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Better prognostic accuracy in younger mild cognitive impairment patients with more years of education

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Abstract

Introduction: Age and years of education influence the risk of dementia and may impact the prognostic accuracy of mild cognitive impairment subtypes.

Methods: Memory clinic patients without dementia (N = 358, age 64.0 ± 7.9) were stratified into four groups based on years of age (≤64 and ≥65) and education (≤12 and ≥13), examined with a neuropsychological test battery at baseline and followed up after 2 years.

Results: The prognostic accuracy of amnestic multi-domain mild cognitive impairment for dementia was highest in younger patients with more years of education and lowest in older patients with fewer years of education. Conversely, conversion rates to dementia were lowest in younger patients with more years of education and highest in older patients with fewer years of education.

Discussion: Mild cognitive impairment subtypes and demographic information should be combined to increase the accuracy of prognoses for dementia.

Keywords: Memory clinic; Mild cognitive impairment; Dementia; Alzheimer's disease; Neuropsychology; Diagnosis

1. Background

Mild cognitive impairment (MCI) [1] is a clinical syndrome, characterized by a decline in cognitive function greater than what is considered normal and different from mild dementia in that activities of daily life are intact or only minimally disturbed. The risk of future dementia is elevated for persons with MCI [2,3]. However, many memory clinic patients with MCI do not develop dementia, that is, an MCI classification yields many false positives [2]. To increase the specificity of the MCI classification and account for the heterogeneity inherent in the MCI syndrome, Petersen et al. [4] and Winblad et al. proposed a subtype paradigm, in which MCI is further divided based on whether or not memory is impaired and whether one or several cognitive domains are affected. The resulting categories were amnestic single-domain (aMCI-sd), amnestic multi-domain (aMCI-md), nonamnestic single-domain (naMCI-sd), and nonamnestic multi-domain (naMCI-md) mild cognitive impairment. We previously reported that aMCI-md results in fewer false positives than non-subtyped MCI and that the other subtypes have little or no prognostic value [5].

Low education is a risk factor for dementia [6,7]. Furthermore, dementia prevalence increases sharply with age, from 1.6% between 60 and 64 years of age, to 4.3% between 70 and 74 years, and 43.1% over the age of 90 [8]. This relationship is also evident in clinical samples [9]. However, there are also indications that both old age and fewer years of formal education attenuate the prognostic accuracy for dementia. Visser et al. [10] reported that the positive predictive value for various definitions of MCI in predicting Alzheimer's disease dementia (ADD) 5 years later was higher in patients older than 65 years, likely because of a higher prevalence of predementia in the older group. However, because both sensitivity and specificity were higher in the younger group, the results can also be interpreted as a better prognostic accuracy among younger

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participants. In another study, Visser et al. [11] reported good prognostic accuracy for subsequent ADD only for amnestic MCI in patients aged 70–85 years, as compared with patients under 69 years of age. Thus, it still remains unclear how patient age influences the prognostic accuracy in MCI. Furthermore, both neuritic plaques and neurofibrillary tangles measured postmortem [12,13] and cerebrospinal fluid Alzheimer's disease biomarkers [14] are more weakly associated with an ADD diagnosis in older people; distinguishing between different states with increasing age is an increasingly difficult task.

In a large population-based study, neuropsychological test results predicted dementia in participants with higher but not lower educational levels [15], possibly because of larger variability in cognitive performance in people with higher educational levels than people with lower educational levels. To the best of our knowledge, there are no clinical studies reporting prognostic accuracy in different education groups or in age and education groups simultaneously.

The aim of the present study was to investigate the influence of years of age and education on the prognostic accuracy of MCI subtypes over a 2-year period.

2. Materials and methods

2.1. Participants

We included 358 consecutive patients from the Gothenburg MCI study [16], a prospective umbrella study conducted at the outpatient memory clinic at the Sahlgrenska University Hospital in Gothenburg, Sweden. First visits took place between 2000 and 2014. All participants were between 40 and 79 years old and experienced cognitive decline (self-reported and/or informant reported) without obvious relation to somatic or psychiatric disorders or traumatic brain injury, with duration of at least 6 months. Cognitive decline was assessed in a clinical interview. In the present study, we included participants who had completed the baseline diagnostic assessment and did not have manifest dementia at baseline (see Section 2.2 for details).

We also included healthy controls, primarily recruited from senior citizen organizations and via information meetings about dementia. Several controls were spouses of patients. All controls were thoroughly interviewed by a research nurse before inclusion. Controls were included if they were physically and mentally healthy and displayed neither self-reported nor observable signs or symptoms of cognitive impairment.

In the Gothenburg MCI study, 742 patient participants were included between 2000 and the end of 2014. Of those, 223 participants (57% women, age at baseline 67.4 ± 7.3, education years 11.1 ± 3.6, Mini–Mental State Examination [MMSE] 24.8 ± 2.7) had dementia (i.e., global deterioration scale [GDS] ≥4) at baseline and were excluded. Sixteen participants (33% women, age at baseline 62.6 ± 8.1, MMSE 28.7 ± 1.4) had inconclusive data on years of education and were excluded. One participant (male, age at baseline 30, MMSE 30) was below 40 years of age and was excluded. One hundred three participants (63% women, age at baseline 61.8 ± 9.5, education years 12.5 ± 3.6, MMSE 28.4 ± 1.4) lacked follow-up data and were excluded. Of the 399 participants (58% women, age at baseline 64.1 ± 7.9, education years 12.6 ± 3.6, MMSE 28.5 ± 1.4) with follow-up data, 41 (49% women, age at baseline 65.7 ± 6.5, education years 11.7 ± 3.7, MMSE 28.1 ± 1.5) had an incomplete neuropsychological data set at baseline. This left 358 participants (59% women, age at baseline 64.0 ± 7.9, education years 12.7 ± 3.6, MMSE 28.5 ± 1.4) for analysis.

2.2. Procedures

2.2.1. Diagnostic procedures

We used the GDS [17] to determine the cognitive stage of the participants. In the Gothenburg MCI study version, GDS is operationalized using the MMSE [18], the Clinical Dementia Rating [19], the Comparative Status Analysis (STEP) [20], and the Investigation of Flexibility, which is a short form of the executive interview [21].

A specialist physician or a registered nurse determined the GDS stage. GDS stage 4 was assigned if STEP was >1, Investigation of Flexibility was >3, Clinical Dementia Rating sum of boxes was >1.0, and MMSE was ≤25. GDS 4 corresponds are equivalent to DSM-IV dementia criteria [22]. GDS stage 4 or higher at follow-up was considered conversion to dementia and was used as outcome or reference standard [23,24].

2.2.2. Instruments and testing procedure

A licensed psychologist or a psychologist in training, supervised by a licensed psychologist, administered the neuropsychological test battery to patients and controls. Two sessions of approximately 1.5–2 hours were needed to complete the examination. The test sequence was designed to minimize the risk of contamination on the memory tests. We used the Digit Symbol test from either the Wechsler Adult Intelligence Scale-revised [25] or the Wechsler Adult Intelligence Scale–3rd Edition [26] and the Trail-Making Test part B (TMT B) [27] to assess processing speed and attention; the delayed recall trials from the Wechsler Memory Scale Logical Memory subtest [28] and the Rey Auditory Verbal Learning Test [29] to assess verbal episodic memory; the copy condition of the Rey Complex Figure test [30] and the silhouettes subtest of the Visual Object and Space Perception Battery [31] to assess visuospatial function; the Boston Naming Test [32] and the Token test part 5 [33] to assess confrontation naming and comprehension of spoken language, respectively; and the interference part of the Stroop test, Victoria version (Stroop III) [34], and the Parallel Serial Mental Operations test [35] to assess executive functions, parallel distributed processing, automaticity, inhibition, mental control, and tracking. In accordance