The role of pre-morbid diabetes on developing of ALS

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Background

- limited number of studies
- age and type of diabetes may be an effect modifier of this association
- later onset of ALS in diabetic patients compared to non-diabetic ones
- conflicting results
Research questions

1. Is there an association between pre-morbid diabetes and ALS?

2. If yes, could age and type of diabetes represent eventual modifying effects?

3. Could diabetics display a later ALS onset?
The Cohort study

Cohort: residents in Turin older than 14 yrs

Follow up: Jan 1st 1998 – Dec 31st 2014 (17 yrs)
(or dates of death, of emigration out of Turin, or 1-yr before date of ALS onset)

N: 727,977
N diab: 82,963
N ALS: 397
N ALS diab: 20
exposure to diabetes was treated as a time-dependent variable, and was truncated at 1 year before ALS onset (3-years truncation as sensitivity analysis)

Cox proportional Hazards models with robust standard errors were performed, adjusted for age, gender, educational level and marital status

the eventual modifying effect of age was assessed categorizing age variable in three classes: <50 years, 50-64 years, 65+ years.
## Results

### Truncation at 1 year before ALS

<table>
<thead>
<tr>
<th>Ever exposure</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.26</td>
<td>0.17 – 0.42</td>
</tr>
<tr>
<td>Stratified by gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.27</td>
<td>0.15 – 0.48</td>
</tr>
<tr>
<td>Female</td>
<td>0.25</td>
<td>0.12 – 0.54</td>
</tr>
<tr>
<td>Stratified by age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-49 years</td>
<td>0.24</td>
<td>0.06 – 0.98</td>
</tr>
<tr>
<td>50-64 years</td>
<td>0.21</td>
<td>0.11 – 0.43</td>
</tr>
<tr>
<td>65+ years</td>
<td>0.27</td>
<td>0.14 – 0.54</td>
</tr>
</tbody>
</table>

### Truncation at 3 years before ALS

<table>
<thead>
<tr>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.18</td>
<td>0.11 – 0.31</td>
</tr>
<tr>
<td>0.16</td>
<td>0.08 – 0.33</td>
</tr>
<tr>
<td>0.22</td>
<td>0.09 – 0.49</td>
</tr>
<tr>
<td>0.24</td>
<td>0.06 – 0.98</td>
</tr>
<tr>
<td>0.14</td>
<td>0.06 – 0.32</td>
</tr>
<tr>
<td>0.18</td>
<td>0.08 – 0.40</td>
</tr>
</tbody>
</table>
Results

- survival analysis by age shown that mean age at ALS onset of diabetic patients was 3-years higher than that of non-diabetic patients:
  - age mean: 67.4 (sd 10.5) years and 70.0 (sd 7.9) years
  - log-rank test p=0.78
Conclusions

- protective association between pre-morbid diabetes and the development of ALS (significant HR of 0.26)

- this association concerned exclusively type 2 diabetes and was not modified by age or sex

- survival analysis by age at ALS onset between diabetic and non-diabetic patients presented different curves, with a 3-years later onset for the former (even if not significant)

- although the mechanisms underlying this association remain mainly unclear:
  - higher serum lipids or glucose may reduce and delay the damage to the motor neuron system;
  - environment and genotype might play a role on this association
Thank you

Fabrizio D’Ovidio Ph.D.
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