Tension-time index of inspiratory muscles in COPD patients: role of airway obstruction

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Inspiratory muscle function has been shown to be related to general muscle weakness, weight loss, blood gas tensions, airway obstruction and hyperinflation. The aim of this study was to define (1) the factor that is the main determinant of the tension-time index of the inspiratory muscles (Trmus), and which thus increases the risk of inspiratory muscle fatigue; and (2) whether a breathing strategy is adopted to avoid inspiratory muscle fatigue.

Twenty-seven normal volunteers and 35 stable COPD outpatients (FEV1, range: 21-89%; and FR/TL, range: 49-77%) were studied. The Trmus was determined as follows: Trmus = Pmax/Ti/Ttot, where Pmax is the maximal inspiratory pressure, Ti is the inspiratory time, and Ttot is the total time of the breathing cycle. COPD patients showed significantly lower Pmax and higher Poi, Pmax, and Trmus than normal subjects. No patient had a Trmus value higher than the inspiratory muscle fatigue threshold of 0.33. The FEV1 was significantly correlated with Trmus and all its components in the patients. The FR/TL was also correlated with all components except Poi. Body weight was only correlated with Pmax. In a forward and backward stepwise regression analysis, FEV1 appeared to be the only significant factor explaining the variance of log(Pmax) and log(Trmus), whereas FR/TL was the principal determinant of Pmax. In COPD patients, a non-linear relationship was found between Ti and Poi, A negative linear relationship was found between Ti/Ttot and Poi/Pmax.

In conclusion, although hyperinflation predominantly affected inspiratory muscle strength in a group of stable COPD patients with a wide range of severity, airway obstruction was the principal factor determining the magnitude of Trmus. In addition, in order to remain below the inspiratory muscle fatigue threshold, as the severity of airway obstruction increased, patients adopted a breathing strategy characterized by decreased Ti/Ttot as inspiratory pressure demand increased.

Introduction

The tension-time index, which reflects the force and timing of inspiratory muscle contraction, is useful for situating patients with chronic obstructive pulmonary disease (COPD) and normal subjects in relation to the fatigue threshold. In COPD and normal subjects, we recently validated a non-invasive tension-time index for all the inspiratory muscles (Trmus) (1) that is analogous to the tension-time index of the diaphragm (Tdi), described by Bellemare and Grassino (2,3). The Trmus is calculated according to the following equation: Trmus = Poi/Pmax Ti/Ttot, where Poi is the mean inspiratory pressure estimated from the mouth occlusion pressure (1,4), Pmax, the maximal inspiratory pressure, and Ti/Ttot, the duty cycle. Several studies have shown that in COPD patients Pmax is reduced as a result of generalized muscle weakness and hyperinflation, which reduce the mechanical advantage of the inspiratory muscles (5). Other factors, such as airway obstruction, impaired nutritional status (5,6) and blood gas tensions (6-8) have also been shown to affect Pmax. The Poi which reflects the load against which the inspiratory muscles must operate, has been shown to be related to pulmonary resistance (9) and airway obstruction, as assessed in terms of FEV1 (10). Furthermore, Poi/Pmax and Ti/Ttot are correlated to changes in FEV1 (10-13). However, the effect of hyperinflation on these parameters has not been reported. In chronically hypercapnic COPD patients, Ti/Ttot and Poi/Pmax are inversely related, probably reflecting an adaptive breathing strategy to avoid fatigue (14).
The aim of this study was to determine in a group of stable COPD patients with a wide range of severity of airway obstruction and hyperinflation but without severe hypercapnia (Paco2 <48 mmHg): (1) the main factors that increase Tmusk; and (2) whether a breathing strategy is adopted to avoid inspiratory muscle fatigue.

Materials and Methods

SUBJECTS

We studied 62 male subjects, 27 normal volunteers and 35 COPD outpatients of comparable age. Each subject was informed of the purpose and methods of the study and gave informed consent. The protocol was approved by the hospital ethics committee. The diagnosis of COPD was made from medical history, clinical examination and pulmonary function tests. At the time of the study all patients were in a clinically stable state (no exacerbation during the previous 4 weeks).

MEASUREMENTS

The FRC was measured with the multibreaths helium equilibrium method (Pulmonet III; SensorMedics, Anaheim, CA) according to recommended procedures (15). About 7 min were allowed for intrapulmonary equilibrium of the mixture of helium, oxygen and air. After this, several slow inspiratory capacity (IC) manoeuvres were performed to enhance equilibrium. We also attempted to measure FRC by the plethysmographic method (2800 Transmural Body Box; SensorMedics). However, several patients with severe COPD were unable to adopt a breathing frequency less than 1 Hz, which is recommended for patients with airway obstruction (15). We therefore report only data obtained with the helium dilution technique. The FEV1 and FVC were measured using standard spiographic techniques and procedures (15). The TLC, FRC/TLC and FEV1/FVC were then calculated. The predicted values were those proposed by the European Community for Steel and Coal (15). Arterial blood gas tensions were measured at rest during room air breathing, using a blood gas analyser (IL meter 1306; Instrumentation Laboratory, Milan, Italy).

The breathing cycle variables were assessed in the sitting position at rest. The subjects breathed through a low resistance valve (0.9 cmH2O l-1 s; dead space: 50 ml). Inspiratory flow was measured with a No. 2 Fleisch pneumotachograph (Fleisch, Lausanne, Switzerland) placed on the inspiratory line and a differential pressure transducer (Model MP45 ± 2 cmH2O; Validyne Corp., Northridge, CA). Tidal volume (VT) was obtained by integration of the flow signal. Mouth occlusions were performed with a silent electromagnetic valve that was closed during expiration and opened automatically about 150 ms after the onset of the occluded inspiration. Since closure was silent, the subjects were unable to anticipate which breath was to be occluded.

The P01 was measured with the Validyne MP45 and a model CD15 carrier demodulator. The Pmax was measured at FRC with the Validyne MP45 transducer (± 300 cmH2O) and the CD15 carrier demodulator, with the technique of Black and Hyatt (16). The subjects were asked to make a maximal inspiratory effort against an occluded airway and to maintain maximal pressure for at least 1 s. The tube into which subjects made maximal efforts had a small airleak to prevent pressure generation by the cheeks with closed glottis instead of with the chest. Repeated measurements were made until three technically satisfactory and reproducible measurements were obtained (variation in Pmax<10%). The reported Pmax data represent the best values.

The mean inspiratory pressure developed by the inspiratory muscles during inspiration (P1) was estimated according to Gaultier al. (4) and Ramonatxo et al. (1). The pressure developed at the end of inspiration (P1) is given by P1=aT10, where a is a constant corresponding to the value of P1 at 1 s (cmH2O), T1 is inspiratory time, and b is a dimensionless constant representing the shape of the pressure profile. If pressure is assumed to increase linearly with time (b=1), it follows that P1=0.5aT1, where a=10P01. Thus P1=0.5aT1 (1). The Tmusk was then computed according to the equation: Tmusk= P1Pmax/T1Ttot. Ramonatxo et al. (1) have validated this tension-time index in patients with COPD and in normal subjects, by comparison with the Trdi described by Bellemare and Grassino (2,3).

All signals were displayed on a Gould ES1000 recorder (Gould Instruments; Cleveland, OH). From an average of 10 respiratory cycles we determined Vr, breathing frequency (f), minute ventilation (Ve), Ttot and T1Ttot. The P01 was calculated from signals displayed at a paper speed of 100 mm s-1. From these values we computed P1, P1/Pmax, and the Tmusk.

PROTOCOL

Subjects were studied at rest in a comfortable sitting position. After their adaptation to the experimental equipment (mouthpiece and noseclip), the ventilatory parameters were recorded for several minutes. At least 10 occlusions were made in each subject, at the rate of 2-3 per minute, with the mean value used to characterize P01. During another 2-min period the measurements were repeated. The reported ventilatory parameters are the mean values obtained before and after the P01 measurements. After 5 min, Pmax was measured.

STATISTICAL ANALYSIS

Data reported in text and tables are mean ± SD. A Student t-test for unpaired observations was used for between-group comparison after confirmation of the normality distribution (Kolomogorov-Smirnov test) and the equality of variance (Levene median test). When these conditions were not met, a Mann-Whitney rank sum test was used. In COPD patients, the correlation of Tmusk and its components with various lung function data was assessed using linear and, when needed, non-linear functions. In order to determine the Pearson correlation coefficients, we performed a logarithmic transformation for variables not
Table 1. Anthropometric, spirometric and blood gas data in COPD patients and control subjects

<table>
<thead>
<tr>
<th>COPD patients</th>
<th>Control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=35)</td>
<td>(n=27)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60 ± 8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170 ± 7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68 ± 11</td>
</tr>
<tr>
<td>FEV₁ (% pred)</td>
<td>43 ± 10</td>
</tr>
<tr>
<td>FVC (% pred)</td>
<td>80 ± 16†</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>42 ± 11</td>
</tr>
<tr>
<td>FRC (% pred)</td>
<td>121 ± 25</td>
</tr>
<tr>
<td>FRC/TLC (%)</td>
<td>65 ± 7</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>73 ± 9</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>39 ± 5</td>
</tr>
</tbody>
</table>

COPD=chronic obstructive pulmonary disease; FEV₁=forced expiratory volume in 1 s; FVC=forced vital capacity; FRC=functional residual capacity; PaO₂=arterial PO₂; PaCO₂=arterial PCO₂; TLC=total lung capacity; f=breathing frequency; P₀₁=mouth occlusion pressure; \( P_l \)=mean inspiratory pressure; \( P_{max} \)=maximal inspiratory pressure; \( R_l \)=pulmonary resistance; \( T/T_{tot} \)=duty cycle; \( T=l \)=inspiratory time; \( T_{di} \)=tension-time index of the diaphragm; \( T_{mus} \)=tension-time index of all the inspiratory muscles; \( T_{tot} \)=total time of the breathing cycle; \( V_l \)=minute ventilation; \( V_l \)=tidal volume.

*Statistically significant difference at the \( P<0.01 \) level.
<br>
<br>

Results

The mean values of anthropometric characteristics and pulmonary function data of the COPD patients are shown in Table 1. Age and height were similar in the two groups. The mean weight was lower in the COPD group, seven patients being underweight (<90% of ideal weight), but only one of them was markedly underweight (75% of ideal weight). Patients exhibited significantly lower forced expiratory flows with, however, a wide range in severity of airway obstruction (FEV₁ range from 21 to 89% pred, and FEV₁/FVC from 23 to 68%). Hyperinflation, as evidenced by higher FRC % pred and FRC/TLC, was present in the COPD patients. Mean arterial blood gas data for COPD are shown in Table 1. Nine patients exhibited moderate hypercapnia (PaCO₂ from 44 to 47 mmHg), but none had severe hypercapnia.

Mean ventilatory data are shown in Table 2. No significant difference was found between the two groups for \( V_l \), \( f \) and \( T/T_{tot} \). However, the COPD patients showed a significantly shorter \( T_l \) (\( P<0.05 \)). Mean respiratory drive and inspiratory muscle function data are shown in Table 3. Patients exhibited significantly higher \( P_0 \), \( P_{max} \), \( T_{di} \) and \( T_{mus} \), resulting in a higher value of \( \frac{P_{di}}{P_{max}} \). The \( T_{mus} \) was significantly increased in patients but did not exceed 0.21 in any of the patients. This is well below the value of 0.33, which is thought to represent the inspiratory fatigue threshold (1).
TABLE 4. Pearson correlation coefficients of tension-time index and its components to body weight, hyperinflation and airway obstruction in COPD patients

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>PImax</th>
<th>R</th>
<th>Ti/Ttot</th>
<th>log (P/t/Pmax)</th>
<th>log (TRmus)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PImax</td>
<td>-0.32*</td>
<td>-0.10</td>
<td>0.16</td>
<td>0.14</td>
<td>-0.10</td>
</tr>
<tr>
<td>R</td>
<td>-0.45†</td>
<td>0.11</td>
<td>-0.33*</td>
<td>0.44†</td>
<td>0.37*</td>
</tr>
<tr>
<td>Ti/Ttot</td>
<td>0.40*</td>
<td>-0.39*</td>
<td>0.45†</td>
<td>-0.63‡</td>
<td>-0.54‡</td>
</tr>
</tbody>
</table>

*Statistically significant correlation at the P<0.05 level.
†Statistically significant correlation at the P<0.01 level.
‡Statistically significant correlation at the P<0.001 level.

TABLE 5. Forward and backward stepwise regression analysis results in COPD patients (independent variables entered in the model were FEV₁ and FRC/TLC)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Step</th>
<th>Variable</th>
<th>r²</th>
<th>P</th>
<th>Percentage of total variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>PImax</td>
<td>1</td>
<td>FRC/TLC</td>
<td>0.200</td>
<td>&lt;0.02</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>FEV₁</td>
<td>0.222</td>
<td>&lt;0.01</td>
<td>+2</td>
</tr>
<tr>
<td>Ti/Ttot</td>
<td>1</td>
<td>FEV₁</td>
<td>0.204</td>
<td>&lt;0.01</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>FRC/TLC</td>
<td>0.209</td>
<td>&lt;0.01</td>
<td>+0.5</td>
</tr>
<tr>
<td>Pr</td>
<td>1</td>
<td>FEV₁</td>
<td>0.148</td>
<td>&lt;0.05</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>FRC/TLC</td>
<td>0.188</td>
<td>&lt;0.05</td>
<td>+4</td>
</tr>
<tr>
<td>log (P/t/Pmax)</td>
<td>1</td>
<td>FEV₁</td>
<td>0.395</td>
<td>&lt;0.001</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>FRC/TLC</td>
<td>0.399</td>
<td>&lt;0.001</td>
<td>+0.4</td>
</tr>
<tr>
<td>log (TRmus)</td>
<td>1</td>
<td>FEV₁</td>
<td>0.296</td>
<td>&lt;0.001</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>FRC/TLC</td>
<td>0.298</td>
<td>&lt;0.001</td>
<td>+0.2</td>
</tr>
</tbody>
</table>

of the total variance (P<0.001) and FRC/TLC added only 0.4% (non-significant). For log (TRmus), FEV₁ explained 30% (P<0.001), while FRC/TLC added only 0.2% (non-significant).

As shown in Fig. 1(a) and (b), by plotting the data of normal subjects and COPD patients, a hyperbolic relationship was found between P/Pmax and FEV₁ (r=0.64, P<0.001) and between TRmus and FEV₁ (r=0.79, P<0.001). This model was also significant when COPD data were analysed (P/Pmax vs FEV₁; r=0.69, P<0.001; TRmus vs FEV₁; r=0.57, P<0.01).

In COPD patients, a significant hyperbolic correlation was found between P/Pmax and FEV₁ (Fig. 2(a)). Figure 2(b) shows the individual values of the control subjects together with the hyperbolic curve of the COPD patients. In all instances, the values of the control subjects were below the regression curve obtained for the COPD patients. In the patients a significant negative linear correlation was found between Ti/Ttot and P/Pmax (Fig. 3).

**Discussion**

We studied a group of stable COPD patients with a wide range in severity of airway obstruction and hyperinflation but without severe hypercapnia. Our results showed that a low FEV₁ (%pred) was the major correlate to increased TRmus, while FRC/TLC was the principal determinant of inspiratory muscle strength. Body weight, PaCO₂ and PaO₂ did not play a major role in this patient population. In order to remain below the fatigue threshold, the patients adopted a breathing strategy characterized by decreased Ti/Ttot as P/Pmax increased.

We studied 35 COPD patients in a stable state, without severe hypercapnia. The ranges in FEV₁ and FRC/TLC were wide and allowed the assessment of the relative contribution of airway obstruction (FEV₁) and hyperinflation (FRC/TLC) to TRmus. As in some previous studies (5,6), we assessed lung volumes using the multibreaths helium equilibration method. This method does not assess trapped gas, and therefore may underestimate FRC. However, the patients performed IC manoeuvres during the measurement of FRC (15), which should have reduced this underestimation. We did not use the plethysmographic data because some of our patients, particularly those with more severe COPD, were unable to adopt a breathing frequency of less than 1 Hz, which is recommended for patients with airway obstruction in order to allow pressure equalization between mouth and alveoli (15,17,18). Indeed, when the latter condition is not respected, plethysmography may result in erroneous overestimation of lung volume (17,18).

Our results showed significant hyperinflation in COPD patients compared with healthy subjects (Table 1), with
(a) Hyperbolic regression analysis with all subjects (n = 62): 
\[ a = 0.31, \quad b = 0.02, \quad r = 0.84; \quad P < 0.001 \]

(b) Hyperbolic regression analysis with all subjects (n = 62): 
\[ a = 0.10, \quad b = 0.02, \quad r = 0.79; \quad P < 0.001 \]

FIG. 1. Relationship of FEV₁ to \( \frac{P_I}{P_{\text{max}}} \) (a) and \( T_{\text{mus}} \) (b) in both COPD patients (●) and control subjects (○). The hyperbolic function used in this figure was: \( y = \frac{(a - x)}{b} \).

\[ P_{0.1} = (3.89/T_1) - 0.36, \quad r = 0.70, \quad P < 0.001 \]

FIG. 2. (a) Relationship between \( P_{0.1} \) and \( T_1 \) in COPD patients (●), where the hyperbolic function was: \( y = \frac{(a - x)}{b} \). (b) Individual data in control subjects (○) in relation to the hyperbolic curve of the COPD patients.

50% of the patients having FRC values ranging from 120 to 174% of predicted.

The tension-time index of the inspiratory muscles was determined from the equation \( T_{\text{mus}} = \frac{T_{\text{IT}}}{{T_{\text{IT}}}} \cdot \frac{P_I}{P_{\text{max}}} \) (1). This equation assumes that inspiratory pressure increases linearly over time during the inspiration. Since this is not always the case in humans (19,20), this method may lead to an overestimation of \( P_i \), as reported by Ramonatxo et al. (1). In the present study, the values of \( P_i \) of normal and COPD subjects were comparable to those previously reported by our group (1). However, these values were higher than those obtained from measurements of \( P_i \) based on oesophageal pressure in both normal subjects and COPD patients (1,9). We also found that our COPD patients exhibited an approximately two-fold increase in \( P_i \) relative to controls, as previously reported by our group (1). Bellemare and Grassino also found similar differences in mean transdiaphragmatic pressure (\( P_{\text{di}} \)) (3).

The usefulness of our estimation of \( T_{\text{mus}} \) is based on several points. First, since this method requires only mouth
In line with previous studies, COPD patients exhibited \( Vt \) comparable to normal subjects, associated with shorter \( T_i \), higher \( P_{m} \) (11, 13, 23, 24) and lower \( P_{m} \) (5, 9, 25, 26). The \( T_{rmus} \) in COPD and normal subjects was similar to that previously reported (1). In all COPD patients the \( T_{rmus} \) was well below the fatigue threshold, in line with previous reports indicating that in stable COPD patients \( T_{rdi} \) is below the fatigue threshold (3).

In the present study, we analysed the various mechanical and non-mechanical factors that may bring COPD patients closer to the fatigue threshold.

\( P_{m} \), a measure of inspiratory muscle strength, was correlated with FRC/TLC, \( \text{FEV}_1 \) and body weight in the COPD group (Table 4). We also found a weak correlation between \( P_{m} \) and body weight, which confirms the minor role of mild-to-moderate weight loss in inspiratory muscle strength. Indeed, a significant effect of nutritional status in inspiratory muscle strength has been found only in patients with severe weight loss (31). The fact that airway obstruction impairs \( P_{m} \) in COPD patients is in agreement with Begin and Grassino (9) and with Heijdra et al. (6). Based on analysis of six different studies, the latter group found that the mean \( P_{m} \) is significantly correlated to the mean \( \text{FEV}_1 \) (%pred) (see Fig. 5 in ref. 6). This may reflect the effects of chronic overload of the diaphragm and the rib cage inspiratory muscles, which are recruited preferentially in COPD patients (22). Indeed, the diameter of the type I and type II fibres of the diaphragm has been shown to be smaller in COPD patients than in normal subjects, and to be linearly correlated with \( \text{FEV}_1 \) (29). In mild COPD the decreased phosphocreatine content in the external intercostal muscle was inversely related to decreased \( \text{FEV}_1/\text{FVC} \) (30), probably reflecting chronic overload of the rib cage inspiratory muscles. In accordance with previous studies (5,6), we found that FRC/TLC was correlated to \( P_{m} \) (Table 5). Hyperinflation decreases inspiratory muscle strength by causing the inspiratory muscles to operate at an unfavourable position of the length-tension curve (26). Indeed \( P_{m} \) declines with increasing volume (32).

We found \( \tilde{P}_i \) to be correlated with \( \text{FEV}_1 \), but not with FRC/TLC (Table 4). This agrees with previous studies in COPD patients where \( \tilde{P}_i \) was found to be related to lung resistance (\( R_L \)) (4,9). \( \tilde{P}_i \) is an expression of the mechanical load that the inspiratory muscles have to sustain to maintain ventilation. In addition, a decrease in \( \text{FEV}_1 \) may elicit expiratory flow limitation with increasing inspiratory work due to intrinsic positive end-expiratory pressure (PEEP) (33). Therefore, change in \( \text{FEV}_1 \) may affect \( \tilde{P}_i \) by changing the load against which the muscles contract. Duranti et al. (10) showed that after administration of a high dose of a \( \beta_2 \)-agonist in severe COPD patients, the changes in mean inspiratory pressure swing were related to the changes in \( \text{FEV}_1 \), and \( R_L \) but not to the changes in FRC. Bellemare and Grassino also found a linear relationship between \( \tilde{P}_i \) and airway resistance (Raw) in COPD patients (3).

The balance between the inspiratory mechanical burden and the ability of the inspiratory muscles to develop force, that is the ratio of \( \tilde{P}_i \) to \( P_{m} \), reflects the relative force required for each inspiration (10). In COPD patients we found that \( \tilde{P}_i/P_{m} \) was thus affected by both airway obstruction (Table 4 and Fig. 1(a)) and hyperinflation (Table 4). A similar relationship with airway obstruction has been reported for the diaphragm by Bellemare and Grassino (3), who found a significant correlation between \( \tilde{P}_i/P_{m} \) and Raw. In COPD patients after inhalation of fenoterol, Duranti et al. (10) also found that the relative decrease in the pleural pressure swing was correlated with the increase in \( \text{FEV}_1 \).

We found that \( T_{V/Tot} \), which is one of the components of \( T_{rmus} \), was also correlated to airway obstruction (Table 4), in line with previous studies (11–13), as well as to hyperinflation. However, these relationships were in inverse relation compared with those between \( \tilde{P}_i/P_{m} \) and \( \text{FEV}_1 \) and FRC/TLC. Therefore, our results suggest that COPD patients use an adaptive breathing pattern to cope with the increased work of breathing.

As discussed above, \( T_{rmus} \) is a useful index for assessing the risk of inspiratory muscle fatigue by situating the individual \( T_{rmus} \) value in relation to the fatigue threshold. We showed that with increasing airway obstruction and hyperinflation, the risk of fatigue increases in COPD patients (Table 4). These results are in agreement with...
those of Bellemare and Grassino (3), who found a similar relationship between Ttdi and Raw.

We expected hyperinflation, the classical factor leading to impaired inspiratory muscle strength, to also be an important determinant of Trmus. In fact, in multiple regression analysis we found hyperinflation to be the principal determinant of Pmax (Table 5), whereas airway obstruction was the predominant factor for increasing Trmus. Thus, our study suggests that the main factor leading the inspiratory muscles closer to the fatigue threshold is the increased inspiratory load rather than the detrimental effects of hyperinflation. Figure 1 describes the relationship of Trmus and P/Pmax to FEV1 in the control subjects and COPD patients. The observed hyperbolic relationship indicates that the risk of inspiratory muscle fatigue, that is, increase in the relative force exhibited during inspiration (P/Pmax) and Trmus, increase with worsening of airway obstruction.

As shown in Table 5, the total variance explained by the model ranged from 21 to 41%, indicating that other factors also influence inspiratory muscle function in COPD patients. The role of physical fitness has also been suggested (6). Indeed, the tension-time index, measured with an esophageal balloon, was shown to be improved by rehabilitation (34).

As previously reported (11-13), in our COPD patients Td decreased with increasing Pp [Fig. 2(a)] in a hyperbolic fashion. This could reflect a breathing strategy adopted by our COPD patients in order to reduce the increase in P, and therefore an adaptation limiting the pressure demands in stable COPD patients. Figure 2(b) indicates that individual data of the control subjects were below the regression curve obtained in the COPD patients. This result may be explained by the lower effective impedance of the respiratory system in healthy subjects when compared to COPD patients.

We found that in the COPD patients Td/Ttot decreased as P/Pmax increased (Fig. 3). This negative relationship between Td/Ttot and P/Pmax, which limited the increase in Trmus, again suggests that COPD patients adopt a breathing pattern which keeps the activity of the inspiratory muscles below the fatigue threshold. This breathing strategy has been previously described in COPD patients with chronic hypercapnia or in acute respiratory failure (14), as well as in normals and COPD patients breathing against fatiguing loads, that is, external inspiratory resistances (2,3,27,28). Such a breathing strategy has also been reported in children with COPD (4) and cystic fibrosis (21). Our results show that such adaptation occurs not only in patients who are chronically hypercapnic or in acute respiratory failure but also in stable eucapnic COPD patients.

In conclusion, in stable eucapnic COPD patients hyperinflation predominantly affected inspiratory muscle strength, while airway obstruction was the principal factor leading to increases in Trmus. In addition, in order to remain below the inspiratory muscle fatigue threshold, with increasing severity of airway obstruction, patients adopted a breathing strategy characterized by decreased Td/Ttot.

References


