Introduction

- Multiple sclerosis (MS) is a chronic, progressive disease, often accompanied by functional impairment due to spasticity.
- Spasticity is a major contributor to disability in MS. It can cause pain, inability to walk and, later, problems with personal hygiene. Indeed, it is spasticity rather than weakness in the limbs that accounts for much of the disability affecting lower limbs.1
- It is hypothesized that as the severity of spasticity increases there is a corresponding impact on health-related quality of life (HRQoL).

Objectives

- To quantify the relationship between physician-reported severity of spasticity and HRQoL, as measured by EuroQol-5D (EQ-5D) and Hamburg Quality of Life Assessment in Multiple Sclerosis (HAQUAMS).3

Methods

- Data were drawn from the Adelphi MS Disease Specific Program, a cross-sectional study of 125 neurologists in the USA.
- Participating neurologists completed a patient record form for the next 12-15 consulting MS patients and the same patients were invited to fill out a patient self-completion form (PSC).
- The full methodology, including limitations, has been published previously.1
- Of the 904 patients who completed a PSC, 439 provided information on all the elements required for this analysis. Preliminary analysis using ANOVA with Bonferroni-corrected t-tests established that the most appropriate split was between the physician-assessed mild and moderate spasticity levels. It was thus deemed appropriate that the two comparator groups for analysis should be patients with no or mild spasticity and those with moderate or severe spasticity.

Due to the progressive nature of MS and its multiple symptomatic manifestations, univariate analysis is influenced by many confounders. The relative impact of spasticity is assessed by adjusting for confounders using propensity scoring and regression as part of a double robust analysis.
- Propensity scoring was used to match patients in each comparator group allowing for the following confounding variables: Expanded Disability Status Scale (EDSS), gender, age, body mass index (BMI), presence and number of concomitant conditions, compliance, MS type.
- Patients who could not be matched because they did not resemble any patient in the opposing group with respect to the confounders were removed from the analysis - Figure 1.

Results

- Double robust estimates (combining the propensity scoring with a weighted regression) were subsequently calculated to show the differences in HRQoL between patients with no/mild spasticity and those with moderate/severe spasticity.
- It should be noted that double robust estimation cannot be used to show a causal effect between the outcome and the study group but does show an association between them independent of the confounding factors.

<table>
<thead>
<tr>
<th>Table 1: Demographics Spasticity</th>
<th>No/mild</th>
<th>Moderate/severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>41.0</td>
<td>48.3</td>
</tr>
<tr>
<td>Gender</td>
<td>Female 76%</td>
<td>Female 63%</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>25.4</td>
<td>25.3</td>
</tr>
<tr>
<td>Employed (full/part time)</td>
<td>59%</td>
<td>20%</td>
</tr>
<tr>
<td>Unemployed</td>
<td>22%</td>
<td>50%</td>
</tr>
<tr>
<td>Unable to work due to MS</td>
<td>57%</td>
<td>83%</td>
</tr>
<tr>
<td>Lives with partner</td>
<td>45%</td>
<td>36%</td>
</tr>
<tr>
<td>Lives with family/friends</td>
<td>36%</td>
<td>41%</td>
</tr>
<tr>
<td>Current EDSS Score (mean)</td>
<td>2.5</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Results from the double robust analysis showed that, compared with patients with no/mild spasticity, the presence of moderate/severe spasticity was, on average, associated with a decrease of 0.12 in EQ-5D score (p=0.006, 95% confidence interval -0.21 to -0.04) – Figure 2.

The authors note that for EQ-5D a lower score represents a poorer quality of life, and a difference in score of 0.05 is considered to be clinically significant.2

Figure 2: Impact of spasticity on EQ-5D

- The HAQUAMS instrument includes an overall score and can be broken down into 5 subscales: fatigue/thinking, upper limb mobility, lower limb mobility, mood, social function. The higher the score on the HAQUAMS the poorer the quality of life.

- Compared with MS patients with no/mild spasticity, the double robust estimation analysis showed that the presence of moderate/severe spasticity was associated with an increased overall score of 0.36 (p=0.005, 95% confidence interval 0.11 to 0.66).

- Significant differences were observed in three of the five subscales - Figure 3.

For the fatigue/thinking domain, the double robust estimation analysis showed that, compared with the patients with no/mild spasticity, the presence of moderate/severe spasticity was associated with an increased score of 0.36 (p=0.018, 95% confidence interval 0.11 to 0.60).

Conclusions

- Moderate/severe spasticity is associated with a significantly worse HRQoL, as measured by EQ-5D and HAQUAMS, versus MS patients with no/mild spasticity.
- In particular, fatigue and upper and lower limb mobility are most significantly impacted by moderate/severe spasticity.
- Patients with moderate/severe spasticity could therefore benefit from a therapy that specifically addresses the severity of spasticity.

Disclosures

The Adelphi MS Disease Specific Programme is an independent study supported by a number of pharmaceutical companies, including XenoPort, Inc.2

1 D Wynn and R Schapiro are consultants for XenoPort, Inc.
2 A AL-Sabbagh and D Lissin were employees of XenoPort, Inc. at the time the study was conducted.
3 E Jones and J Pike are employees of Adelphi Real World.
4 This poster was funded by XenoPort, Inc.

References


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