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Original Study

Association of Antidementia Drugs and Mortality in Community-Dwelling Frail Older Patients With Dementia: The Role of Mortality Risk Assessment

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A B S T R A C T

Objective: To evaluate whether treatment with antidementia drugs is associated with reduced mortality in older patients with different mortality risk at baseline.
Design: Retrospective.
Setting: Community-dwelling.
Participants: A total of 6818 older people who underwent a Standardized Multidimensional Assessment Schedule for Adults and Aged Persons (SVaMA) evaluation to determine accessibility to homecare services or nursing home admission from 2005 to 2013 in the Padova Health District, Italy were included.
Measurements: Mortality risk at baseline was calculated by the Multidimensional Prognostic Index (MPI), based on information collected with the SVaMA. Participants were categorized to have mild (MPI-SVaMA-1), moderate (MPI-SVaMA-2), and high (MPI-SVaMA-3) mortality risk. Propensity score-adjusted hazard ratios (HR) of 2-year mortality were calculated according to antidementia drug treatment.
Results: Patients treated with antidementia drugs had a significant lower risk of death than untreated patients (HR 0.82; 95% confidence interval [CI] 0.73–0.92 and 0.56; 95% CI 0.49–0.65 for patients treated less than 2 years and more than 2 years treatment, respectively). After dividing patients according to

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The authors declare no conflicts of interest.

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their MPI-SVaMA grade, antidementia treatment was significantly associated with reduced mortality in the MPI-SVaMA-1 mild (HR 0.71; 95% CI 0.54–0.92) and MPI-SVaMA-2 moderate risk (HR 0.61; 95% CI 0.40–0.91, matched sample), but not in the MPI-SVaMA-3 high risk of death.

Conclusions: This large community-dwelling patient study suggests that antidementia drugs might contribute to increased survival in older adults with dementia with lower mortality risk.

In 2013, official death certificates recorded 84,767 deaths from Alzheimer disease (AD), making AD the sixth leading cause of mortality in the United States and the fifth leading cause of death in Americans aged older than 65 years.[1]

Some factors have been associated with a decrease in AD survival.[2–5] On the contrary, symptomatic antidementia drugs, such as acetylcholinesterase inhibitors (AChEIs) (donepezil, galantamine, and rivastigmine) and the N-methyl-d-aspartate receptor antagonist (memantine), can have some beneficial effects in people with AD, such as delay nursing home placement alone [6–8] or in combination[9] and may reduce mortality for patients living in nursing homes and in the community.[10,11] However, these medications are associated with several side effects such as cardiovascular[12] and gastrointestinal[13] events. Therefore, applying the correct prescription indications and identifying patients with AD potentially benefiting from antidementia therapy is a priority.

Decision-making for therapeutic options in older patients with dementia is a major challenge for health practitioners, particularly in frail older patients. In fact, frailty is associated with a greater risk for adverse health-related outcomes[14,15] or cognitive-related outcomes.[16] Mortality risk stratification in frail older patients should be based on information on comorbidity and functional status,[17] possibly using a multidimensional Comprehensive Geriatric Assessment (CGA) that integrates information of several domains of health and function.[18] Recently, a Multidimensional Prognostic Index (MPI) derived from a standardized CGA has been developed and validated for mortality risk assessment in several independent cohorts of hospitalized[19] and community-dwelling older adults[20] with acute or chronic diseases, including older adults with dementia.[21,22]

The main aim of the present observational study was to estimate the all-cause mortality risk linked to antidementia drug use in frail older community-dwelling persons with dementia with a different grade of mortality risk.

Methods

Study Population

This was a retrospective observational study conducted according to the World Medical Association's 2008 Declaration of Helsinki, the guidelines for Good Clinical Practice, and the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[23] All consecutive community-dwelling older adults aged 65 years and older who underwent a CGA-based multidimensional assessment according to the Standardized Multidimensional Assessment Schedule for Adults and Aged Persons (Scheda per la Valutazione Multidimensionale delle persone adulte e Anziane) (SVaMA)[20] from January 1, 2005 to December 31, 2013 were screened for inclusion in the study. Inclusion criteria were: (1) diagnosis of dementia according to the *International Classification of Diseases, Ninth Revision* 290 and subgroups or according to the main diagnosis record P70 of the SVaMA; and (2) a SVaMA evaluation within 2 months from the date of the first registration of the dementia diagnosis in the database. The Institutional Review Board of the Social and Healthcare Local Unit (Unità Locale Socio Sanitaria, ULSS) 16, Padova, Italy approved this retrospective observational study. Informed consent was given by participants who underwent SVaMA evaluation and/or their proxies for their clinical records to be used in clinical studies. All patient records and information were anonymized and deidentified prior to the analysis.

Main Exposure

Antidementia drug users were defined as participants with dementia using donepezil, galantamine, rivastigmine, with or not memantine. The "enrollment" was defined as the first prescription that succeeded the date of the registration of the dementia diagnosis. According to the Italian law, donepezil, galantamine, and rivastigmine are given to patients with a diagnosis of AD and a Mini-Mental State Examination score between 21 and 26, whereas memantine is allowed only if the Mini-Mental State Examination score is between 10 and 20. These medications are prescribed by specialists trained in dementia and monitored by the Italian National Healthcare System. For nonusers, the "enrollment" was defined as the date of the SVaMA completion that succeeded the date of the first registered dementia diagnosis in the database. If the date of SVaMA completion preceded the date of the diagnosis registration, the time interval between these dates was lower than 2 months. Our cohort was linked to the Pharmaceutical Prescription database of the Azienda ULSS 16 Padova to extract the individual medication use. Drug prescriptions were determined according to the anatomic therapeutic chemical codes.

Main Outcome

Participants were followed for a mean follow-up of 2.2 ± 2.1 years. Vital status was assessed by consulting the Registry Offices of the cities in which the patients were residents at the time of the evaluation. Dates of death were identified from death certificates. All data regarding the evaluations were extracted from the Administrative Repository Database of the ULSS 16, Padova, Italy.

The MPI Based on the SVaMA

The SVaMA is the officially recommended multidimensional assessment schedule used by the health personnel of the National Healthcare System to perform a multidimensional assessment in community-dwelling older persons introduced by the Veneto Regional Health System since 2000 to establish accessibility to some healthcare resources (homecare services or nursing home admission).[20] For the purposes of our study, we included people attending nursing homes only because this is the most common reason of accessing SVaMA.[20]

To calculate the MPI, the following domains of the SVaMA were considered: (1) age, (2) sex, (3) main diagnosis, (4) nursing care needs (VIP) evaluated according to a validated numeric scale; (5) cognitive status (VCOG), evaluated by the Short Portable Mental Status Questionnaire (SPMSQ); (6) the pressure sores risk (VPIA), evaluated by the Exton-Smith Scale; (7) the activities of daily living (VADL) and (8) mobility (VMOB) evaluated by the Barthel index; and (9) social support (VSOC), evaluated by a numeric scale of 16 items that explores the presence of a support network during the day and the night.