Parkinson’s disease burden and comorbidities: a cross-sectional cohort-study

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OBJECTIVE
To evaluate the influence of comorbidity on clinical phenotype, dopaminergic function and CSF biomarkers in a population of de novo Parkinson’s disease (PD) patients.

BACKGROUND
Whilst neurodegeneration in the substantia nigra is the primary contributor to cardinal motor symptoms of PD, it is unclear whether co-occurring comorbidities may also be contributory to PD pathology, and whether they have an impact on clinical phenotype. There is a natural increased likelihood of being diagnosed with other diseases of urinary/digestive/circulatory system, because of the autonomic and clinical features of PD, and the higher prevalence of non-motor symptoms in PD patients compared to healthy controls [1, 2]. Though several studies have established that PD is accompanied by substantial comorbidity, the impact of comorbidity on motor and non-motor symptoms, imaging and CSF biomarkers remains to be explored.

RESULTS
Thirty-six PD patients had 0 comorbidities, 162 had 2-4 and 168 had ≥5. Compared to those who had 0-1 or 2-4 comorbidities, PD patients with ≥5 comorbidities were significantly older (\(p=0.003\) vs 0-1; \(p=0.006\) vs 2-4) with a longer disease duration (\(p=0.05\) vs 0-1; \(p=0.006\) vs 2-4) and exhibited higher burden of non-motor symptoms (MDS-UPDRS part 1, \(p=0.011\) vs 0-1; \(p=0.027\) vs 2-4) and autonomic dysfunction (SCOPA-AUT, \(p=0.005\) vs 0-1; \(p=0.001\) vs 2-4). Among non-motor symptoms, comorbidity was correlated with anxiety (Pearson’s Correlation \([C]=0.107, p=0.042\), apathy (\(C=0.134, p=0.010\)), sleep problems (\(C=0.123, p=0.019\), sleepiness (\(C=0.236, p=0.0001\)), constipation (\(C=0.154, p=0.003\)), dizziness (\(C=0.104, p=0.048\), and fatigue (\(C=0.208, p<0.0001\)). There was no difference in motor burden (MDS-UPDRS part 3, H&Y stage), nigrostriatal dysfunction or any CSF biomarkers between comorbidity groups.

METHODS
Using the Parkinson’s Progression Marker’s Initiative database, 366 PD patients that had data on comorbidity were extracted and divided into three groups of 0-1, 2-4 or ≥5 comorbidities. Comorbidity was evaluated using a semi-structured questionnaire and correlated with motor and non-motor features, [123]IP-F-CIT SPECT molecular imaging and CSF biomarkers.

CONCLUSION
Our findings demonstrate that increased comorbidities in PD patients is related to higher burden of non-motor symptoms and autonomic dysfunction. We show that PD patients with 5 or more comorbidities have a longer disease duration and are significantly older. We also illustrate that anxiety, apathy, sleep disturbances, constipation, dizziness and fatigue are strongly associated with comorbidity, suggesting that comorbidity negatively influences non-motor symptom burden, therefore impacts significantly on the quality of life of these patients. Our study highlights the detrimental impact of health comorbidities on PD patient’s non-motor symptoms. The greater the number of comorbidities, the higher the risk of adverse outcomes including disability, increased health care costs, institutionalization, and morbidity. Therefore, early identification of non-motor symptoms and suitable interventions is pivotal for the effective care of patients with PD.

TABLE 1 Demographic Characteristics for PD-comorbidity groups

<table>
<thead>
<tr>
<th>Number of subjects</th>
<th>0-1 comorbidities</th>
<th>2-4 comorbidities</th>
<th>≥5 comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at screening, mean ±SD*</td>
<td>58.70 ±9.10</td>
<td>60.70 ±10.17</td>
<td>63.65 ±9.03</td>
</tr>
<tr>
<td>Gender male, % (n)</td>
<td>77.80 (28)</td>
<td>65.40 (106)</td>
<td>61.30 (103)</td>
</tr>
<tr>
<td>Age at onset, mean ±SD</td>
<td>58.21 ±8.95</td>
<td>60.22 ±10.19</td>
<td>63.01 ±8.98</td>
</tr>
<tr>
<td>PD duration (months), mean ±SD*</td>
<td>5.81 ±5.83</td>
<td>5.80 ±5.59</td>
<td>7.72 ±7.36</td>
</tr>
<tr>
<td>Family history of PD, % (n)</td>
<td>16.70 (6)</td>
<td>27.80 (45)</td>
<td>25 (42)</td>
</tr>
<tr>
<td>Year of Education, mean ± SD</td>
<td>15.78 ±3.16</td>
<td>15.04 ±3.09</td>
<td>15.94 ±2.92</td>
</tr>
</tbody>
</table>

Figure 1 Scatter plots demonstrating the distribution of disease duration, age, UPDRS-Part 1 and autonomic dysfunction scores according to comorbidity burden.

Figure 2 Correlations between comorbidity burden and non-motor symptoms

References