Pulmonary function in patients with hereditary motor and sensory neuropathy: A comparison of patients with and without spinal deformity

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Received 8 March 2012; received in revised form 16 May 2012; accepted 18 May 2012

Abstract

We assessed pulmonary function in hereditary motor and sensory neuropathy. Fourteen neuropathy patients without spinal deformity (group 1), 14 with spinal deformity (group 2), and 16 individuals with idiopathic spinal deformity (group 3) matched to group 2 for age, height and Cobb angle, were included. Hereditary motor and sensory neuropathy severity was measured with Charcot–Marie–Tooth Neuropathy Score. All participants exhibited mild decrease in maximal inspiratory pressure at the mouth. One-way analysis of variance yielded significant main effects for lung volumes – slow vital capacity, forced expiratory volume in 1 s, and total lung capacity ($p$’s < .01), attributable to greater volumes in group 1 compared to groups with spinal deformity – and transfer factor for carbon monoxide ($p=.013$), reflecting differences between groups 1 vs. 2. Slow vital capacity and total lung capacity correlated with maximal inspiratory pressure in group 2, whereas slow vital capacity correlated with muscle work in group 3 ($p$’s < .05). Decreased lung volume may be due to impaired respiratory muscle strength in hereditary motor and sensory neuropathy with spinal deformity and due to spinal deformity in idiopathic patients.

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Keywords: Hereditary motor and sensory neuropathy; Charcot–Marie–Tooth disease; Spinal deformity; Respiratory muscle function; Static lung volume

1. Introduction

Hereditary motor and sensory neuropathy (HMSN), also known as Charcot–Marie–Tooth disease (CMT), is the most common type of inherited neuropathy [1]. The most common clinical symptom is bilateral distal muscle weakness of the legs, with some patients also exhibiting weakness of the arms as well. Gait abnormalities, foot deformity and distal sensory deficits of the legs are also typical [2,3]. Finally, spinal deformities are present in some patients [4–7].

Some individuals with HMSN report a variety of respiratory problems, although this is usually not a dominant symptom [8]. Previous studies have described excessive weakness of the diaphragm and other respiratory muscles in HMSN patients, including severe cases of respiratory failure as a result of diaphragmatic paresis [9–11]. However, the current scientific literature usually considers abnormalities in ventilation to be marginal in HMSN patients. There are only a few studies available describing...
in detail the pulmonary function changes associated with HMSN [8,12,13]. Several theories exist that explain the respiratory problems found in HMSN. Besides true neurogenic paresis of the respiratory muscles [9–11], other factors like vocal cord dysfunction [8,14,15], autonomic nervous system dysfunction [16], musculoskeletal dysfunction reflected in insufficient integrated postural-respiratory function of the diaphragm [17], along with other abnormalities of the respiratory muscles and structural spinal deformities [18,19] may significantly impact pulmonary function.

The main purpose of this study was to examine whether pulmonary function in HMSN patients might be affected by structural spinal deformity. Based on previous research, we expected respiratory muscle strength and ventilatory volumes to be decreased in HMSN patients with spinal deformity. We also expected that the degree of spinal deformity would correlate with the extent of pulmonary dysfunction. 

The sample consisted of all 28 patients with an electromyographically confirmed diagnosis of HMSN who came to the Clinic of Rehabilitation and Sports Medicine, University Hospital Motol, Prague, Czech Republic and consented to this research. In 25 patients, the neuropathy was classified as demyelinating and in 3 patients it was classified as of the axonal type. The Charcot–Marie–Tooth Neuropathy Score (CMTNS) [20] was utilized to measure HMSN impairment in each patient. The CMTNS for the entire sample of HMSN patients ranged from 9 to 30 points (see Table 1). The patients were subcategorized into two groups. Group 1 consisted in 14 HMSN patients with normal spinal curves. Group 2 included 14 HMSN patients with spinal deformity of various severity and shape. Standing radiographs of anterior–posterior and lateral views of the cervical, thoracic, and lumbosacral spinal regions were taken in all patients to identify the presence, character (i.e., hyperkyphosis vs. lateral curvature), and degree of spinal curvature. Cobb angles were determined for any frontal and sagittal plane deviations [21]. In accordance with the Scoliosis Research Society, we have defined scoliosis as a lateral spinal curvature with a Cobb angle exceeding 10° [22]. All kyphotic curvatures over 40° were considered pathologic [23]. For the purpose of this paper, the primary or greatest curve was reported (Table 1), even in cases where multiple scoliotic curves were present. For better assessment of the influence of respiratory muscle function and spinal deformity on lung volumes we also included patients with idiopathic spinal deformity (scoliosis or kyphoscoliosis; group 3, n = 16), who were matched for age, height and Cobb angle to the patients in group 2.

All patients underwent a comprehensive examination of pulmonary function. Spirometric assessments were performed using a calibrated spirometer (ZAN 100 flowhandy II, ZAN, Oberthulba, Germany). Static lung volumes were measured by methane dilution with synchronous measurement of transfer factor for carbon monoxide (TLCO) using the single-breath method (ZAN 300, ZAN, Oberthulba, Germany). The predicted values for the lung function parameters were derived from those published by the European Community for Coal and Steel [24]. Measurements of maximal inspiratory and expiratory pressures at the mouth (PImax, PEmax), pressure at the mouth 100 ms after the beginning of a quiet inspiration (P0,1) and duty cycle were performed using a commercially available system (ZAN 100 flowhandy II with automatic shutter, ZAN, Oberthulba, Germany) according to the American Thoracic Society/European Respiratory Society standard [25] and normal values were adopted from those published by Black et al. [26]. The non-invasive tension-time index for inspiratory muscles was calculated according to the following equation:

$$TT_mus = PI / PI_{max} * TI / T_{tot}$$

where $PI = 5P_{0.1} * TI$ and $TI / T_{tot}$ is the ratio of mean inspiratory time to total time of respiratory cycle. Neuro-muscular coupling was assessed by the ratio of $P_{0.1} / Vt$ (tidal volume). All measurements were performed in triplicate and expressed as percent predicted or absolute values, where the best of at least three reproducible values were used for data processing. Restrictive lung function was defined as $TLC < 80\%$ predicted [24].

### 2.1. Statistical analysis

Results are expressed as mean ± SD. The Kolmogorov–Smirnov test was used to confirm normality of scores.
distribution. Associations between variables were examined by Pearson correlation coefficients and comparisons among the groups were conducted using one-way analysis of variance (ANOVA) with posthoc Bonferroni’s multiple comparisons. Statistical significance was assessed using the conventional two-tailed .05 level. All analyses were performed using the statistical software GraphPad Prism, version 4.0.

3. Results

Values for pulmonary function measures across the three groups are presented in Table 2 and correlations across these measures are shown in Tables 3 and 4. Patients with HMSN without spinal deformity (group 1) had normal lung volumes and transfer factor for carbon monoxide, but only three of them (21%) had strength of inspiratory muscles within normal limits. For the group as a whole, some decrease in maximal inspiratory pressure at the mouth (PImax) was identified (5.4 ± 3.5 kPa, 58.4 ± 30.5% predicted) [26]. On the contrary, none of the participants in group 1 had expiratory muscle strength within normal limits, with moderate to severe decrease of the mean PEmax value to 6.9 ± 2.7 kPa, 43.0 ± 14.0% predicted [26]. The decrease of respiratory muscle strength apparently had no influence on slow vital capacity (SVC) and total lung capacity (TLC), which were found to be normal in all subjects. However, it was correlated with the ratio of residual volume to total lung capacity (RV/TLC), which were found to be normal in all subjects. The patients with HMSN and spinal deformity (group 2) had borderline impaired lung volumes (relative to the normal) with HMSN without spinal deformity (group 1) had normal TLC, while the rest had restrictive or mixed ventilatory defect. Similar as group 1, patients in group 2 also presented with a mild PImax decrease (5.7 ± 1.9 kPa, 58.4 ± 20.1%predicted). Lung volumes and the inspiratory muscle function have shown a close relationship; PImax (%predicted) correlated significantly with SVC (%predicted, r = .55, p = .044), TLC (%predicted, r = .54, p = .047) and transfer coefficient for carbon monoxide (KCO, %predicted, r = -.78, p = .001), while TTmus correlated with SVC (%predicted, r = -.58, p = .031), functional residual capacity (FRC, %predicted, r = -.56, p = .038), KCO (%predicted, r = .59, p = .028) and the neuromuscular coupling expressed as the ratio of P0,1/Vt (kPa/l, r = .78, p = .001). The scoliotic curve angle had the closest relationship to age (years, r = 67, p = .008). It also correlated negatively with the ratio of forced expiratory volume in 1 s to slow vital capacity (FEV1/SVC %, r = -.64, p = .015) and positively with the ratio of RV/TLC (%, r = .59, p = .028). CMTNS correlated negatively with TLC (%predicted, r = -.56, p = .036), while the relationship with SVC (%predicted) approached statistical significance (r = -.50, p = .068). Expiratory muscle strength did not correlate significantly with lung volumes, Cobb angle, or CMTNS.

The patients with idiopathic spinal deformity (group 3) had similar lung volumes as patients in group 2 with TLC 87.9 ± 18.8 (%predicted), only 4 patients (29%) had restrictive and 1 patient (7%) obstructive ventilatory defect. PImax (%predicted) was only slightly reduced in this group of patients, 6 patients (43%) had inspiratory muscle strength within normal limits. Among tests of respiratory muscle function, only TTmus showed correlation with lung volumes (SVC, TLC and FRC), with the strongest

Table 2  
Pulmonary function in subgroups of patients, mean ± SD.

<table>
<thead>
<tr>
<th>Group</th>
<th>Simple HMSN</th>
<th>Scoliotic HMSN</th>
<th>Idiopathic scoliosis</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVC (%pred)</td>
<td>102.6 ± 9.8</td>
<td>76.9 ± 12.7</td>
<td>84.7 ± 22.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FEV1 (%pred)</td>
<td>100.1 ± 10.2</td>
<td>77.3 ± 15.1</td>
<td>81.5 ± 21.0</td>
<td>.001</td>
</tr>
<tr>
<td>FEV1/SVC (%)</td>
<td>82.8 ± 6.4</td>
<td>82.9 ± 8.4</td>
<td>83.1 ± 6.1</td>
<td>.970</td>
</tr>
<tr>
<td>TLC (%pred)</td>
<td>102.6 ± 7.2</td>
<td>80.3 ± 14.5</td>
<td>87.9 ± 18.8</td>
<td>.002</td>
</tr>
<tr>
<td>FRC (%pred)</td>
<td>110.0 ± 16.7</td>
<td>94.3 ± 20.3</td>
<td>97.4 ± 25.0</td>
<td>.219</td>
</tr>
<tr>
<td>RV (%pred)</td>
<td>130.4 ± 29.0</td>
<td>109.7 ± 27.6</td>
<td>114.7 ± 28.6</td>
<td>.222</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>37.6 ± 6.4</td>
<td>40.1 ± 6.1</td>
<td>38.4 ± 9.2</td>
<td>.411</td>
</tr>
<tr>
<td>P0.1/Vt (kPa)</td>
<td>98.1 ± 8.1</td>
<td>81.4 ± 16.2</td>
<td>86.7 ± 17.1</td>
<td>.013</td>
</tr>
<tr>
<td>KCO (%pred)</td>
<td>101.4 ± 9.2</td>
<td>110.2 ± 22.8</td>
<td>108.5 ± 18.2</td>
<td>.404</td>
</tr>
<tr>
<td>PImax (%predicted)</td>
<td>58.4 ± 30.5</td>
<td>58.4 ± 20.1</td>
<td>71.7 ± 16.0</td>
<td>.104</td>
</tr>
<tr>
<td>PImax (kPa)</td>
<td>5.4 ± 3.4</td>
<td>5.7 ± 1.9</td>
<td>6.1 ± 1.9</td>
<td>.729</td>
</tr>
<tr>
<td>PEmax (%predicted)</td>
<td>43.0 ± 14.0</td>
<td>37.9 ± 16.0</td>
<td>49.2 ± 14.5</td>
<td>.139</td>
</tr>
<tr>
<td>PEmax (kPa)</td>
<td>6.9 ± 2.7</td>
<td>6.6 ± 2.3</td>
<td>7.1 ± 2.4</td>
<td>.837</td>
</tr>
<tr>
<td>P0.1 (kPa)</td>
<td>0.18 ± 0.08</td>
<td>0.2 ± 0.06</td>
<td>0.2 ± 0.11</td>
<td>.553</td>
</tr>
<tr>
<td>TTmus</td>
<td>0.17 ± 0.12</td>
<td>0.14 ± 0.07</td>
<td>0.14 ± 0.09</td>
<td>.625</td>
</tr>
<tr>
<td>P0.1/Vt (kPa/l)</td>
<td>0.32 ± 0.15</td>
<td>0.41 ± 0.21</td>
<td>0.37 ± 0.35</td>
<td>.613</td>
</tr>
</tbody>
</table>

Notes: HMSN – hereditary motor and sensory neuropathy; SVC – slow vital capacity; pred. – predicted; FEV1 – forced expiratory volume in 1 s; FEV1/SVC – forced expiratory volume in 1 s to slow vital capacity; TLC – total lung capacity; FRC – functional residual capacity; RV – residual volume; RV/TLC residual volume to total lung capacity; TLCO – transfer factor for carbon monoxide; KCO – transfer coefficient for carbon monoxide; PEmax – maximal inspiratory pressure at the mouth; PEmax – maximal expiratory pressure at the mouth; P0.1 – pressure at the mouth 100 ms after the beginning of a quiet inspiration; TTmus – tension–time index for inspiratory muscles; P0.1/Vt – pressure at the mouth 100 ms after the beginning of a quiet inspiration to tidal volume; Data presented as mean ± SD, p-values relate to separate one-way analyses of variance.

Please cite this article in press as: Horacek O et al., Pulmonary function in patients with hereditary motor and sensory neuropathy: A comparison of patients with and without spinal deformity, Neuromuscular Disord (2012), http://dx.doi.org/10.1016/j.nmd.2012.05.008
correlation being with SVC (%predicted, r = -.72, p = .003). Expiratory muscle strength showed correlation with neither lung volumes nor Cobb angle. Besides to TLCO and KCO, SVC (%predicted) showed inverse relationship to P0,1 (r = .66, p = .008) and to the ratio of P0,1/Vt (r = -.56, p = .029). The Cobb angle showed inverse relationship with lung volumes (SVC, TLC and FRC), namely FRC (%predicted, r = -.72, p = .005) and positive correlation with P0,1 (kPa, r = .57, p = .033). Its relationship with TTmax approached statistical significance (r = .48, p = .083). (Table 4).

Comparison among all three groups (Table 2) showed virtually no difference in respiratory muscle function, while there were statistically significant main effects for lung volume measures, namely the SVC (F[2,40] = 9.95, p < .001), FEV1 (F[2,40] = 7.85, p = .001) and TLC (F[2,40] = 7.35, p = .002), with all three main effects attributable to greater average lung volume scores in group 1 compared to group 2 (p’s < .01), and group 1 compared to group 3 (p’s < .05). There was also a significant main effect for TLCO (F[2,40] = 4.85, p = .013), which reflected better scores in group 1 compared to group 2 (p < .05).

4. Discussion

The results of the study indicate that respiratory muscle function is often at least slightly impaired in patients with HMSN, independent of the presence of spinal deformity. HMSN involves predominantly peripheral nerves of lower and upper extremities. The most common clinical symptoms are bilateral muscle weakness of the legs and often of the arms as well, distal sensory deficit of the legs, foot deformities and gait abnormalities [2,3].

There are several studies focusing on respiratory muscle function in HMSN [8–13], however, to the best of our knowledge, this study is the first to assess respiratory muscle function in HMSN patients with spinal deformities. To further delineate the effects of HMSN and spinal deformity on pulmonary function, we also used patients with idiopathic spinal deformity as positive controls, paying special attention to including only those patients with idiopathic spinal deformity who matched the HMSN patients with spinal deformity for age, height and Cobb angle.

The number of patients who have PImax within normal limits was rather low in all groups (three, four and two patients in group 1, 2 and 3, respectively), suggesting that
respiratory muscle dysfunction may not be an accidental finding among patients with HMSN or spinal deformity. In accordance with previous reports [12,13], we noticed a larger observed decrease in PE\textsubscript{max} than PI\textsubscript{max} in all three groups, which may be attributed to greater involvement of abdominal muscles in pulmonary function of the participants in this study. However, this possibility requires further investigation [13]. We used percent predicted values to classify a decrease of respiratory muscle strength, but there is disagreement in the literature with regard to what represents normal values, particularly in healthy adults [27]. Generally, the reported threshold indicative of muscle weakness tends to be lower than 80% predicted [27], which was used here. Therefore, the level of impairment of respiratory muscle function reflected in our results could be less severe than that indicated by the percent predicted.

The mean values of an array of parameters of respiratory muscle function were not statistically different among groups. However, the group difference in PI\textsubscript{max} was not so far from statistical significance ($p = .104$), with highest values in patients with idiopathic spinal deformity (group 3). Group 3 also had the lowest mean values of P\textsubscript{0.1} and TT\textsubscript{mus}, albeit these were not statistically different among groups ($p > .05$). Future research should examine the possibility that HMSN may have greater impact on respiratory muscle function than spinal deformity per se.

The abnormality of lung function found in all groups of patients was restrictive in type, characterized by decrease of SVC and TLC with normal expiratory airflow. Despite the fact that respiratory muscle function was impaired similarly in all groups of patients, there were statistically significant group differences in measures of lung volume, with patients with HMSN with spinal deformity (group 2) having the lowest mean values for lung volume measures. A relatively consistent pattern of results emerged for the lung volume measures. The Bonferroni’s multiple comparison posthoc test consistently pointed to statistical differences between groups 1 and 2, and 1 and 3, respectively. The same was true for transfer factor for carbon monoxide (TL\textsubscript{CO}). While mean values of K\textsubscript{CO} were increased in all groups, TL\textsubscript{CO} reflected the magnitude of impairment of lung volumes and hence the magnitude of alveolar volume (VA). This finding has already been established in patients with extrapulmonary lung volume restriction, either in respiratory muscle dysfunction or in decreased compliance of the chest wall [28,29]. In our study, both groups with spinal deformity had lower lung volumes than patients with simple HMSN. Therefore, lung volume seemed to be primarily influenced by the presence of spinal deformity. This is in accordance with Aboussouan et al. [8] who reported that reduction of lung volume in HMSN patients with spinal deformities may be independent of phrenic nerve dysfunction.

Despite careful matching of patients with spinal deformities, the association between lung volumes and the degree of Cobb angle was somewhat different between the groups 2 and 3. We found statistically significant correlation between lung volumes and the Cobb angle in patients with idiopathic spinal deformity (group 3), while in group 2 the Cobb angle was mildly associated only with the airway patency. Previously, Newton et al. [30] were able to show such associations even in patients with mild to moderate spinal deformity. Other research has also suggested an increasing probability of lung volume restriction with a greater Cobb angle [30,31]. The severity of pulmonary impairment, however, cannot be derived from the angle of scoliosis alone [30,32,33]. In this study, 3 out of 5 patients in group 2 and 2 out of 4 patients in group 3 with a Cobb angle greater than 50 degrees had normal lung function. These findings go along with previous reports which found many other characteristics of spinal deformity besides the angle of the scoliotic curve which we did not measure, such as degree of kyphosis [33], number of involved vertebrae [30,32], uppermost vertebra involved in scoliosis [32] the degree of spine rotation [33–35], or curve rigidity [35,36], significantly influencing the pulmonary function. Therefore, the Cobb angle seems to be only partially responsible for the reduced lung volumes.

The association of lung volume and respiratory muscle function was also different between the groups 2 and 3. In group 2, both SVC and TLC were closely related to PI\textsubscript{max} and TT\textsubscript{mus}, while in patients with idiopathic spinal deformity (group 3), SVC showed close correlation with P\textsubscript{0.1}, TT\textsubscript{mus} and the ratio of P\textsubscript{0.1}/Vt. These findings suggested that, in group 3, the decreased lung volumes

<table>
<thead>
<tr>
<th>Angle and other study measures</th>
<th>Scoliotic HMSN</th>
<th>Idiopathic scoliosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVC (%pred)</td>
<td>–.03</td>
<td>–.58*</td>
</tr>
<tr>
<td>FEV\textsubscript{1} (%pred)</td>
<td>–.42</td>
<td>–.63*</td>
</tr>
<tr>
<td>FEV\textsubscript{1}/SVC (%)</td>
<td>–.64*</td>
<td>–.26</td>
</tr>
<tr>
<td>TLC (%pred)</td>
<td>–.22</td>
<td>–.59*</td>
</tr>
<tr>
<td>FRC (%pred)</td>
<td>–.29</td>
<td>–.72**</td>
</tr>
<tr>
<td>RV (%pred)</td>
<td>–.29</td>
<td>–.20</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>–.59*</td>
<td>–.46</td>
</tr>
<tr>
<td>TL\textsubscript{CO} (%pred)</td>
<td>–.11</td>
<td>–.31</td>
</tr>
<tr>
<td>K\textsubscript{CO} (%pred)</td>
<td>.27</td>
<td>.51</td>
</tr>
<tr>
<td>PI\textsubscript{max} (%pred)</td>
<td>.25</td>
<td>.38</td>
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<tr>
<td>PI\textsubscript{max} (kPa)</td>
<td>–.17</td>
<td>–.37</td>
</tr>
<tr>
<td>PE\textsubscript{max} (%pred)</td>
<td>.21</td>
<td>.10</td>
</tr>
<tr>
<td>PE\textsubscript{max} (kPa)</td>
<td>–.14</td>
<td>.06</td>
</tr>
<tr>
<td>P\textsubscript{0.1} (kPa)</td>
<td>.33</td>
<td>.57*</td>
</tr>
<tr>
<td>TT\textsubscript{mus}</td>
<td>.29</td>
<td>.48</td>
</tr>
<tr>
<td>P\textsubscript{0.1}/Vt (kPa/l)</td>
<td>.41</td>
<td>.37</td>
</tr>
</tbody>
</table>

Notes: Pearson correlations are shown; "p < .05, "p < .01. HMSN – hereditary motor and sensory neuropathy; SVC – slow vital capacity; pred. – predicted; FEV\textsubscript{1} – forced expiratory volume in 1 s; FEV\textsubscript{1}/SVC – forced expiratory volume in 1 s to slow vital capacity; TLC – total lung capacity; FRC – functional residual capacity; RV – residual volume; RV/ TLC residual volume to total lung capacity; TL\textsubscript{CO} – transfer factor for carbon monoxide; K\textsubscript{CO} – transfer coefficient for carbon monoxide; PI\textsubscript{max} – maximal inspiratory pressure at the mouth; PE\textsubscript{max} – maximal expiratory pressure at the mouth; P\textsubscript{0.1} – pressure at the mouth 100 ms after the beginning of a quiet inspiration; TT\textsubscript{mus} – tension-time index for inspiratory muscles; P\textsubscript{0.1}/Vt – pressure at the mouth 100 ms after the beginning of a quiet inspiration to tidal volume.

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potentially attributable to spinal deformity had an important impact on respiratory muscle function. Elevated respiratory drive expressed as \( P_{0.1} \) and the non-invasive index of inspiratory muscles expressing energy demand on ventilation seemed to reflect mainly ventilatory compensation of decreased lung volumes. On the other hand, in group 2, the extent of lung volume restriction seemed to be at least in part attributable to the respiratory muscle function.

Further research is required to determine if compromised respiratory muscle function is a result of polyneuropathy itself or, rather, decondition, since the patients with HMSN may be less active and participate less in sports and exercise than their age- and sex-matched peers. Studies addressing diaphragm and phrenic nerve function in HMSN exist, confirming frequent prolongation of phrenic nerve conduction (up to 96–100%). However, only a few patients report having respiratory problems [8]. Also more research is required to establish respiratory impairment in relation to genetic characterization of HMSN.

Exercise intolerance and fatigue are common complaints in patients with HMSN and decondition in HMSN population has been reported [37]. Nathanson [38] found that HMSN individuals with abnormal lung function tended to be older than those with normal lung function and it can be assumed that older patients would be more prone to sedentary lifestyle with subsequent physical deconditioning. A combined protocol of electromyographic studies of respiratory musculature and cardiopulmonary exercise testing may help to clarify this issue in HMSN patients. Future research should also explore whether scoliosis, kyphoscoliosis and hyperkyphosis impact respiratory function differentially.

Finally, several limitations should be acknowledged. A small sample size was used. However, the prevalence of cases with both CMT and spinal deformity is very low in the Czech Republic. In our previous study [4], these patients comprised only 26% of the overall study sample that underwent examination. Movement limitations, commuting, and the non-intervention nature of this study are additional barriers with respect to patient recruitment. It is likely that more results would reach the threshold for statistical significance with a larger sample. Although the groups were similar with respect to age, there were significant group differences with respect to sex. However, these differences were at least partially accounted for by the use of age- and sex-adjusted anthropometric parameters expressed as norm-based percentage, not the raw values.

It may be argued that the observed deficits in respiratory muscle function in group 2 could be attributable to the differences in the CMTNS score between groups 1 and 2. However, the CMTNS score can increase not only as muscles weaken because of the increasing severity of the disease, but also due to other factors. Spinal deformity in CMT is considered neuromuscular in nature. Therefore, greater impairment is associated with greater occurrence of scoliosis. Supporting the line of reasoning that CMTNS does not reflect respiratory muscle function accurately is the lack of differences between \( P_{\text{max}} \) and \( PE_{\text{max}} \) between groups 1 and 2 (see Table 2), which suggests that these two groups are comparable with respect to the strength of the diaphragm, or that the diaphragm exerts greater strength in group 2 (due to the CMTNS-related deficits in trunk muscles). More thorough assessment of muscle function that includes the evaluation of pressure in the esophagus and the transdiaphragmatic pressures may be necessary in order to confirm the specific function of individual respiratory muscle groups in these patients and hence determine the exact contribution of muscle impairment to deficits in lung function.

Finally, a control group was not available. Again, it can be argued that the use of normative data ameliorates this limitation to some point. In addition, great variability exists in values that are considered “normal”, partly stemming from general lifestyle factors and individual fitness, which could introduce a bias into comparisons with a healthy control group. Recent research suggests that muscle weakness is indicated at \( P_{\text{max}} \) values lower than 40 cm H\(_2\)O for men and 35 cm H\(_2\)O for women [27], which is substantially below the 80% norm we used. Finally, the stated purpose of this study was comparisons of the three groups of patients distinct with regard to neuropathy and spinal deformity.

5. Conclusions

Our findings indicate that dysfunction of respiratory muscles is quite common in patients with HMSN and cannot be easily predicted from the magnitude of lung volumes. Furthermore, expiratory muscles appear more affected than inspiratory ones. Patients with HMSN who develop spinal deformity usually have decreased lung volume, which seems to be primarily caused by impaired respiratory muscle strength. On the other hand, in patients with idiopathic spinal deformity, the magnitude of lung volumes seems to be mainly influenced by the spinal deformity itself.

Acknowledgements and support

This study was supported by the foundation Movement without Help, Prague, Czech Republic, and by Grant OPPK CZ.2.16/3.1.00/24022.

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