Cognitive scores, even within the normal range, predict death and institutionalization

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Abstract

Background: dementia is a predictor of death and institutionalization. It is less clear if variations in cognition within the normal range predict adverse outcomes.

Objective: to determine if variation at the high end of cognitive test scores predicts mortality or institutionalization, independent of the effect of potential confounders.

Design: secondary analysis of the Canadian Study of Health and Aging, a population-based longitudinal study with an initial data collection in 1991 and follow-up five years later.

Setting: community-dwelling seniors living in Canada.

Participants: 9008 consenting seniors were sampled from representative population registries in Canada.

Measures: age, gender, marital status, the Mini-Mental State Examination, self-rated health, and activities of daily living.

Outcomes: death or institutionalization over the five years of follow-up.

Results: Mini-Mental State Examination scores predicted mortality and institutionalization. The unadjusted odds ratio of mortality was 0.85 (95% confidence interval 0.84, 0.86) per point on the Mini-Mental State Examination, and the adjusted odds ratio was 0.95 (95% confidence interval 0.93, 0.97). The unadjusted odds ratio for institutionalization was 0.83 (95% confidence interval 0.82, 0.85), and the adjusted odds ratio was 0.91 (95% confidence interval 0.90, 0.94). This effect was present even in analyses restricted to those within the normal range of Time 1 Mini-Mental State Examination scores.

Conclusions: low normal cognitive test scores predict adverse outcomes. Clinicians should consider close clinical follow-up of those with low normal cognitive test scores. Further research is needed to target seniors for follow-up and possible intervention to decrease mortality and institutionalization risk.

Keywords: elderly, cognition, mini-mental state examination, mortality, institutionalization

Introduction

Cognitive impairment has a high prevalence in the elderly, especially in the oldest old. Approximately one third of those with cognitive impairment suffer from dementia [1] and these persons have a higher mortality [2–5] and exhibit progressive cognitive and functional deterioration [6]. Those with dementia are also at higher risk of nursing home placement [7–10]. Cognitive impairment with no dementia (CIND) is also common in the elderly. This is a constellation of disorders associated with poor cognitive test scores which do not meet the criteria for a diagnosis of dementia. It includes a variety of conditions which interfere with cognition or cognitive status testing, such as delirium, psychiatric problems, social isolation, and low intellect [11]. Persons with low cognitive test scores but no dementia have poor health outcomes, including a higher probability of mortality, institutionalization, and development of dementia [12]. This association appears to be independent of other health factors.

In summary, it is clear that abnormal cognition predicts mortality [13–17]. Traditionally, interventions directed at preserving health and function have been aimed at this group. However, there may be a gradient in risk across the entire range of cognitive test scores: variations in cognitive test scores even at the high end of the range may predict death, or other adverse outcomes.
If this is the case, there are large numbers of seniors with low normal cognition who might potentially benefit from interventions to improve cognition and functioning.

The objectives of this study are to use a secondary analysis of an existing data set: i) to determine whether scores within the normal range of the Mini-Mental State Examination (MMSE) predict death and institutionalization; and ii) to determine if these associations are independent of potential confounders such as age, functional status, and health status.

Methods
The sample
The Canadian Study of Health and Aging [1] is a longitudinal, population based epidemiological study whose original objectives were to determine the prevalence, incidence, risk factors and patterns of care for people with dementia in Canada. Supplementary objectives covered broader aspects of health and disability among elderly Canadians. The study began in 1991 (CSHA-1); the first follow-up began in 1996 (CSHA-2).

In CSHA-1, representative samples of people aged 65 or over on October 31, 1990 were drawn in 39 urban and surrounding rural areas in the ten Canadian provinces. The study involved 9,008 people from the community and 1255 from long-term care institutions; this paper considers only the community sample. The community sampling frame was based on the Canadian provincial universal health insurance plans, with the exception of Ontario, where technical limitations with the health insurance plan list at the time prevented its use. Here, we used the Enumeration Composite Record, a composite list of all citizens in Ontario based on electoral lists, updated between elections from information such as property sales. The response rate in the community was 72.1%.

The same approach to data collection was used in both phases of the study. In the community, participants were interviewed in their homes; the interview covered general health, functional status, and social circumstances. Cognitive status was assessed using the Modified Mini-Mental State Examination (3MS) [18]. A clinical examination was performed on all those who scored below 78 on the 3MS, plus a random sample of those who scored 78 or above. The clinical examination included neuropsychological testing, an informant interview, a physical exam, and clinical history.

In CSHA-2, participants were followed. Seven hundred and twenty people in the community sample could not be contacted or declined to participate. For those who had died, information on date and cause of death were obtained from a proxy respondent. All others were re-interviewed and examined using the same methods as in CSHA-1.

The sample for these analyses includes the 8512 community residents who had complete data at CSHA-1 and who were not lost to follow-up at CSHA-2. The multivariable analyses include only those with complete data for all Time 1 variables. Reasons for non-inclusion in these analyses include loss to follow-up, refusal to participate, unable to participate, or missing data. Those who were excluded had lower Time 1 MMSE scores. Had they been included, it is likely that the effects we observed would have been stronger. The study was approved by local institutional review boards at all participating study sites, and was in compliance with the Declaration of Helsinki.

Measures
Time 1 predictors
The 3MS [18] was used as the cognitive screening test for cognitive impairment and dementia. However, we also asked questions to allow the calculation of an MMSE [19, 20] score. Since the MMSE is more widely used than the 3MS, we present these analyses here.

Functional status was based on self-report and was assessed using the 7-item Activities of Daily Living (ADL) and the 7-item Instrumental ADL (IADL) scales from the Older American Resources Utilization Study [21]. For our analyses, each item was scored either as 1 (can perform without help) or 0 (needs assistance or unable to perform.) Summated scores, ranging from 0–7 were calculated for the ADL and IADL scales. Self-rated health was assessed using a 5-point scale ranging from very good to poor; this too was taken from the Older Americans Resources Utilization Study [21]. For these analyses, self-rated health was dichotomized as either 1 (very good and good) or 0 (not too good, poor and very poor).

Education was measured as number of years of completed schooling; age is in years. Marital status was classified as never married, previously married (widowed, divorced and separated), and currently married.

Outcome measures
Mortality was coded as either 1 (deceased by the end of CSHA-2) or 0 (alive at the end of the study). Similarly, institutionalization was coded as either 1 (institutionalized during the study period) or as 0 (remained in community). In Canada, nursing homes are not used for post-hospitalization convalescence, and very few people who are institutionalized return to the community.
Statistical analyses

Analysis of mortality and institutionalization: all participants for whom complete data were available were included in this analysis. Associations between the Time 1 variables and mortality or institutionalization were studied using Student’s t-test assuming unequal variance, and Chi-square tests. To adjust for the effect of confounding variables, logistic regression models were constructed. Covariates included age, gender, education, Time 1 MMSE, and self-rated health. Continuous variables were entered directly into the model, while categorical variables were entered as dummy variables. Models were constructed both by forcing all variables into the model, and by backwards stepwise selection of variables, which gave similar results. Since there was considerable collinearity between the initial MMSE score and education, sensitivity analyses were conducted, with education excluded from the model.

Models were constructed for the entire population. Models were also constructed for a restricted population with MMSE scores within the previously established normal range (scores of 24–30). We subsequently repeated all analyses using the 3MS score instead of the MMSE.

Results

At Time 1, 60% of the sample were women; the average age was 75.7 years; 20.4% completed the study in French and 79.6% in English. The mean education was 10.2 years. At follow-up, 24.3% of the sample had died; 12.4% had been institutionalized. These were not mutually exclusive events: 4.4% were institutionalized during the study period, and subsequently died.

Figure 1 shows the relationship of initial MMSE score to mortality for the entire range of MMSE scores. There is a clear gradient in this effect, with those scoring lower having higher mortality. For each point increase on the MMSE, the unadjusted odds of mortality was 0.85 (95% confidence interval (CI), 0.84, 0.86). Multi-variable models are presented in Table 1. After controlling for age, gender, education and self-rated health, the association between cognition and mortality remained statistically significant: the adjusted odds ratio (OR) for mortality was 0.95 (95% CI, 0.93, 0.97). Since this represents the decreasing risk per point of the MMSE, over the entire scale, the effect is quite large. We also conducted analyses restricted to those with normal initial Time 1 scores, which gave similar results. Analyses using the 3MS score gave similar results.

Figure 2 shows the relationship of initial MMSE scores to subsequent institutionalization. Again, even after controlling for confounding variables, the association between MMSE score and institutionalization remained significant, with an OR of 0.91 (95% CI 0.90, 0.94). Analyses using the 3MS score gave similar results.

Discussion

Our results demonstrate a strong association between cognition and adverse outcomes; this extends across the entire range of the MMSE score. This association...
Table 2. Odds ratio of institutionalization from multivariable models, in the entire sample, and in those with an MMSE of greater than 23 at Time 1. The Odds Ratios represent the adjusted risk of institutionalization per point on the MMSE. Even after accounting for the effect of age, gender, education, and health and functional status, the MMSE score predicted institutionalization

<table>
<thead>
<tr>
<th></th>
<th>Entire population (n=8073)</th>
<th>Normal MMSE score (n=6934)</th>
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<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.09 (1.08, 1.11)</td>
<td>1.10 (1.08, 1.11)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1.02 (0.86, 1.21)</td>
<td>1.15 (0.93, 1.42)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>0.99 (0.97, 1.01)</td>
<td>0.97 (0.95, 1.00)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>0.91 (0.70, 1.20)</td>
<td>0.92 (0.67, 1.28)</td>
</tr>
<tr>
<td>Married</td>
<td>0.65 (0.54, 0.78)</td>
<td>0.62 (0.50, 0.77)</td>
</tr>
<tr>
<td>Divorced/separated/widowed</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Basic ADL impairment (number of impairments)</td>
<td>1.07 (0.97, 1.07)</td>
<td>1.14 (1.01, 1.29)</td>
</tr>
<tr>
<td>Instrumental ADL impairment (number of impairments)</td>
<td>1.21 (1.15, 1.28)</td>
<td>1.27 (1.19, 1.36)</td>
</tr>
<tr>
<td>Self-rated health (good vs not good)</td>
<td>1.23 (1.03, 1.47)</td>
<td>1.36 (1.10, 1.69)</td>
</tr>
<tr>
<td>MMSE Score at Time 1</td>
<td>0.91 (0.90, 0.94)</td>
<td>0.88 (0.83, 0.93)</td>
</tr>
</tbody>
</table>

Odds ratios are adjusted for the effects of other confounding variables. Please note that for continuous variables, the odds ratios represent the increased (or decreased) risk for each unit of change in the predictor.

Our findings also corroborate previous observations about predictors of death. We observed that men had a higher mortality, and we observed the powerful effect of self-rated health status [24] and functional impairment on mortality. Surprisingly, we observed no effect of level of education on mortality or institutionalization once we adjusted for cognitive test scores. However, in models with education, but not MMSE scores, education had a strong effect on mortality or institutionalization. It is possible that the effect of education is exerted through cognition: those with a high educational attainment have higher cognitive test scores, and lower mortality and institutionalization rates. However, it is more likely that the effects of education are masked by the collinearity between education and cognition, making the regression models difficult to interpret.

Limitations

There may be other confounding variables that we did not measure, or measured incompletely. We did not examine attitudes to health, lifestyle behaviours, or sense of control, nor have we measured the impact of specific disease states or socioeconomic status (SES). It is well known that cognitive test scores vary across socioeconomic levels [25, 26] and that SES is associated with mortality. Finally, there was some bias in persons who were unable to be included in the analyses. Those who were not included had lower Time 1 MMSE scores. However, if they were included, it is likely that the associations which we observed would have been stronger rather than weaker.

An alternative explanation for the associations we observed is that cognitive decline is an epiphenomenon of comorbid medical conditions: cognitive scores may be a symptom of an underlying pathology that was subsequently fatal. However, this alternative explanation does not undermine the potential predictive value of cognitive scores, or the value of using a brief cognitive screen in the clinical setting to identify those at risk. The fact that this association persisted even after controlling for some known risk factors underscores the value of a cognitive screening test.

Interpretation

Our results show that cognitive test scores predict mortality and institutionalization. However, we do not propose that this association is necessarily causal. Indeed, it is unlikely that the increased mortality we have observed is due to dementia: incident cases of dementia are unlikely to have died in the five-year study interval.

The finding that low normal cognition predicts poor outcomes is important for clinicians. Traditionally, interventions have targeted seniors with definite cognitive impairment. But the benefits of intervention may extend to those with low normal cognition. Further
research is needed into identifying those persons with low normal cognition who are at risk for progression of cognitive loss and death. As well, further research is needed into interventions which may benefit this group.

A second implication of our findings is to reconsider the common interpretation of cognitive test scores. Traditionally, cognitive screening tests such as the MMSE and 3MS assumed a threshold below which is considered cognitive impairment and above which is considered normal. As the risk of adverse outcomes increases with decreasing cognitive ability over the entire scale, a single cut-point may be misleading. Several articles have discussed the virtues of setting variable cut-points [27–31]. It may be reasonable for clinicians to consider cognitive scores as a continuous risk for adverse outcomes, as is done for other parameters, such as blood pressure.

**Key points**

- Cognitive test scores predict mortality in community-dwelling seniors: this effect is a gradient extending into the normal range.
- Cognitive test scores predict institutionalization in community-dwelling seniors: this effect is also a gradient extending into the normal range.
- These associations persist after adjustment for age, gender, functional status, and self-reported health.

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**References**


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