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Mild cognitive impairment

Concepts, cut-offs, and clinical relevance

Akademisk avhandling

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av Mattias Göthlin

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Avhandlingen baseras på följande delarbeten

I. Göthlin, M., Eckerström, M., Rolstad, S., Wallin, A., Nordlund, A., 2017, Prognostic accuracy of Mild Cognitive Impairment subtypes at different cut-off levels, Dementia & Geriatric Cognitive

II. Göthlin, M., Eckerström, M., Rolstad, S., Kettunen, P., Wallin, A., 2018, Better prognostic accuracy in younger MCI patients with more years of education, Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring

III. Göthlin, M., Eckerström, M., Lindwall, M., Rolstad, S., Eckerström, C., Jonsson, M., Kettunen, P., Svensson, J., Wallin, A., Latent cognitive profiles differ between incipient Alzheimer's disease and dementia with subcortical vascular lesions in a memory clinic population, Manuscript

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Mild cognitive impairment - concepts, cut-offs, and clinical relevance

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Abstract

Mild cognitive impairment (MCI) is a diagnosis frequently used in dementia research and in memory clinics. MCI is meant to identify patients without dementia, but with cognitive decline beyond what is considered normal, and with an increased risk of progressing to dementia. Typically, cognitive test performance 1.5 standard deviations (SD) or more below normal controls is considered impaired. To account better for heterogeneity in etiology and prognosis in MCI, clinical subtypes of MCI have been suggested; MCI with or without memory impairment as one dimension, and impairment in one or more than one cognitive domain as another dimension. The aim of this thesis is to clarify the prognostic value of MCI and MCI subtypes in memory-clinic patients.

All participants in papers I-III were either patients seeking care at the Sahlgrenska memory clinic in Mölndal or healthy controls examined at the same unit. Paper I included 317 patients, 55 of whom progressed to dementia. Paper II included 358 patients, 68 of whom progressed to dementia. Paper III included 383 patients, 70 of whom progressed to dementia. All patients included in paper I were also included in paper II and III, all patients included in paper II where also included in paper III.

In paper I, 317 patients were followed for 2 years, and 168 patients were followed for 4-6 years. The probability of a patient progressing to dementia after 2 years was 17%, and 14% after 4-6 years. One-third of the memory-clinic patients did not meet standard criteria for MCI at baseline, and had a reduced probability of progressing to dementia (from 17% to 1% within 2 years and from 14% to 9% after 4-6 years). Meeting standard criteria for MCI only slightly increased the risk of progressing to dementia (from 17% to 26% after 2 years and from 14% to 20% after 4-6 years). Amnestic multi-domain MCI was the only subtype that significantly increased a patient's probability of progressing to dementia (from 18% to 46% after 2 years and from 14% to 37% after 4-6 years). A more liberal MCI cut-off (i.e. 1.0 SD instead of 1.5 SD or 2.0 SD) did not improve the prognostic accuracy of MCI or the MCI subtypes.

In paper II, amnestic multi-domain MCI was associated with a much larger increase in probability of progression to dementia in younger patients under 65 with more than 12 years of education than in other demographic groups, as compared with patients with other subtypes and those who did not meet MCI criteria.

In paper III, cognitive subtypes derived from a latent profile analysis differentiated between patients who two years after baseline progressed to Alzheimer's disease dementia vs. dementia with subcortical vascular features, where the traditional MCI subtypes did not.

In conclusion, a large group of memory-clinic patients do not display significant cognitive impairments and have a very low probability of progressing to dementia. Prognosticating progression to dementia is easier in younger patients with more years of education than in other demographic groups. However, even among younger patients with more years of education, it may be better to use absence of amnestic multi-domain MCI to rule out progression to dementia, than to use presence of amnestic multi-domain MCI to find patients who will progress. Statistically derived cognitive subtypes may separate the risk of AD dementia from the risk of dementia with subcortical vascular features where the established MCI subtypes do not.

Keywords: mild cognitive impairment, cognition, dementia, Alzheimer's disease, memory clinic, diagnostic assessment

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