Behavioral Symptoms Improve Prediction Models of Mortality in Patients With Dementia

To the Editor: The recent cohort study by Cheng et al[1] that focused on mortality predictors in Taiwanese patients with dementia yielded interesting results. The long follow-up period is a strength of the study. The authors chose a prediction model in which comorbidities and demographic variables were included in the analysis. In the Cox regression model, the use of antipsychotic drugs was not associated with mortality (hazard ratio = 1.09; 95% CI, 0.98–1.22).[1] This result helps clarify the controversy regarding an association of antipsychotic use and mortality in patients with dementia. I agree that there is not enough evidence to support this association, as was stated in a systematic review of mine published last year.[2] The lack of association of antidepressants with mortality is also reassuring and in agreement with a previous report.[3]

Although the prediction model presented is useful for clinicians, I would have welcomed a model including any scale measuring behavioral disturbances (depression, agitation, aggression, hallucinations), which are highly prevalent and predictive of mortality.[2–6] It would also be interesting to know the proportion of patients with Alzheimer's type dementia and that of other types of dementia to compare the results with those of the cohorts from Western countries. It seems that vascular dementia is more frequent in Asia than in these countries.

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Dr Cheng and Colleagues Reply

To the Editor: We thank Dr Modrego for the response to our article.[1] We acknowledge that Drs Modrego and Lobo, in their systematic review,[2] stated that there is still not enough evidence to conclude that a link exists between antipsychotic use and mortality in dementia patients. Confounding factors may limit the results of observational studies investigating this question, but randomized controlled trials may fail to reflect real-world clinical situations because of their inclusion and exclusion criteria.[3] A similar limitation also exists for investigations of the association between antidepressant use and mortality in dementia patients. To date, findings regarding the impact of antidepressants on mortality in dementia patients have been inconsistent.[1,4–6]

On the other hand, the presence of behavioral and psychological symptoms of dementia (BPSD) may be a valuable factor in predicting mortality in dementia patients.[2] For example, agitation and aggression may cause head trauma or fractures due to falls and therefore increase the risk of death.[7] Lopez et al[7] found that the increased risk of death in patients with probable Alzheimer's disease was associated with the presence of psychiatric symptoms rather than exposure to antipsychotics. Our registry database, the National Health Insurance Research Database, did not provide information about BPSD or neuropsychiatric inventory results. Consequently, we could not evaluate the influence of these factors. However, the severity and type of BPSD may change over time.[8] BPSD symptoms may elevate the risk of falls and fracture events, which were evaluated as the factor "femoral neck fracture" in our article.[1]

The proportions of patients with Alzheimer's type dementia (*ICD-9* code = 331.0) and vascular type dementia (*ICD-9* code = 290.4) in the derivation cohort were 9.9% and 15.9%, respectively. We performed another analysis to add those factors of different dementia types into our Cox proportional hazards regression model, which was equal to the creating process described in our article.[1] The results showed that neither Alzheimer's type nor vascular type dementia was significant as a factor for the final variables selection (vascular type: $P = .79$, Alzheimer's type: $P = .974$) compared with other predicting variables. This result was generally in accord with previous findings. In a brain neuropathology study, the authors found few dementia cases that did not have a mixed component of both Alzheimer's-type pathologies and vascular lesions.[9] According to the literature, although vascular dementia may be associated with a slightly higher mortality rate, the excess mortality in patients with certain stroke features may be driven greatly by cardiovascular disease outside the brain.[10,11] Stroke or vascular dementia may demonstrate a phenomenon of worse generalized vascular disease that is not specific to the brain. More investigations will be required to clarify if type of dementia (especially vascular and Alzheimer's type dementia) impacts significantly as an independent predictor in the prediction model with adjustment for comorbidity variables (ie, competing mortality risks).

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