



Predictors of functional disability in mild cognitive impairment and dementia



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ABSTRACT

Objective: Knowledge about factors predicting functional disability in mild cognitive impairment (MCI) and dementia would help health care providers to identify those patients who are at high risk of functional disability. Previous research is scarce and focused on only a small number of possible predictors. The aim of this study was to identify predictors of functional disability in patients with MCI and dementia.

Study design: Cross-sectional cohort study.

Main outcome measures: Data from patients who visited a memory clinic between 2011 and 2015 were evaluated. The Disability Assessment for Dementia (DAD) was used to assess functional disability. Patients diagnosed with MCI or dementia and with a DAD score available were included. This led to the inclusion of 474 patients. Univariate analyses with a broad range of variables were performed to detect factors that had a significant relationship to the DAD score. Age, gender and variables with a *p*-value of 0.1 or lower in the univariate analyses were taken into a multivariable analysis. This multiple linear regression analysis was performed to determine which variables were independently associated with the DAD score.

Main results: Our multivariable model explained 42% of the variance in the DAD score. Independent predictors of the DAD score were age ($B = 0.03$, 95%CI = 0.002–0.05), gender ($B = -0.43$, 95%CI = -0.78 to -0.07), score on the Clinical Dementia Rating scale (CDR) ($B = 1.53$, 95%CI = 1.07–1.99 for CDR 1, $B = 2.93$, 95%CI = 2.28–3.58 for CDR 2, $B = 3.96$, 95%CI = 2.65–5.27 for CDR 3) and level of physical activity ($B = 0.56$, 95%CI = 0.05–1.07).

Conclusion: Older age, male gender, higher CDR score and lower levels of physical activity are independent predictors of functional disability in MCI and dementia.

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1. Introduction

Dementia is a neurocognitive disorder which causes cognitive impairment and consequently impairment of social and practical functioning [1]. Mild cognitive impairment (MCI) is described as a state between normal cognitive ageing and dementia [2]. A difference between dementia and MCI is that the ability to function independently in usual daily activities is (largely) preserved in MCI. It is found that impairment of activities of daily living (ADL) is the main factor influencing the health related quality of life [3]. Therefore, in patients with MCI and dementia, it is important to make an estimation of their degree of functional disability. The level of impairment in ADL is related to the diagnosis [4,5], but also to other patient characteristics. In the general population, other factors that have been shown to affect functional status in elderly

include age, education, comorbidities, depression, visual impairment, functional limitations, gait speed, body mass index (BMI), unintentional weight loss, physical activity level, alcohol abstinence and smoking [4,5]. Only a few studies [6–8] were published concerning the predictors of disability in ADL in patients with MCI and dementia. Rist et al. [7] only examined five factors and found that smoking, alcohol abstinence and low income were predictors of ADL disability. Benke et al. [6] focused on neuropsychological factors and included only few demographical factors and depression, of which age, gender (women performed better) and disease duration were significant predictors in the multivariate analysis. Hesseberg et al. [8] examined basic demographical variables, diagnosis (MCI or dementia), depression and comorbidities and found diagnosis, age, gender and depression to be predictors of disability in instrumental ADL. In these previous studies, only a small number of the above mentioned factors influencing functional disability in the general elderly population were examined, and only three (age, gender and depression) in more than one cohort. Thus, not enough information is available to draw a conclusion about

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which factors predict functional disability in patients with dementia and MCI. Regarding the high disease burden, especially the high impact on quality of life, knowledge about these factors is important. It helps health care professionals to detect patients with a high risk of functional disability. This is even more essential when there is no (reliable) information available from people close to the patient. Health care providers should be more alert if patients have a higher risk of functional disability so that a better inventory can be made of the needs of (professional) help. Therefore, we decided to study a broad range of possible predictors of disability in ADL, including demographical predictors, comorbidity, lifestyle factors and functional tests. The aim of this study was to examine which factors predict functional disability in patients diagnosed with MCI or dementia.

2. Methods

2.1. Data collection and study population

Between January 2011 and August 2015, data of patients attending the memory clinic in the University Medical Centre of Utrecht were collected. The patients were referred by general practitioners or by other physicians because of a suspicion of cognitive or behavioral impairment. The study protocol for data collection was approved by the local research ethics committee and all patients gave their informed consent for the use of their anonymous data. Patients with a diagnosis of MCI or dementia were included. Dementia or MCI was diagnosed by an experienced multidisciplinary geriatric team. Diagnoses were based on the diagnostic criteria of McKhann et al. [9] for dementia and Albert et al. [10] for MCI. Patients were excluded if there was no Disability Assessment for Dementia (DAD) score available.

2.2. Outcome

2.2.1. Functional disability

Disability in ADL was measured using the DAD [11]. The DAD is a validated questionnaire for scoring disability in ADL in patients with cognitive impairment. It contains 40 items. The subdomains hygiene, dressing, continence, eating, meal preparation, telephoning, going on an outing, finance and correspondence, handling medications, leisure and homework are scored. Information for the questionnaire was given by an informant of the patient. Subdomains can be scored as yes or no on the ability to initiate, to plan and to perform the activity. It was scored Not Applicable if the patient never did this activity before or if there was no information available. Scores are presented in percentages ranging from 0 to 100%, where a higher score corresponds with a higher performance state. If something was Not Applicable it was not included in the percentage.

2.2.2. Demographic, clinical and neuropsychological determinants

For every patient attending the memory clinic, a structured questionnaire was completed at study entry. Demographic determinants included age, sex, level of education and living situation. The Clinical Dementia Rating (CDR) [12] scale was used to determine the disease stage. This scale quantifies impairment in cognitive function and routine activities by means of a five-point scale where 0 stands for no impairment, 0.5 for very mild or questionable impairment (MCI or very light dementia), 1 for mild impairment, 2 for moderate impairment and 3 for severe impairment. The Mini Mental State Examination (MMSE) was used to assess global cognitive function. The MMSE includes eleven questions measuring cognitive functions with higher values indicating better cognitive function [13]. If patients reported feeling depressed

or a loss of interest, the Geriatric Depression Scale (GDS) was taken. The GDS focuses on detecting depression in geriatric patients [14]. The cut-off point for a depression was set at a score greater than 5 [15]. Overall comorbidity was assessed through the Charlson comorbidity index [16]. In this weighted index certain severe conditions get 1–6 points depending on by their mortality risk. For this study a difference was made between no or mild comorbidity (Charlson comorbidity index 0–1) and severe comorbidity (Charlson comorbidity index ≥ 2). Visual impairment was considered positive when patients reported having problems with their vision. Patients were defined as smokers when they were currently smoking or had quit less than 6 months ago. Alcohol use was split up in no alcohol use, moderate alcohol use (≥ 10 and < 150 g alcohol per week) and severe alcohol use (≥ 150 g alcohol per week). Physical activity was rated low in case patients did not exercise more than half an hour a day at moderate intensity for at least five days a week [17]. Moderate intensive physical activities included cycling, sports, gardening or doing odd jobs. Obesity was defined as having a body mass index (BMI) of 30 or higher [18]. Unintentional weight loss was defined as weight loss of three kilograms or more in the last month. Low handgrip strength was defined as handgrip strength under 85% of the normal value adjusted for sex and age [19]. A four meter walking test was performed to determine gait speed in meters per second. Cut-off point for low gait speed was set at 0.8 m/s [20].

2.3. Data analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 21 for Windows [21]. Some variables appeared to have missing data. Most of the missing data was 'Missing At Random' [22] and this can cause bias when performing an analysis with only the complete cases. Therefore multiple imputations were performed [23]. These were performed via the Fully Conditional Specification method [24]. The missing values of all the independent variables were imputed. Because of the exclusion of patients without a DAD score available, no DAD scores were imputed. All patients with a DAD score available were included for the multiple imputations, regardless of their percentage of missing independent variables. The variables were imputed on the raw scale with no restrictions on the range [25]. The number of imputations was set at 20 [26].

Linear regression models were used to detect significant predictors of functional disability. The DAD score was the dependent variable in these models. Assumptions of a linear regression model were violated (highly negatively skewed distribution of the residuals and no homoscedasticity). Therefore, the DAD score was transformed. The DAD scores were reversed and thereafter a square root transformation was made. Univariate linear regression analyses were performed with the different variables. Age, gender and variables with a p -value at or under 0.10 were taken into a multivariable linear regression analysis. The forced entry method was used to include the variables into the model. Significance level for the p -value in the multivariable model was set at 0.05. To see if there were evident differences in predictors between patients in different disease stages, the sample was split in patients with a lower CDR-score (CDR 0–1) and patients with a higher CDR-score (CDR 2–3). To examine if there were differences between sexes, the study population was split in men and women. The same analyses were performed for the subgroups.

3. Results

Between January 2011 and August 2015, 712 participants visited the memory clinic. MCI was diagnosed in 112 patients and

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