Clinical Estimation of Vascular Elastic Function
and Practical Application

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Abstract: We have developed an aortic pulse wave velocity method (aortic PWV method) and an ultrasonic phase locked echo tracking system (β method) that enable a non-invasive estimation of the elastic function of the aorta and cervical arterial system, and have carried out basic, clinical, and epidemiological studies to validate these methods. Aortic PWV is determined by the simultaneous recording of carotid artery pulse wave, femoral artery pulse wave and heart sounds and measurement of the actual length of the aorta. The β value is determined by the diameter of the artery, displacement of the diameter and blood pressure. PWV and β values increased with ageing in normal subjects and in patients with arteriosclerotic diseases. PWV and β values in the elastase administered group shifted within a lower range than the arteriosclerotic group. Both methods are non-invasive, qualitative, simple and convenient and are useful because they enable repeated examination at the outpatient clinic.

Key words: aortic pulse wave velocity (aortic PWV), aorta, ultrasonic phase locked echo tracking system (β method), cervical artery

INTRODUCTION

Arteriosclerosis develops when ageing and congenital factors accompany so-called risk factors such as hypertension, diabetes mellitus, and hyperlipemia. One feature of arteriosclerosis is that it develops with individual differences in subjects in their 40-50s or older. Pathomorphologically, it begins as a proliferation of morbid cells and connective tissues, and vascular remodeling progresses to calcification and finally atheroma. At the same time, functional changes such as blood flow disturbance, thrombogenicity, or deterioration of vascular elastic function also occur. Although invasive methods such as angiography and non-invasive methods such as digital subtraction angiography, computed tomography, magnetic resonance angiography, and ultrasonic diagnosis have been used for clinical imaging, there are few methods that enable estimation of vascular function, particularly the vascular elastic function. We have developed an aortic pulse wave velocity method (aortic PWV method) and an ultrasonic phase locked echo tracking system (β method) that enable a non-invasive estimation of the elastic function of the aorta and cervical arterial system, and have carried out basic1-8, clinical9-17, and epidemiological18 studies to validate these methods. The clinical applications and basic procedures of both test methods are described in this Minireview.

Parameters for Evaluation of Vascular Elastic Function

Major parameters used to express vascular elastic function and several expressions for blood vessel function are listed in Table 1, respectively. Vascular elastic function can be determined as a dynamic response of vascular transversal specificity in terms of a temporal series of variations in blood flow volume, blood flow velocity, and blood flow resistance under pulsatile conditions that are regulated by cardiac output, heart rate, viscosity of the blood, blood pressure and other factors. The relationship between these factors can be described by the general expression $C = f(Eh/D)$, in which vascular elastic function ($C$) is expressed by the function of Young's modulus of the wall ($E$), diameter ($D$), and thickness of the wall ($h$). Since the arterial wall consists of a multilayer structure (intima, media and adventitia) together with a mosaic structure (atheroma and calcification), vascular function deteriorates as materials in the arterial wall vary quantitatively.
Table 1. Parameters of vascular elastic function and various equations for blood vessel function

<table>
<thead>
<tr>
<th>Vascular elastic function</th>
<th>Expressions for blood vessel function</th>
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<tr>
<td>1. Volume elasticity $(K)$</td>
<td>$V \cdot \frac{dP}{dV}$</td>
</tr>
<tr>
<td>Compliance</td>
<td>$\frac{1}{K}$</td>
</tr>
<tr>
<td>PWV $\sqrt{K/\rho}$</td>
<td>$\frac{K}{\rho}$</td>
</tr>
<tr>
<td>Young's modulus $K(1-\sigma^2)D/h$</td>
<td>$\ln(P_s/P_d)$ $D_d/D$</td>
</tr>
<tr>
<td>$\beta$</td>
<td>$\frac{P_s}{\rho} \Delta D + \frac{D}{\Delta P}$</td>
</tr>
<tr>
<td>$\Delta T$</td>
<td>$\frac{P_s}{\Delta D} + \frac{D}{\Delta P}$</td>
</tr>
</tbody>
</table>

$V$: Blood vessel volume  
$P_d$: Diastolic blood pressure  
$\rho$: Blood viscosity  
$C$: Blood vessel function  
$E$: Young's modulus  
$h$: Wall thickness  
$L$: Blood vessel length  
$s$: Occupied area  
$P_s$: Systolic blood pressure  
$f$: function

and qualitatively with the progression of arteriosclerosis and ageing. Furthermore, one of the characteristics of the vascular elastic function is that the function itself varies with changes in arterial internal pressure. Elastin, collagen, and smooth muscle cells each exert a physiological effect on arterial internal pressure, abnormal hypertension, and abnormal hypotension, respectively, and as a result, the relationship between arterial internal pressure and the elastic modulus is non-linear. Accordingly, when attempting to determine the elastic modulus, arterial internal pressure must be taken into consideration. As a result, the PWV values obtained were uniformly converted to PWV values at a diastolic pressure of 80 mmHg using the table showing the relation between PWV and diastolic pressure. As for the $\beta$ method, correction for a specific arterial internal pressure is not required since the ratio of the natural logarithm of systolic and diastolic pressure ($\ln P_s/P_d$) is introduced into the expression.

**Aortic PWV Method**

1. **Principle and Method**

The aortic PWV method estimates the average spatial elastic function from directly above the aortic valve area to the femoral artery by measuring the velocity of pulse wave transmission between these two points non-invasively. The method of measurement and procedure are shown in Fig. 1. PWV is determined by the simultaneous recording of the carotid artery pulse wave, femoral artery pulse wave and heart sounds and measurement of the actual length of the aorta. Here, $tc$ is the time of pulse transmission from the aortic valve area (point A) to the carotid artery (point C). When a pulse is transmitted to point X on the aorta, $tc$ means the time of pulse transmission between point A and point X. In the same way, the time of pulse...
transmission between point X and point F (femoral artery) corresponds to \( t \). From these, the time of pulse transmission from point A to point F is determined \((t+tc)\). Accordingly, PWV is determined by dividing the actual length of the aorta \((D \times 1.3)\) by the pulse transmission time \((t+tc)\).

Stress and extension (strain) show a linear relation when material in question is uniformly like rubber. However, in arteries that consist of cells and various connective tissues, the relationship between both is characteristically non-linear, in other words, the elasticity value varies with fluctuations in arterial internal pressure.

As shown in Fig. 2, elastin, collagen, and smooth muscle cells function within the range of physiological pressure; and as a result, the relation between arterial internal pressure and the elastic modulus shows a sigmoid trace. This fact indicates that the elastic modulus increases (the wall becomes stiffer), in hypertension, and decreases (the wall becomes softer), in hypotension. During this process, non-fibrotic connective tissues such as glycosaminoglycans and glycoprotein envelop elastin and collagen, respectively, like a sheath and assist them in exhibiting an elastic function with smooth extension and contraction. As mentioned above, since the elastic modulus and arterial internal pressure have a non-linear relation in the blood vessels of the living body, PWV requires a correction for particular arterial internal pressures when the elastic function is compared among individuals or the time course variation in elastic function is examined.

Figure 3 shows the relation between diastolic blood pressure and PWV in an isolated aorta obtained by autopsy and in an aorta in the living body. In either case, PWV increases with the rise in diastolic blood pressure, and is seen to be dependent on arterial internal pressure\(^{11}\). Based on these data, a table for pressure correction has been prepared, and the PWV obtained is uniformly corrected to the PWV at a diastolic pressure of 80 mmHg according to the table.

The sensor to the skin\(^{4}\). Furthermore, the upstroke points of the pulse wave are automatically recognized, \( t \) and \( tc \) are measured, and then by inputting the diastolic pressure, the PWV value corrected for pressure is output.

2. Relationship between PWV and the Compositions of Aortic Intimal and Medial Tissues

PWV was measured prior to death and then after autopsy together with the degree of atheroma formation and calcification. A total of 14 compositions including smooth muscle cells and various kinds of connective tissue were quantified by microspectrophotometry\(^{20,21}\). The result of a multiple regression analysis in which
PWV was taken as an independent variable and each element of the arterial wall was treated as a dependent variable.

**3. Clinical Applications of PWV**

1) A change of PWV values with ageing

Average PWV values of 106,968 normal subjects without any arteriosclerotic disease are shown in Fig. 5 by age group. An increase in PWV with ageing is clearly evident as PWV ranges from 4.72 m/sec in their 0s to 9.60 m/sec in their 70s. This indicates that blood vessels continue to develop up to their 20s and attain maturity in their 50s, and afterwards PWV increases with ageing. After their 50s, standard deviation increases and differences among individuals become greater. Table 2 shows average PWV values as a function of age. This table makes it possible to estimate a subject's degree of ageing or degree of youthfulness. For example, when a 60-year-old person's PWV is 7.4 m/sec, his estimated age according to the PWV is 48–50 years old, and he is judged to be about 10 years younger than his actual age.

2) PWV values in arteriosclerotic diseases

In Fig. 6, PWV values of the patients with arteriosclerotic diseases such as hypertension, diabetes mellitus, and hyperlipemia are compared with PWV values of normal subjects. PWV values in any disease group were significantly higher than for normal subjects in any age group. In particular, in patients undergoing hemodialysis, with diabetes mellitus, or with cerebral infarction, an increase in PWV values is evident. In addition, continual measurement of PWV values in a patient makes it possible to determine the rapidity with which arteriosclerosis is progressing or the estimation of efficacy of a drug.

A PWV shift in cases where an anti-arteriosclerotic agent, elastase extracted from pig pancreas and act on connective tissue metabolism, was administered on 126 patients over a period of 14 years is shown in Fig. 7. PWV values in the drug administered group shifted within a lower range than in the arteriosclerotic

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**Fig. 4** A multiple regression analysis in which PWV is taken as an independent variable and each element of the arterial wall is treated as a dependent variable.

**Fig. 5** Average PWV values of 106,968 normal subjects. Average PWV values and standard deviation are $4.7 \pm 0.4$ m/sec in 0 to 4 years old (5), $5.1 \pm 0.6$ m/sec in 5 to 9 years old (68), $5.2 \pm 0.5$ m/sec in 10 to 14 years old (153), $5.5 \pm 0.6$ m/sec in 15 to 19 years old (183), $6.3 \pm 0.5$ m/sec in 20s (2,495), $6.7 \pm 0.5$ m/sec in 30s (27,901), $7.2 \pm 0.5$ m/sec in 40s (44,208), $7.7 \pm 0.6$ m/sec in 50s (25,315), $8.5 \pm 0.7$ m/sec in 60s (6,084) and $9.6 \pm 0.9$ m/sec in 70s (556), respectively. ( ): numbers of normal subjects.
group, and the ameliorative effect of the vascular function of this drug which has a metabolic effect on connective tissue, particularly an eliminatory effect on degenerated elastin or calcium phosphate, is evident. From the aspect of distribution of arteriosclerosis to various arteries, it is known that arteriosclerosis develops the earliest in the abdominal aorta, and then the coronary arteries, and cerebral arteries. Accordingly, an estimation of sclerosis in the aorta by PWV is thought to be useful in predicting the degree of sclerosis in organ arteries such as coronary arteries and cerebral arteries.
Blood pressure measured at the neck is higher by some ten mmHg in systolic pressure and lower by some mmHg in diastolic pressure than that at the forearm. Therefore, the value for blood pressure measured at the forearm ($X_s, X_d$) converted to cervical arterial pressure according to the expression shown below was used to determine the $\beta$ value. For the common carotid artery and carotid sinus,

$$P_s = 76.8 + 1.89X_s - 0.0016(X_s)^2$$
$$P_d = 10.5 + 1.13X_d - 0.0003(X_d)^2$$

For the internal carotid artery and vertebral artery,

$$P_s = 23.0 + 1.03X_s - 0.0011(X_s)^2$$
$$P_d = 10.82 + 0.88X_d - 0.0021(X_d)^2$$

As mentioned above, the PWV method requires an uniform conversion to PWV values at a diastolic pressure of 80 mmHg due to its dependence on arterial internal pressure, while the $\beta$ method is independent of blood pressure and does not require correction because it adopts a ratio of the natural logarithm, $\ln P_s/P_d$.

2. Clinical Applications of the $\beta$ Method

The device developed here is the Aloka SSD 610 with a built-in ultrasonic phase locked echo tracking system. An electronic scanning type probe was used at a frequency of 7.5 mHz. The ultrasonic beam is shifted toward the site of the maximum arterial diameter towards a right angle as viewed through the B mode image, and
A comparison of the $\beta$ values of patients with arteriosclerotic diseases such as hypertension, diabetes mellitus, and hyperlipemia with those of normal subjects is shown in Fig. 8. The $\beta$ values for four arteries in the sclerotic group are significantly higher than those in the normal group at any age, which shows that the $\beta$ method is useful in estimating cervical arterial sclerosis. Moreover, continual observation of $\beta$ values is also a useful means of estimating the rate of advance of cervical arteriosclerosis or judging the efficacy of a drug treatment.

Figure 9 shows the shift in $\beta$ values in the internal carotid artery in which the elastase administered group and sclerotic patient group are compared. In the elastase-administered group, $\beta$ values shifted on a significantly lower gradient as compared with patients in the sclerotic group, clearly showing the suppressive effect of elastase on progression of arteriosclerosis.

**CONCLUSION**

The basic principles and clinical applications of the aortic PWV method and $\beta$ method for estimating the elastic function of the aorta and cervical arteries were outlined. Both methods are non-invasive, qualitative, simple and convenient and are useful because they enable repeated examination at the out-patient clinic.
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