Assessment of Physiologic Variables and Subjective Comfort Under Different Levels of Pressure Support Ventilation*

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Study objectives: To evaluate the effects of 12 ventilator settings (pressure support ventilation [PSV] plus positive end-expiratory pressure [PEEP], 30 + 0 cm H2O; 25 + 0 cm H2O; 20 + 0 cm H2O; 15 + 0 cm H2O; 10 + 0 cm H2O; 5 + 0 cm H2O; and 0 cm H2O) on physiologic variables; the percentage of ineffective efforts; patient comfort; and whether the diagnosis of COPD may influence results.

Design: Prospective, randomized, physiologic study.

Setting: Three weaning centers.

Patients: Thirty-six consecutive patients (20 patients with COPD).

Intervention: Patients were randomly submitted to the 12 settings.

Measurements and results: Breathing pattern, respiratory drive (p0.1), arterial oxygen saturation (SatO2), heart rate, percentage of ineffective efforts per minute, patient comfort measured by means of a visual analogue scale (VAS), and BORG scale were recorded under each setting. Under different levels of assistance, breathing pattern, SatO2, and p0.1 significantly and linearly changed (p < 0.0001) while VAS and BORG scale presented a significant (p < 0.027) U-shaped trend; high or low assistance caused the most discomfort. Under high levels of assistance, a higher (analysis of variance, p < 0.023) frequency of ineffective effort percentage was observed in the subgroup of 26 patients who presented this phenomenon. Breathing pattern significantly (p = 0.013) changed when compared to PSV alone (PSV plus zero end-expiratory pressure [ZEEP]) at the same total inspiratory pressure assistance (PSV plus PEEP). A huge variability among patients in breathing pattern and comfort was found under the setting rated as the most comfortable by patients. The diagnosis of COPD did not influence the overall results.

Conclusions: The following conclusions are made: (1) physiologic variables followed a linear trend, while comfort followed a U-shaped trend under different levels of PSV (irrespective of COPD diagnosis); (2) high assistance caused an increase in ineffective efforts; (3) only the breathing pattern significantly changed when total assistance was given as PSV plus PEEP when compared to PSV alone (PSV plus ZEEP); and (4) the extreme levels of PSV are not associated with the best comfort.

Key words: COPD; mechanical ventilation; symptoms; weaning

Abbreviations: ABG = arterial blood gas; ANOVA = analysis of variance; Fio2 = fraction of inspired oxygen; HR = heart rate; MV = mechanical ventilation; p0.1 = respiratory drive; PEEP = positive end-expiratory pressure; PSV = pressure support ventilation; SatO2 = arterial oxygen saturation; VAS = visual analogue scale; Ve = minute ventilation; Vt = tidal volume; ZEEP = zero end-expiratory pressure

Pressure support ventilation (PSV) is widely used in the ICU for weaning attempts1–3 aimed at improving patient comfort and at the same time at reducing ventilatory work.4 Previous studies have shown that the use of PSV is able to affect the breathing pattern,5 arterial blood gases (ABGs),5 work of breathing,5,6 and hemodynamics.7 Although

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ABGs, tidal volume (VT), respiratory rate, accessory muscles or diaphragmatic activity, and controlled computerized closed-loop systems have been proposed as useful parameters to set the ideal level of PSV.\textsuperscript{1,5,8,9} Specific guidelines or criteria have not yet been published. The PSV setting is often based on the physicians' clinical intuition and predictions.\textsuperscript{1} Traditional approaches to mechanical ventilation (MV) are aimed at providing levels of support able to produce a VT of 8 to 15 mL/kg or a respiratory rate between 25 breaths/min and 30 breaths/min.\textsuperscript{1,10} The application of positive end-expiratory pressure (PEEP) has been extensively used to improve oxygenation, hemodynamics, ventilation/perfusion mismatching, and recruitment of unventilated alveoli, and especially to counteract dynamic intrinsic PEEP.\textsuperscript{11} The sensation of well-being, comfort, or dyspnea has already been studied in patients who received MV\textsuperscript{12,13} by comparing different modalities of ventilation,\textsuperscript{1,14,15} as well as by comparing different ways of delivering PSV.\textsuperscript{16} Moreover, it is well known that the intensity of discomfort increases as the delivered pattern of ventilation deviates from that spontaneously chosen by the subject.\textsuperscript{5,13,17} Leung and coworkers\textsuperscript{18} demonstrated a correlation between the increase in the number of ineffective ventilation triggering and the increase in level of ventilator assistance. Up to now, studies comparing physiologic changes and patient comfort during application of different levels of PSV, with and without adjunctive PEEP, are still lacking. Therefore, the aims of the present study, carried out on a miscellaneous group of patients with prolonged/difficult weaning, were as follows: (1) to evaluate the effects of different levels of total assistance, obtained with PSV alone or PSV plus PEEP, on physiologic variables, the number of ineffective efforts, and on patient comfort; and (2) to determine if a diagnosis of underlying COPD influences the results.

**Materials and Methods**

The study was conducted according to the Declaration of Helsinki and with approval of the protocol by the ethics committee of each hospital. Patients gave their informed consent to the study.

**Patients**

From March 1, 2002, to July 31, 2002, we studied 36 consecutive patients coming from general ICUs and admitted to the weaning centers of three hospitals: two Fondazione S. Maugeri IRCCS centers in Gussago (27 patients, 66%) and Montescano (2 patients, 5%), the Fondazione ONLUS Villa Pineta (7 patients, 17%). The weaning centers were separate units with four to six monitored beds each. The Gussago, Montescano, and Gaia to weaning centers belong to rehabilitation institutions, which are referral rehabilitation and chronic care centers for a large geographic area in northern Italy. Besides caring for long-term patients, patients receiving MV are admitted to these institutions to undergo a program of progressive discontinuation from MV, and are then discharged to a home ventilation program. Most of our patients (66%) were receiving long-term oxygen therapy before ICU admission. At the time of study entry, all the patients were in a posttracheotomy status and in stable physiologic condition, as assessed by the following: (1) ABG analysis (pH > 7.35), (2) hemodynamics (no need to change dose of vasoactive catecholamine), and (3) \( FIO_2 \) values under MV with a \( FIO_2 \leq 40\% \) and PEEP \( \leq 5 \) cm H\(_2\)O. Patients were classified according to the underlying diagnosis: COPD, neuromuscular diseases (amyotrophic lateral sclerosis, two patients; Duchenne muscular dystrophy, three patients; myasthenia gravis, two patients), and sequelae of surgery (cardiovascular surgery, six patients; thoracic surgery, one patient; upper abdomen surgery, one patient). For statistical purposes, patients were classified as COPD or non-COPD. Exclusion criteria were concomitant diseases of the CNS, cancer, inability to answer to a symptom visual analogue scale (VAS)\textsuperscript{19} and/or to a questionnaire (BORG),\textsuperscript{20} presence of psychiatric problems, signs of delirium, or refusal to participate. Two days before the study, a physician not involved in the protocol assessed the patients' temporal orientation by means of the Italian version of the Benton test.\textsuperscript{21}

**Study Protocol and Definitions**

Patients received continuous MV throughout the study period. On admission to the weaning centers, all patients underwent a preliminary T-piece trial to rule out their ability to breathe spontaneously. The T-piece trial was considered unsuccessful if the patients showed severe distress signs (tachypnea, tachycardia, diaphoresis, and worsening in ABG values and in neurologic status) within 48 h. In case of T-piece trial failure, patients were assigned to a defined weaning protocol either of increasing spontaneous breathing trials or of decreasing levels of PSV. The study protocol was initiated within 7 days after admission to the weaning center; in all patients, PSV had been delivered during the last 7 consecutive days prior to the beginning of the study. On weaning center admission, patients used the following ventilators: EVITA 2 (Dräger Medizintechnik; Lübeck, Germany) [20 patients], EVITA 4 (Dräger Medizintechnik) [10 patients], IV Ent-201 (VersaMed; Kadima, Israel) [1 patient], Nellcor Puritan Bennett 840 (Nellcor Puritan Bennett, Pleasanton, CA) [3 patients], and Horus (Tsamma; Antony, France) [2 patients]. The day before the study, the patients were switched to a ventilator with a built-in algorithm to measure respiratory drive (p0.1) [Evita 2 and Evita 4]. The inspiratory phase of ventilator assistance was pressure triggered; the sensitivity was set at 1 cm H\(_2\)O below the baseline pressure (the flow-by mode was not activated). The expiratory trigger sensitivity, when available, was set at 30% of peak flow. Due to different pulmonary mechanics characteristics of the patients, the slope rise of the inspiratory flow was set at the fastest available setting on the machine in patients with COPD (0.10 s) and slower in the non-COPD patients (0.50 s). No back up of respiratory rate was added. The study was a single-blind, cross-over protocol comparing 12 ventilator settings as follows: 30 cm H\(_2\)O of PS plus zero end-expiratory pressure (ZEEP); 25 cm H\(_2\)O of PS plus 5 cm H\(_2\)O PEEP; 25 cm H\(_2\)O of PS plus ZEEP; 20 cm H\(_2\)O of PS plus 5 cm H\(_2\)O of PEEP; 20 cm H\(_2\)O of PS plus ZEEP; 15 cm H\(_2\)O of PS plus 5 cm H\(_2\)O of PEEP; 15 cm H\(_2\)O of PS plus ZEEP; 10 cm H\(_2\)O of PS plus 5 cm H\(_2\)O of PEEP; 10 cm H\(_2\)O of PS plus ZEEP; 5 cm H\(_2\)O of PS plus ZEEP; 5 cm H\(_2\)O of PS plus ZEEP; 5 cm H\(_2\)O of PS plus ZEEP; 5 cm H\(_2\)O of PS plus ZEEP; and 0 cm H\(_2\)O of PS plus 5 cm H\(_2\)O of PEEP. The sequence of the 12

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settings was computer generated and randomly assigned to each patient. Each step lasted 5 consecutive min without pauses. Among the six settings with PEEP, the patient’s comfort setting was defined as that which offered the best level of comfort, as assessed by the VAS.

**Measurements**

Patients’ demographic (age, sex), anthropometric (body weight as known before admission into the general ICU), and clinical data (days spent in the weaning center) were obtained from each center’s register. Physiologic and symptom measurements were collected at baseline and within the last minute of each of the 12 ventilator setting steps. The following measurements were recorded.

**Breathing Pattern:** Vt, minute ventilation (Ve), and respiratory rate were obtained by the flow signal of the ventilator (EVITA 2 Dräger in 24 patients, EVITA 4 Dräger in 12 patients) according to the analogue data reported on the ventilator display. The number of breaths per minute was calculated as the number of triggered ventilator cycles with a pressure tracing on the ventilator display.

**pH:** pH was measured with the semiautomatic built-in algorithm. The mean value of three consecutive measurements was considered for statistics.

**Arterial Oxygen Saturation:** Arterial oxygen saturation (SatO₂) was assessed by pulse oximetry while the patients, in a sitting position, breathed at an FiO₂ able to maintain a target SatO₂ of > 92%.

**Heart Rate:** Heart rate (HR) was recorded continuously by means of an ECG monitoring system.

**Patient Comfort:** The level of comfort was measured by means of a VAS and modified BORG scale as previously described. The dyspnea VAS consisted of a 20-cm horizontal line with the left and right extremes indicating the best and worst comfort sensation, respectively; physicians asked subjects placed in their most comfortable position to put a vertical mark on the line on a sheet held in front of them in response to the question: “How is your level of comfort in this moment?” For each step, patients drew a vertical mark that best represented their comfort assessment at that moment. The level of comfort was calculated as the distance in centimeters from the left side of the horizontal line to

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**Table 1—Clinical and Physiologic Characteristics of Studied Patients**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>COPD</th>
<th>No COPD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>20</td>
<td>16</td>
<td>36</td>
</tr>
<tr>
<td>Men</td>
<td>13</td>
<td>9</td>
<td>22 (61%)</td>
</tr>
<tr>
<td>Women</td>
<td>7</td>
<td>7</td>
<td>14 (39%)</td>
</tr>
<tr>
<td>Age, yr</td>
<td>70 ± 5</td>
<td>63 ± 17</td>
<td>67 ± 12</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>62 ± 14</td>
<td>65 ± 12</td>
<td>63 ± 13</td>
</tr>
<tr>
<td>COPD</td>
<td>20</td>
<td>0</td>
<td>20 (55.5%)</td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>0</td>
<td>8</td>
<td>8 (22.2%)</td>
</tr>
<tr>
<td>Postsurgical</td>
<td>0</td>
<td>8</td>
<td>8 (22.2%)</td>
</tr>
<tr>
<td>Stay in ICU before weaning</td>
<td>31 ± 8</td>
<td>28 ± 7</td>
<td>28 ± 7</td>
</tr>
<tr>
<td>center admission, d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stay in weaning center, d</td>
<td>28 ± 8</td>
<td>27 ± 9</td>
<td>29 ± 8</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>14 ± 1</td>
<td>14 ± 3</td>
<td>14 ± 2</td>
</tr>
<tr>
<td>PaO₂/FiO₂</td>
<td>286 ± 63</td>
<td>296 ± 43</td>
<td>292 ± 52</td>
</tr>
<tr>
<td>pH</td>
<td>7.39 ± 0.01</td>
<td>7.38 ± 0.01</td>
<td>7.38 ± 0.01</td>
</tr>
</tbody>
</table>

*Data are presented as No. or mean ± SD unless otherwise indicated. APACHE = acute physiology and chronic health evaluation.

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**Table 2—Time Course of Variations for Breathing Pattern, SatO₂, and pH Under Different Settings**

<table>
<thead>
<tr>
<th>Variable</th>
<th>FS + PEEP, cm H₂O</th>
<th>FS + PEEP, cm H₂O</th>
<th>FS + PEEP, cm H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate, bpm</td>
<td>12 ± 6</td>
<td>14 ± 6</td>
<td>16 ± 6</td>
</tr>
<tr>
<td>Ventilation rate, L/min</td>
<td>54 ± 11</td>
<td>54 ± 12</td>
<td>54 ± 12</td>
</tr>
<tr>
<td>FiO₂</td>
<td>0.46 ± 0.01</td>
<td>0.46 ± 0.01</td>
<td>0.46 ± 0.01</td>
</tr>
<tr>
<td>SatO₂ (%)</td>
<td>98 ± 3</td>
<td>98 ± 3</td>
<td>98 ± 3</td>
</tr>
<tr>
<td>pH</td>
<td>7.39 ± 0.01</td>
<td>7.38 ± 0.01</td>
<td>7.38 ± 0.01</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD. The variations in respiratory rate, Ventilation rate, FiO₂, SatO₂, and pH were found to be statistically and linearly different (p < 0.0001) under all settings. The distribution of assistance with PEEP compared to assistance without PEEP was correlated with decreased Ventilation rate and Ventilation rate and increased respiratory rate (p < 0.0001).
The mark placed by the patient, expressed as the percentage value of the maximum possible level of discomfort. The modified Borg scale consisted of a vertical line labeled 0 to 10 with verbal descriptors at fixed points on the scale (0 = no discomfort, 3 = moderate discomfort, 5 = strong discomfort, 10 = intolerable discomfort). Patients were asked to indicate their perceived level of discomfort by pointing to a number or phrase on the scale set in large type on a sheet held in front of them. Our patients were carefully instructed on the appropriate use of both scales before the protocol began. A new scale was presented each time the measurements were made.

**Ineffective Efforts.** According to a previous article, any inspiratory effort unable to trigger a ventilator cycle (lack of pressure tracing on ventilator display) was defined as an ineffective effort; the physician observed the parameters on-line on the ventilator monitor. Ineffective effort was assessed as a lack of ventilator triggering in the presence of a spontaneous breathing inspiratory flow signal. The number of ineffective efforts were recorded during the last minute of assistance for each setting. The number of ineffective efforts thus recorded was then standardized by dividing this value by the calculated respiratory rate in the same minute; the final data expressed as ineffective efforts/respiratory rate ratio × 100 (percent-

**Figure 1.** Mean ± SD values for comfort and ineffective efforts at different levels of assistance from 30 to 0 cm H₂O (with or without the application of 5 cm H₂O of PEEP). VAS (top, this page), Borg scale (bottom, this page), and percentage of ineffective efforts per minute (top, next page) were found to be statistically different under described settings (p < 0.027 for comfort and p < 0.023 for ineffective efforts) in the 26 patients presenting ineffective efforts.
Statistical Analysis

Statistical analysis was performed using the SPSS software package (SPSS release 10.1; SPSS; Chicago, IL). All the results are shown as mean and SDs or frequencies, and percentage distributions when appropriate. Analysis of variance (ANOVA) for repeated measures was applied to detect the within- and between-subject (COPD and non-COPD) effects due to the application of different settings of PSV and PEEP on different physiologic and subjective variables; a Bonferroni adjustment for multiple comparison was then added. A linear variation of data revealed by ANOVA (the higher the PSV assistance, the lower or the higher the studied parameter) was defined as a linear trend; a parabolic variation (higher and lower assistance causing similar results in the studied parameter) was defined as U-shaped. Relationships between VAS and p0.1, ineffective efforts, respiratory rate, and total level of assistance chosen by the patients as the most comfortable (comfort setting) were assessed by means of a bivariate Spearman correlation for nonparametric data. Any p value < 0.05 was considered statistically significant.

Results

Anthropometric and clinical characteristics of all patients enrolled in the study classified according to underlying disease are shown in Table 1. All patients included in the study completed the protocol. Among the 16 non-COPD patients, 8 patients (50%) had neuromuscular diseases (amyotrophic lateral sclerosis, three patients; Duchenne muscular dystrophy, three patients; myasthenia gravis, two patients), while 8 patients (50%) were recovering from cardiovascular (six patients), thoracic (one patient), and upper abdomen surgery (one patient). The time elapsed from intubations to tracheotomy ranged from 9 to 29 days; the time from intubations to weaning center admission ranged from 15 to 50 days. The reasons for which MV had been initiated in the ICU were as follows: relapse of a chronic respiratory failure with (42%) or without (20%) pneumonia, muscular failure (20%), sepsis (6%), and cardiac failure (12%). All patients had a long period of stay both in the ICU of provenience (ranging from 15 to 55 days) and in the weaning center (18 to 60 days). The stability of clinical condition under MV at study entry was verified by ABGs, pH, and APACHE (acute physiology and chronic health evaluation) II score. The non-COPD patients were younger than those with COPD; all other variables were similar between the two groups. Two of the 36 studied patients died before hospital discharge. The day prior to the study, patients received MV under PSV ranging from 12 to 28 cm H2O with a level of PEEP ≤ 5 cm H2O; their VT per kilogram ranged between 4.6 mL and 11 mL (mean, 8.15 ± 1.3 mL).

Effects on Breathing Pattern, Oxygenation, p0.1, and HR

Table 2 shows that VT and \( \dot{V}_E \) significantly increased, and respiratory rate significantly decreased as the level of assistance increased. Breathing pattern was significantly changed when total assistance was given as PSV plus PEEP when compared to PSV alone (PSV plus zero end-expiratory pressure [ZEEP]). SatO₂ significantly increased while p0.1 decreased under high levels of assistance (Table 2).
The application of PEEP did not change the results found with PSV alone. HR remained unchanged under all levels of assistance.

**Patient Comfort**

Comfort levels, assessed by VAS and BORG scale, followed a U-shaped trend (p = 0.027) when the level of assistance was modified (Fig 1, top and middle panels). In fact, the extreme (both lowest and highest) levels of assistance generated the least comfort. Moreover, these results were not affected by the addition of PEEP (Fig 1, top and middle panels). Interestingly, no significant relationship was found between comfort and p0.1, comfort and ineffective efforts (p = 0.634), or comfort and respiratory rate (p = 0.385).

**Effects on Ineffective Efforts**

Ineffective efforts were observed in 26 of 36 patients (72%), irrespective of the applied PSV setting. Among these patients, 14 patients (54%) had COPD (70% of 20 COPD patients), 6 patients (23%) had neuromuscular diseases (75% of 8 patients with neuromuscular diseases [Duchenne muscular dystrophy, 3 patients; myasthenia gravis, 2 patients; amyotrophic lateral sclerosis, 1 patient]), and 6 patients (23%) were postsurgical patients (75% of 8 postsurgical patients [cardiovascular surgery, 5 patients; thoracic surgery, 1 patient]). In the whole studied group, ineffective efforts (expressed as the percentage of ineffective efforts per minute) increased under high level of assistance even if this change was not statistically significant. This trend reached statistical significance when the subgroup of 26 patients who experienced ineffective efforts was taken into account: the percentage of ineffective efforts increased under high level of assistance (ANOVA, p = 0.023) [Fig 1, bottom]. The application of PEEP did not change the results found with PSV alone.

**Comfort Setting**

The level of assistance allowing the highest comfort (comfort setting) varied widely among the patients: the PSV assistance of 30 cm H2O was chosen as the most comfortable in 2.8% of cases, 25 cm H2O was chosen in 13.8%; 20 cm H2O was chosen in 33.3%; 15 cm H2O was chosen in 25%; 10 cm H2O was chosen in 22.3%; and 5 cm H2O was chosen in 2.8%. Table 3 shows the huge SDs and extremely wide range of values for level of assistance chosen, VT, and VT per kilogram, respiratory rate, VE, ineffective efforts, and comfort under the setting defined by patients as the most comfortable. There was no statistically significant correlation between comfort (as assessed by the VAS) and setting of assistance chosen by the patients (comfort setting). The diagnosis of COPD (55.5%) or non-COPD (44.4%) did not affect the overall results of the study.

### Table 3—Physiologic Data Under Comfort Setting*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Comfort Setting</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of assistance, cm H2O</td>
<td>17.08 ± 5.8</td>
<td>5–30</td>
</tr>
<tr>
<td>Vt per kilogram</td>
<td>8.11 ± 2.3</td>
<td>3.3–14</td>
</tr>
<tr>
<td>Vt, ml</td>
<td>569 ± 316</td>
<td>230–1,560</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min</td>
<td>18 ± 6</td>
<td>9–29</td>
</tr>
<tr>
<td>Ve, L/min</td>
<td>8.99 ± 3.7</td>
<td>4.2–17</td>
</tr>
<tr>
<td>Ineffective efforts per minute, %</td>
<td>3.99 ± 10</td>
<td>0–56</td>
</tr>
<tr>
<td>VAS, %</td>
<td>20 ± 21</td>
<td>0–77</td>
</tr>
<tr>
<td>BORG scale</td>
<td>1.41 ± 1.9</td>
<td>0–7</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD unless otherwise indicated.

**Discussion**

This study, carried out on a miscellaneous group of patients with prolonged/difficult weaning, showed that different levels of PSV are associated with significant changes in breathing pattern, oxygenation, and p0.1, as well as ineffective efforts and changes in patient comfort. Extreme high or low levels of PSV are not associated with the best comfort. Breathing pattern significantly changed when total assistance was given as PSV plus PEEP when compared to PSV alone (PSV plus ZEEP). The presence of an underlying disease (COPD or non-COPD) does not seem to influence the results.

The most appropriate PSV setting is generally considered crucial for the success of the weaning process. The lack of a well-defined relationship between patients’ perception of comfort and physiologic measures continues to frustrate clinicians worldwide. Technology tries to pay more attention to the patient’s requirements and comfort during application of external positive pressure. The results of previous studies indicate a direct correlation between the level of PSV and the increase in Vt or decrease in respiratory frequency. Our study confirms previous observations, and is the first to show that breathing pattern may be significantly changed when total assistance is given as PSV plus PEEP when compared to PSV alone (PSV plus ZEEP). Other authors found that p0.1 varied inversely with the level of PSV; opposing results demonstrated that the higher variability of p0.1 may be found both under high and low levels of assistance. Our study, confirming that neuromuscular drive is highly affected by the level of assistance, indicates that
partitioning of a given peak level of assistance with PSV alone or PSV plus an adjunctive fixed level of PEEP has no role in modifying this effect.

**Ineffective Efforts**

Leung et al.\(^\text{18}\) showed that increasing the level of ventilator assistance produces a progressive decrease in inspiratory muscle energy expenditure, but also an increase in the rate of ineffective triggering and wasted inspiratory efforts. To our knowledge, our study is the first showing variations in ineffective efforts under different levels of PSV, applied during a weaning attempt in postracheotomy status. Surprisingly, the diagnosis of COPD was not associated with a higher risk of ineffective efforts compared to other diagnosis (non-COPD). Moreover, not all patients, under high levels of assistance, experienced ineffective efforts; in fact, only a subgroup of our patients (26 of 36 patients) had ineffective efforts under all levels of PSV. Confirming previous reports,\(^\text{19}\) we showed that the likelihood of experiencing ineffective efforts statistically and linearly decreased with reducing the level of assistance (ANOVA, \(p = 0.023\)) [Fig 1]. However, we failed to demonstrate that the application of 5 cm H\(_2\)O of PEEP causes a change in the percentage of ineffective efforts, whatever the level of PSV applied (Fig 1).

**Patient Comfort**

Dyspnea, or “pathologic” breathlessness, has been defined as an uncomfortable awareness of breathing or an increased respiratory effort that is unpleasant and regarded as inappropriate by the patient. Despite the frequency with which the symptom is encountered in clinical practice, dyspnea has been difficult to evaluate because it is a subjective sensation, and its apparent severity may or may not correlate with physiologic measurements.\(^\text{28}\) Knebel et al.\(^\text{10}\) compared breathing comfort during weaning with PSV and synchronized intermittent mandatory ventilation by means of the VAS, and concluded that the sensation of dyspnea and anxiety intensity remained stable across different PSV levels in patients receiving MV. On the contrary, Manning et al.\(^\text{13}\) chose the term *breathing discomfort* to define breathlessness under MV. Both the VAS and BORG scale have been shown to be applicable\(^\text{29}\) and reproducible\(^\text{30}\) to test dyspnea or breathing discomfort. The subjective feeling of respiratory comfort under different modes of MV has been studied in healthy volunteers.\(^\text{31}\) Despite some indications that high levels of ventilator support may improve comfort\(^\text{8}\) or decrease dyspnea overall,\(^\text{19}\) the intensity of discomfort increases as the delivered pattern of ventilation deviates from that spontaneously chosen by the patient.\(^\text{17}\) In particular, Manning et al.\(^\text{13}\) provided evidence that both low and very high inspiratory flow rates are associated with breathing discomfort. Chiumello et al.\(^\text{32}\) showed that modulating the peak inspiratory flow throughout changes in the pressurization rate may affect the patient’s respiratory effort and subjective sensation of breathing comfort measured by a VAS. Our study showed that discomfort, as assessed through VAS and BORG scale, can be perceived both at high and low levels of PSV assistance, demonstrating that the relationship between different levels of assistance and comfort could be described as a U-shaped curve, with the lowest and the highest assistance corresponding to the highest magnitude of dyspnea. Our study is the first to demonstrate that the application of PSV, either with or without 5 cm H\(_2\)O of PEEP, did not modify this U-shaped trend of comfort. Besides, we showed a marked interindividual variability in the values of PSV at which patients felt most comfortable. The absence of a correlation between comfort and other physiologic variables (respiratory rate, \(p = 0.1\), and ineffective efforts) confirms that comfort is an independent variable. In other words, maximal comfort can be perceived at a rate of 15 breaths/min in one individual while another subject can perceive maximal comfort at a higher rate.

**Comfort Setting**

Table 3 shows that the comfort setting encompasses a huge range of PSV levels, a high range for breathing pattern, percentage of ineffective efforts, and perceived level of comfort. Finally, our study shows that the underlying diagnosis (COPD or non-COPD) does not appear to be a major factor influencing the physiologic parameters and patient comfort assessments discussed above.

**Limitations of the Study**

While our study clearly sheds new light on the field of ventilatory assistance and setting in stable patients undergoing weaning, its main objective was to investigate each patient’s comfort in response to different levels of applied PSV. Our results cannot be extended to all types of ICU patients due to the fact that our patients had a postracheotomy status and had received MV for a very long time. We did not perform serial measurements of ABGs. This was due to the limited time (5 min) set for each step stabilization. A longer time (at least 30 min) would be necessary to obtain stable and reproducible ABG values; this would mean a longer period of study for all the 12 settings that would be uncomfortable for patients with subsequent influence on comfort. Although this was not the aim of our study, we cannot exclude a possible influence of ABG changes (espe-
cially for \( \text{PaCO}_2 \) on patient comfort. We are aware that ABG measurement remains the “gold standard” to correct the level of assistance and hence the effectiveness of ventilation, but we are also aware that in everyday practice the physician would never perform repeated ABG samples any time settings of the ventilator are changed. However, breathing pattern, ineffective efforts, and comfort are noninvasive and immediate parameters to be practically used to continuously change settings of the ventilator. The overall duration of the study was approximately 2 h, which is quite a long time for a physiologic study. We cannot absolutely exclude a time effect, although the randomized allocation of the ventilatory mode should overcome such a problem. In our protocol, only the effects associated with a level of 5 cm H\(_2\)O of adjunctive PEEP were taken into account. The data produced do not allow us to conclude that the PSV level associated with the best comfort level is better than others in reducing the duration of mechanical ventilation and complications, or that the setting found more comfortable would be the same when applied for a longer period of time. The present study draws the practitioner’s attention to considering patient comfort assessment as an indicator for ventilatory strategy and careful selection of the PSV level. Indeed, the lack of any relationship between the patient’s perception of comfort and physiologic measures somehow further complicates patient-ventilator interactions. In practical terms, PSV assistance during weaning attempts could be adjusted firstly on the basis of the patient’s comfort, and secondarily readjusted on the basis of V\(_t\), respiratory rate, and ABG parameters.

In conclusion, this study, undertaken on a miscellaneous group of patients with prolonged/difficult weaning, showed the following: (1) physiologic variables followed a linear trend, while comfort followed a U-shaped trend under different levels of PSV (irrespective of COPD diagnosis); (2) high assistance caused an increase in ineffective efforts; (3) only breathing pattern significantly changed when total assistance was given as PSV plus PEEP when compared to PSV alone (PSV plus ZEEP); and (4) the extreme levels of PSV are not associated with the best comfort.

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ACKNOWLEDGMENT: The authors thank Mrs. Donna D’Agostino for English editing, and Giovanni Bader, MD, for statistical assistance.

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