*Original Article*

# Altered Aortic Properties in Elderly Orthostatic Hypertension

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**To investigate the impact of arterial properties on orthostatic blood pressure (BP) dysregulation in older hypertensives, orthostatic BP dysregulation, a common phenomenon in elderly hypertensives, is associated with target organ damage and falls. However, the mechanism of orthostatic BP dysregulation remains unclear. The pulse wave velocity (PWV), related arterial stiffness, and the augmentation index (AI), a measure of arterial wave reflection, were measured in 365 older hypertensives. We classified the study patients into an orthostatic hypertension (OHT) group with orthostatic increase of systolic BP (SBP) of ≥20 mmHg (*n*=27) and an orthostatic normotension (ONT) group with an orthostatic increase of SBP of <20 mmHg and orthostatic SBP decrease of <20 mmHg (*n*=338). Orthostatic AI was significantly greater in the OHT group than in the ONT group (OHT: 6.5±12% *vs.* ONT: −5.6±12%, *p*<0.001), while supine AI and supine and orthostatic pulse rate were comparable between the two groups. There was no significant difference in the PWV between the OHT and ONT groups. Orthostatic hypertension was affected by altered aortic properties and associated with augmented wave reflection of arterial pressure. (*Hypertens Res* 2005; 28: 15–19)**

***Key Words*: aortic properties, augmentation index, orthostatic hypertension**

## Introduction

Orthostatic hypotension, often found in elderly hypertensives with autonomic nervous dysfunction (a large subgroup of elderly hypertensives), is well recognized as a risk factor for falls, syncope and cardiovascular events (*1*–*4*). However, there have been few reports on orthostatic hypertension (OHT), in which the blood pressure (BP) increases with orthostatic postural change (*5*–*11*). Although some reports have suggested that an orthostatic BP increase predicts an increased risk of developing coronary artery disease (*5*, *7*) and cerebrovascular disease (*8*, *10*), the clinical significance and mechanism of OHT remain unclear.

One report showed that the patients with OHT had higher seated systolic BP (SBP) than those without OHT (*7*). Generally, the progressive appearance of the reflected wave in systole and eventual summation with the forward incident wave results in augmentation of the SBP (*12*).

We speculated that aortic properties play an important role in orthostatic BP increase. However, there have been no reports about the relationship between aortic properties and orthostatic BP change. In this study, we investigated the relationship between aortic properties and orthostatic BP increase.

## Methods

### Patients

We enrolled 382 hypertensive patients who satisfied the following criteria: 1) supine BP (measured by standard cuff methods after resting 5 min in a supine position) ≥140 mmHg for SBP and/or ≥90 mmHg for diastolic BP (DBP); or 2) treatment of hypertension ≥ 3 months without a change of anti-hypertensive drugs at either of two Japanese hospital

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**Table 1. Clinical and BP Characteristics**

| | Normal group ($n$=338) | Orthostatic hypertension ($n$=27) |
|---|---|---|
| Age (years) | 60±12 | 65±10 |
| Male (%) | 55 | 48 |
| Body mass index (kg/m$^2$) | 24±3.2 | 25±2.7 |
| Smoking (%) | 24 | 12 |
| Hyperlipidemia (%) | 32 | 19 |
| Diabetes mellitus (%) | 10 | 29* |
| Coronary artery disease (%) | 14 | 29 |
| Cerebrovascular disease (%) | 8 | 0 |
| Treated hypertension (%) | 64 | 63 |
| Ca antagonist (%) | 40 | 28 |
| ARB (%) | 30 | 28 |
| β-Blocker (%) | 11 | 12 |
| ACE inhibitor (%) | 13 | 16 |
| Diuretics (%) | 11 | 8 |
| α1-Blocker (%) | 7 | 0 |
| Supine brachial | | |
| SBP (mmHg) | 142±18 | 136±18 |
| DBP (mmHg) | 86±11 | 83±12 |
| HR (bpm) | 68±11 | 67±12 |
| Standing brachial | | |
| SBP (mmHg) | 142±19 | 163±19** |
| DBP (mmHg) | 91±13 | 97±13* |
| HR (bpm) | 74±13 | 74±12 |

*$p$<0.05, **$p$<0.001 *vs.* normal group. BP, blood pressure; ARB, angiotensin receptor blocker; ACE, angiotensin converting enzyme; SBP, systolic BP; DBP, diastolic BP; HR, heart rate.

clinics. The entry period was January 2002 to December 2002. Informed consent was obtained from all study participants, and the study was approved by the Research Ethics Committee of the Department of Cardiology, Jichi Medical School.

## Pules Wave Velocity (PWV) and Augmentation Index (AI) Measurements

BP, PWV and AI were measured with the subject in a supine position after 5 min of rest using an automatic waveform analyzer (formPWV/AI; Colin Co., Komaki, Japan). The validity and reproducibility of brachial-ankle PWV using this autonomic waveform analyzer have been reported in type 2 diabetes patients (*13*), patients with coronary artery disease (*14*, *15*), and patients on chronic dialysis (*16*). AI was determined by arterial applanation tonometry incorporating an array of 15 micropiezoresistive transducers placed on the right carotid artery (formPWV/AI; Colin Co. ) and was calculated from the aortic pressure waveform (*17*). Carotid BP was estimated by the pressure signal obtained using tonometry, by equating the carotid mean arterial pressure to the brachial artery measurement as previously described (*18*). PWV and supine AI were simultaneously recorded. Standing AI was measured with the subject in a standing position for at least 3 min. The orthostatic AI change was taken as the difference between the supine and standing AI.

**Table 2. Profiles of Aortic Properties**

| | Normal group ($n$=338) | Orthostatic hypertension ($n$=27) |
|---|---|---|
| PWV (cm/s) | 1,754±390 | 1,707±369 |
| Supine AI (%) | 23±17 | 21±18 |
| Standing AI (%) | 17±19 | 28±16* |

*$p$<0.05 *vs.* normal group. PWV, pulse wave velocity; AI, augmentation index.

## Definition of OHT

Brachial BP and heart rate (HR) were measured with the subject in a supine position after resting 5 min in the supine position, and then with the subject in a standing position for at least 3 min. No patients developed presyncope or syncope in the standing position. We classified the patients into an OHT group with an orthostatic SBP increase ≥ 20 mmHg ($n$=27) and an orthostatic normotension group (ONT) with an orthostatic SBP increase < 20 mmHg and orthostatic SBP decrease < 20 mmHg ($n$=338). We excluded 17 patients who had an orthostatic SBP decrease ≥ 20 mmHg, because the prevalence of α-adrenergic blockade use (40%) in this group was significantly higher than that in the OHT (0%, $p$<0.001) or ONT (7%, $p$<0.001) group.

## Statistical Analysis

A two-tailed paired $t$-test was used to compare mean values between the two groups. An $\chi^2$ test was applied to examine differences in prevalence between the two groups. A value of $p$<0.05 was considered to be statistically significant.

# Results

There were no significant differences in the frequency of antihypertensive drug use between the two groups. The prevalence of diabetes mellitus and the standing SBP and DBP were higher in the OHT group than in the ONT group, while the supine SBP was lower in the OHT group than in the ONT group (Table 1).

There was no significant difference in the estimated carotid BP ofthe supine position between the OHT and ONT group (137±18 *vs*. 143±22 mmHg). However, the carotid BP of the standing position was higher in the OHT group than in the ONT group (167±19 *vs*. 141±22 mmHg, $p$< 0.001).

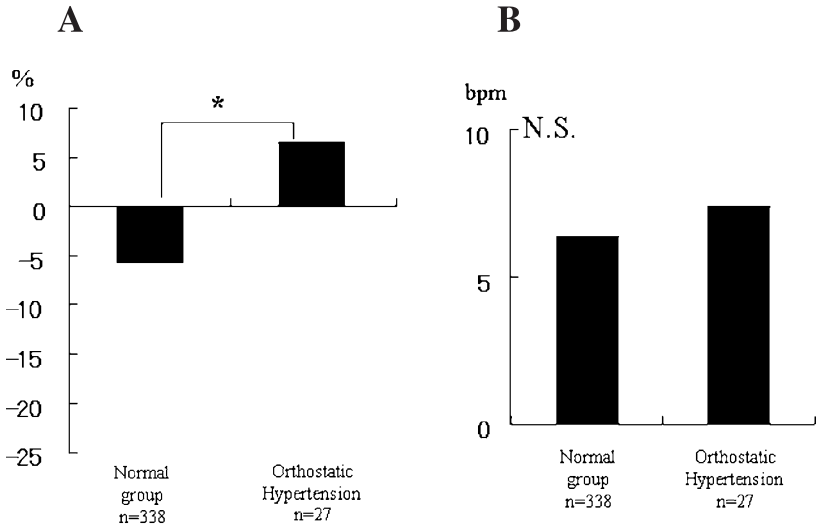


**Fig. 1.** *Orthostatic changes in augmentation index (A) and heart rate (B).* *$p < 0.001$ *between the indicated colums.*

There was no significant difference in the PWV or supine AI between the two groups. Standing AI was higher in the OHT group than in the ONT group (Table 2).

Figure 1 shows the orthostatic changes in AI and HR in the two groups. The orthostatic change in AI was higher in the OHT group than in the ONT group. There was no significant difference in the change of HR between the two groups.

## Discussion

In this study, the orthostatic AI change of the OHT group was significantly higher than that of the ONT group, indicating that OHT might be determined by functional arterial properties related to the orthostatic change in the amount and site of wave reflection. We observed an excessive augmentation of the reflected pressure wave in the OHT patients.

In regard to PWV, there was no significant difference between the OHT and ONT group. PWV is related to aortic distensibility and compliance by the Bramwell-Hill equation (*19*). PWV is known to be an indicator of arterial stiffness (*20–23*), and has been regarded as a marker reflecting vascular damage (*24*, *25*). Therefore, the mechanism of OHT might not be simply progressed in arterial stiffness.

There was no significant difference in PWV or AI in the supine position between the OHT group and ONT group. However, AI in the standing position and orthostatic AI change were significantly higher in the OHT group than in the ONT groups. AI is determined by the intensity and timing of reflected pressure waves (*26*). The intensity of aortic wave reflection is a determinant of the vascular tone of the peripheral artery (*27*, *28*). The augmentation of a reflected pressure wave occurs earlier as a consequence of the new reflecting site provided by the increased peripheral resistance (*27*, *28*). The mechanism of OHT remains unclear, although some pathogenic processes have been reported (*6*). In an earlier study, we reported that plasma norepinephrine and vasopressin levels during tilting were significantly higher and that the orthostatic norepinephrine increase tended to be higher in a group of subjects with OHT than in those with ONT (*10*). This finding suggests that orthostatically induced sympathetic activation might play some role in the pathogenesis of OHT. In OHT, sympathetic activation accompanied by orthostatic change might increase the vascular tonus, which is related to the augmentation of reflected pressure waves. In the present study, the prevalence of diabetes mellitus was 40% in the OHT group. Orthostatic hypotension is a well-known complication caused by autonomic denervation in patients with long-term poor control of blood glucose levels. One report demonstrated (*29*) that OHT was a novel complication in normotensive diabetic patients and that the hypersensitivity of the cardiopulmonary baroreflex and sympathetic nervous system might contribute to the pathogenesis of OHT. The incidence of diabetes mellitus in this study might have played a role in the orthostatic BP increase.

In addition, cardiac factors are among the important determinants of AI (*12*). One report demonstrated a linear relation between AI and HR in a pacing study, with AI decreasing by 4% for every 10 bpm increments in HR (*30*). Because of the proportionality between ejection time and cardiac cycle duration, the peak of the forward traveling wave occurs earlier at faster HR. In this study, there were no significant differences in orthostatic BP change between the OHT and ONT groups. Therefore, orthostatic AI change appears not to be explained by the orthostatic HR change.

In a recent study in which the study groups findings were adjusted for age and 24-h SBP, we reported that elderly hypertensive patients with OHT often have advanced silent cerebrovascular diseases, and they may be at elevated risk of overt clinical cerebrovascular events (*10*). In addition, other authors have reported that AI was an independent predictor of

mortality due to end-stage renal failure in hemodialysis patients with normal PWV (*31*). In the present study, there was no significant difference in AI or PWV between the OHT and ONT group. This result suggests that the OHT group may have consisted of hypertensives without abnormal arterial structure but with impaired functional arterial properties that were detected as an excess augmentation of arterial wave reflection.

Increased BP variability may contribute to an increase in the risk for hypertensive target organ damage (*32*). Morning BP increase is reported to be associated with cardiac hypertrophy in hypertensive patients (*33*), and this may trigger cardiovascular events (*34*). We previously reported that ambulatory BP variability was increased more markedly in a group of patients with OHT than in an ONT group (*10*). This BP variability may have been partly due to the augmentation of reflected waves.

In this study, the prevalence of administration of α-adrenergic blockers was higher in the OHT group than in the ONT group. Postural hypotension, one of the side effects of using α-adrenergic blockers, is often seen in the early phase, and is not rare in the chronic phase, of drug therapy (*35*). In this study, all patients had taken anti-hypertensive drugs for at least 3 months. In our previous study, we reported that the orthostatic BP increase was selectively abolished by α-adrenergic blockers (*10*). This might indicate that administration of α-adrenergic blockers diminished the orthostatic AI increase. In the present study, the ONT group showed a higher rate of calcium antagonist use that the OHT group. Slavachevsky *et al*. suggested that calcium antagonists might induce a greater decline in orthostatic BP than angiotensin converting enzymes (*36*). This may also indicate that administration of a calcium antagonist diminished the orthostatic BP increase in the present study.

In a previous study by Safer *et al*., carotid BP was shown to be a more sensitive marker of mortality in end-stage renal disease than brachial BP (*18*). In the present study, there was no significant difference in supine carotid BP between the ONT and OHT group, but standing carotid BP was higher in the OHT group than the ONT group. In the OHT group, standing carotid BP was higher than standing brachial SBP. In addition, the present study that altered aortic properties in elderly patients with orthostatic hypertension could be successfully assessed by carotid BP. Carotid BP might be a better predictor of target organ damages than brachial BP.

Our findings indicated that excessive augmentation of arterial wave reflection was the predominant mechanism of OHT. The OHT group may have consisted of hypertensive patients without abnormal arterial structure but with abnormal functional properties resulting in elevated risk of hypertensive cerebrovascular disease.

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