Noninvasive Measurement of Baroreflex Sensitivity Index Using an Indirect and Continuous Blood-Pressure Recorder

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SUMMARY

The index of the baroreceptor reflex sensitivity (BRS) was measured noninvasively by monitoring the arterial pressure (AP) of the finger and R-R interval on the ECG during a Valsalva maneuver. An indirect finger AP measurement system was newly designed on the basis of the so-called vascular unloading technique. The BRS index was determined as the slope of the linear regression equation between the R-R interval and the virtual brachial AP which was evaluated from the finger AP. The data on both parameters were taken from the second period of the fourth phase in the Valsalva maneuver. The measurement was carried out on 24 inpatients (29–65 years) with essential hypertension. The conventional invasive method using phenylephrine or nitroglycerine was also performed on the same subjects. The correlation coefficient between the invasive and noninvasive methods was 0.81 when phenylephrine was used and 0.90 with nitroglycerine (p<0.001). The present method was found useful in routine clinical examination because of its easy and repeatable noninvasive application to patients without causing stress.

Additional Indexing Words:
Finger arterial pressure Noninvasive method Essential hypertension

The diminished baroreceptor reflex sensitivity (BRS) in hypertensive patients was first reported by Bristow et al.1) According to their method, the BRS index can be calculated as the ratio between changes in the R-R interval on the electrocardiograph (ECG) and intra-arterial systolic blood pressure following the intra-venous administration of alpha-adrenergic agents such as

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Because of the risk in applying such pressor amines to patients, Palmero et al. did not use an alpha-adrenergic agent, but instead induced a pressure rise by the Valsalva maneuver. They obtained a good correlation with the conventional phenylephrine method. These methods, however, require the measurement of intra-arterial pressure which involve an invasive procedure and causes stress to patients.

Recent technical developments put the indirect finger arterial pressure (AP) measurement into practice. This method, called the "vascular unloading technique", can measure the finger AP indirectly and continuously so that it can be easily applied to the BRS index measurement. The present paper describes a semi-automatic system including the finger AP recording device for measuring the BRS index noninvasively. The BRS indices obtained by both noninvasive and conventional invasive methods were measured and compared in hypertensive patients.

**MATERIALS AND METHODS**

*Noninvasive BRS index measurement system:*

Fig. 1 shows the functional diagram of a noninvasive BRS index measurement system. It consists of a finger AP measurement unit, brachial systolic/diastolic blood pressure measurement device, ECG processing unit and data processor (microcomputer).

The mechanism of the finger AP measurement unit is similar to the system developed by Yamakoshi et al., except for the mechanics used in fixing and compressing the finger. In our system the finger is fixed at its root with a 32-mm wide rubber cuff which is covered with a stainless steel girdle (Fig. 2). The girdle is pulled by a spring so as to match the cuff and the finger,
and stabilized by a tightener. The mechanics minimize the dead space between the cuff and the finger. The cuff was made to fit fingers having an approximate diameter of 12–26 mm. The appearance of the finger cuff unit is shown in Fig. 3.

The principle of the finger AP measurement is described in several references. Briefly, the photoplethysmograph using LEDs (light-emitting diodes) and a photo-transistor detects a relative change in the vascular volume (Fig. 2), the signal of which is compared with the reference value previously set. The difference between these signals drives the diaphragm pump to compress the finger so as to maintain a constant vascular volume. When the vascular volume change is compensated for by the water flowing
into and out from the cuff, the cuff pressure begins to change, tracing the finger AP. The finger AP can be therefore obtained by measuring the cuff pressure.

The indirect brachial AP measurement device (UA-254, Copal Takeda Medical Co., Ltd.) measures systolic and diastolic blood pressures for continuous evaluation of the virtual brachial AP from the finger AP. The systolic/diastolic blood pressure values obtained are manually fed into the microcomputer through the keyboard.

The ECG processing unit detects the electrocardiographic events and feeds the signal on R-R intervals into the microcomputer. The microcomputer (PC-9801, NEC) receives the finger AP, systolic/diastolic blood pressure and R-R interval, displays the variations of finger AP, virtual brachial AP (described below), R-R interval and heart rate, and calculates the BRS index when a Valsalva maneuver is performed.

**Noninvasive BRS index measurement:**

The noninvasive BRS index measurement requires the changes of the AP and R-R interval following the Valsalva maneuver. In order to compare the results with the invasive BRS index using the intra-brachial AP, it is necessary to evaluate the indirect brachial AP from the finger AP. In this study, the systolic and diastolic blood pressures of the upper arm were measured 5 times by the above indirect device during continuous finger AP measurement. Two regression equations were then formed concerning the systolic and diastolic pressures, expressing the relation between the upper arm and finger APs. These equations were used to transform the finger AP continuously into the upper arm AP. The estimated upper arm AP is called the “virtual AP” in this study. The calculation of the regression equations and the virtual AP were performed automatically by the microcomputer.

As stated by Palmera et al., phase 4 of the Valsalva maneuver can be split into two short periods: a first one in which the AP increases gradually but no significant change can be seen on the R-R interval, and a second one characterized by a lengthened R-R interval in addition to the increased AP. The data of the virtual AP and R-R interval obtained during the second period of phase 4 were used for the BRS index calculation. The linear relationship between them was obtained by the least squares method and the BRS index (BRS\text{val}) was calculated from the slope (coefficient) of the regression equation.

**Invasive BRS index measurement:**

The invasive BRS index measurement followed the method by Bristow et al. A catheter (0.6 mm ID) with a needle tip was inserted into the left brachial artery and was connected to the strain-guage pressure transducer (P50, Gould Statham Instruments Inc.). Firstly, phenylephrine (100 µg)
was injected into the right cubital vein, and the brachial AP and R-R interval changes were monitored. Both signals were fed into the computer so as to obtain the linear regression equation between the systolic blood pressure and R-R interval. The period from the onset of the systolic pressure rise until it reached the peak was used for the calculation. The slope (coefficient) of the equation was determined as the index $BRS_{ph}$. The $BRS_{ph}$ measurement was carried out twice at more than a 15-min interval. The averaged value of two $BRS_{ph}$ on each subject was used for the statistical analysis. The significance of the correlation coefficient between the $BRS_{val}$ and $BRS_{ph}$ was checked statistically with the t-test.

Secondly, at an interval of at least 15 min after $BRS_{ph}$ measurement, trinitroglycerine (100 $\mu$g) was injected, the index $BRS_{ng}$ was calculated and its correlation with the $BRS_{val}$ was determined by the same method used with phenylephrine.

Subjects and experimental protocol:

Measurements were carried out on 24 inpatients (18 males and 6 females) with untreated essential hypertension. Their ages ranged from 29 to 68 years (mean±SD=45.5±8.2). The noninvasive BRS measurement was performed initially with the patient in a sitting position, preceding the invasive BRS measurements. The invasive BRSs ($BRS_{ph}$ and $BRS_{ng}$) were measured in the supine position.

RESULTS

Accuracy of continuous finger AP measurement:

Fig. 4 demonstrates an example of the simultaneous beat-to-beat recordings of the indirect finger AP and the direct brachial AP. It is clear from the figure that the wave shape of the finger AP is quite similar to that of the brachial AP while the finger AP is approximately 20 mmHg lower than the brachial AP in this subject. This tendency is also found in Fig. 5 where a typical pattern of the AP variation following the Valsalva maneuver (VM) is shown with the heart rate (HR) change.

Table I summarizes the comparison between both APs, where 20 pairs of APS picked randomly from simultaneous AP recordings, such as those shown in Fig. 5. In the table, $r$, $A$ and $B$ respectively indicate the correlation coefficient and regression coefficients $[(brachial AP)=A\times(finger AP)+B]$. The upper row for each subject shows the results for systolic blood pressure and the lower row for diastolic pressure. The columns BAP–FAP and BAP–VAP show the averaged differences (mean±SD) between the brachial AP (BAP) and finger AP (FAP) and between BAP and virtual AP (VAP), respect-
Fig. 4. An example of the simultaneous beat-to-beat recording of the indirect finger and the direct brachial arterial pressures.

Table I. Results of the Comparison between the Arterial Pressures of the Finger and the Upper Arm

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>r</th>
<th>A</th>
<th>B</th>
<th>BAP-FAP (mmHg)</th>
<th>BAP-VAP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MT</td>
<td>M</td>
<td>64</td>
<td>0.95</td>
<td>1.26</td>
<td>-21.2</td>
<td>15.4±8.4</td>
<td>5.1±2.8</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.97</td>
<td>1.42</td>
<td>-30.8</td>
<td>6.1±4.6</td>
<td>2.0±1.8</td>
</tr>
<tr>
<td>SY</td>
<td>M</td>
<td>48</td>
<td>0.87</td>
<td>1.50</td>
<td>-5.0</td>
<td>16.2±9.5</td>
<td>5.4±3.1</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.86</td>
<td>1.26</td>
<td>21.8</td>
<td>2.0±3.8</td>
<td>0.6±1.2</td>
</tr>
<tr>
<td>FU</td>
<td>M</td>
<td>60</td>
<td>0.99</td>
<td>1.18</td>
<td>6.7</td>
<td>28.3±5.2</td>
<td>14.0±3.1</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.98</td>
<td>1.31</td>
<td>1.2</td>
<td>12.9±8.8</td>
<td>0.2±10.0</td>
</tr>
<tr>
<td>KO</td>
<td>M</td>
<td>66</td>
<td>0.90</td>
<td>1.21</td>
<td>29.7</td>
<td>49.3±7.1</td>
<td>0.3±6.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.95</td>
<td>1.18</td>
<td>31.3</td>
<td>40.0±3.4</td>
<td>0.2±3.1</td>
</tr>
<tr>
<td>TA</td>
<td>F</td>
<td>42</td>
<td>0.96</td>
<td>1.42</td>
<td>-36.0</td>
<td>10.6±7.9</td>
<td>-0.7±5.4</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.92</td>
<td>1.16</td>
<td>-11.4</td>
<td>0.8±4.0</td>
<td>0.0±3.8</td>
</tr>
<tr>
<td>KK</td>
<td>F</td>
<td>50</td>
<td>0.98</td>
<td>1.53</td>
<td>-22.4</td>
<td>61.5±6.3</td>
<td>-0.2±3.4</td>
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<tr>
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<td></td>
<td></td>
<td>0.88</td>
<td>1.17</td>
<td>19.5</td>
<td>35.7±3.6</td>
<td>-0.4±3.4</td>
</tr>
<tr>
<td>SU</td>
<td>M</td>
<td>48</td>
<td>0.99</td>
<td>1.52</td>
<td>-17.4</td>
<td>23.8±20.5</td>
<td>-0.4±4.0</td>
</tr>
<tr>
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<td></td>
<td>0.98</td>
<td>1.33</td>
<td>3.4</td>
<td>26.4±3.6</td>
<td>-7.1±2.5</td>
</tr>
</tbody>
</table>

BAP=direct brachial arterial pressure; FAP=indirect finger arterial pressure; VAP=virtual arterial pressure (see text).

A and B: regression coefficients between BAP and FAP expressed by the equation $BAP = A \times FAP + B$.

r: correlation coefficient between BAP and FAP.

Upper row: results on systolic blood pressure; lower row: results on diastolic blood pressure. BAP-FAP and BAP-VAP are expressed as mean±SD.
Fig. 5 (left). A simultaneous recording of the heart rate (HR), indirect finger arterial pressure and direct brachial arterial pressure before, during and after the Valsalva maneuver.

Fig. 6 (right). A recording of the heart rate (HR) and the systolic (SBP) and diastolic (DBP) outlines of the virtual brachial pressures (A), and the regression equation between the SBP and R-R interval for BRS index determination (B).

tively. The virtual APs were obtained by adjusting the finger AP using the regression equations between the finger AP and auscultatory brachial AP. The results suggested that the indirect beat-to-beat brachial AP variation could be estimated from the finger AP recording when the auscultatory measurement of systolic and diastolic pressures is carried out in advance.

**Comparison between noninvasive and invasive BRSs:**

An example of the virtual AP and heart rate variations following the Valsalva maneuver, and the relation between the systolic blood pressure and the R-R interval are shown in Fig. 6A and B, respectively. The plots in the scattergram were obtained from the period indicated by the solid bar in Fig. 6A. The index of the baroreceptor reflex sensitivity was defined by the gradient of the regression equation in Fig. 6B: the $BRS_{\text{val}}$ could be determined as 2.8 msec/mmHg in this example.
Fig. 7. Correlations of the noninvasive BRS index measurement (BRSval) with the invasive phenylephrine method (BRSph: A) and the invasive trinitro-glycerine method (BRSng: B).

The scattergrams in Fig. 7 show the relation between the BRSs by the conventional invasive method (BRSph and BRSng) and by our noninvasive method (BRSval). As shown in the figure, the BRSval values were about half of the BRSng, but the correlation coefficient was high (r=0.81). BRSng, on the other hand, correlated better with BRSval (r=0.90), and the absolute values corresponded well with each other. It was clear from these results that our noninvasive determination of BRS index has a high degree of accuracy.

DISCUSSION

Gribbon et al\textsuperscript{1)} stated that the BRS index decreases with increases of age and blood pressure. Watson et al\textsuperscript{6)} and Mancia et al\textsuperscript{7)} reported that the blood pressure of patients with a lower BRS index tends to be unstable. It was confirmed, moreover, that idiopathic orthostatic hypertension and congestive heart failure influence the BRS index\textsuperscript{8),9)} From these facts, the BRS index can be seen to be a useful clinical index for expressing the cardiovascular control characteristics of patients. It may also be of use in determining differences in the pharmacological action of drugs\textsuperscript{10)}

Despite its importance, the BRS index has not been used often clinically because the measurement requires intra-arterial cannulation and administration of an adrenergic agent, both of which are stressful to the patients. Our method, on the other hand, using the indirect finger AP measurement and the Valsalva maneuver is totally noninvasive, so that it can be performed repeatedly in the same patient as a routine examination.

The accuracy of the vascular unloading technique for measuring the finger AP was discussed in detail by Yamakoshi et al\textsuperscript{5)} As is also stated in their report, the measurement error is often caused by the inappropriate size...
cuff which does not fit well to the finger. To minimize this error, the system was modified mechanically to fit one cuff to any finger with a diameter ranging from 12 to 26 mm.

Since the measurement of finger blood pressure has only very recently been developed, its clinical significance has not as yet been clearly demonstrated. Even its relationship to the brachial blood pressure is not exactly known. According to our previous study on the peripheral circulation of healthy and hypertensive subjects, there are many variations in the diameter and distribution of the arterial vessels in the finger. Thus, it is not easy to find a general equation expressing the blood-pressure drop between the upper arm and the finger. However, the relative difference between the finger AP and the brachial AP is almost constant at rest and during a Valsalva maneuver (as shown in Fig. 5). It is therefore possible to obtain indirectly the variation in brachial AP continuously from the finger AP by calibrating it with auscultatory systolic and diastolic pressures beforehand. The virtual brachial AP into which the finger AP is transformed is then available for the calculation of the indirect BRS index measurement using the Valsalva maneuver.

REFERENCES