Correlation between Wave Components of the Second Derivative of Plethysmogram and Arterial Distensibility

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SUMMARY

The ratio of two wave components |b/a| constituting the second derivative of the plethysmogram (SDPTG) was correlated with arterial distensibility. Eighty-two subjects (33–93 years old) were classified into three groups according to the thickness of the intima-media complex of the common carotid artery measured by B-mode ultrasonography. One group was non-atherosclerotic (without pathologic thickening) (nAS) and the other two groups atherosclerotic (mild and severe thickening, or plaque formation) (AS-1 and AS-2). Distensibility (D) of the common carotid artery was calculated from arterial dimensions and blood pressure: $h/p = D$, where $h = (Ds-Dd)/Dd$; Ds, Dd and p represent the inner diameter of the carotid artery at peak systole, at end diastole and brachial pulse pressure, respectively. The plethysmogram was recorded at the cuticle of the 2nd digit of the left hand, and the SDPTG was determined with a 10 msec time constant. D showed a significant negative correlation with age in all subjects and in the three separate groups. The correlation between age and |b/a| was significantly negative in all subjects. This negative correlation was not observed in the nAS group, while it was significant in both AS-1 and AS-2. The correlation between |b/a| and D was significantly positive in all subjects and in each group. Significant differences were found among the three groups for |b/a| and D. These results suggest that a decrease in |b/a| or in D was proportional to the thickness of the intima-media complex of the carotid artery, that is, the development of atherosclerosis. These results provide direct evidence that |b/a| of the SDPTG is related to the distensibility of the peripheral artery, and suggest that |b/a| is a useful non-invasive index of atherosclerosis and altered arterial distensibility. (Jpn Heart J 1998; 39: 775–784)

Key words: Second derivative of plethysmogram, Plethysmogram, Arterial distensibility, Atherosclerosis

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THE second derivative wave of the plethysmogram (PTG), the SDPTG, can notably expose the inflection points of the original PTG wave which contains information related to hemodynamics and organic or functional characteristics of peripheral arteries. Therefore, the amplitude and contour of components a, b, c, d, and e (Figure 1) constituting the SDPTG have been analyzed in relation to hemodynamics, including cardiac and peripheral circulatory functions and the SDPTG has been evaluated as a useful non-invasive clinical method.[1-4]

It has been observed that the ratio of the magnitudes |b/a| of the SDPTG is significantly correlated with age.[5-8] In addition, indices of atherosclerosis, such as thickening of the vascular wall, are also associated with the aging process.[9] These observations have aroused our interest as to whether |b/a| reflects changes in arterial distensibility.

Takazawa *et al.*[2,3,10] observed that the effect of angiotensin on the value of |b/a| was contrary to that of nitroglycerin, and moreover, the value of |b/a| was clearly affected by atherosclerotic indications. They suggested that the change in |b/a| was associated with a change in arterial distensibility. From evidence that the value of |b/a| was shifted in the juvenile direction by nitroglycerin, Ozawa[8] also reported the possibility that |b/a| was related to distensibility of the elastic arteries. Suzuki *et al.*[11] observed that |b/a| was remarkably influenced by hemodynamic changes during VVI mode pacing performed on patients with complete A-V block and suggested that the distensibility or compli-

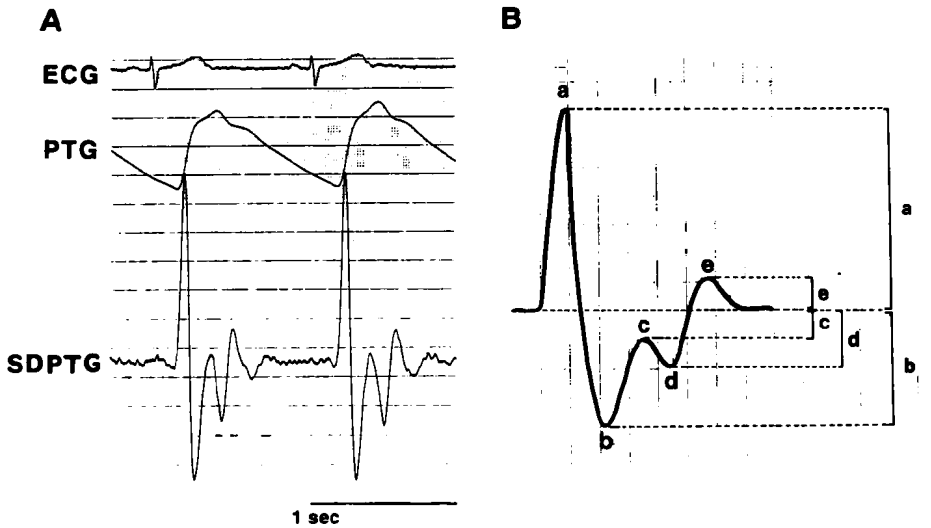

Figure 1. **A:** Original records of the ECG (upper), PTG (middle) and SDPTG (lower trace). **B:** Schematic drawing of the SDPTG. The SDPTG consists of five waves, a, b, c, d and e. Upward and downward deflections from the baseline are defined as positive and negative, respectively.

ance of the peripheral arteries could be evaluated by the value of |b/a|.

This is indirect evidence that the |b/a| of the SDPTG is related to arterial distensibility. Further studies will be needed for direct evidence of a correlation between |b/a| and arterial distensibility.

Therefore, in this study, we investigated the correlation between |b/a| of the SDPTG and the distensibility of the carotid artery, with reference to aging and the degree of atherosclerosis (thickness of the intima-media complex).

Our results confirmed directly that |b/a| is related to arterial distensibility and suggest that atherosclerosis could be evaluated by |b/a| of the SDPTG. Preliminary reports of this investigation have appeared previously in abstract form.[12-14]

Materials and Methods

Materials and groups: The 82 male and female subjects studied comprised healthy volunteers and hospital patients. Their ages ranged from 33 to 93 years old (71.9 ± 1 8, Mean ± SEM). The thickness of the intima-media complex of the carotid artery was measured by B-mode by ultrasonographic examination (ALOKA Japan D-2200) of the left and right common carotid arteries within 15 mm proximal to the bifurcation toward the internal and external carotid arteries, with the subjects in the supine position and at rest. The average value of the thickness measured for the left and right side was used for the thickness of the subject. The subjects were classified into three groups according to the thickness of the intima-media complex of the carotid artery: less than 0.9 mm, between 1.0 and 2.5 mm, and greater than 2.6 mm or local formation of plaques. The latter two groups were assumed to be atherosclerotic. The subjects were subsequently defined as nAS (non-atherosclerotic) (15 subjects), or AS-1 (39 subjects) and AS-2 (28 subjects) (atherosclerotic).

Distensibility: Estimation of distensibility of the carotid artery by the ultrasonogram image was conducted based on the method described by Blankenhorn *et al.*[15] The inner diameter of the common carotid artery within 15 mm proximal to the bifurcation toward the internal and external carotid arteries was measured on the left and right sides by ultrasonic scanning (M-mode) at systole (Ds) and diastole (Dd). Systemic blood pressure was measured at the left brachial artery using a conventional sphygomanometer (pulse pressure, p). Distensibility (D) was then calculated by the following formula;

$$h/p = D$$

where h = (Ds-Dd)/Dd. The average value of D calculated for the right and left common carotid arteries was used as the D for the subject. The values of disten-

sibility appeared in the text and the values are 1000 times greater than the calculated D.

Plethysmogram (PTG) and second derivative of PTG (SDPTG): The SDPTG was recorded (FCP-3116; sensor; TG-17, Fukuda Electric Co., Ltd., Tokyo) (10 msec in time constant) at the cuticle of the 2nd digit of the left hand, three times every 10 minutes following the ultrasonographic examination, with the subjects supine and at rest.

The SDPTG wave consists of five wave components, a, b, c, d and e (Figure 1). The amplitude of each wave from the baseline was measured, with the values above the baseline defined as positive and those below as negative (Figure 1). The b to a ratio was determined as the absolute value, $|b/a|$. The average of three measurements was used for correlation with age and D.

Statistical analysis: Data are presented as mean ± SEM. Statistical analysis was conducted using Student's *t*-test (unpaired) and differences were evaluated to be significant at $p < 0.01$ and $p < 0.05$. Correlations were evaluated by Pearson's correlation coefficient and differences were evaluated to be significant at $p < 0.01$ and $p < 0.05$ (Fisher's r to z).

Results

Correlation between age and D: The correlation between age and D was significant and negative for all subjects ($r = -0.813$, $p < 0.01$) (Figure 2A). The correlations were significant and negative within the nAS, AS-1 and AS-2 groups ($r = -0.439$, $p < 0.05$; $r = -0.648$, $p < 0.01$ and $r = -0.474$, $p < 0.01$, respectively) (Figure 2B). D was 3.681 ± 0.270 ($p < 0.01$ vs AS-1, and AS-2) in the nAS group, 1.408 ± 0.088 ($p < 0.01$ vs nAS, AS-2) in the AS-1 group and 1.023 ± 0.090

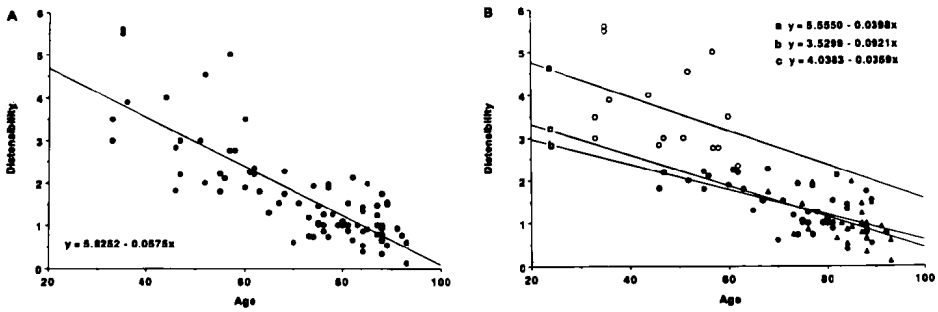

Figure 2. **A:** Correlation between age (years old) and distensibility for all subjects ($r = -0.813$, $p < 0.01$). **B:** Correlation between age and distensibility within the three groups. ○(a), nAS ($r = -0.439$, $p < 0.05$); ●(b), AS-1 ($r = -0.648$, $p < 0.01$); ▲(c), AS-2 ($r = -0.474$, $p < 0.01$). The distensibility values are 1000 times greater than the calculated D.

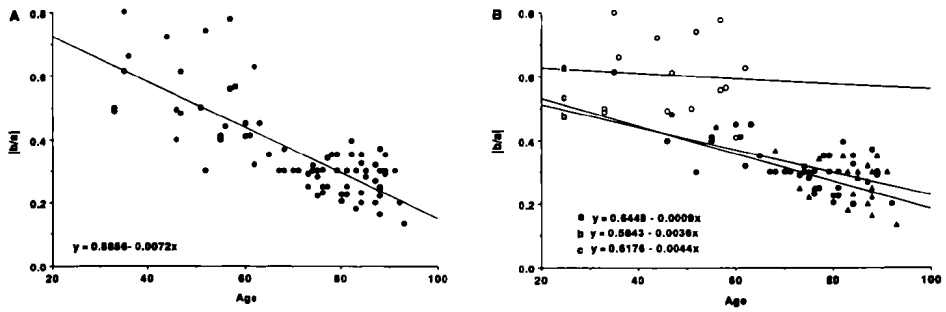

Figure 3. **A:** Correlation between age (years old) and |b/a| for all subjects ($r = -0.790$, $p < 0.01$). **B:** Correlation between age and |b/a| within the three groups. ○ (a), nAS ($r = -0.078$, $p > 0.1$ not sig.); ●(b), AS-1 ($r = -0.601$, $p < 0.01$); ▲(c), AS-2 ($r = -0.418$, $p < 0.05$).

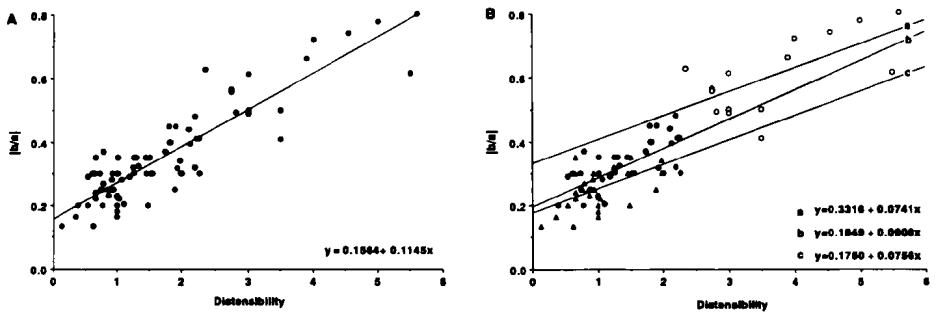

Figure 4. **A:** Correlation between |b/a| and distensibility for all subjects ($r = 0.892$, $p < 0.01$). **B:** Correlation between |b/a| and distensibility within the three groups. ○(a), nAS ($r = 0.659$, $p < 0.01$); ●(b), AS-1 ($r = 0.683$, $p < 0.01$); ▲(c), AS-2 ($r = 0.550$, $p < 0.01$). The distensibility values are 1000 times greater than the calculated D.

($p < 0.01$ vs nAS, AS-1) in the AS-2 group (Figure 5A).

Correlation between age and |b/a|: A significant negative correlation was found between age and |b/a| for all subjects ($r = -0.790$, $p < 0.01$) (Figure 3A). Subjects in the nAS group did not show a significant correlation ($r = -0.078$, $p > 0.1$), however, subjects in groups AS-1 and AS-2 showed significant negative correlations ($r = -0.601$, $p < 0.01$ and $r = -0.418$, $p < 0.05$, respectively) (Figure 3B). |b/a| was 0.604 ± 0.030 ($p < 0.01$ vs AS-1 and AS-2) in the nAS, 0.323 ± 0.012 ($p < 0.01$ vs nAS, and AS-2) in the AS-1 and 0.252 ± 0.012 ($p < 0.01$ vs nAS, and AS-1) in the AS-2 group (Figure 5B).

Correlation between |b/a| and D: The correlation between |b/a| and D was significant and positive ($r = 0.892$, $p < 0.01$) for all subjects (Figure 4A). The

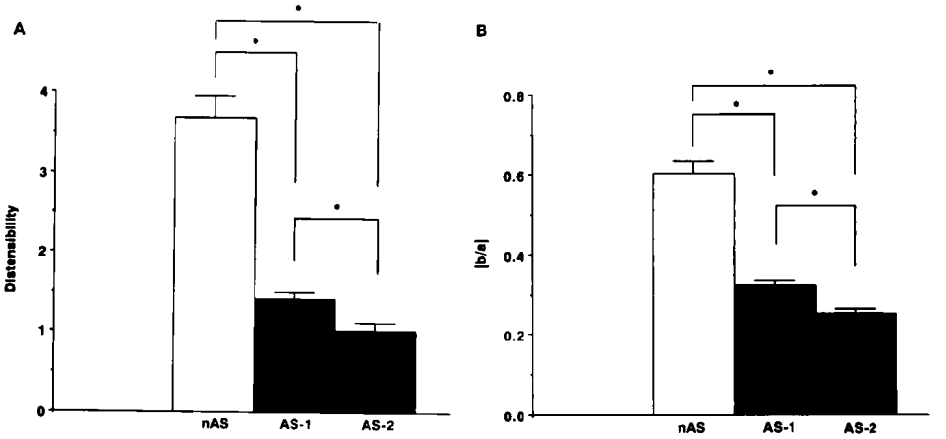

Figure 5. Differences among the three groups for distensibility (A) and |b/a| (B). The distensibility values are 1000 times greater than the calculated D. Mean ± SEM, $*p < 0.01$.

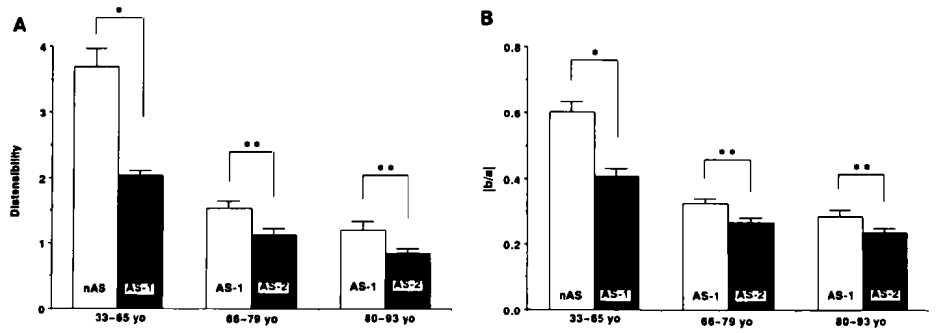

Figure 6. Comparison of distensibility (A) and |b/a| (B) among the three groups, (nAS, AS-1, AS-2) in three different age ranges, (33～65, 66～79, and 80～93 years old). nAS, AS-1 and AS-2 are defined in the Materials and Methods. There are no values for AS-2 for 33～65 year old subjects. Mean ± SEM. $*p < 0.01$, $**p < 0.05$.

intragroup correlations for groups nAS, AS-1 and AS-2 were significant and positive ($r = 0.659$, $p < 0.01$; $r = 0.683$, $p < 0.01$; and $r = 0.550$, $p < 0.01$; respectively) (Figure 4B).

Discussion

The second derivative of plethysmogram (SDPTG): The finger plethysmogram (PTG) described by Yoshimura[16] has been used extensively for evaluation of hemodynamics and the peripheral circulation. To make inflection points of the original PTG wave prominent, the use of the second derivative of the PTG, that

is, the SDPTG (it has been hitherto called the acceleration plethysmogram) has been suggested by Seki[17] and Ozawa.[18] Components constituting the SDPTG have been analyzed in relation to hemodynamics and various forms of circulatory diseases.[1-4]

During systole, the PTG consists of two components, the early and late systolic components. The former component corresponds to a phase of increase in the aortic pressure with a rise in aortic flow velocity, and the latter to a progressive increase in aortic pressure despite a fall in aortic flow velocity. These features have already been described elsewhere.[3,19,20] This means that the PTG reflects contours of the ascending aortic pressure wave,[21,22] although the PTG is basically recorded as a peripheral volume wave. In other words, the PTG reflects the central pressure wave affected by peripheral vascular factors. The SDPTG consists of four wave components during systole, a, b, c and d, and one wave component during diastole, e. The a and b waves and the c and d waves correspond to the early and late systolic component of the PTG, respectively.[2,3,10] Consequently, components of the SDPTG reflect components of the PTG and we can recognize the central pressure wave from the SDPTG components. The a and b waves reflect the early systolic phase (rapid ejection phase). Therefore, the amplitudes and contours of the a and b waves, or the value of |b/a| of the SDPTG are considered to be influenced by organic or functional changes in peripheral arteries, such as stiffness, compliance or distensibility. Since atherosclerotic lesions of the carotid artery are closely correlated to those of other arteries, such as the aorta, coronary, and upper and lower limb arteries,[23-26] a relation was sought between the ratio |b/a| and distensibility of the carotid artery.

Correlation between |b/a| and D: Takazawa *et al.*[2,3,10] reported that a marked decrease in |b|, a slight decrease in a, and then a decrease in |b/a| were induced by application of angiotensin. On the other hand, nitroglycerin application increased |b/a| due to a moderate increase in a and a marked increase in |b|. Moreover, Orita *et al.* showed that |b/a| was reduced by atherosclerosis, and from these observations on the SDPTG, suggested |b/a| may possibly represent the stiffness of the elastic arteries.[7] Ozawa[8] observed that a decrease in |b/a| was dependent on aging and this correlation was shifted in the juvenile direction by application of nitroglycerin, suggesting that |b/a| reflected the distensibility of peripheral arteries. Since arterial impedance is altered by angiotensin or nitroglycerin,[27] their suggestions are pertinent. Suzuki *et al.*[11] observed a decrease in stroke volume without alteration of diastolic blood pressure during VVI mode pacing performed on patients with complete A-V block. They suggested that this hemodynamic phenomenon was caused by an increase in distensibility of the elastic arteries and they observed that the phenomenon was

followed by marked increases in |b| and |b/a|.

Studies by other investigators constitute indirect evidence that |b/a| is associated with the distensibility of peripheral arteries. However, further investigations are required for direct evidence of a correlation between |b/a| and distensibility using subjects with alterations in arterial stiffness or compliance.

It was previously reported that the dependency of an increase in thickness of the intima-media complex of the carotid artery on age was caused by atherosclerotic lesions.[9] Therefore, the dependency of arterial distensibility on aging, which was observed in this study, may possibly result from a progressive increase in thickness of the intima-media complex of the carotid artery caused by atherosclerotic development. This possibility is seen in Figure 5. The value of the distensibility (D) is significantly different between the three groups. Distensibility (D) in the non-atherosclerotic (nAS) group is higher than that in the atherosclerotic (AS-1 or the AS-2) groups, and the value in the AS-2 group is lower than that of the AS-1 group.

Age dependent decreases in |b/a| have been previously reported.[5-8] In this study, we confirmed this relation. Moreover, as shown in Figure 5, the value of |b/a| was lower in the atherosclerotic groups than in the non-atherosclerotic group. The finding that the value of |b/a| in the AS-2 group was lower than that of |b/a| in the AS-1 group indicates that |b/a| is decreased due to the development of atherosclerosis. A statistically significant negative correlation between the thickness of the intima-media complex and distensibility, and the same correlation between the intima-media complex and |b/a| were clearly observed in this study. It would thus be expected that |b/a| and distensibility should show a positive correlation. This is clearly shown in Figure 4.

Our results provide direct evidence of an association between |b/a| and the distensibility of peripheral elastic arteries.

Evaluation of atherosclerosis with |b/a|: It was previously observed that |b/a| was significantly decreased with atherosclerosis[7] and that the amplitude of a and b were influenced by atherosclerotic lesions of peripheral arteries.[28] In this study, we also demonstrated that |b/a| was lowered in proportion to the development of atherosclerosis. As shown in Figure 6, the values of the distensibility and |b/a| are significantly different between the atherosclerotic groups (between nAs and AS-1; between AS-1 and AS-2) in the same age range. This suggests that |b/a| of the SDPTG is useful for the evaluation of atherosclerosis, especially in subjects 65 years old or younger. Further analysis as to whether and how the other components of SDPTG, c/a, d/a and e/a, are correlated with distensibility will be forthcoming in future studies.

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