

EDITORIAL

Cognitive impairment: an (in)dependent risk factor for mortality in older men?

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Awareness of the mortality risk of people diagnosed with mild cognitive impairment (MCI) has recently emerged, increasing scientific interest in the particularities of this neurocognitive syndrome.¹⁻⁴ Mortality in MCI is studied far less than in dementia. Population-based studies have found lower mortality rates than those found in specialized clinics and research settings, which could be due to selection bias and different methods of characterizing impairment.^{2,5} Additionally, while published data on the association between cognitive decline and mortality from high-income countries is abundant, there is little data from low- and middle-income populations.

The results of Campos et al.⁶ provide important detail that higher mortality is associated with cognitive impairment in community-dwelling older adults from a middle-income country. In this interesting and relevant study, a branch of the Bambuí Cohort Study of Aging,⁷ 1,281 older adults from a small rural town in southeastern Brazil were followed for 13.3 years. The large sample size, the fact the investigators sought to include the entire older adult population of the study area, and the long observational time are clear strengths. The investigators managed to collect baseline data on cognitive and clinical parameters and explored the association between different severity levels of cognitive impairment and long-term mortality risk. A positive association was found between moderate cognitive decline, male gender, and higher mortality rates. The authors stratified the severity of cognitive impairment according to standard deviation patterns of Mini-Mental State Examination scores. Mild and moderate cognitive impairment were respectively defined by scores of -1.0 and -2.0 standard deviations below the cutoff means. The default procedure when ascertaining the severity of cognitive decline and establishing a dementia diagnosis must also rely on functionality parameters, such as performing activities of daily living. Although the authors did investigate functional impairment in abilities such as dressing, walking across a room, bathing/showering, eating, getting in/out of bed, and toilet use, this data was not specifically contemplated for discriminating between degrees of cognitive impairment. Nevertheless, moderately impaired participants, as defined by Mini-Mental State Examination scores, had a higher prevalence of

functional disability (28.6%) than those with MCI (13.5%) or those who were unimpaired (8.8%) ($p = 0.003$).

Another important methodological aspect was that cognition was only assessed upon enrollment using screening instruments. No longitudinal follow-up data on cognition and functional status was performed. MCI is a heterogeneous syndrome that could involve underlying neurodegenerative diseases,⁸ but may also be due to potentially reversible conditions, such as depression, vitamin deficiencies, or metabolic (e.g. thyroid) disorders. Although this limitation must be taken into account, previous populational studies have used similar methodologies to address long-term mortality risks in mild and moderate cognitive decline.⁴ Sub-categorizing MCI by its distinct endophenotypes (i.e., amnesic vs. non-amnesic, single- vs. multiple domain MCI) could provide important details about the association between mortality and specific underlying etiologies. In fact, one longitudinal study compared mortality rates from 1,292 healthy participants and 862 participants with MCI, which was stratified according to the number and type of affected cognitive domains.² A higher overall mortality risk was found in the MCI group than healthy controls, as well as in the non-amnesic vs. amnesic MCI group. Male gender, lack of physical activity, and a history of heart disease (which suggests the importance of the vascular disease burden) were also associated with higher mortality risk.

With respect to baseline socio-demographic features, the three cognitive impairment groups (none, mild, and moderate) were significantly different ($p < 0.0001$) concerning age and education. Participants with mild and moderate cognitive impairment were older, while the percentages of those with less than four years of education were 59.5%, 93.6%, and 95.2%, respectively, for subjects with no, mild, and moderate cognitive dysfunction. A number of clinical characteristics also deserve attention. There were statistically significant differences ($p < 0.0001$) among groups with no, mild, or moderate cognitive dysfunction regarding *Trypanosoma cruzi* infection (34.4, 54.8, and 76.2%, respectively) and depressive symptoms (34.9, 47.6, and 76.2%, respectively). *T. cruzi* infection is endemic to rural southeastern Brazil (where the study was conducted) and is a major cause

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of Chagas cardiomyopathy. Therefore, there is a likely association between *T. cruzi* infection and cognitive impairment, given the well-established association between congestive heart failure and cognitive impairment.⁹ In fact, previous studies from the same Bambuí cohort indicated that *T. cruzi* infection is associated with cognitive impairment in older adults.¹⁰ Therefore, mortality in cognitively impaired members (both MCI and dementia patients) of this cohort might represent an underlying effect of chronic heart disease, although there were no significant differences between the study groups regarding cardiovascular disease factors. Regarding late-life depression, however, there is profuse evidence in the literature indicating that depression in older adults is largely associated with cognitive impact and increased rates of deterioration and mortality.¹¹

The authors recognized the above-mentioned disparities, and, after adjusting for socio-demographic, lifestyle and health parameters, the study's main finding was that male patients with moderate cognitive decline have a higher mortality risk. This finding underscores the importance of MCI prevention, investigation and treatment when modifiable risk factors are identified. Moreover, the study highlights specific characteristics found in a rural Brazilian population of older adults. This could serve as an encouragement for new future initiatives to determine the associations between cognitive status and long-term outcomes, such as mortality risks, in middle- and low-income countries.

Disclosure

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