Rates and Predictors of Progression from Mild Cognitive Impairment to Dementia: The Mayo Clinic Study of Aging

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Rosebud Roberts, M.B. Ch.B., M.S.
Professor of Epidemiology
College of Medicine, Mayo Clinic
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Background Issues on MCI Progression

• Estimates of progression frequently based on prevalent cases
• Limited information on progression in incident cases
• Predictors of MCI progression may differ from predictors of incidence
• Limited insights on outcomes in MCI cases who revert to normal
Learning Objectives

• To understand the rates of MCI progression to dementia
• Gain insight into rates of MCI reversion to normal
• Gain insight into the predictors of progression and reversion
Mayo Clinic Study of Aging

Objectives

• Estimate prevalence and incidence of MCI
• Identify risk factors for MCI
• Identify predictors of MCI progression to dementia
Mayo Clinic Study of Aging

• Prospective, population-based study
• Sampling frame: Olmsted County, MN
  – Rochester Epidemiology Project (REP)
  – 70-89 years old
  – Index Date: October 1, 2004
• Target population: 9,953
  – Randomly Selected: 5,233
• Stratified sampling by:
  – Age (70-79 years, 80-89 years)
  – Gender
Study Protocol

- Nurse interview
  - Memory questions
  - Clinical Dementia Rating
  - Medications
  - Comorbid medical conditions

- Neurological evaluation by physician

- Cognitive testing battery
  - Memory
  - Language
  - Executive Function
  - Visuospatial (WAIS-R)
Diagnosis by Consensus

• MCI: Clinical Criteria
  – Cognitive decline or impairment
  – Impairment in ≥1 cognitive domains
  – Essentially normal functional activities
  – Absence of dementia

• MCI
  – amnestic vs. non-amnestic
  – Single vs. multiple domain
1,969 normal cognition or MCI at baseline

1,640 Cognitively normal
190 Lost to follow-up
39 Died
26 Moved
125 Refused

1,450 ≥1 follow-up

348 incident MCI
(Total MCI: 677)

329 prevalent MCI

18 incident dementia
MCI Progression to Dementia

Prevalent MCI, 329
282 ≥1 follow-up

Incident dementia
96

Incident MCI, 348
196 ≥ 1 follow-up

Incident dementia
36

Progression to dementia
132 (of 478 MCI cases)
### Characteristics of MCI Subjects*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Prevalent</th>
<th>Incident</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>282</td>
<td>196</td>
<td>478</td>
</tr>
<tr>
<td>% ≥ 80, yr</td>
<td>66</td>
<td>72</td>
<td>68</td>
</tr>
<tr>
<td>% Men</td>
<td>57</td>
<td>58</td>
<td>58</td>
</tr>
<tr>
<td>Education, ≤ 12 yrs</td>
<td>58</td>
<td>55</td>
<td>57</td>
</tr>
<tr>
<td>APOE ε4</td>
<td>31</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Moderate exercise†</td>
<td>47</td>
<td>58</td>
<td>51</td>
</tr>
<tr>
<td>Mean follow-up, yrs</td>
<td>2.8</td>
<td>2.5</td>
<td>2.7</td>
</tr>
</tbody>
</table>

* At diagnosis of MCI
† Moderate exercise at least once a week; *p < .05
Results
MCI Progression to Dementia
MCI Outcomes

• Transitions
  – 121 (25.3%) progression to dementia without reversion
  – 189 (39.5%) stable MCI
  – 168 (35.2%) ≥ 1 reversion to normal

• Annual progression rates
  – ~10.2% per year in MCI cases
  – < 1% in cognitively normal

• Progression to dementia: MCI vs. normal
  – HR: 21.3 (95% CI, 12.9, 35.2)
Progression to Dementia: Prevalent and Incident MCI

Cumulative incidence (%) vs Age, yrs

- Prevalent MCI
- Incident MCI

p value: .001
Probability of Progression Over Time

Cumulative incidence ([1-KM] %)

Time from MCI diagnosis, yrs

- 1 year: 6.9%
- 2 years: 18.8%
- 3 years: 25.5%
- 4 years: 33.2%
- 5 years: 45.8%
MCI Progression to Dementia by Age and Sex

Incidence/1000 pyrs
Men: 67.7
Women: 94.3
Combined: 82.1
<table>
<thead>
<tr>
<th>Risk factors</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow gait</td>
<td>1.59</td>
<td>1.05, 2.39</td>
<td>.03</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.54</td>
<td>1.03, 2.31</td>
<td>.04</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>1.77</td>
<td>1.24, 2.53</td>
<td>.002</td>
</tr>
<tr>
<td>APOE ε4</td>
<td>1.38</td>
<td>0.95, 1.98</td>
<td>.09</td>
</tr>
<tr>
<td>Subjective memory complaint</td>
<td>1.88</td>
<td>0.92, 3.86</td>
<td>.09</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protective factors</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate exercise</td>
<td>0.66</td>
<td>0.45, 0.97</td>
<td>.04</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No association</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>1.17</td>
<td>0.83, 1.67</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Adjusted for gender and education, age as the time variable
## Predictors of MCI Progression by Subtype and Domains

<table>
<thead>
<tr>
<th>MCI Subtype</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>aMCI vs. naMCI</td>
<td>1.24</td>
<td>0.83, 1.86</td>
<td>.30</td>
</tr>
<tr>
<td>Multi- vs. single domain</td>
<td>1.64</td>
<td>1.15, 2.34</td>
<td>.007</td>
</tr>
<tr>
<td>Factor</td>
<td>Men</td>
<td>Women</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>----------------------</td>
<td>-----------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1.00 (0.54, 1.87)</td>
<td>2.39 (1.38, 4.16)</td>
<td></td>
</tr>
<tr>
<td>Slow gait speed</td>
<td>1.43 (0.82, 2.49)</td>
<td>1.87 (0.97, 3.61)</td>
<td></td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>1.57 (0.97, 2.54)</td>
<td>1.98 (1.18, 3.32)</td>
<td></td>
</tr>
<tr>
<td>FAQ score ≥ 10</td>
<td>4.63 (2.20, 9.74)</td>
<td>1.72 (0.77, 3.86)</td>
<td></td>
</tr>
<tr>
<td>Moderate exercise</td>
<td>0.55 (0.33, 0.92)</td>
<td>0.88 (0.48, 1.59)</td>
<td></td>
</tr>
<tr>
<td>Not married</td>
<td>1.11 (0.66, 1.87)</td>
<td>0.55 (0.32, 0.93)</td>
<td></td>
</tr>
</tbody>
</table>
### Progression of MCI to Dementia Neuropsychological Factors

<table>
<thead>
<tr>
<th>Domain z Scores</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global domain score ≤ -1 SD</td>
<td>2.65</td>
<td>1.69-4.16</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Language ≤ -1 SD</td>
<td>2.20</td>
<td>1.51-3.19</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Executive function ≤ -1 SD</td>
<td>1.76</td>
<td>1.18-2.62</td>
<td>.005</td>
</tr>
<tr>
<td>Memory ≤ -1 SD</td>
<td>1.74</td>
<td>1.20-2.52</td>
<td>.004</td>
</tr>
<tr>
<td>Visuospatial ≤ -1 SD</td>
<td>1.74</td>
<td>1.18-2.57</td>
<td>.005</td>
</tr>
</tbody>
</table>
Outcomes Following MCI Reversion to Normal
Progression to Dementia

- No reversion
- $\geq 1$ reversion

p value: .001
Outcomes* by Age and Time

No Reversion: outcome is dementia
≥1 Reversion: outcome is MCI or dementia
<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased reversion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate exercise</td>
<td>1.45</td>
<td>1.03, 2.03</td>
<td>.03</td>
</tr>
<tr>
<td>Reduced reversion</td>
<td></td>
<td></td>
<td></td>
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<td>0.57</td>
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<td>.04</td>
</tr>
<tr>
<td>FAQ score ≥ 10</td>
<td>0.24</td>
<td>0.06, 0.98</td>
<td>.05</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>0.40</td>
<td>0.26, 0.63</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.87</td>
<td>0.63, 1.21</td>
<td>.42</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.70</td>
<td>0.45, 1.10</td>
<td>.13</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>0.80</td>
<td>0.59, 1.10</td>
<td>.17</td>
</tr>
</tbody>
</table>
# Reversion by Subtype and Domains

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>95% CI</th>
<th>(p)</th>
</tr>
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<tbody>
<tr>
<td>Reduced reversion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aMCI vs naMCI</td>
<td>0.63</td>
<td>0.45, 0.87</td>
<td>.005</td>
</tr>
<tr>
<td>Multiple vs. single domain</td>
<td>0.58</td>
<td>0.40, 0.83</td>
<td>.003</td>
</tr>
</tbody>
</table>
Conclusions

• Progression from MCI to dementia is much higher than from normal cognition
• Predictors of MCI progression differ from predictors of incidence
• Multi-domain MCI:
  – Higher risk of progression and lower reversion
  – Suggests greater brain pathology
• Predictors of progression differ from predictor for MCI incidence
• Subjects who revert to normal progress to MCI or dementia in 4-5 years
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