Lung Function Accurately Predicts Hypercapnia in Patients With Duchenne Muscular Dystrophy

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Lung Function Accurately Predicts Hypercapnia in Patients With Duchenne Muscular Dystrophy*

Michel Toussaint, PT; Marc Steens, PT; and Philippe Soudon, MD

Background: In patients with Duchenne muscular dystrophy (DMD), implementation of mechanical ventilation depends on sleep investigation and measurement of CO₂ tension. The objective of this cross-sectional study was to determine which noninvasive lung function parameter best predicts nocturnal hypercapnia and diurnal hypercapnia in these patients.

Methods: According to transcutaneous CO₂ (TcCO₂) measurement, 114 DMD patients were classified into three groups: nocturnal hypercapnia (n = 38) [group N], diurnal hypercapnia (n = 39), despite nocturnal ventilation (group D), and 24-h normocapnia and spontaneous breathing (n = 37) [group S] as control. TcCO₂ tension and lung function variables included vital capacity (VC) and maximal inspiratory pressure (MIP), and breathing pattern variables included tidal volume (Vt) and respiratory rate (RR), measured at the time of group inclusion. The rapid and shallow breathing index (RSBI [RR/Vt]) and Vt/VC ratio were calculated. Areas under the curve from the receiver operating characteristic (ROC) were calculated for those parameters.

Results: Compared to group S, lung function was significantly worse in group N and group D. VC, RR, and RSBI distinguished group S from group N by ROC comparison. Cut-off values of VC ≤ 680 mL (ROC, 0.968), MIP ≤ 22 cm H₂O (ROC, 0.928), and Vt/VC > 0.33 (ROC, 0.923) accurately discriminated group D from group N, but RSBI, RR, and Vt did not. Conclusions: Lung function is useful to predict nocturnal hypercapnia in patients with DMD. Moreover, VC < 680 mL is very sensitive to predict daytime hypercapnia.

Key words: Duchenne; hypercapnia; neuromuscular; noninvasive ventilation; ventilation; vital capacity

Abbreviations: ANOVA = analysis of variance; BMI = body mass index; DMD = Duchenne muscular dystrophy; D-NIPPV = diurnal noninvasive intermittent positive pressure ventilation; PvcO₂ = venous P CO₂; MIP = maximal inspiratory pressure; NIPPV = noninvasive intermittent positive pressure ventilation; N-NIPPV = nocturnal noninvasive intermittent positive pressure ventilation; ROC = receiver operating characteristic; RR = respiratory rate; RSBI = rapid and shallow breathing index; SpO₂ = pulse oximetric saturation; TcCO₂ = transcutaneous CO₂; VC = vital capacity; V̇e = minute ventilation; Vt = tidal volume

The prognosis for patients with progressive neuromuscular disorders is dependent on the degree of respiratory involvement. Respiratory muscle involvement is characterized by a progressive fall in vital capacity (VC); decreased VC results from decreasing respiratory muscular strength1 and from increasing elastic load. Increasing elastic load is induced by reduced lung and thorax compliance2; the latter also enhances the work of breathing.3 To compensate for an increased work of breathing, a rapid and shallow breathing pattern will be adapted,4 and has typically been described in different neuromuscular disorders.5–7

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This work was performed at Inkendaal Rehabilitation Hospital, Neuromuscular Centre VUB-Inkendaal and Centre for Home Mechanical Ventilation.
The authors have no conflicts of interest to disclose.
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The rapid and shallow breathing index (RSBI) is calculated by the ratio of respiratory rate (RR) to tidal volume (Vt).\textsuperscript{8} Initially, any increase of RSBI observed in adolescents with Duchenne muscular dystrophy (DMD) is interpreted as a strategy to minimize respiratory effort\textsuperscript{9} and dyspnea perception.\textsuperscript{10} However, a high RSBI leads to progressive alveolar hypoventilation by increasing dead space ventilation.\textsuperscript{4} Despite the limited predictive power, the RSBI is an index commonly used to predict the possibility for sustaining spontaneous ventilation\textsuperscript{9} whatever the obstructive or restrictive origin of the respiratory failure.\textsuperscript{11} In DMD patients, however, the RSBI has not previously been validated to discriminate those hypercapnic patients needing ventilation from normocapnic patients able to breathe unassisted.

Implementations of nocturnal noninvasive intermittent positive pressure ventilation (N-NIPPV) and, later, of daytime extension of nocturnal ventilation (daytime noninvasive intermittent positive pressure ventilation [D-NIPPV]) are important milestones in the DMD disease progression. The timing of initiation of N-NIPPV should be considered carefully. Hypercapnia during sleep is the standard criterion to decide for N-NIPPV.\textsuperscript{12} Ward et al\textsuperscript{13} recently supported the appropriateness of this approach. The present study aims at determining which noninvasive lung function parameters best predict nocturnal hypercapnia in DMD patients with spontaneous ventilation. Similarly, we investigated parameters best associated with diurnal hypercapnia in older DMD patients effectively treated with N-NIPPV for years but in whom hypercapnia developed during daytime spontaneous ventilation. The latter would yield additional diurnal ventilation.

**Materials and Methods**

**Study Design**

Patients who met inclusion criteria for one of the groups on this study were followed up at our center. These patients were included in the present cross-sectional study. Patients were systematically assessed every 6 months during a 24-h scheduled hospital admission.

**Patients**

During the period from January 1, 1995, until December 31, 2004, 168 DMD patients were referred to Hospital Inkendaal, a specialist center for patients with neuromuscular disease. Study inclusion criteria comprised wheelchair-bound DMD patients > 12 years old. At hospital admission, respiratory assessment comprised nocturnal continuous blood gases monitored at night and daytime lung function tests. Three groups of patients with more and more advanced disease were defined based on transcutaneous Pco\textsubscript{2} tension (Tc\textsubscript{CO\textsubscript{2}}).

The first group, nocturnal hypercapnia (group N), included patients presenting with episodes of hypercapnia defined as Tc\textsubscript{CO\textsubscript{2}} tension > 45 mm Hg during sleep.\textsuperscript{14} This group started N-NIPPV.\textsuperscript{15} The second group, daytime hypercapnia (group D), included nocturnal normocapnic patients thanks to N-NIPPV but presenting with diurnal hypercapnia > 45 mm Hg during spontaneous respiration. In addition to N-NIPPV, this end-stage DMD group started D-NIPPV via mouthpiece. The third group included patients with 24-h normocapnia and spontaneous breathing (group S). Conventionally, it was not expected that this group would need mechanical ventilation in the next 12 months. Exclusion criteria included patients receiving continuous ventilation in the emergency department after acute respiratory insufficiency leading to permanent hypercapnia (Tc\textsubscript{CO\textsubscript{2}} > 60 mm Hg). Patients with a tracheostomy or with severe cognitive impairment were excluded. Finally, patients with low compliance to N-NIPPV and patients with temporarily inadequate N-NIPPV were excluded from group D.

Of the 168 patients, 114 participated in this study. Fifty-four patients were excluded due to tracheostomy (n = 14; n = 11 for acute respiratory failure, n = 3 for impaired swallowing function), 29 patients had severe cognitive impairment, and 11 patients received ventilation immediately for > 20 of 24 h because N-NIPPV was ineffective (n = 3) or insufficient (n = 8). The ethics committee of our institution approved the study, and informed consent was obtained from patients and/or families prior to the study.

**Measurements**

Pulse oximetric saturation (Sp\textsubscript{o\textsubscript{2}}) [Oxicap 4700; Ohmeda; Louisville, CO] and Tc\textsubscript{CO\textsubscript{2}} were recorded noninvasively (TCM3; Radiometer; Copenhagen, Denmark) over 9 h of sleep. Waking venous blood pH and venous Pco\textsubscript{2} (Pv\textsubscript{CO\textsubscript{2}}) were obtained from blood samples in the morning. In 1984, our group described Tc\textsubscript{CO\textsubscript{2}} as a useful proxy of Pco\textsubscript{2} tension shifts.\textsuperscript{15} This finding
determined our choice for noninvasive TcCO₂ to monitor PaCO₂ at night in all DMD patients. Janssens et al.15,17 confirmed that in noninvasive ventilation, TcCO₂ is in excellent agreement with PaCO₂. In patients receiving N-NIPPV, TcCO₂ was also measured during the last 2 h of the day while the patient was breathing spontaneously (Fig 1). In those N-NIPPV patients, end-diurnal hypercapnia > 45 mm Hg was, in our protocol, the criterion to extend noninvasive intermittent positive pressure ventilation (NIPPV) to D-NIPPV on the condition that N-NIPPV was adequate.

Patients underwent lung function testing using a noninvasive portable spirometer in sitting position with a face mask (model NIPPV) to D-NIPPV on the condition that N-NIPPV was adequate.

Statistics

Data from the three groups were analyzed by one-way analysis of variance (ANOVA). The Student-Newman-Keuls test was used for all post-ANOVA comparisons between group S, group N, and group D. Pearson correlations gave the relationship between respiratory parameters from the 114 patients. Sensitivity, specificity, and area under the curve from the receiver operating characteristic (ROC) were computed (MedCalc Software; Mariakerke, Belgium) for VC, V̇t, VE, V̇t/VE, RR, MIP, and RSI.

Table 1—Patient Characteristics and Lung Function at Three Progressive Respiratory Stages in Duchenne Dystrophy Evolution*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group S</th>
<th>Group N</th>
<th>Group D</th>
<th>ANOVA, p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>37</td>
<td>38</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Age, yr†</td>
<td>16.5 ± 3.1</td>
<td>17.9 ± 3.0</td>
<td>23.1 ± 4.6</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>Height, cm†</td>
<td>166 ± 7</td>
<td>165 ± 8</td>
<td>166 ± 9</td>
<td></td>
</tr>
<tr>
<td>Weight, kg†</td>
<td>53.2 ± 14.6</td>
<td>55.4 ± 18.8</td>
<td>42.2 ± 12.2</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>Weight, %†</td>
<td>97.3 ± 29.0</td>
<td>103.1 ± 36.1</td>
<td>69.8 ± 21.2</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>BMI†</td>
<td>19.4 ± 5.2</td>
<td>20.3 ± 6.7</td>
<td>16.1 ± 5.4</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>VC, mL†</td>
<td>1,822 ± 662</td>
<td>1,381 ± 545</td>
<td>557 ± 193</td>
<td>&lt; 0.05‡§</td>
</tr>
<tr>
<td>V̇t, mL/RR†</td>
<td>36.9 ± 13.1</td>
<td>28.4 ± 11.7</td>
<td>11.5 ± 4.1</td>
<td>&lt; 0.05§</td>
</tr>
<tr>
<td>RR, breaths/min†</td>
<td>18.8 ± 3.6</td>
<td>22.8 ± 5.0</td>
<td>24.0 ± 5.8</td>
<td>&lt; 0.05‡</td>
</tr>
<tr>
<td>MIP, cm H₂O₂†</td>
<td>42 ± 17</td>
<td>34 ± 14</td>
<td>16 ± 7</td>
<td>&lt; 0.05§</td>
</tr>
<tr>
<td>V̇e, mL</td>
<td>6,136 ± 1,869</td>
<td>5,814 ± 1,618</td>
<td>5,184 ± 1,437</td>
<td>&lt; 0.05§</td>
</tr>
<tr>
<td>RSI, breaths/min/mL†</td>
<td>0.07 ± 0.03</td>
<td>0.10 ± 0.05</td>
<td>0.12 ± 0.06</td>
<td>&lt; 0.05§</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
†ANOVA significance (p < 0.001).
‡Student-Newman-Keuls test significance, group S vs group N.
§Student-Newman-Keuls test significance, group N vs group D.
¶Student-Newman-Keuls test significance, group S vs group D.

Table 2—Sleep Measurements in the Three Groups of DMD Patients*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group S</th>
<th>Group N</th>
<th>Group D</th>
<th>ANOVA, p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>37</td>
<td>38</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TcCO₂, mm Hg†</td>
<td>41.9 ± 2.6</td>
<td>61.4 ± 8.8</td>
<td>47.9 ± 4.4</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>Mean SpO₂, %</td>
<td>95.8 ± 0.8</td>
<td>95.3 ± 1.4</td>
<td>95.5 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>Percentage of time with SpO₂ &lt; 90%, %</td>
<td>0</td>
<td>0.7 ± 1.4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Waking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaCO₂, mm Hg†</td>
<td>40.9 ± 2.8</td>
<td>48.2 ± 4.4</td>
<td>43.9 ± 3.2</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>TcCO₂, mm Hg†</td>
<td>39.6 ± 2.7</td>
<td>47.3 ± 4.8</td>
<td>42.9 ± 3.9</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>pH†</td>
<td>7.37 ± 0.02</td>
<td>7.30 ± 0.02</td>
<td>7.36 ± 0.02</td>
<td>&lt; 0.05‡</td>
</tr>
<tr>
<td>End diurnal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TcCO₂, mm Hg†</td>
<td>43.2 ± 3.63</td>
<td>59.3 ± 7.1</td>
<td>&lt; 0.05§</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD.
†ANOVA significance (p < 0.001).
‡Student-Newman-Keuls test significance, group S vs group N.
§Student-Newman-Keuls test significance, group N vs group D.
¶Student-Newman-Keuls test significance, group S vs group D.
measurements to determine the discriminative value of these indexes. The cut-off value was calculated by providing the best compromise between the optimal sensitivity and the optimal specificity. An area under the ROC curve of 1 suggests that the cut-off value is a perfect discriminator, and an area of 0.5 suggests that the cut-off value is no better than random in predicting outcome. Significance was accepted at p < 0.05.

**Results**

Table 1 reports patient characteristics from group S, group N, and group D. The mean height was similar in the three groups. Despite the older age, VC and Vt were progressively lower in the three groups (p < 0.001). The patients breathed shallower and more rapidly in group N compared to group S (p < 0.05), but this pattern was not different from group D. The VC, Vt, MIP, Vt/VC ratio, VE, and BMI but not RR and RSBI were significantly lower in group D compared to group N. Finally, the VE at rest was not different in group S compared to group N, but decreased significantly in group D. As expected, all patients from group S remained 24-h normocapnic within 2 years after inclusion (Table 2). Patients from group N presented with nocturnal hypercapnia with spontaneous ventilation. According to Ward et al., they subsequently started N-NIPPV. Finally, patients from group D presented end-diurnal hypercapnia despite normocapnia with N-NIPPV. They started D-NIPPV as N-NIPPV extension. The decreasing weight confirmed the significant difference in BMI in group D vs group N.

Table 3 shows the discriminative value of the most important respiratory parameters to differentiate between patients with nocturnal hypercapnia (group N) from those without nocturnal hypercapnia (group S). RSBI was intermediately sensitive and specific, but VC was a more sensitive but less specific discriminator of nocturnal hypercapnia. As shown in Table 4, discrimination of diurnal hypercapnia was accurately achieved by sensitive and specific cut-off values such as VC ≤ 680 mL, Vt/VC > 0.33, and MIP ≤ 22 cm H₂O. By contrast, other variables such as RR, VE, and RSBI poorly discriminated for daytime hypercapnia. Figure 2 compares ROC curves of VC and RSBI in predicting nocturnal hypercapnia (Fig 2, top, A) and diurnal hypercapnia (Fig 2, bottom, B). Figure 3 reports the strong relation between VC and MIP (r = 0.89, p < 0.001) in the 114 DMD patients. Figure 4 describes the breathing pattern in the three groups investigated. VE was maintained in group N vs group S.

### Table 3—Prediction of Nocturnal Hypercapnia by Noninvasive Lung Function Tests in DMD (Group N vs Group S)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cut-off*</th>
<th>ROC (95% Confidence Interval)†</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC, mL</td>
<td>≤ 1,820</td>
<td>0.710 (0.594–0.809)‡</td>
<td>87</td>
<td>51</td>
</tr>
<tr>
<td>Vt, mL</td>
<td>≤ 256</td>
<td>0.691 (0.573–0.792)‡</td>
<td>66</td>
<td>66</td>
</tr>
<tr>
<td>Vt/VC</td>
<td>&gt; 0.27</td>
<td>0.549 (0.429–0.664)‡</td>
<td>32</td>
<td>84</td>
</tr>
<tr>
<td>RR, breaths/min</td>
<td>&gt; 23</td>
<td>0.723 (0.608–0.820)‡</td>
<td>45</td>
<td>89</td>
</tr>
<tr>
<td>MIP, cm H₂O</td>
<td>≤ 39</td>
<td>0.636 (0.517–0.744)‡</td>
<td>71</td>
<td>54</td>
</tr>
<tr>
<td>VE, mL</td>
<td>≤ 4,321</td>
<td>0.533 (0.414–0.649)‡</td>
<td>26</td>
<td>87</td>
</tr>
<tr>
<td>RSBI, RR/Vt</td>
<td>&gt; 0.07</td>
<td>0.724 (0.608–0.821)‡</td>
<td>71</td>
<td>73</td>
</tr>
</tbody>
</table>

*Cut-off: value from the best compromise between sensitivity and specificity.†ROC values: 1 = perfect discrimination between group N vs group S; 0.5 = hazardous discrimination at 50% chance for error.‡Probability that ROC area = 0.5, p < 0.01.

### Table 4—Prediction of Diurnal Hypercapnia by Noninvasive Lung Function Tests in DMD (Group D vs Group N)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cut-off*</th>
<th>ROC (95% Confidence Interval)†</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC, mL</td>
<td>≤ 680</td>
<td>0.968 (0.900–0.994)‡</td>
<td>90</td>
<td>95</td>
</tr>
<tr>
<td>Vt, mL</td>
<td>≤ 225</td>
<td>0.631 (0.513–0.738)‡</td>
<td>56</td>
<td>66</td>
</tr>
<tr>
<td>Vt/VC</td>
<td>&gt; 0.33</td>
<td>0.923 (0.839–0.971)‡</td>
<td>77</td>
<td>95</td>
</tr>
<tr>
<td>RR, breaths/min</td>
<td>&gt; 21</td>
<td>0.535 (0.417–0.649)‡</td>
<td>72</td>
<td>45</td>
</tr>
<tr>
<td>MIP, cm H₂O</td>
<td>≤ 22</td>
<td>0.928 (0.845–0.974)‡</td>
<td>92</td>
<td>87</td>
</tr>
<tr>
<td>VE, mL</td>
<td>≤ 5,860</td>
<td>0.635 (0.517–0.741)‡</td>
<td>80</td>
<td>55</td>
</tr>
<tr>
<td>RSBI, RR/Vt</td>
<td>&gt; 0.06</td>
<td>0.604 (0.486–0.714)‡</td>
<td>92</td>
<td>26</td>
</tr>
</tbody>
</table>

*Cut-off: value from the best compromise between sensitivity and specificity.†ROC values: 1 = perfect discrimination between group D vs group N; 0.5 = hazardous discrimination at 50% chance for error.‡Probability that ROC area = 0.5, p < 0.001.
The lower $V_e$ obtained in group D was due to a reduction in $V_t (p < 0.05)$ without compensatory increase in RR.

**Discussion**

The present study suggests that patients with DMD remain normocapnic as long as $VC$ remains $>1,820$ mL. If $VC$ drops below this value, nocturnal hypercapnia is likely to be present. If $VC$ further decreases to $<680$ mL, patients may start to be hypercapnic by the end of the day despite treatment with effective N-NIPPV. Hypercapnia during the night (yielding N-NIPPV) and during the day (requiring D-NIPPV) is not entirely obtained from the same variables.

In DMD, distinction should be made between the need for nighttime mechanical ventilation only, with the need for mechanical ventilation during both night and day. Hypercapnia during the night may not result from respiratory muscle weakness only. Other factors may contribute to respiratory failure and the development of alveolar hypoventilation.

Central hypopneas during rapid eye movement sleep, upper airways obstruction, sleep fragmentation, positioning, eventually obesity, respiratory muscle asynchronism, impaired ventilatory drive, and reduction in chest wall compliance decrease may all deter alveolar ventilation.

When awake, the sleep-related hypopneas and upper airway obstruction disappear. Obesity plays a less important role when patients are sitting. Respiratory muscle coordination is better when awake, and inspiratory compensations are more pronounced. Finally, ventilatory control is reported to be reset with prolonged use of nocturnal NIPPV.

In DMD patients, daytime hypoventilation progression is likely to be highly associated with inspiratory muscle weakness on the condition that patients are properly ventilated at night.

The present data clearly support the use of continuous sleep monitoring of $TcCO_2$ and $SpO_2$ in assessing alveolar ventilation. However, lung function and noninvasive assessment of breathing pattern give useful prognostic information about the progression in the stage of permanent ventilation. Easily measurable clinical predictors are clinically very important. Polysomnography is not universally available, is time consuming, expensive, and not available during routine consultation. Hence, it is important to gain insight in these parameters at different stages of DMD severity. Specific and sensitive surrogate markers for patients at risk for hypercapnia during the night or during the day may prevent overconsumption of expensive and more invasive tests.

**Prediction of Nocturnal Hypercapnia (Group N vs Group S)**

In patients with DMD, Lyager et al showed that a $VC < 1,200$ mL characterized patients with hypercapnea 24 h/d. In the present study, we instituted
earlier N-NIPPV as soon as patients presented with nocturnal hypercapnia without diurnal hypercapnia. We found that VC < 1,820 mL was the best discriminator for sleep-related hypercapnia. The predictive power of VC, however, is limited since the specificity is low (Table 3). This is consistent with the results of Hukins and Hillman, who predicted sleep hypercapnia from FEV$_1$ < 40%. Despite the high sensitivity of FEV$_1$, comparable to that of VC in the present study, FEV$_1$ was not very specific. This demonstrates that prediction of sleep hypercapnia from lung function tests or from breathing pattern indexes is not very

![Figure 3. Relation between MIP and VC in 114 Duchenne patients.](image3)

![Figure 4. Spontaneous resting Ve at three stages of progressive chronic respiratory failure in DMD: comparison with iso-Ve curves at 2, 4, 6, and 8 L/min in group S, group N, and group D.](image4)
accurate. Hence, polysomnography should be recommended more regularly (eg, yearly) when VC falls to < 1,820 mL because a significant ROC prediction of 0.710 warrants attention.

**Prediction of Daytime Hypercapnia (Group D vs Group N)**

Daytime hypercapnia is likely to appear in end-stage DMD patients. In patients who have been effectively ventilated at night for years with NIPPV, daytime hypercapnia typically appears at the end of the day, as illustrated in Figure 1. In nonrestrictive pathologies, RSBI and RR but not VC and MIP were previously reported as good predictors for the ability to sustain a few hours of spontaneous ventilation during weaning trials. Manthous et al suggested that in patients with neuromuscular diseases, no data support a different approach to assess the ability to breathe unassisted. Our results, however, suggest this statement should be reconsidered. First, in group D, RSBI was neither sensitive nor specific in predicting daytime hypercapnia (Table 4). Second, in contrast to the RSBI, the VC, MIP, and Ve/VC were found more sensitive and specific in forecasting impending daytime hypercapnia and ventilation implementation as suggested elsewhere. VT/VC is a novel index that calculates the depth of the Ve as a proportion of the VC used during rest. This ratio summarizes in one value the sum of the inspiratory and expiratory reserve volumes. In our study, VC ≤ 680 mL, MIP < 22 cm H2O, and Ve/VC ratio > 0.33 were all sensitive parameters in predicting daytime hypercapnia. VC was the most appropriate predictor because it tolerated the lowest proportion of false-positive results (patients with hypercapnia at the end of the day despite VC > 680 mL). This finding is clinically useful because VC is very easy to measure by portable monitors, for example, during a home visit. In the DMD population, the VC maneuver is very reproducible. The prediction of daytime respiratory failure from Ve was associated elsewhere with Ve during rest < 5 L. We could not confirm this finding because Ve was neither sensitive nor specific. Especially in the end stage of DMD disease evolution, the reduction in alveolar ventilation may be larger than what is suggested from Ve values only (Fig 3).

The present data suggest certain cut-off values as sensitive and specific predictors of nocturnal and diurnal hypercapnia. We included all patients referred to our center over a period of 10 years. However, before they can be widely accepted, the present predictive variables should be validated prospectively on consecutive patients visiting similar specialist centers.

In conclusion, VC was useful in predicting nighttime hypercapnia but was extremely accurate in predicting daytime hypercapnia. Nocturnal hypercapnia is likely to develop in DMD patients when VC falls to < 1,820 mL, but they are at high risk for diurnal hypercapnia when VC falls to < 680 mL.

**REFERENCES**

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