Experimental Gerontology 110 (2018) 146–150

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Combined effects of mild cognitive impairment and slow gait on risk of dementia

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ARTICLE INFO

Section Editor: Diana Van Heemst

Keywords:
Cognition
Mobility
Frailty
Gait
Dementia

ABSTRACT

Background: Mild cognitive impairment (MCI) is a high risk of conversion to dementia and gait dysfunction is also a risk for dementia. The goal of the study was to examine if co-occurrence of MCI and slow gait (SG) increases the risk of dementia.

Methods: A prospective study was conducted in 3937 older adults who did not have dementia at baseline. Participants were classified into groups based on status of MCI and SG: without MCI and SG (control), without MCI and with SG (SG), without SG and with MCI in a single domain (sMCI) or multiple domains (mMCI), sMCI and SG (sMCI + SG), and mMCI and SG (mMCI + SG). Incident dementia was followed monthly. Cox proportional hazards regression models were used to calculate the hazard ratio for incident dementia in each group.

Results: During a mean follow-up period of 43 months, 182 subjects had incident dementia. MCI was a risk factor for dementia and SG increased the risk, even after adjusting for covariates (SG: HR = 1.31 (0.81–2.14), 95% CI = 0.276, sMCI: HR = 1.87, 95% CI = 1.21–2.88, $p = .005$; mMCI: HR = 3.36, 95% CI = 1.98–5.71, $p < .001$; sMCI + SG: HR = 3.33, 95% CI = 1.92–5.77, $p < .001$; mMCI + SG: HR = 5.02, 95% CI = 2.75–9.14, $p < .001$).

Conclusions: Co-occurrence of MCI and SG has a high risk of dementia compared to that of each condition alone. Evaluation of both gait and cognition is useful in risk assessment of dementia.

1. Introduction

Dementia is a critical health problem with major and increasing worldwide costs estimated to be over 1 trillion dollars in 2018 (Wimo et al., 2017). Development of a strategy for treatment and prevention requires assessment of the risk for dementia and the effectiveness of intervention. Mild cognitive impairment (MCI) has a high risk of conversion to dementia and is modifiable, with the possibility of reversion to a cognitive intact status (Petersen, 2011). In a community setting, the prevalence of MCI is about 15–20% (Jia et al., 2014; Manly et al., 2008; Shimada et al., 2013a) and the annual conversion rate of MCI to dementia is approximately 5% (Mitchell and Shiri-Feshki, 2009).

Gait dysfunction is thought to be a marker of a risk for dementia (Verghese et al., 2002), and slow gait speed is also thought to be a risk factor for cognitive impairment, including MCI (Buracchio et al., 2010) and dementia (Beauchet et al., 2016; Dumurgier et al., 2016). Simultaneous gait and cognitive impairments, such as those in motoric cognitive risk syndrome (MCR) (Verghese et al., 2014), increase the risk of dementia compared to each respective impairment (Verghese et al., 2014; Waite et al., 2005). Evaluation of gait speed is a simple and widely accepted method for assessment of gait ability. However, the definition of co-occurrence of gait and cognitive impairment has varied among studies. MCR definitions used worldwide include a combination of slow gait (SG) and subjective cognitive complaint (Verghese et al., 2014), while the risk of dementia in subjects with co-occurrence of MCI and SG is unclear. Evaluation of this risk would provide insights into development of a preventive strategy for dementia. Thus, this prospective study was performed in community-dwelling older adults to test the hypothesis that co-occurrence of MCI and SG has a greater risk of future dementia compared to that of MCI or SG only.

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https://doi.org/10.1016/j.exger.2018.06.002
Received 8 November 2017; Received in revised form 8 May 2018; Accepted 1 June 2018
Available online 04 June 2018

2. Methods

2.1. Study design and samples

The study was performed prospectively. A baseline survey was conducted in the Obu Study of Health Promotion for the Elderly (OSHPE), which is part of the National Center for Geriatrics and Gerontology: Study of Geriatric Syndromes (NCGG-SGS), a cohort study with the primary goal of establishing a screening system for geriatric syndromes in the community-dwelling population (Shimada et al., 2016). Participants for the current study were selected from 5104 OSHPE participants (aged ≥65 years), based on inclusion criteria of independence in basic activities of daily living and aged ≥65 at baseline. The exclusion criteria were a history of dementia and Parkinson's disease, MMSE < 24 at baseline, and no definition of MCI and SG due to missing values. The presence of dementia was confirmed in a clinical interview and from medical records. Participants not using Japanese National Health Insurance or Latter-Stage Medical Care were also excluded due to lack of collection of prospective data on dementia. A total of 3937 participants were considered eligible for the study and were included in the analysis. The follow-up period was defined from the time of the examination at baseline until 2015 (mean ± SD: 43 ± 6 months, median 44 months). The ethics committee of the National Center for Geriatrics and Gerontology approved the study. Consent for participation was obtained from all subjects.

2.2. Mild cognitive impairment

MCI was diagnosed using the National Center for Geriatrics and Gerontology Functional Assessment Tool (NCGG-FAT) (Makizako et al., 2013) and a detailed protocol described elsewhere (Makizako et al., 2016). The NCGG-FAT consists of multiple domains of cognition for identification of MCI status, including attention, executive function, processing speed and memory. Attention and executive function were assessed by the electronic tablet version of the Trail Making Test, parts A and B. Processing speed was assessed using the electronic tablet version of the Symbol Digit Substitution Test. Memory was evaluated by Word list memory, including immediate recognition and delayed recall. The detailed procedures for these tests are described elsewhere (Makizako et al., 2016; Makizako et al., 2013). NCGG-FAT has adequate test-retest reliability and validity among community-dwelling older adults (Makizako et al., 2013). All tests used in this study had standardized thresholds for definition of MCI based on objective cognitive impairment (score < 1.5 SDs below age- and education-specific means), based on our own algorithm derived from a database of > 10,000 community-dwelling older Japanese individuals (Makizako et al., 2016). In addition, the definition of MCI in this study required evidence of functional independency, based on no need for supervision or external help in performing basic activities of daily life, and normal general cognitive functioning, which was defined as MMSE ≥ 24. MCI cases were classified as those in single (sMCI) and multiple (mMCI) domains, based on results for cognitive functions.

2.3. Gait speed

Gait speed was measured using a previously described protocol. (Shimada et al., 2013a) Gait time was measured over 2.4 m in the middle of a straight walkway of 6.4 m, between marks at 2.0 m and 4.4 m from the start of the walkway. The gait speed (m/s) was calculated and SG was defined as < 1.0 m/s, as validated (Shimada et al., 2013b) and widely accepted (Abellan van Kan et al., 2009; Dumurgier et al., 2016).

2.4. Incident dementia

During follow-up, incident dementia was monitored for all participants without dementia at baseline, using data from the Japanese Health Insurance System, which is a national system of medical insurance (Association; Welfare). All Japanese citizens (including permanent residents and non-Japanese people residing in Japan with a visa lasting three months or longer) have to enroll in an insurance system and most Japanese people are enrolled in Employees' Health Insurance, Japanese National Health Insurance, or Later-Stage Medical Care (about 87% of older adults in Japan) (Association; Welfare). The detailed procedure of collection of incident dementia cases using medical records has been described elsewhere (Makizako et al., 2016). Medical records, residents moving out of Obu, and mortality data were evaluated monthly. Moving out of Obu and death were treated as censoring events.

2.5. Covariates

Potential covariates were selected based on cumulative evidence (Barnes and Yaffe, 2011; Norton et al., 2014; Xu et al., 2015). In a face-to-face interview, information was collected for age, sex, body mass index (weight/height^2), educational history, medication use, and lifestyle, including physical inactivity, smoking and alcohol intake. Information on specific diseases (hypertension, heart disease, diabetes, cerebrovascular disease) related to dementia (Barnes and Yaffe, 2011; Norton et al., 2014; Xu et al., 2015) was also collected. Medical conditions were determined in interviews conducted by well-trained nurses.

2.6. Statistical analysis

Subjects were classified into the following groups according to their status of cognitive impairment and gait speed: control (no MCI and no SG), SG (SG without MCI), MCI (MCI without SG), and MCI + SG (MCI with SG). Analysis of variance or χ^2 test was used to compare characteristics among these groups. For continuous variables, a Tukey-HSD test was conducted as a post hoc analysis for comparison between groups. Analyses using crude (model 1) and adjusted (model 2) Cox proportional hazards regression models were conducted to examine the relationship of MCI and SG with incident dementia, and hazard ratios (HR) for incident dementia were calculated with 95% confidential intervals (CI). Model 2 was adjusted for covariates including age, sex, BMI, hypertension, heart disease, diabetes, cerebrovascular disease, medication use, educational history, physical exercise, smoking, and alcohol intake. The four groups were also further classified into subgroups according to subtypes of MCI (control, SG, sMCI, sMCI + SG, mMCI, mMCI + SG) and sub-analysis was conducted using Cox proportional hazards regression analysis. All calculations were performed using SPSS ver. 20 (IBM Corp., Armonk, NY, USA) and $p < .05$ was considered to be significant in all analyses.

3. Results

Classification of participants based on gait speed and cognitive function resulted in the following groups: control ($n = 2698$), SG ($n = 384$), MCI ($n = 674$), and MCI + SG ($n = 181$). Most characteristics had significant differences between groups ($p < .05$), except for sex ($p = .130$) and smoking habit ($p = .374$) (Table 1). Incident dementia occurred in 182 subjects (4.6%) during follow-up (control: $n = 77$, 2.9%; SG: $n = 24$, 6.2%; MCI: $n = 45$, 6.7%; MCI + SG: $n = 36$, 19.9%). According to subtypes of MCI, the incident dementia rates were as follows: sMCI: $n = 28$, 5.5%; mMCI; $n = 17$, 10.1%; sMCI + SG: $n = 21$, 17.8%; mMCI: $n = 15$, 23.8%. Data were censored due to 100 deaths (control: $n = 48$, 1.8%; SG: $n = 21$, 5.5%; MCI: $n = 21$, 3.1%; MCI + SG: $n = 10$, 5.5%) and 35 subjects who moved out of the area (control: $n = 23$, 0.9%; SG: $n = 5$, 1.3%; MCI: $n = 6$, 0.9%; MCI + SG: $n = 1$, 0.6%).

The results of Cox regression analysis in the SG, MCI and MCI + SG