*Original Article*

# The Influence of Wave Reflection on Left Ventricular Hypertrophy in Hypertensive Patients Is Modified by Age and Gender

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**It has been established that a positive association exists between the augmentation index (AIx) and left ventricular mass (LVM) in hypertensives, but it remains unclear whether this association is affected by age or gender. The aim of the study was to assess the effect of age and gender on the association between carotid AIx and LVM in hypertensive patients. We performed arterial tonometry and echocardiography in 512 treated hypertensive patients who were divided into 4 groups by gender and age (older or younger than 65 years). Correlations between carotid AIx and echocardiographic indices were evaluated by univariable and multivariable models. In females, carotid AIx increased with age up to 60 years, but decreased thereafter. In univariable analyses, carotid AIx was positively correlated with the LVM index in younger females ($r$=0.25, $p$=0.04) and males ($r$=0.48, $p$<0.001), but not in the older age groups. Multivariable analyses showed that this positive correlation in younger males remained significant ($\beta$=0.39, $p$<0.001) after adjusting for age, body mass index, and mean arterial pressure. In contrast, in the older subjects, carotid AIx was negatively correlated with relative wall thickness in females ($\beta$=–0.14, $p$=0.034) and males ($\beta$=–0.17, $p$=0.037) independent of age and mean arterial pressure. A significant association between carotid AIx and LVM index was seen only in younger males. The lack of any such association in older hypertensives can be explained by both the plateau in the values of carotid AIx, and the fact that LVM increased with age. (*Hypertens Res* 2008; 31: 649–656)**

***Key Words*: carotid augmentation index, hypertension, aging, gender, left ventricular mass and geometry**

## Introduction

The augmentation index (AIx) has been widely used to assess the pulsatile properties of the arterial system (particularly in relation to pulse wave reflection) and to characterize its impact on the heart (*1*). Previous studies have demonstrated that AIx is positively correlated with left ventricular (LV) mass (LVM) in normotensive subjects (*2*), hypertensive patients (*3–6*), and patients with end-stage renal disease (*7*, *8*), independently of brachial systolic blood pressure (BP), mean arterial pressure (MAP), and pulse pressure.

Age-related changes in the arterial pulse can be explained by an increase in arterial stiffness and progressively earlier wave reflection with age (*9*). However, it has been reported that both carotid and aortic AIx either tend to plateau or decline in value at around 60 years of age, despite a continued increase in aortic pulse wave velocity (PWV) and augmentation pressure (*10–13*). This phenomenon occurs much more frequently in females. Therefore, in older subjects, it is suggested that the measurement of AIx fails to detect the progressive increase in aortic stiffness with advancing age.

The Second Australian National Blood Pressure Study (ANBP2) has recently reported that there was no association

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Received July 9, 2007; Accepted in revised form November 1, 2007.

**Table 1. Characteristics of the Study Patients Grouped by Age and Gender**

| Variables | Females | | Males | | *p* | | |
|---|---|---|---|---|---|---|---|
| | <65 years (*n*=63) | ≥65 years (*n*=227) | <65 years (*n*=65) | ≥65 years (*n*=157) | Age | Gender | A×G |
| Clinical parameters | | | | | | | |
| Age (years) | 53±6 | 73±6 | 52±7 | 73±6 | <0.001 | 0.38 | 0.53 |
| Height (cm) | 153±6 | 147± 6 | 166±7 | 160±6 | <0.001 | <0.001 | 0.79 |
| Body mass index (kg/m$^2$) | 25±5 | 24±3 | 25±3 | 23±3 | <0.001 | 0.30 | 0.64 |
| Duration of hypertension (years) | 9±8 | 12±9 | 9±8 | 12±10 | 0.003 | 0.72 | 0.67 |
| Medications | | | | | | | |
| Calcium channel blockers (%) | 65 | 64 | 66 | 61 | 0.53 | 0.87 | 0.70 |
| Angiotensin converting enzyme inhibitors (%) | 22 | 19 | 17 | 21 | 0.96 | 0.74 | 0.34 |
| Angiotensin II receptor blockers (%) | 44 | 51 | 51 | 47 | 0.79 | 0.80 | 0.33 |
| Diuretics (%) | 16 | 20 | 17 | 20 | 0.34 | 0.88 | 0.90 |
| α1-Blockers (%) | 6 | 3 | 5 | 4 | 0.40 | 0.93 | 0.45 |
| Hemodynamic parameters | | | | | | | |
| Systolic BP (mmHg) | 155±18 | 157±18 | 156 ±16 | 159 ±19 | 0.23 | 0.49 | 0.77 |
| Diastolic BP (mmHg) | 89±10 | 81±10 | 91±11 | 82±11 | <0.001 | 0.11 | 0.38 |
| MAP (mmHg) | 111±11 | 106±11 | 113±10 | 107±11 | <0.001 | 0.16 | 0.69 |
| Pulse pressure (mmHg) | 67±16 | 76±17 | 65±13 | 77±18 | <0.001 | 0.79 | 0.39 |
| Heart rate (bpm) | 65±10 | 65±9 | 65±10 | 64±9 | 0.24 | 0.46 | 0.43 |
| baPWV (cm/s) | 1,643±268 | 2,025±381 | 1,644±303 | 1,961±359 | <0.001 | 0.42 | 0.39 |
| Carotid AIx (%) | 29±11 | 34±11 | 19±13 | 28±12 | <0.001 | <0.001 | 0.03 |
| Echocardiographic parameters | | | | | | | |
| IVSTd (mm) | 10±2 | 10±2 | 11±2 | 11±2 | 0.38 | 0.002 | 0.66 |
| PWTd (mm) | 10±1 | 10±2 | 10±2 | 10±2 | 0.28 | 0.003 | 0.67 |
| LVDd (mm) | 46±4 | 45±5 | 47±4 | 48±5 | 0.60 | <0.001 | 0.005 |
| LVDs (mm) | 28±4 | 28±5 | 28±4 | 30±5 | 0.06 | 0.002 | 0.004 |
| Stroke volume (mL) | 69±16 | 63±17 | 75±16 | 73±17 | 0.02 | <0.001 | 0.11 |
| Ejection fraction (%) | 70±8 | 69±9 | 71±7 | 67±9 | 0.002 | 0.63 | 0.07 |
| LV mass index (g/m$^2$) | 121 ±29 | 124 ±33 | 121±34 | 135±33 | 0.01 | 0.08 | 0.08 |
| Relative wall thickness | 0.43±0.08 | 0.45±0.09 | 0.44±0.07 | 0.44±0.08 | 0.44 | 0.82 | 0.17 |
| E/A ratio | 0.87±0.17 | 0.75±0.27 | 0.92±0.27 | 0.75±0.23 | <0.001 | 0.32 | 0.31 |
| DcT (ms) | 228±54 | 252±55 | 228±53 | 267±55 | <0.001 | 0.16 | 0.17 |

BP, blood pressure; MAP, mean arterial pressure; baPWV, brachial-ankle pulse wave velocity; AIx, augmentation index; IVSTd, interventricular septal thickness in diastole; PWTd, posterior wall thickness in diastole; LV, left ventricular; LVDd, LV diameter in diastole; LVDs, LV diameter in systole; E, early diastolic filling; A, atrial filling; DcT, deceleration time of E wave; A×G, interaction term between age and gender. Data are shown as mean±SD.

between carotid AIx and cardiovascular events in older female hypertensive patients (≥65 years) (*14*). Weber *et al*. demonstrated that aortic AIx was not associated with an increased risk of coronary artery disease (CAD) in older male patients with suspected CAD (>60 years), although the association was positive in younger male patients (*15*). In a study of older subjects (≥65 years), including 71% male and 98% hypertensives, aortic AIx did not stratify the risk for new cardiovascular events (*16*). In light of these results, it has been hypothesized that AIx may be a good marker for cardiovascular risk in younger male subjects, but not in older female and male subjects. However, no study has positively identified any effect of age and gender on the association between carotid AIx and hypertensive target organ damage. The aim of the present study was thus to assess the effect of aging and gender on the relationship between carotid AIx and LVM in hypertensive patients.

## Methods

### Study Patients

We enrolled 523 consecutive hypertensive patients from the Department of Internal Medicine for outpatients in Miwa Municipal Hospital, Japan, who had been under a consistent antihypertensive regimen for at least 6 months. Patients who had secondary hypertension, arrhythmias, valvular heart disease (more than a moderate degree by quantitative Doppler

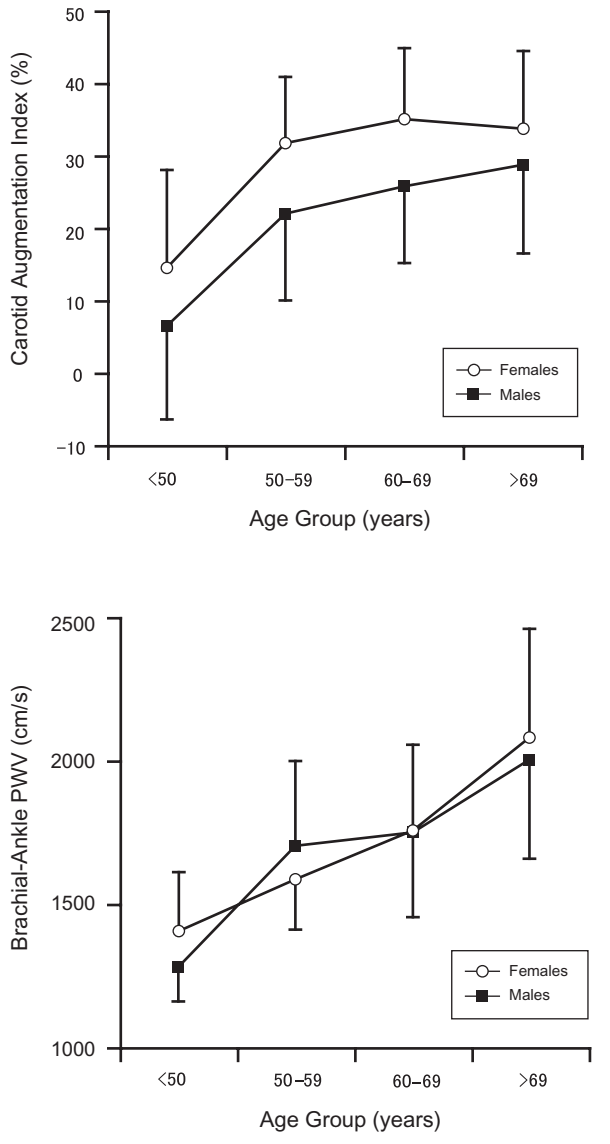


**Fig. 1.** *Age-related changes in the carotid augmentation index (upper panel) and brachial-ankle PWV (lower panel) by decade of age and gender. The numbers per group (females/males) were as follows: < 50 years, n = 10/15; 50 to 59 years, n = 27/36; 60 to 69 years, n = 70/45; and > 69 years, n = 183/126. Values are the means ± SD.*

methods), histories of clinical stroke and CAD, renal insufficiency (serum creatinine >2 mg/dL), dementia, malignancy, peripheral arterial disease defined as an ankle-brachial blood pressure index <0.9, or chronic inflammatory disease were excluded. Patients who were taking β-blockers or had impaired LV systolic function (LV ejection fraction [LVEF] <45%) were also excluded, since carotid AIx can be affected by these factors (*1*). The patients were stratified by age and gender, and classified into 4 groups (females aged <65 years; females aged ≥65 years; males aged <65 years; and males aged ≥65 years) based on previous reports in which the cutoff age was 65 years (*14*, *16*). This study was approved by the Institutional Review Board of Miwa Municipal Hospital, and written informed consent was obtained from all of the subjects.

## Clinical Measurements

At the first visit, these patients underwent a medical interview and anthropometric measurements. All patients were investigated in the morning after an overnight fast. Before the pulse wave analysis, and after 5 min of rest in a sitting position, brachial BP was measured twice at a 1 min interval using an automated cuff oscillometric device (HEM-907; Omron Healthcare, Kyoto, Japan). The average of the two BP readings was used as the BP value.

## Carotid AIx and PWV Measurements

A pulse wave analysis was performed using a vascular testing device (form/BP-203RPE II; Omron Healthcare) which simultaneously measured electrocardiograms, phonocardiograms, bilateral brachial and ankle BPs, and carotid pulse wave. Measurement of carotid AIx was performed using a multi-element applanation tonometry sensor for the left common carotid artery. A multi-element tonometry sensor consisting of 15 pressure-sensitive small elements aligned side-by-side was coupled to the device. The quality of the carotid pulse wave and the downward force were checked visually on a tonogram, and pulse waves were recorded and stored over a period of 30 s. The validity and reproducibility of this tonometry sensor have been reported previously (*8*, *17*).

In this study, arterial stiffness was noninvasively assessed by brachial-ankle PWV (baPWV). The baPWV was measured by using the volume-plethysmographic method. The details of the measurements and the reproducibility of this automatic method have been described in previous reports (*8, 17*, *18*). The mean of the right and left baPWV values was used for the analysis. Carotid AIx and baPWV were measured by a trained investigator (who did not obtain the previous measurements) in a quiet and temperature-controlled laboratory (23°C) after a 5 min rest in the supine position.

## Echocardiographic Measurements

Two-dimensional and M-mode echocardiography were performed using an echocardiographic instrument (model EUB 6500; Hitachi, Tokyo, Japan) with a 2.5-MHz transducer, by a cardiologist who was unaware of the patients' clinical data. The interventricular septal thickness (IVSTd), LV posterior wall thickness (PWTd), LV diameter at end-diastole (LVDd), and LV diameter at end-systole (LVDs) were measured using leading-edge methodology, according to the recommendations regarding quantitation in M-mode echocardiography by the American Society of Echocardiography (ASE) (*19*).

**Table 2. Univariable Correlations with Carotid AIx in the Study Patients Grouped by Age and Gender**

| Variables | *r* | | | |
|---|---|---|---|---|
| | Females | | Males | |
| | <65 years ($n$=63) | ≥65 years ($n$=227) | <65 years ($n$=65) | ≥65 years ($n$=157) |
| Age (years) | 0.39** | 0.02 | 0.29* | 0.11 |
| Height (cm) | −0.15 | −0.12 | −0.33* | −0.31*** |
| Body mass index (kg/m$^2$) | −0.28* | −0.10 | −0.19 | −0.19* |
| Systolic BP (mmHg) | 0.10 | 0.10 | 0.38** | 0.25** |
| Diastolic BP (mmHg) | −0.26* | 0.08 | 0.22 | 0.04 |
| Heart rate (bpm) | −0.53*** | −0.45*** | −0.39** | −0.43*** |
| baPWV (cm/s) | 0.17 | 0.03 | 0.23 | 0.13 |
| LV mass index (g/m$^2$) | 0.25* | 0.06 | 0.48*** | 0.10 |
| Relative wall thickness | 0.20 | −0.13 | 0.26* | −0.16* |
| Ejection fraction (%) | −0.18 | −0.04 | −0.17 | −0.03 |
| E/A ratio | 0.03 | 0.03 | −0.01 | 0.13 |
| DcT (ms) | 0.27* | 0.14* | 0.15 | 0.04 |

Abbreviations as in Table 1. *$p$<0.05; **$p$<0.005; ***$p$<0.001.

When an optimal orientation of the M-mode line could not be obtained, correctly oriented two-dimensional linear measurements were made by the leading-edge convention according to the ASE recommendations (*20*). LVM was calculated using the anatomically validated formula reported by Devereux (*21*). The LVM index (LVMI) was calculated as the LVM divided by the body surface area. LV relative wall thickness (RWT) was calculated at end-diastole as (IVSTd+PWTd)/LVDd. LV volume was calculated by the method of Teichholz. Stroke volume was calculated as the difference between end-diastolic volume and end-systolic volume. Linear measurement-derived LVEF was calculated as the percentage reduction of LV volume from end-diastole to end-systole. Next, the parameters of LV diastolic function were measured by recording the LV diastolic inflow using pulsed Doppler echocardiography. The LV diastolic filling pattern was recorded from the apical transducer position with the sample volume situated between the mitral leaflet tips. The peak velocity of early rapid filling (E-wave velocity) and the peak velocity of atrial filling (A-wave velocity) were recorded, and the ratio of the E-wave to the A-wave (E/A) was calculated. The deceleration time (DcT) of the E-wave velocity was measured as the time interval from the E-wave peak to the decline of the velocity to baseline values.

The reproducibility of LVMI and RWT measurements was evaluated in a randomly drawn subsample of 30 patients in whom echocardiography was repeated at 3-d intervals. The intraobserver coefficient of variation for LVMI was 6.2%, and that for RWT was 6.7%.

## Statistical Analysis

Values are expressed as the means±SD values for continuous variables and as percentages for categorical variables. The two-way analysis of variance (ANOVA) was performed to detect any differences in the continuous variables between groups. For categorical variables, pairwise comparisons were analyzed with a $\chi^2$ test or Fisher's exact test as appropriate. Pearson's correlation coefficient was used to examine the univariable correlations between carotid AIx and the examined variables. Multivariable linear regression analyses were performed to estimate and test the independent effect of carotid AIx on LVMI and RWT, adjusting for confounding factors. The null hypothesis was rejected when the two-tailed $p$ value was <0.05. All statistical analyses were performed with SPSS version 11.0 (SPSS Inc., Chicago, USA).

## Results

A total of 512 patients completed the study protocol and their data were analyzed. The mean age was 67.7±9.8 years (range, 30–83 years); there were 290 females and 222 males. Because 11 patients had either impaired LV systolic function or significant valvular disease on echocardiography, they were excluded from the study.

The characteristics of the study patients grouped by age and gender are shown in Table 1. In comparison to younger (age <65 years) patients, older (age ≥65 years) patients had a lower height and body mass index. The older patients also had a longer history of hypertension than the younger patients, while there were no significant differences in the antihypertensive drug classes among the 4 groups. The percentages of current smokers, hyperlipidemia, and diabetes were similar among the 4 groups. The older patients had higher baPWV, carotid AIx, and LVMI, and lower stroke volume and LVEF than the younger patients. As expected, the LV diastolic function (lower E/A ratio and longer DcT) in the older patients was impaired to a greater extent than in the younger patients.

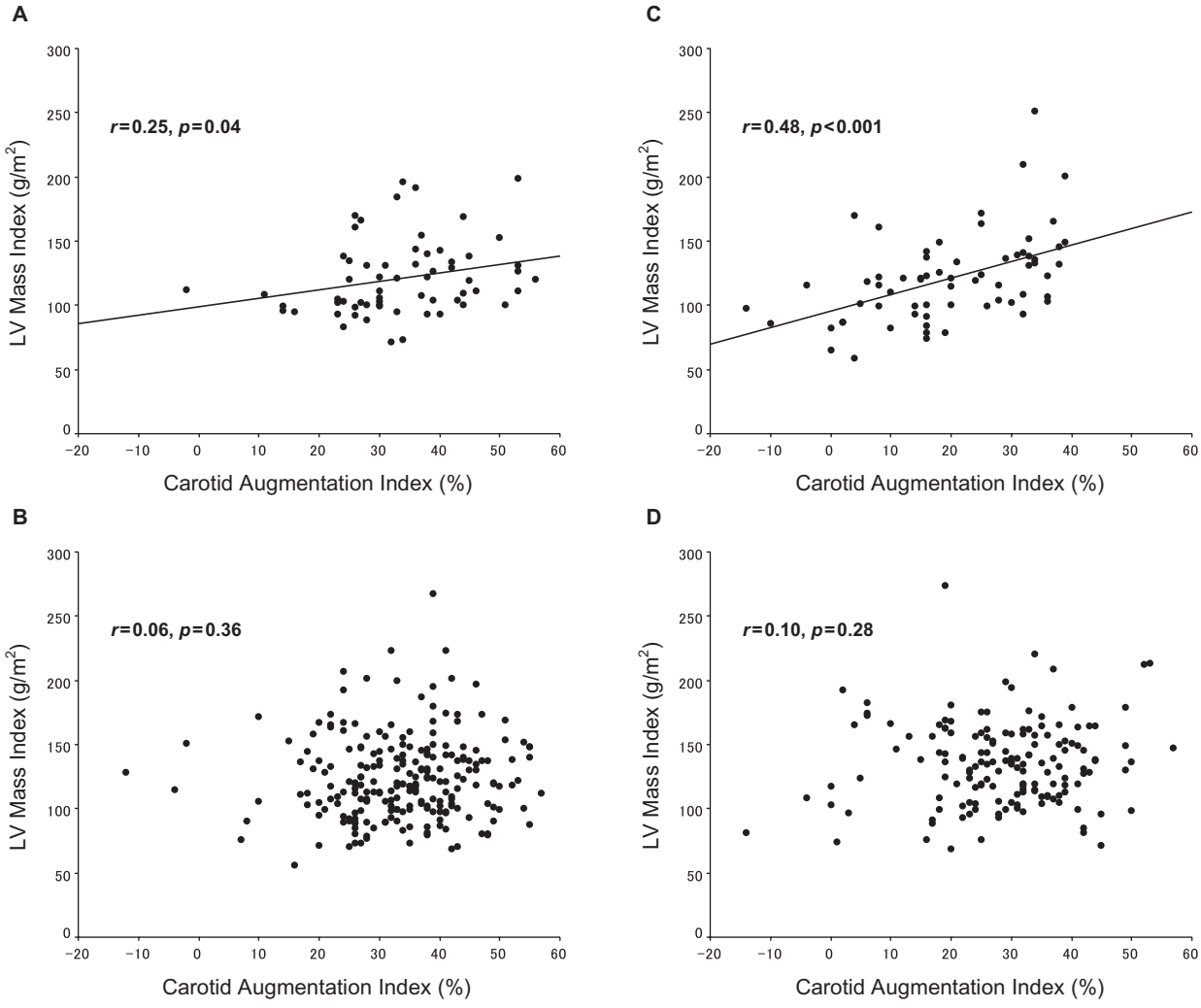


**Fig. 2.** *Correlation between the carotid augmentation index and LV mass index grouped by age and gender. A: Females aged < 65 years. B: Females aged ≥65 years. C: Males aged < 65 years. D: Males aged ≥65 years.*

Carotid AIx was significantly correlated with age both in all patients ($r$=0.25, $p$<0.001) and in the younger group ($r$=0.37, $p$<0.001), but not in the older group ($r$=0.06, $p$=0.27). As shown in Fig. 1, the age-related changes in carotid AIx were more prominent in the younger group. Carotid AIx was higher in females than in males at each decade of age ($p$<0.001). In addition, carotid AIx in females increased with age up to 60 years, then tended to decrease thereafter. The significant interaction term in carotid AIx also indicates that the increase in carotid AIx with age was greater in males than in females, and that the gender difference in carotid AIx was larger in the younger patients (Table 1 and Fig. 1). In contrast, baPWV continued to increase with age in both genders. LVMI was also significantly and positively correlated with age in both genders ($r$=0.17, $p$<0.001). In contrast to the age-related changes in carotid AIx, however, the age-related increase in LVMI was found in the older group ($r$=0.15, $p$=0.003), but not in the younger group ($r$=0.13, $p$=0.14). These age-related increases in LVMI observed in subjects overall and in the older groups remained significant even after adjusting for body mass index and systolic BP.

In univariable analyses, carotid AIx was significantly correlated with LVMI in all patients ($r$=0.13, $p$=0.004). When the subjects were separately analyzed by gender, a significant correlation was observed in males ($r$=0.25, $p$<0.001), but not in females ($r$=0.10, $p$=0.09). On the other hand, when they were divided by age (older or younger than 65 years), a significant correlation was observed in the younger ($r$=0.34, $p$<0.001) but not in the older ($r$=0.03, $p$=0.59) subjects. Univariable analyses were then performed in each subgroup (Table 2). Carotid AIx was positively correlated with LVMI in younger females and males (Fig. 2A, C), but not in older females and males (Fig. 2 B, D). On the other hand, no significant association between baPWV and LVMI was observed in

**Table 3. Multivariable Regression Analyses for Left Ventricular Mass Index**

| Independent variables | Females | | | | Males | | | |
|---|---|---|---|---|---|---|---|---|
| | <65 years ($n$=63) | | ≥65 years ($n$=227) | | <65 years ($n$=65) | | ≥65 years ($n$=157) | |
| | $\beta$ | $p$ | $\beta$ | $p$ | $\beta$ | $p$ | $\beta$ | $p$ |
| Age (years) | 0.27 | 0.06 | 0.19 | 0.004 | 0.13 | 0.38 | 0.14 | 0.09 |
| Body mass index (kg/m$^2$) | 0.20 | 0.16 | 0.15 | 0.03 | 0.19 | 0.13 | 0.12 | 0.15 |
| MAP (mmHg) | 0.12 | 0.36 | 0.15 | 0.02 | 0.15 | 0.28 | 0.12 | 0.17 |
| Carotid AIx (%) | 0.25 | 0.08 | 0.07 | 0.38 | 0.39 | <0.001 | 0.11 | 0.20 |
| | $r^2$=0.34 | | $r^2$=0.28 | | $r^2$=0.38 | | $r^2$=0.26 | |

$\beta$, standardized regression coefficient; $r^2$, multiple coefficient of determination, other abbreviations as in Table 1.

any of the groups. In females, carotid AIx was positively correlated with DcT in both the younger and older groups. In males, carotid AIx was positively correlated with RWT in the younger males, but negatively correlated with RWT in the older males.

Multivariable linear regression analyses for LVMI were performed in each subgroup (Table 3). Carotid AIx was associated with LVMI ($\beta$=0.39, $p$<0.001) independent of age, body mass index, and MAP in younger males, but this association was not observed in the other subgroups. In the older groups, carotid AIx was negatively correlated with RWT (females: $\beta$=−0.14, $p$=0.034; males: $\beta$=−0.17, $p$=0.037) independent of age and MAP.

## Discussion

The major findings of this study were the positive correlation between carotid AIx and LVMI in younger hypertensive patients; however, the correlation was lost in the older groups. Even after adjusting for confounders, this correlation was only observed in younger males. These results may be partly due to the fact that the age-related changes in carotid AIx were more prominent in younger patients. These findings imply that carotid AIx may not be useful for measuring the LV load in older patients. Furthermore, in contrast to our expectations, carotid AIx was negatively correlated with RWT in the older patients. These new findings deserve further discussion.

### Influence of Age on the Association between Carotid AIx and LVM

LV hypertrophy is an adaptive process occurring in response to long-term increases in myocardial work caused by pressure or volume overload (*1*). The earlier wave reflection, which impedes LV ejection as a pulsatile load, increases LV load by increasing the aortic pressure in late systole (*22*). In fact, several studies have demonstrated that AIx is positively correlated with LVMI (*2–8*). Nevertheless, this association has not been analyzed separately by age and gender. In the present study, the age-related changes in carotid AIx were non-linear; carotid AIx increased with age in younger patients, but this increase slowed down and plateaued after the age of 50. These results are consistent with the previous observations of age-related changes in AIx in the general population (*10–13*, *23*, *24*). In more recent studies, particularly in older subjects, the significance of AIx as a predictor of cardiovascular risk has been questioned (*14–16*).

In our older patients, in contrast to the age-specific changes in carotid AIx, LVMI increased linearly with age. Conrady *et al*. reported that LVMI increases with advancing age in hypertensive patients, and they showed that the relation of LVMI to age could be explained by increasing hypertensive duration (*25*). The older hypertensive patients might have a prolonged opportunity to acquire LV load, because LV load may be accumulated for a certain period before it is sufficient to affect LVM. The absence of any association between carotid AIx and LVMI in our older patients might have been due to the discrepancy between the age-related changes of carotid AIx and LVMI. Two physiological mechanisms can be considered as possible reasons for the non-linear relationship between age and carotid AIx in our study.

First, Mitchell *et al*. suggested that age-related changes in carotid AIx are consistent with the hypothesis that a marked increase in elastic artery PWV with little change in muscular artery PWV leads to impedance matching between the central aorta and proximal muscular arteries, which reduces proximal wave reflection and shifts reflecting sites distally (*10*). Therefore, carotid AIx declines in older subjects. A second mechanism is the change in the pattern of LV ejection and the decrease in the ejection duration that occur as a result of depressed LV systolic function. Together, these changes could cause a further reduction in AIx (*1*). Nürnberger *et al*. found that carotid AIx was correlated significantly with age only in young healthy subjects, but not in those with cardiovascular disease, which included patients with impaired LV function (*26*). The lack of an association between age and carotid AIx in older subjects may have been due to alterations in the LV ejection pattern. In the present study, the older patients had lower LVEF than the younger patients, suggesting that in cases of impaired LV contractility, such as with aging, hypertensive heart disease, and CAD, we should exer-

cise caution when using the carotid AIx as a measure of wave reflection.

### Influence of Gender on the Association between Carotid AIx and LVM

In younger patients, males showed a higher correlation between carotid AIx and LVMI than females. The predictors of AIx (height, heart rate [HR]) and the impact of gender on AIx were consistent with previous studies (*17*, *26–29*). The authors of these studies also suggested that the observation of a high AIx in females was predominantly due to their lower height and thus the closer physical proximity between the heart and the reflecting site, rather than an effect on large artery stiffening (*30*). In a general population aged ≤65 years, it was demonstrated that AIx was significantly correlated with the risk of CAD ($p<0.001$), and this correlation was more pronounced in males ($r=0.51$) than in females ($r=0.31$) (*12*). These results are in agreement with our results. Therefore, AIx may be insufficient to provide precise information on the magnitude of the wave reflection in females. Because females are generally shorter than males, there may be no visible reflected wave foot or inflection point on the pressure wave, because the forward and reflected waves merge together (*31*). Actually, in our older females, carotid AIx was particularly high, and this may have been related to their lesser height. In our data, the age-related increase of carotid AIx exhibited a plateau when it approached a mean value of 35%, as shown in Fig. 1. This value of AIx at the carotid artery is considered to be the saturation level because it corresponds to an aortic AIx of approximately 50% (*22*), and thus to the maximal magnitude of wave reflection in the aorta (*1*). Therefore, there is no capacity for carotid AIx to be influenced by other pathological factors in this age group. These limitations indicate that carotid AIx is a poor marker for LV load and vascular aging, particularly in females (*10*, *12*, *28*).

### Impact of Wave Reflection on LV Remodeling

In the present study, negative associations were observed between the carotid AIx and RWT in the older age groups. In contrast, previous reports have demonstrated that healthy subjects with higher AIx have higher values of RWT (*2*, *32*), and these results are partially consistent with our observations in younger males. Because these previous reports studied younger and healthier subjects than those included in the present study (*2*, *32*), the association between carotid AIx and RWT may have been modified by aging and concurrent cardiovascular risk factors in our report. However, there is another possible explanation for our results. The older patients in the present study had lower LV stroke volume than the younger patients. For the same cardiac output, there is an inverse association between stroke volume and HR. Lower stroke volume was found in subjects with higher RWT (*32*). These physiological principles explain the positive association between RWT and HR (lower stroke volume, faster HR) (*33*). In addition, AIx appears to be strongly affected by the HR, a faster HR being almost invariably associated with decreased AIx (*27*). These facts could account for the negative correlations between carotid AIx and RWT in our older patients. Because carotid AIx and echocardiography were not evaluated at the same time, it is not possible to determine a more detailed mechanism.

### Study Limitations

Several limitations of this study bear mentioning. First, because the present study was cross-sectional, the cause-effect relationships can not be discussed. Second, the mean age of the study patients was high, and the numbers of patients in the 2 groups (<65 and ≥65 years) were not balanced. Third, because all of our patients were taking antihypertensive medications, these drugs may have affected both the wave reflections and the LV structure and functions. However, the proportion of drug classes was similar among the 4 groups, and it has been demonstrated that the significance of the effect of AIx on the cardiovascular risk is not influenced by cardiovascular drugs (*26*, *29*). Fourth, the carotid AIx values measured by carotid tonometry may have fluctuated, because this method requires a high degree of technical expertise. Finally, we used the baPWV as a proxy measure of aortic stiffness, instead of the carotid-femoral PWV, an established surrogate measure of aortic stiffness. However, baPWV has been validated against invasive measure of aortic PWV (*18*).

### Conclusion

Among our treated hypertensive patients, carotid AIx was associated with cardiac target organ damage in younger males, but no such association was observed in older or female patients. The ventricular-vascular interaction could be modified by various factors, so clinicians should exercise caution when using carotid AIx as an index of cardiac damage in hypertension.

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