing.

**Heart rate spectral analysis.**—Heart rate variability was measured by ECG telemetry (Syna Act MT11, NEC Medical Systems, Tokyo, Japan) from lead V5 and recorded using a data recorder (RD135T, TEAC, Tokyo, Japan). The sampling accuracy of the recorded data was 1 kHz, and analog-digital conversion was performed on a computer (AD98, Canopus, Kobe, Japan). An R-R interval analysis program (Pasherver, Kissei Comtec Co., LTD, Nagano, Japan) was used to calculate the mean R-R interval and standard deviation. Spectral analysis was performed by fast Fourier transform (FFT). The Hanning window method was used to pre-treat the signal data for FFT analysis. Spectral analysis was performed 3 minutes before and 3 minutes after standing (FFT algorithm yielding a 256-point). The data were condensed into 2-minute sampling periods to better view the detailed changes during each 3-minute period. Spectral analysis was performed at 30-second intervals for a total of 6 time points before and after standing to evaluate time sequence changes (Figure 1).

The total power of the heart-rate spectral data provided by FFT was separated into a low-frequency component (LF: 0.04–0.15 Hz) and a high-frequency component (HF: 0.15–0.4 Hz). Each respective power component was divided by the total power (TP) and expressed as LF/TP and HF/TP. These values were used as an index of changes in ANS activity. In particular, the LF:HF ratio was used as an index of sympathetic nervous system activity.

To evaluate cardio-vagal nerve activity separately from sympathetic nervous activity, testing was performed while
each subject maintained a respiratory rate of at least 9 breaths per minute.

Near-infrared spectroscopy.—For the purpose of monitoring cerebral circulation, cerebral perfusion was measured using a near-infrared cerebral oxygen monitor (OM-200, Shimadzu Corp., Kyoto, Japan), with its sensor unit placed over the right eyebrow. The area was cleaned with alcohol before the sensor unit was affixed. This device utilizes near-infrared light rays to measure changes in hemoglobin in biological tissue by spatial analysis on the basis of the light diffusion theory. The device’s light source consists of three different wavelength laser beams (780 nm, 805 nm, and 830 nm), and the beams are irradiated in order. According to the variations in optical density (OD) of each wavelength, oxygen-hemoglobin (HbO2), deoxyhemoglobin (HbD), and total hemoglobin (HbT) are calculated on the basis of the Lambert-Beer law (9):

\[ \text{OD} = \text{ absorption coefficient} \times \text{path length} \times \text{concentration} \]

Where OD = the variations in optical density from the initial value, and Hb = changes in the concentration of hemoglobin.

In addition, this device shows the difference between actual biological tissue and theoretical concentration, and the difference is represented by values that have been revised on the basis of the light diffusion formula (10,11). Because this device provides the relative changes in concentration in each subject, we used an arbitrary unit (AU) to express the concentration.

Statistical Analysis

The respective changes in pre- and post-standing blood pressure for the young and elderly groups were analyzed and compared by one-way ANOVA. For changes in other pre- and post-standing parameters, the Student’s paired t test was used to analyze linear distribution variables (median R-R, LF/TP and HF/TP, HbT, HbO2, and HbD). The Wilcoxon signed rank test was used to analyze nonlinear data variables (LF and HF power and the LF:HF ratio). Comparison between the young and elderly subjects was conducted using the Student’s t test and Mann-Whitney U test. Significance was established at the $p < .05$ level for all analyses.

RESULTS

Blood Pressure and Heart-Rate Spectra

Table 1 shows comparisons in heart rate variability for 3 minutes before and after standing. The mean R-R interval (in milliseconds) decreased significantly after standing in both the young and elderly subjects ($p < .01$). This decrease tended to be greater in the young subjects than in the elderly subjects. The R-R standard deviation (in milliseconds) was significantly higher in the young subjects than in the elderly subjects. Both LF power and HF power were higher in the young subjects than in the elderly subjects. LF power was significantly higher ($p < .01$) before active standing in the young subjects, and HF power was significantly higher ($p < .05$) before passive standing in the elderly subjects. The LF: HF ratio increased after active standing in both the young and elderly subjects but tended to decrease after passive standing. In particular, the LF:HF ratio was significantly higher ($p < .05$) after active standing in the young subjects.

Blood pressure was higher in the elderly subjects than in the young subjects at all time points. There were no significant blood pressure changes before and after standing in either of the age groups. Blood pressure decreased immediately after standing but tended to return to baseline levels after 3 minutes. Furthermore, there were no significant differences in blood pressure changes between active standing and passive standing (Table 2).

Figure 2 shows heart-rate variability data for 3 minutes before and after standing in a typical case from each group. Comparison of the waveform changes in the R-R interval

<table>
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<tr>
<th>Table 1. R-R Interval Variability Before and After Standing</th>
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<td><strong>Active Standing</strong></td>
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Notes: Values are mean ± SD. n = 9 young subjects; n = 8 elderly subjects.
Before vs after: *p < .05, **p < .01
Young vs elderly: †p < .05, ‡p < .01.
between the young and elderly subjects revealed regular and rhythmic variations in the young subjects but more blunted variations in the elderly subjects. We observed transient shortening of the R-R interval for approximately 10 seconds immediately after standing. The degree of shortening was more pronounced with active standing than with passive standing. The elderly subjects demonstrated less shortening of the R-R interval after standing, including a more gradual response, than the young subjects.

A comparison of the frequency power distribution between the young and elderly subjects revealed greater power values in the young subjects. Evaluation of the changes in total power showed a decrease in the HF power component after standing in the young subjects but showed very little change in the elderly subjects.

Serial Changes in Heart-Rate Spectra Before and After Standing

Figure 3 shows time sequence changes in LF/TP, HF/TP, and the LF:HF ratio before and after active standing. There were no significant differences in the LF/TP changes. However, the young subjects showed a significantly lower HF/TP (p < .05) at 0 to 2 minutes and 0.5 to 2.5 minutes after standing than immediately before standing. The young sub-
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jects showed a significantly increased LF:HF ratio \( p < .05 \) immediately after standing, whereas this ratio increased in the elderly subjects only after some delay.

Figure 4 shows time sequence changes in LF/TP, HF/TP, and the LF:HF ratio before and after passive standing. The young subjects showed a significantly increased LF/TP \( p < .05 \) at 0.5 to 2.5 minutes after standing, whereas the elderly subjects had a significantly decreased LF/TP \( p < .05 \) immediately after standing. The elderly subjects showed a decreased HF/TP \( p < .05 \) immediately after standing. The young subjects showed a significantly increased LF:HF ratio \( p < .01 \) at 0.5 to 2.5 minutes after standing, whereas the elderly subjects had a significantly lower LF:HF ratio \( p < .05 \) immediately after standing, followed by a slow subsequent increase.

Changes in Cerebral Circulation

Figure 5 shows the changes in HbT, HbO\(_2\), and HbD in the young subjects every 2 seconds after standing. The HbT and HbO\(_2\) showed the greatest decrease during the 10-second period after standing and returned to baseline levels approximately 20 seconds after standing. The HbD rose slightly after standing, although not significantly, and returned to baseline values approximately 20 seconds after standing. A comparison of the maximum variation in HbO\(_2\) and HbT during active standing and passive standing revealed significantly greater changes during passive standing (HbT, \( p < .01 \); HbO\(_2\), \( p < .05 \)).

Figure 6 shows the changes in HbT, HbO\(_2\), and HbD in the elderly subjects every 2 seconds after standing. The HbT and HbO\(_2\) showed the greatest decrease during the 15-second period after standing and tended to be slightly delayed compared with the young subjects. Furthermore, unlike in the young subjects, these values had still not returned to baseline levels even 20 to 25 seconds after standing. A comparison of the maximum variation in HbO\(_2\) and HbT during standing revealed a significant difference in the change in the HbT \( p < .01 \) during passive standing compared with active standing.

DISCUSSION

The changes in the LF:HF ratio of the elderly subjects after passive standing was delayed significantly in comparison with the young subjects, which proves the blunt reaction of the sympathetic nervous system of the elderly subjects after standing. This implies that it is necessary to pay attention to activating the function of the ANS of elderly subjects when they stand passively. As for the changes in cerebral circulation, there appeared to be a transient decrease in the

Figure 3. Comparison of heart-rate variability of the young and elderly subjects in active standing.

Figure 4. Comparison of heart-rate variability of the young and elderly subjects in passive standing.

Figure 5. A, Changes in HbT, HbO\(_2\), and HbD in the young subjects every 2 seconds after standing. B, Comparison of the maximum variation in HbT and HbO\(_2\) in the young subjects during active and passive standing.
cerebral perfusion during a period of 10 to 20 seconds after standing in both young and elderly subjects. In particular, the decrease in cerebral perfusion was more significant in passive standing than in active standing. The main reasons are a decrease in venous return due to the lack of contractility of the lower limbs’ skeletal muscle and a decrease in heart-rate variability caused by a decrease in venous return. As for healthy persons, the increase in heart-rate variability due to an activated sympathetic nerve will compensate even under a condition of this kind. However, such a compensation can hardly be expected in elderly persons with lowered autonomic nervous function, and, in particular, it is unlikely that compensation will occur in elderly subjects who suffer from diabetes and ANS dysfunction (12). ANS dysfunction is a morbid state caused by aging; it is therefore necessary to take into account the changes in morbid states caused by aging.

The present study established two conditions, active standing and passive standing, to control experimentally whether or not skeletal muscle contractility arises. These two methods of care are generally taken in clinical situations, and the results of the present study demonstrate the influence given to the venous return by the difference of skeletal muscle activity, which is applicable to actual situations where care is given.

The present study analyzed heart-rate variation to reflect ANS activity during postural changes. This method of analysis, particularly with reference to the evaluation of the effects of changes in posture on OH, has been discussed by other investigators (13,14). Some researchers have reported different characteristic trends between elderly patients, who often experience ANS dysfunction and decreased muscle strength, and healthy younger individuals (15–17).

Pagani and colleagues (18) compared heart rate variability between young and elderly subjects and found that the LF:HF ratio tended to be lower with a head-up tilt posture in the elderly subjects. Lipsitz and colleagues (8) evaluated the characteristics of heart-rate variability in elderly subjects during a head-up tilt procedure and concluded that the low frequency power component tended to increase less remarkably (0.06–0.10 Hz) than that observed in younger subjects, suggesting that abrupt postural changes present a risk factor for syncopal attacks in this group. Our results are in general agreement with these previous findings. Thus, during assisted standing in the elderly persons, who may already be experiencing some autonomic nervous dysfunction, sufficient precautions must be taken to ensure adequate autonomic nerve function (e.g., allowing the elderly persons to stand up with as little assistance as possible).

Furthermore, we found that changes in heart-rate variability and cerebral perfusion were greatest during the 30-second period immediately after standing. Until recently, rapid changes in these parameters induced by standing were difficult to measure due to limitations in the available measurement devices. However, recent improvements in measurement devices have enabled more accurate assessment of these parameters immediately after standing. Tanaka and colleagues (19) applied a volume clamp technique to continuously monitor finger blood-pressure variations immediately after active and passive standing and found a substantial reduction in blood pressure during the first 10 seconds after standing. Bloomfield and colleagues (6) analyzed and compared heart-rate variations in subjects during passive head-up posturing and active standing up and found a marked reduction of the R-R interval immediately after active standing. On the basis of their results, they suggested the importance of monitoring these variations immediately after standing in the diagnosis of OH. We noted similar variations in the present study (Figure 2).

One purpose of the present study was to clarify the influence of changes in blood pressure when standing on cerebral circulation. However, measurements in the present study did not find remarkable changes in blood pressure immediately after standing. That is to say, the manchette measuring method did not allow us to measure the rapid changes in blood pressure immediately after standing, which was one of the study purposes. The R-R interval variability shows an abrupt increase in heart rate during an instantaneous period of 10 to 20 seconds immediately after standing. A sharp drop in blood pressure seems to have occurred with the increase in heart rate. It is necessary to develop in-depth studies on the changes in blood pressure by developing a testing method that can monitor the blood pressure’s serial changes during the entire process of the test.

The influence of postural changes on cerebral perfusion, which was clarified by this experiment, has also been studied by others, along with the development of measuring instruments. In 1948, Shenkin and colleagues (20) measured cerebral blood flow changes from a head-up to a head-down position by the Kety method utilizing radioisotopes. Since then, advanced imaging technologies, including computed tomography, single photon emission computed tomography, and positron emission tomography, have been developed. These technologies assist in medical diagnosis by allowing the monitoring of cerebral perfusion during head-up tilt testing as well as other postures. Recently, several studies have
began to focus on the relation between impaired cerebral autoregulation and orthostatic hypotension. Aaslid and colleagues (21) examined the reduced cerebral blood flow associated with postural changes in healthy subjects and reported that the autoregulatory function associated with cerebral vascular constriction was evident within 10 seconds and returned to baseline within 60 seconds. In contrast, this autoregulatory function appears to be impaired in patients with autonomic nervous dysfunction, thus predisposing these patients to the development of symptoms such as syncpe.

The present study included the use of a near-infrared cerebro oxygen monitor to measure changes in cerebral perfusion immediately after standing. This device monitors intracerebral blood flow via a sensor placed on the forehead. We chose this device because it is noninvasive and imposes minimal burden on the study subjects. Several studies, including those by Hampson and colleagues (22), Kurth and colleagues (23), and Li and colleagues (24), have verified that this device can accurately monitor cerebral blood flow and cerebral oxygenation. Jobsis (9) stated that the changes in HbO2 detectable by near-infrared monitoring reflect relative changes in cerebral perfusion. Similarly, in the present study, relative changes in HbO2 served as an index of changes in cerebral perfusion upon standing. The measurement technique currently used, although capable of determining relative changes in a specific subject, is still not able to provide absolute values. Thus, interpretation of the changes at each measurement point can be considered only on an individual basis because it is often difficult for the relation between the concentration and optical density based on the Lambert-Beer law to be applied directly to biological tissue. It can be pointed out that the measurement based on the Lambert-Beer law needs contrastive materials of “zero-concentration,” which are difficult to obtain in biological tissue, and that it is difficult to determine optical axis distance because biological tissue is a strong scattering medium. In some studies, the variability gained from the NIRS measurement is expressed in μmol/l. However, for the above-mentioned reasons, the use of μmol/l when measured with this device may result in questionable findings. We and others (25,26) express by the arbitrary unit.

Cerebral blood flow and metabolism are known to gradually decrease after reaching adulthood as part of the aging process. Hock and colleagues (27) reported that the magnitude of increase in HbT and HbO2 and the magnitude of decrease in HbD during brain activity (measured over the forehead) is lower in elderly individuals than in younger individuals. In addition, the amount of brain parenchyma differs between younger and elderly individuals. Although cerebral atrophy is generally most prominent in patients with presenile and senile dementia, these atrophy changes may also be present in healthy elderly individuals. From the perspective of the monitoring principles used in the present study, the distance from the skin site of the sensor to the brain parenchyma was longer in the elderly subjects than in the young subjects (28,29); thus, differences in the amount of cerebrospinal fluid occupying the space between the skull and brain parenchyma may also have influenced our findings. Because a comparison of the differences in absolute cerebral blood flow between elderly and young subjects was not possible, our study focused on the assessment of the relative changes in each group of subjects.

We evaluated autonomic nervous function and cerebral perfusion primarily on the basis of the premise that the ANS plays a major role in the regulation of cerebral circulation. However, regulation of cerebral circulation is not influenced only by the ANS. Higher-functioning circulatory centers in the central nervous system (CNS) have also been shown to play an important role in this process. A study in cats by Ninomiya and colleagues (30) describes the involvement of higher CNS centers in the regulation of increased cardiac sympathetic nerve activity just prior to spontaneous movement and in the regulation of increased heart rate and myocardial contractility during actual movement. These findings indicate that spontaneous movement may also play a key role in circulatory regulation. Thus, sudden passive postural changes of a person in an assisted care setting likely contribute to the development of OH. Further in-depth research should be conducted, including an investigation of the specific role of higher CNS function in these conditions.

The worldwide increase in the aging population is expected to increase the necessity to assist elderly persons with their postural changes, which may consequently increase accidents due to OH while they are assisted with standing. Our findings indicate that it is important to make elderly persons aware of the necessity to activate their autonomic nervous function before they are assisted with standing and to take care of them in a way that sufficiently utilizes the function of their skeletal muscles. Further studies are needed that examine situations where elderly persons are assisted with standing, and it is necessary to develop bioengineered means that allow elderly persons to exert themselves for the maintenance and improvement of muscle contractility and ANS function.

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Address correspondence to Takayasu Kawaguchi, RN, PhD, College of Nursing Art and Science Hyogo, 13-71, Kitaoji-cho, Akashi 673-8588, Japan. E-mail: takayasu_kawaguchi@cnas-hyogo.ac.jp

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