Variability of Breath-by-Breath Tidal Volume and its Characteristics in Normal and Diseased Subjects
Ventilatory Monitoring with Electrical Impedance Pneumography

Yushiro Kuratomi, MD, Nobuo Okazaki, MD, Teruo Ishihara, MD, Tatsuo Arai, MD and Shiro Kira, MD

To assess clinical significance of breath-by-breath variation of tidal volume and its distribution pattern displayed as a histogram, continuous measurement of tidal volume was made with electrical impedance pneumography for about 60 minutes. Subjects were composed of 26 normal male and 46 patients including 17 patients with restrictive lung disease and 29 patients with obstructive lung disease. To evaluate variation of tidal volume quantitatively, coefficient of variance (C.V.) was used. In comparison to the normal pattern of distribution (C.V. = 26.0 ± 7.5%, mean ± S.D.), patients with restrictive lung disease showed extremely narrow pattern of the distribution and significantly smaller C.V. (17.5 ± 4.6% in old pulmonary tuberculosis, P < 0.005 and 18.9 ± 9.3% in pneumonitis, P < 0.025). Whereas, patients with obstructive lung disease showed widespread pattern of the distribution and significantly greater C.V. (43.2 ± 13.0% in pulmonary emphysema with hypercapnia, 33.0 ± 7.5% in normocapnia and 35.8 ± 9.4% in asthmatic attack, P < 0.005). In all the patients with bronchial asthma after the treatment, the extremely widespread pattern of histogram was returned toward the normal one and the C.V. was decreased (22.4 ± 6.4%). It was suggested that the distribution pattern of tidal volume was affected by the change of clinical condition, and was well correlated to the pathophysiological process related to restrictive or obstructive lung disease. We conclude that analysis of tidal volume distribution by the histogram is one of the useful approach to manage patients with respiratory diseases.

Key Words: Electrical impedance pneumography, Non-invasive ventilatory monitoring, Breathing pattern, VT histogram

It is well known that physical airway attachments such as a facemask or mouthpiece with a noseclip produce a significant increase in tidal volume with unaltered, or decreased respiratory rate1−3). It is also suggested that these devices could alter periodicity and variability of breathing components4, 5). To analyze clinical information embedded in natural and spontaneous breathing, non-invasive approach without physical connection to the airway is indispensable.

In view of this status of respiratory monitoring, we, at present, can use several kinds of non-invasive method for monitoring and measuring ventilation6). One of them, electrical impedance plethysmography (pneumograph) has a specific advantage of its non-invasiveness and easy applicability to any subjects, even in the severely ill condition7). Through the basic investigations8, 9), we have been applying this technique to respiratory monitoring and recognized its usefulness for daily clinical use.

In this study, we investigated clinical signifi-
cance of breath-by-breath variation of tidal volume in normal subjects and patients with various respiratory diseases.

**METHODS**

**Subjects**

Twenty-six normal male, aged from 19 to 46 who had no history of respiratory disease were studied for the control. Forty-six patients were composed of 10 patients with old pulmonary tuberculosis whose vital capacity was under 50% of the predicted value, 7 patients with pneumonitis in severe respiratory failure, 22 patients with pulmonary emphysema, 5 of whom were with hypercapnia (Paco₂ > 45 mmHg), the remaining 17 were with normocapnia, and 7 patients of bronchial asthma during attack and after the treatment. All but 3 patients with bronchial asthma were male. Diagnosis of all patients were confirmed by medical history, clinical examination, and pulmonary function tests. Morphometric data, pulmonary function test and arterial blood gas values for all the subjects are shown in Table 1.

**Apparatus and Procedure**

The impedance pneumograph employed was a four-electrode system (Toshiba Electric Co., Japan). A constant high frequency alternative current (50 kHz, 1.5 mA) was applied to the thorax through the outer pair of electrode, E₁ and E₄, placed bilaterally on the posterior axillary lines at the level of mamilla. Transthoracic impedance changes accompanying respiration were detected as voltage changes between the inner pair of electrodes, E₂ and E₃, placed 3 cm medi- ally to E₁ and E₄ at the same level respectively. The electrode used was a disposable disc electrode for ECG monitoring (3M Co., USA). The relationship between impedance change (ΔZ) and ventilatory volume change (ΔV) was essentially linear in the normal tidal volume range. However, non-linear relationship was sometimes seen for small tidal volume, especially when it was less than 300 ml. To solve this problem and improve the accuracy, a Butterwoth low-pass filter to eliminate the cardiac impedance change on pneumographic recording and a microprocessor aided calibration system were installed as detailed in our previous report. At the beginning of measurement, sequential changes of ΔZ and ΔV obtained with Wright respirometer (BOC Co., England) attached to a face mask were simultaneously and directly stored in the memory for a period of several tidal breathing. From these stored data, best fitted correlation curve, either linear or non-linear, between the two variables was processed. Once the reproducible correlation curve was established, it was memorized as calibration curve in the system. Thereafter the impedance change was automatically converted to the ventilatory

<p>| Table 1. Morphometric, pulmonary function and arterial blood gas values for all the subjects |
|---|---|---|---|---|---|---|---|---|---|---|</p>
<table>
<thead>
<tr>
<th>n</th>
<th>age</th>
<th>height</th>
<th>weight</th>
<th>%VC</th>
<th>FEV₁/FVC%</th>
<th>Paco₂</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Normal Subject</td>
<td>26</td>
<td>26.2± 8.2</td>
<td>171.7±4.9</td>
<td>62.9± 5.8</td>
<td>80</td>
<td>70</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Old Pulmonary Tuberculosis</td>
<td>10</td>
<td>65.8± 5.6</td>
<td>158.3±7.5</td>
<td>45.6±10.1</td>
<td>41.7± 6.3</td>
<td>65.6±19.7</td>
<td>68.8±16.1</td>
<td>40.8± 4.4</td>
<td></td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>7</td>
<td>53.6±6.3</td>
<td>159.6±5.5</td>
<td>55.3± 5.8</td>
<td>51.8±12.6</td>
<td>84.0±10.4</td>
<td>70.2±17.5</td>
<td>36.5± 3.0</td>
<td></td>
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<tr>
<td>Pulmonary Emphysema</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>hypercapnic</td>
<td>5</td>
<td>63.8±13.0</td>
<td>156.4±3.8</td>
<td>41.8± 3.0</td>
<td>67.4±21.4</td>
<td>37.6± 3.5</td>
<td>61.9±17.8</td>
<td>62.1±14.8</td>
<td></td>
</tr>
<tr>
<td>normocapnic</td>
<td>17</td>
<td>67.1± 5.0</td>
<td>160.1±4.3</td>
<td>50.4± 9.6</td>
<td>69.2±13.4</td>
<td>40.1±10.7</td>
<td>72.9±10.2</td>
<td>39.3± 4.0</td>
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<tr>
<td>Bronchial Asthma</td>
<td>7</td>
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<td></td>
<td></td>
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<tr>
<td>during attack</td>
<td>42.4±11.2</td>
<td>157.9±7.8</td>
<td>57.3± 7.1</td>
<td>NA</td>
<td>NA</td>
<td>60.0±14.9</td>
<td>34.0± 9.6</td>
<td></td>
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<tr>
<td>after treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>116.4±24.4</td>
<td>63.8±10.1</td>
<td>83.4±12.1</td>
<td>35.9± 4.9</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD, *Values during oxygen inhalation (Mean FIO₂ = 62%).

Definition of abbreviations: %VC = vital capacity of % predicted normal values, FEV₁/FVC% = forced expiratory lung volume in one second per forced expiratory volume, Pao₂ = arterial Po₂, Paco₂ = arterial Pco₂, NA = not available.
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volume. With this calibration method, the tidal volume could be measured within ±10% accuracy. After at least 15 minutes rest, measurements were made in the supine position for about 60 minutes. The signals from the impedance pneumograph were recorded on a 4-channel paper recorder (Watanabe Instrument Co., Japan). Subjects were asked to avoid any major change in body position and open their eyes not to fall asleep. Each recording was usually consisted of 500 to 1500 breaths of tidal volume.

Data analysis

Breath-by-breath tidal volumes measured were classified into each 50 ml interval, then histogram displayed as a relative frequency (given as percentages of total numbers of breaths) was made. To evaluate variation of tidal volume quantitatively, coefficient of variance (C.V.), which normalizes the variability by dividing the standard deviation by the mean, was used. Mean respiratory rate was obtained by dividing the total numbers of breaths by the each recording time in minutes. It was confirmed that the C.V. in normal subjects showed a normal distribution because the values, if plotted on normal probability paper, yield an almost straight line. So we thought distribution of C.V. in diseased subjects could be assumed, a priori, to be normal. From this point, statistical analysis was performed using paired and unpaired Student's t tests. A p value less than 0.05 was considered significant.

RESULTS

Typical tidal volume histograms of each group of subjects are shown in the following.

Fig. 1 shows a histogram of 40 years old normal man. In this case, the peak value of frequency is 27%, mean VT 370 ml, S.D. 85 ml, and C.V. 23.3%. The pattern of distribution is nearly symmetrical around the mean VT indicated with letter X. Fig. 2 shows another histogram of 20 years old normal man who shows the highest value of C.V. among all the normal subjects. Compared to Fig. 1, VT is distributed widely and the peak value of frequency is decreased to 12%, S.D. and C.V. are increased to 183 ml, 37.1% respectively. But the pattern of distribution has a similar tendency to the Fig. 1 that is
symmetrical distribution around the mean VT.

Figs. 3 and 4 show representative histograms of patients with restrictive lung disease. Fig. 3 shows a histogram of 63 years old patient with old pulmonary tuberculosis who has a history of thoracoplasty, and whose vital capacity is 35% of the predicted value. The peak value of frequency is markedly increased to 44%, and about 80% of total breaths are included between the range of 250 to 350 ml of VT. S.D. and C.V. are decreased to 57 ml, 18.5% respectively. Narrowing of the distribution is clearly seen in comparison to the normal one. Fig. 4 shows a histo-

![Fig. 3. VT histogram of a 63-year-old patient with old pulmonary tuberculosis.](image)

![Fig. 4. VT histogram of a 53-year-old patient with pneumonitis.](image)

![Fig. 5. VT histogram of a 56-year-old patient with pulmonary emphysema accompanying hypercapnia.](image)

![Fig. 6. VT histogram of a 64-year-old patient with pulmonary emphysema with normocapnia.](image)
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gram of critically ill patient with pneumonitis. It is characterized by a markedly increased respiratory rate to 34 breaths/min. S.D. is 62 ml and C.V. is 23.6%. The distribution shows similar narrow pattern to the Fig. 3.

Through Figs. 5 to 9, results of patients with obstructive lung disease are represented. Figs. 5 and 6 are of patients with pulmonary emphysema, the former one is 56 years old man with hypercapnia (PaCO₂ 67 mmHg), the later one is 64 years old man with normocapnia. In Fig. 5, the peak value of frequency is decreased to 17%, S.D. and C.V. are increased to 150 ml, 51.5% respectively. The distribution shows widespread pattern. It is also characteristic that the frequencies of smaller VT are increased, and the distribution is unsymmetrical being more inclined toward the left side and extended long toward the right side. In Fig. 6, the peak value of frequency is increased compared to the Fig. 5, but the distribution shows some widespread pattern. S.D. is 132 ml and C.V. is 36.4%.

Fig. 7 shows an analogue tracing of breathing pattern in patient with bronchial asthma. Upper half of the figure is a recording during asthmatic attack which is characterized by unstable FRC level and markedly prolonged expiratory time. Fairly large variation in breath-by-breath tidal volume can be observed. In lower half recording after the treatment, stable FRC level, normalization of expiratory time and decrement in variation of VT are clearly demonstrated.

Figs. 8 and 9 are histograms of the same patient showing in Fig. 7, the former one is during asthmatic attack, the latter one is after the treatment. During attack, the tidal volume is distributed in

During Attack

After Treatment

Fig. 7. Analogue tracing of the breathing pattern in a 25-year-old patient with bronchial asthma during attack (upper half, impedance respiratory wave and VT) and after the treatment (lower half).
Table 2. Mean, SD, CV of tidal volume (VT), Mean respiratory rate (RR) and minute volume (VE) for all the subjects

<table>
<thead>
<tr>
<th></th>
<th>Mean VT (ml)</th>
<th>SD (ml)</th>
<th>CV (%)</th>
<th>Mean RR (breaths/min)</th>
<th>Mean VE (L/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Subject</td>
<td>409 ± 96</td>
<td>105±38</td>
<td>26.0±7.5</td>
<td>14.5±2.2</td>
<td>5.9±1.2</td>
</tr>
<tr>
<td>Old Pulmonary Tuberculosis</td>
<td>325 ± 68</td>
<td>56±15</td>
<td>17.5±4.6</td>
<td>22.2±4.1</td>
<td>7.0±0.9</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>480±223</td>
<td>79±28</td>
<td>18.9±9.3</td>
<td>31.1±5.5</td>
<td>14.5±6.5</td>
</tr>
<tr>
<td>Pulmonary Emphysema</td>
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<tr>
<td>hypercapnic</td>
<td>288±47</td>
<td>121±27</td>
<td>43.2±13.0</td>
<td>15.0±2.0</td>
<td>4.2±0.2</td>
</tr>
<tr>
<td>normocapnic</td>
<td>329±70</td>
<td>108±34</td>
<td>33.0±7.5</td>
<td>16.7±2.6</td>
<td>5.5±1.5</td>
</tr>
<tr>
<td>Bronchial Asthma</td>
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<tr>
<td>during attack</td>
<td>526±96</td>
<td>192±74</td>
<td>35.8±9.4</td>
<td>17.3±3.2</td>
<td>8.9±0.7</td>
</tr>
<tr>
<td>after treatment</td>
<td>371±113</td>
<td>83±38</td>
<td>22.4±6.4</td>
<td>16.0±3.1</td>
<td>5.7±1.6</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD.
* P < 0.005, ** P < 0.01, # P < 0.025 when compared to normal subject.

wide range, the distribution shows extremely widespread pattern with the large mean VT. After the treatment, the distribution returned toward the normal symmetrical pattern with the smaller mean VT. S.D. and C.V. are decreased from 229 ml to 119 ml, 38.4% to 28.2% respectively.

Mean, S.D., C.V. of tidal volume, mean respiratory rate, and mean minute volume for all the subjects are given in Table 2. The mean VT for the normal subjects was 409 ± 96 ml, C.V. of VT 26.0 ± 7.5%, respiratory rate 14.5 ± 2.2 breaths/min and minute volume 5.9 ± 1.2 L/min. In comparison to the normal subjects, C.V. of VT is significantly smaller in the patients with old pulmonary tuberculosis, pneumonitis and greater in the patients with pulmonary emphysema and bronchial asthma during attack. Mean RR is significantly elevated in the patients with old pulmonary tuberculosis, pneumonitis, pulmonary emphysema with normocapnia and bronchial asthma during attack. Mean VE is significantly increased in the patients with old pulmonary tuberculosis, pneumonitis, pulmonary emphysema accompanying hypercapnia and bronchial asthma during attack. Mean VE is significantly increased in the patients with old pulmonary tuberculosis, pneumonitis and bronchial asthma during attack, and decreased in the patients with pulmonary emphysema accompanying hypercapnia. Patients with pneumonitis are characterized by the highest value of mean RR and VE among all the subjects. Although there is no statistical significance, patients with pulmonary emphysema accompanying hypercapnia shows smaller mean VT than the normocapnic patients. In bronchial asthma after the treatment, every parameters return to the levels that are not significantly different from those of the normal subjects.

Fig. 10 presents pooled results of the values of C.V. among each groups of the subjects. As stated before, compared to the normal subjects, the values of C.V. are significantly smaller in the patients with old pulmonary tuberculosis (p < 0.005), pneumonitis (p < 0.025) and greater in the patients with pulmonary emphysema and bronchial asthma during attack (p < 0.005). In comparison between each groups of patients, no significant difference is observed between patients with old pulmonary tuberculosis and those with pneumonitis. Patients with pulmonary emphysema accompanying hypercapnia shows significantly greater C.V. than those with normocapnia (p < 0.025). In all the patients with bronchial asthma, the values of C.V. are decreased after the treatment (p < 0.005).

DISCUSSION

In the detailed review by Baker, we can see many investigations and reports about the physiological aspect of the impedance changes accompanying respiration and clinical application of impedance pneumograph for respiratory monitoring 7. From the standpoint of respiratory moni-
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Fig. 10. Pooled results of the C.V. in normal and diseased subjects. Y-axis gives the value of C.V. in %. Horizontal bars on each plot indicate the means and one standard deviations. Asterisks over the plots indicate significant difference from normal subjects (* P < 0.005, * P < 0.025). P values between two groups of patients are shown under the plots. Connecting lines in patients with bronchial asthma show the trend during attack and after the treatment.

Bendixen and associates appear to be the first to introduce a histogram for displaying variation of breath-by-breath tidal volume in normal young adults, but they mainly stated about the physiological significance of sighing, not about the variability of VT per se. Thereafter, Spencer et al., Zikria et al. and Askanazi et al. observed narrowing of the VT histogram which resulted from a loss of the normal breath to breath variation of VT following upper abdominal operation, in septic and acutely ill patients. Hanning and Spence observed restoration of the
VT distribution from narrow pattern to normal variation in patient during weaning from mechanical ventilation. These observations provide an important clue that analysis of breathing pattern by the VT histogram could be a promising approach for the management of patients with respiratory disease. We attempted to clarify the characteristics of VT histogram in normal subjects and patients with various kinds of respiratory disease, and assess their clinical significance for respiratory monitoring.

In our normal subjects, values of mean tidal volume, respiratory rate and minute ventilation were similar to that observed in other study for normal subjects using non-invasive apparatus such as a canopy system or respiratory inductive plethysmograph. Person to person variance of the C.V. was 12.5% to 37.1%. As shown in Figs. 1 and 2, the patterns of distribution were different between individuals, but the tendency to show a symmetrical distribution around the mean VT was generally observed. In the present study, there was no significant correlation between age and C.V. (r = -0.24). In a study of 235 normal subjects aged 6 to 80 years, Jammes et al. reported that C.V. of VT were independent of age. Tobin et al., however, suggested that rhythmicity of respiration and tidal volume change were more irregular in the elderly beyond 60 years old. It is not clear about the reason of this difference, but the former results might be related to the method using spirometer with a mouthpiece and noseclip and small size of sample which was only 20 or 30 successive breaths. In our study, elderly subjects are not included in normals, so influence of age to variability of tidal volume remains to be elucidated.

Patients with restrictive lung disease such as an old pulmonary tuberculosis or pneumonitis showed the narrow pattern of VT histogram with high peak value of frequency and less values of C.V. at a relatively fixed VT in these patients. On the other this pattern reflected a tendency to breathe at a relatively fixed VT in these patients. On the other hand, patients with obstructive lung disease such as a pulmonary emphysema or bronchial asthma showed the widespread pattern of VT histogram with low peak and scattered values of frequency and greater values of C.V. Mechanisms accounting for this striking contrast between two groups of patients may be related to the difference of pathophysiological condition that is decreased compliance of the lung or thoracic cage per se in restrictive lung disease, or the degree of airflow limitation in obstructive lung disease.

In the patients with bronchial asthma, as patients were recovered from the attack, reversibility of the VT histogram from the widespread pattern to the normal one was confirmed. This phenomenon support the estimation that airflow limitation is one of the regulation factors to characterize the pattern of VT histogram. In addition, it may be suggested that serial measurements of tidal volume histogram on their courses of the treatment provide indices in assessing the recovery from attack or effectiveness of the therapeutic modalities.

Parot et al. reported significant decrease of VT in hypercapnic patients with COPD compared to nonhypercapnic patients, and suggested reduction of VT was responsible for CO2 retention in these patients. In our study, there was a significant difference in C.V. but no difference in mean and S.D. of VT between hypercapnic and nonhypercapnic patients with pulmonary emphysema. It may be related to not significant but smaller VT and greater S.D. in hypercapnic patients. These hypoventilatory state could be recognized from the VT histogram as shown in Fig. 5, which had a distribution distorted toward the range of smaller tidal volume. On the other hand, as shown in Fig. 8, the increase of frequencies of larger tidal volume indicated hyperventilatory state.

We conclude that graphical analysis of tidal volume distribution by the histogram is one of the useful approach to manage patients with respiratory diseases.

REFERENCES

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