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Development of a risk score for the prediction of incident dementia in older adults using a frailty index and health checkup data: The JAGES longitudinal study

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ABSTRACT

In Japan, the prevalence of dementia is expected to reach 4.7 million by 2025. This study aimed to develop a risk score for the prediction of incident dementia in community-dwelling older adults. In this longitudinal observational study, we used data from the Japan Gerontological Evaluation Study (JAGES) conducted in K City. We performed Cox regression analyses to develop three risk score models for the prediction of incident dementia in older adults using a frailty index and health checkup data. Analyses of the area under the receiver operating characteristic curve were conducted to compare the models' predictive abilities.

We identified 6656 (9.2%) individuals who developed incident dementia during the observation period. The C-statistics of the risk scores ranged from 0.733 to 0.790.

The risk score models were able to predict incident dementia in older adults and may help non-medical professionals detect dementia risk at an early stage.

1. Introduction

The World Health Organization has reported that the total number of people with dementia has risen sharply throughout the world over the past few decades (World Health Organization, 2012). However, the incidence of new dementia cases has recently declined due to higher education and an increased awareness of preventative healthcare (Langa et al., 2017; Satizabal et al., 2016). Primary prevention strategies aimed at improving the control of lifestyle-related risk-factors may have reduced the risk of dementia (Deckers et al., 2015).

Japan has a super-aging population with a long life expectancy, and there is a rapidly increasing need for older adults' care, including medical and long-term care (LTC) services (Nomura et al., 2017). Japanese insurers use a frailty index known as the “Kihon Checklist” (Appendix Table A1) (Arai and Satake, 2015) to identify frail community-dwelling older adults in order to assess potential care needs and prevent avoidable increases in the number of LTC service users. The validity of the Kihon Checklist as an indicator of frailty has been previously demonstrated (Sampaio et al., 2016; Satake et al., 2016), and studies have applied the checklist to the assessment of physical function, frailty, and self-reported health in older adults (Fukutomi et al., 2015; Kera et al., 2017; Makizako et al., 2015; Matsushita et al., 2017; Yamada et al., 2017). A previous study suggested that the Kihon Checklist's cognitive function items alone had inadequate predictive ability for the screening of dementia in community-dwelling older adults may due to the non-inclusion of physical function and other risk factors (Tomata et al., 2016).

It was estimated that there were 2.8 million people with dementia in 2010 throughout Japan, and this number is projected to reach 4.7 million by 2025 (Health and Welfare Bureau for the Elderly, 2013). In order to address this surge in dementia prevalence, the government announced a five-year plan (designated the “Orange Plan”) for the promotion of dementia measures that began in 2012 (Cabinet Office of Government of Japan, 2013). This plan was revised into the “New Orange Plan” in 2015 (Labour and Welfare of Ministry of Health, 2016), which aims to systematically support older adults with dementia and their families through seven components, including the early diagnosis of dementia and prompt treatment (Cabinet Office of Government of Japan, 2013). Identifying dementia in its early stage can reduce the impact on patients and their families by allowing them to anticipate and

Abbreviations: LTC, long-term care; FBS, fasting blood sugar levels; HbA1c, hemoglobin A1c levels; HDL, high-density lipoprotein levels; LDL, low-density lipoprotein; HR, hazard ratio; ROC, receiver operating characteristic

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plan for eventual problems (Moyer and Force, 2014; Stephan et al., 2016), but dementia is often underdiagnosed (Sampson et al., 2009; Wilcock et al., 2016) due to its complicated disease progression (Buntinx et al., 2011). It is therefore important to develop a simple tool that allows family members and other close associates to identify the preclinical signs of dementia in older adults. The prediction accuracy of previous dementia risk models varied, and the model with high c-statistic was built based on the laboratory test results (Stephan et al., 2016). This study was undertaken to develop a new risk score for the prediction of incident cases of dementia identified using LTC eligibility certification data in community-dwelling older adults.

2. Methods

As risk factors related to dementia incidence suggested in former studies were included in the Kihon Checklist (Alzheimer's Association, 2016; Chen et al., 2009; Deckers et al., 2015; Qizilbash et al., 2015), we constructed the dementia risk score model based on sex, age, the items on the frailty index (from "Kihon Checklist"), and physical health status (from health checkup).

2.1. Study design and population

We retrospectively collected data of older adults (aged ≥65 years) residing in K city who had answered the Kihon Checklist between April 2011 and March 2012. The data were obtained from the Japan Gerontological Evaluation Study. The Kihon Checklist, which is a self-administered questionnaire developed by the national government, was sent to community-dwelling older adults who had yet to receive LTC eligibility certification. Municipal governments use the results of this checklist to formulate policies aimed to prevent excessive increases in the number of individuals who require LTC services. Between April 2011 and March 2012, the municipal government of K city sent the Kihon Checklist to 142,376 subjects aged 65 years or older and had an even-numbered age at the end of March 2012. We excluded 50,660 individuals due to invalid responses (lack of answers for > 10 items in Q1 to Q20) or failure to return the questionnaire. From the 91,716 remaining respondents, we further excluded 19,589 individuals who had answered the questionnaire later than January 2012. This resulted in a total of 72,127 subjects for analysis. To identify older adults with dementia who eventually became eligible for LTC services, we linked the subjects' data with information on LTC eligibility certification from April 2011 to March 2015.

2.2. Dementia identification

The procedure of LTC certification involves the submission of an application by the candidate or their families to the relevant municipal government (insurer) for care needs assessment including the daily living independence level for people with dementia. Using LTC eligibility certification data, we identified new cases of dementia by assessing the degree of independence in daily living in older adults with dementia (Appendix Table A2) (Kawagoe et al., 2013). This ranking system comprises nine levels, with higher levels indicating more severe dementia. Under this system, people with dementia were identified as those with a rank of IIa or higher.

2.3. Frailty index (Kihon Checklist)

The Kihon Checklist comprises 25 question items, which are presented in Appendix Table A1 (Arai and Satake, 2015). These items assess each subject's instrumental activities of daily living (IADL) (Q1–Q5), physical function (Q6–Q10), nutritional status (Q11–Q12), oral function (Q13–Q15), houseboundness (Q16–Q17), cognitive function (Q18–Q20), and risk of depression (Q21–Q25) (Ministry of Health Labour and Welfare, 2006). Responses that indicate a lack of independence in daily activity or poor physical/mental function were given a value of 1; other responses were given a value of 0. With regard to body mass index (BMI), being underweight has been shown to have a more influential role in frailty (Bucholz et al., 2016). Accordingly, a BMI below 18.5 was used to indicate poorer physical condition.

2.4. Health checkup

Health checkup data were obtained from specific health checkups for 1) enrollees in National Health Insurance, 2) enrollees in Japan Health Insurance Association or Social Health Insurance/Employees' Health Insurance who underwent health checkups administered by the K City Medical Association or H Prefecture Health Service Association, and 3) enrollees in the Medical Care System for Older Adults in the Latter Stage of Life (this system was implemented in 2009 for older adults aged ≥75 years). First, we determined if the subjects underwent a health checkup in 2011, and obtained data on items such as systolic blood pressure, diastolic blood pressure, fasting blood sugar (FBS) levels, hemoglobin A1c (HbA1c) levels, triglyceride levels, high-density lipoprotein (HDL) levels, low-density lipoprotein (LDL) levels, BMI, and waist circumference. Because these health checkups are not compulsory, we included non-participation in the health checkups as a category in these items. Because of > 80% of health checkup participants aged 75 years or older did not measure their waist circumference. Diagnoses of metabolic syndrome were not available in the data, and this condition was not included in analysis.

2.5. Subject characteristics

Subject characteristics included sex and age at the end of March 2012. We categorized age and sex into the following 10 categories: 65–69-year-old female, 70–74-year-old female, 75–79-year-old female, 80–84-year-old female, ≥85-year-old female, 65–69-year-old male, 70–74-year-old male, 75–79-year-old male, 80–84-year-old male, and ≥85-year-old male.

2.6. Statistical analysis

We first conducted descriptive analyses of the 10 age-sex categories, the 25 items of the Kihon Checklist, hypertension (systolic blood pressure > 130 mm Hg or diastolic blood pressure > 85 mm Hg), FBS (> 110 mg/dl), HbA1c (> 5.6% based on the criteria set by the Committee of the Japan Diabetes Society et al., 2010), triglycerides (> 150 mg/dl), HDL (< 40 mg/dl), LDL (> 140 mg/dl), and BMI (< 18.5). These factors were compared between incident dementia cases and non-dementia cases.

The main outcome measure was the identification of dementia through the certification of a rank of IIa or higher (according to the criteria outlined in Appendix Table A2). The follow-up period began when a subject responded to the Kihon Checklist (between April 2011 and March 2012) and ended when they received a certification of IIa or higher or until March 31, 2015, whichever was earlier.

The risk score was developed using an approach similar to those of Kivipelto et al. (2006) and Reitz et al. (2010). Briefly, we conducted Cox hazard regression analyses adjusted by the age-sex categories of each candidate variable, and we identified variables that showed statistical significance for use in the development of three risk score models to predict incident dementia in older adults. We estimated hazard ratios (HRs) and 95% confidence intervals of the independent variables using forward stepwise selection with an entry probability of $F = 0.001$ and a removal probability of $F = 0.01$ in the three models. Receiver operating characteristic (ROC) curve analyses were performed to compare the predictive abilities of the three models. Bootstrap resampling using 5000 replications was conducted to test the models' robustness.

Model 1 focused only on age and sex as the independent variables