Effects of Age and Hypertension on Autonomic Nervous Regulation During Passive Head-Up Tilt

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Abstract To study the effects of age and hypertension on autonomic nervous activity with passive postural change, we examined 31 normotensive subjects (25 to 85 years old) and 31 hypertensive patients (21 to 71 years old) without any cardiac disease, diabetes mellitus, or neurological disorders. Subjects were passively placed in a 60° head-up tilting position after 15 minutes in the supine position. Autonomic nervous function was evaluated by frequency domain analysis of heart rate variability with the autoregressive method. Using low-frequency (0.1 Hz) and high-frequency (0.25 Hz) peaks, the ratio of low- to high-frequency power (L/H) was calculated as an index of sympathetic activity and the ratio of high to total power (%HF) as that of parasympathetic activity. With the patient in the supine position, total power spectral density declined logarithmically with age in normotensive subjects and hypertensive patients, but %HF and L/H showed no changes. In response to passive tilting, L/H increased and %HF was decreased in the normotensive subjects, and these responses declined with age logarithmically. In contrast, hypertensive patients exhibited less autonomic response to postural change regardless of age. These results suggest that autonomic neural response to tilt is decreased with age; however, attenuation of the response by hypertension is not associated with an increase in age.

Key Words • aging • autonomic nervous system • spectrum analysis

Methods

Subjects
The subjects were 31 hypertensive patients (World Health Organization stages I and II) aged 21 to 71 years (mean±SD, 55±14 years) and 31 normotensive subjects (25 to 85 years, 52±17 years). Patients with cerebrovascular disease, diabetes mellitus, neuromuscular dysfunction, cardiac disease, or arrhythmia were excluded. Exclusion of cerebrovascular disease was based on normal findings on brain computed tomography and physical examination. The diagnosis of hypertension was based on normal findings on brain computed tomography and during admissions to the hospital and kept on a diet with a salt content of 7 to 10 g/d. Drugs affecting neural regulation including sedatives and antihypertensive agents were discontinued at least 1 week before the study.

Power Spectral Analysis
Patients were kept in the supine position in a temperature-controlled, quiet room for 30 minutes before postural change. After baseline data were obtained for 15 minutes, patients were passively placed in a 60° head-up tilting position, then returned to the supine position for 15 minutes. Heart rate and blood pressure were continuously measured throughout the study with a monitoring apparatus (CBM-3000, Nippon Colin, Nagoya, Japan). Blood pressure was measured on a beat-to-beat basis through a sensor placed on the wrist over a radial artery, which was calibrated every 2 minutes by blood pressure in the brachial artery of the opposite side with a sphygmomanometer. A total of 512 RR intervals were obtained from each recording, usually for 7 to 10 minutes of each data acquisition. We used stationary RR intervals free from noise or ectopic beats. When an ectopic beat existed, we excluded the consecutive three beats including the ectopic beat.

Heart rate variability was then assessed by power spectral analysis with an autoregressive model using a computer program (AUTONOMIC NERVOUS SYSTEM PACKAGE, version 1.09, Nippon Colin). For analysis, total power was defined as power at 0.03 Hz or greater, low frequency (LF) as the peak at 0.1 Hz, and high frequency (HF) as the peak at 0.25 Hz. The ratio of low- to high-frequency power (L/H) was calculated as an index of sympathetic activity and the ratio of high-frequency to total power (%HF) as that of parasympathetic activity.

The study protocol was approved by the Ethics Committee of Osaka University Hospital, and informed consent was obtained from each subject.
Statistical Analysis

The correlation between age and spectral power was analyzed by a simple regression model. Differences of changes in heart rate and the power spectral indexes (total power, $L/H$, and $\%HF$) between normotensive subjects and hypertensive patients were assessed by two-way analysis of variance (ANOVA) with repeated measures. Differences in changes of these variables within groups were analyzed by a two-tailed, paired $t$ test. A value of $P<.05$ was considered statistically significant.

Results

In normotensive subjects in the supine position, total power declined with age (Fig 1). Absolute power of HF and LF decreased with age similar to total power, and $\%HF$ and $L/H$ showed no age-related changes (Fig 1). Similarly, a decline in total power with no age-related change in $\%HF$ and $L/H$ was observed in hypertensive patients (Fig 2). Systolic blood pressure was not significantly altered by passive postural change in the normotensive subjects (from $114\pm3$ to $113\pm3$ mm Hg), but it was decreased in the hypertensive patients (from $149\pm3$ to $145\pm3$ mm Hg, $P<.05$). Diastolic blood pressure was unchanged in normotensive (from $64\pm2$ to $67\pm2$ mm Hg) and hypertensive groups (from $82\pm2$ to $84\pm2$ mm Hg). In response to tilt, heart rate was similarly increased in normotensive subjects (from $64\pm2$ to $76\pm3$ beats per minute, $P<.01$) and hypertensive patients (from $64\pm2$ to $76\pm2$ beats per minute, $P<.01$). The heart rate response to passive tilt decreased with age in both groups. During passive tilt, $\%HF$ decreased and $L/H$ increased in both groups (Figs 3 and 4). $L/H$ response was significantly attenuated in the hypertensive patients compared with the normotensive subjects ($P=.016$). In normotensive subjects, the responses of $\%HF$ and $L/H$ declined with age (Fig 5), whereas those in hypertensive patients showed no age-related changes (Fig 6).

Discussion

In this study, we examined the effects of age and hypertension on the autonomic nervous function at rest and during passive postural tilt. Results obtained with patients in the supine position confirmed previous reports that heart rate variability, as shown by total power of spectral analysis, decreased with age.\cite{6,8,10} These changes may be explained by vascular sclerosis,\cite{3} de-
In response to passive postural tilt, normotensive subjects showed a significant increase in L/H and decrease in %HF, indicating sympathetic activation and reduction of vagal tone during postural change. These responses declined with age. Thus, autonomic nervous response was reduced in the elderly.

In hypertensive patients, L/H response to tilt was significantly attenuated compared with that in normotensive subjects. Although it did not reach statistical significance, %HF in the hypertensive patients also showed a lower response. These poor responses were observed even in young patients, resulting in no age-related decline of sympathetic and parasympathetic responses to tilt. Therefore, the effect of hypertension on autonomic function was masked in the elderly patients. Gribbin et al showed an independent effect of age (19 to 66 years) and hypertension on baroreceptor reflex sensitivity in response to phenylephrine injection. In their study, decrease of baroreceptor function in hypertension was observed even in patients more than 50 years of age. It was also

**Figure 3.** Graphs show example of power spectral density before, during, and after head-up tilt in a 27-year-old normotensive man. HF indicates high frequency; LF, low frequency.

**Figure 4.** Line graphs show response of %HF and L/H to passive head-up tilt (TILT). Data are mean±SEM; n=31 for each group. Open circles show normotensive subjects; closed circles, hypertensive patients (*P<.05 between groups). %HF indicates percentage of high-frequency power in total power; L/H, ratio of low- to high-frequency power. Response of L/H was significantly attenuated in hypertensive patients compared with normotensive subjects (F=0.0159).
reported that increases in blood pressure and age (21 to 68 years) are associated with a reduction in β-adrenergic receptor response of heart rate. In contrast, similar to our results, Kawamoto et al demonstrated a limited influence of hypertension in older subjects (56 to 76 years) because their autonomic functions have already declined with aging. The lack of interaction between age and hypertension in the elderly in the former two studies may be due to the relatively younger age composition of the aged group as well as the difference in methods used to evaluate autonomic function.

Schwartz et al reported that age-related decline in L/H was observed only in patients under controlled breathing. However, this study needed 45 minutes for the entire recording. Because keeping patients in controlled breathing for 45 minutes is not only difficult but also stressful and may affect autonomic nervous activities, we did not ask for controlled breathing but observed the effects of aging on the autonomic response during head-up tilt. These results suggest that the method used in this study does not require controlled breathing for the assessment of autonomic nervous activity from heart rate variability.

In conclusion, autonomic neural response to tilt is decreased with age; however, attenuation of the response by hypertension is not associated with the increase in age.

Fig 5. Scatterplots show effects of age on the response of %HF and L/H to passive tilt in normotensive subjects. Data are expressed as percent change of values for patients during tilt to those with patients in the supine position. %HF indicates percentage of high-frequency power in total power; L/H, ratio of low- to high-frequency power. n=31.

Fig 6. Scatterplots show effects of age on the response of power spectral components to tilt in hypertensive patients. Data are expressed as percent change of values for patients during tilt to those with patients in the supine position. %HF indicates percentage of high-frequency power in total power; L/H, ratio of low- to high-frequency power. n=31.
References


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