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Featured Article

Practical risk score for 5-, 10-, and 20-year prediction of dementia in elderly persons: Framingham Heart Study

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Abstract

Introduction: With a rapidly aging population, general practitioners are confronting the challenge of how to determine those who are at greatest risk for dementia and potentially need more specialized follow-up to mitigate symptoms early in its course. We created a practical dementia risk score and provided individualized estimates of future dementia risk.

Methods: Using the Framingham Heart Study data, we built our prediction model using Cox proportional hazard models and developed a point system for the risk score and risk estimates.

Results: The score system used total points ranging from −1 to 31 and stratifies individuals into different levels of risk. We estimated 5-, 10-, and 20-year dementia risk prediction and incorporated these into the points system.

Discussion: This risk score system provides a practical tool because all included predictors are easy to assess by practitioners. It can be used to estimate future probabilities of dementia for individuals.

Keywords: Dementia; Prediction; Risk score; Risk factor; Framingham Heart Study

1. Introduction

Dementia is a general term used to describe a chronic and/or progressive decline in cognitive and functional ability. It is a disease of worldwide significance; the World Health Organization estimated that 47.5 million people worldwide were living with dementia in 2015 [1]. Along with the difficulties experienced by those living with the disease, dementia places extremely high stressors on caregivers. The economic impact is also substantial; in the United States alone, the health care costs are estimated at 604 billion dollars per year at present and are expected to increase [2]. As a result of these wide-ranging impacts, the medical field has devoted much time and resources in studying the causes and prevention of this disease [1].

Currently, despite substantial efforts, there is no effective treatment for the cure or prevention of dementia [3]. In recent years, attention has turned to the identification of effective early intervention strategies, implemented at a stage when there is the time and potential to modify or slow disease progression [3–5]. The development of a risk profile for dementia is predicated upon evidence that the modification of several potent risk factors will reduce the probability of developing dementia. A similar approach has been followed successfully in the cardiovascular field in the Framingham Heart Study (FHS) in 1970s [6–8], but its application to dementia has been more limited.

In 2006, the Cardiovascular Risk Factors, Aging, and Dementia (CAIDE) study developed a score index to predict the risk of dementia on the basis of risk factor profiles present in middle age [9]. This analysis found that midlife vascular risk

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factors could be combined to predict the risk of dementia, but at that time, there was still a lack of research about other potential types of risk factors that could be used to improve the model and more accurately predict dementia risk in late life. To fill this gap, Barnes et al. developed a dementia risk index for use in late life based on 6 years of follow-up in the larger Cardiovascular Health Study [10]. However, this index includes measures that may not be readily available from all patients, such as cerebral magnetic resonance imaging and Doppler sonography of the carotid arteries [11]. Following these efforts, other researchers focused on developing a simpler risk score to enable primary care clinicians to determine the risk of developing dementia in elderly populations. Using 8 years of follow-up data from a New York-based sample, a score system was developed for predicting late-onset Alzheimer disease risk in elderly individuals using more commonly available measures [11]. More recently, research on dementia risk scores was conducted by analyzing four separate longitudinal cohorts in the United States, including the FHS [12]. This analysis identified high-risk patients by defining a cutoff on scores and targeted this high-risk group as those most likely to benefit from increased cognitive screening in a primary care setting [12]. However, for individual patients and their primary care physicians, it may be more useful to predict their future dementia probability risk with a personalized risk score system. This type of prediction system requires lengthier follow-up data to capture the relevant risk factors and the corresponding dementia incidence. The FHS has monitored the cognitive status of Original Cohort participants since 1976, and detailed dementia surveillance data have been collected over the last 30 years [13–15]. In this study, we purposely centered our analysis on potential predictors that are readily available to the general practitioner (GP), and avoided risk factors, such as APOE status, which are not usually used in general practice to develop a risk score that predicted the 5-, 10-, and 20-year individual dementia risk in older individuals.

2. Method

2.1. Participants

Initiated in 1948, the FHS is an ongoing, multigenerational longitudinal cohort study. At the time of recruitment, the town of Framingham was considered adequately the representative of the US population at that time [16]. Members of the Original Cohort of 5209 residents, which were a 2/3 sample of the entire town population, have undergone biennial examinations, which have included medical history, physical examinations, and laboratory testing since study inception [17]. The first detailed cognitive assessment battery was administered to participants from the Original Cohort between examination cycles 14 and 15 (1976–1978); and the ongoing surveillance for cognitive decline and dementia began with the 15th examination cycle. Therefore, we chose the 15th examination (1977–1979) as baseline and included 30 years of follow-up data in the analysis [18]. To meet the eligibility criteria for this study, participants had to be 60 years or older and dementia free at the time of the 15th examination cycle. All FHS protocols and participant consent forms were approved by the Institutional Review Board of Boston University School of Medicine; all participants provided written informed consent.

2.2. Surveillance for dementia

The dementia-free cohort population was established by screening all participants using a brief neuropsychological test battery 1 year prior and concurrent to the 15th examination cycle [19]. Since 1976, participants' cognitive status has been monitored regularly at cycle examinations, as described in the following.

The Mini–Mental State Examination (MMSE) screening test was administered to participants beginning at the 17th examination cycle [20]. Between 1981 and 1999, a participant was flagged for more detailed cognitive assessment using education-adjusted MMSE cutoffs and also by comparing their MMSE performance at each examination to their own scores at previous examinations. A drop of 3 or more points from an immediately preceding examination or a drop of 5 or more points across all examinations triggered recommendation for further follow-up. Participants were also asked to participate in this additional assessment if they self-reported memory loss, if a family member reported symptoms of memory loss in the participant, or if an FHS physician or study staff member referred them for this assessment. Beginning in 1999 in addition to continued administration of the MMSE at the regular health examination, all surviving members of the cohort were invited for a more extensive cognitive assessment and administered a battery of neuropsychological tests regardless of prevalent cognitive status. The entire cohort continued to be followed for dementia progression until the date of death.

A panel of at least one neurologist and one neuropsychologist reviewed each case of possible dementia. The details of this consensus diagnostic process have been previously described [21].

2.3. Risk factors

Demographic characteristics, lifestyle factors, and medical histories were collected during the 15th examination through self-report questionnaires, and a physical examination was performed by a physician. The candidate risk factors extracted from the 15th examination included the following: age, gender, marital status, weight, height, smoking status, alcohol use, daily consumption of coffee and tea, low-salt diet, and coexisting conditions. Marital status included five categories (single, married, widowed, divorced, and separated).

Height and weight were measured, and body mass index (BMI) (kg/m^2) was calculated. BMI was divided into