

Point of View

Potential modifications on verbal-language/orientation-memory ratio from Addenbrooke's cognitive examination III to predict mild cognitive impairment from healthy controls

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Dear Sir,

With an increase in the global burden of dementia,^[1] screening and diagnostic tools for early diagnosis is of paramount importance. At present, the biomarkers being explored for early diagnosis of dementia includes cerebrospinal fluid biomarkers like amyloid- β , total tau, and phosphorylated tau, genetic biomarker like Apolipoprotein E,^[2] and neuroimaging biomarkers such as amyloid and tau imaging.^[3] However, these biomarkers are costly, invasive, time-consuming, and not widely available or accessible. Furthermore, it is difficult to implement them as screening tools at a population level.

Addenbrooke's Cognitive Examination III (ACE III) is a neuropsychological test that screens the major cognitive domains such as attention, language, learning and memory, verbal fluency and visuospatial function. It has previously been used as a screening tool in detection of dementia at early stages.^[3] ACE III has also been standardized across seven regional languages. In a study by Mathuranath *et al.* an earlier version of ACE was used to differentiate Alzheimer's disease (AD) and frontotemporal dementia (FTD) by deriving the verbal-language/orientation-memory (VLOM) ratio demonstrating that the orientation, attention, and memory were worse in patients with AD whereas language functions were more impaired in patients with FTD.^[4] A study by Bruno and Vignaga (2019) demonstrated that ACE III had high diagnostic accuracy for mild cognitive impairment (MCI).^[5] However, the VLOM ratio derived from the current version of ACE which is ACE III-R, has not yet been validated.

A similar attempt has been made here to explore the utility of VLOM ratio modifications for prediction power in detecting MCI instead.

We considered the possibility of modifying VLOM ratio to language and memory (L/M) ratio in order to explore such an

analysis. Instead of adding verbal and orientation components in the ratio, we are only taking L/M ratio. Since Memory is a more predominant factor in clinical dementia rating (CDR) scale,^[6] it is expected that people with CDR 0.5 will have a lower Memory score and hence the L/M ratio could be potentially used to differentiate between MCI and normal. Moreover, language has been shown to be relatively more intact in MCI as compared to memory.^[7] Also using only L/M makes the test easier to conduct since only two cognitive domains are required to be evaluated as compared to four in VLOM ratio.

A cross-sectional analysis was performed using the baseline data from the Tata longitudinal study of ageing based in urban Bengaluru, India.^[8] CDR was used to classify participants into normal cognition (CDR = 0) and MCI (CDR = 0.5) category. ACE III-R was administered and L/M ratio was calculated for all participants. A Random Forest Model using scikit learn^[9] in python was built with VLOM ratio and L/M ratio respectively and the area under the precision recall curve (AUC PR) was calculated in order to compare the relative performance of each of the metric. We used random undersampling from the normal participants to account for data imbalance between normal and MCI participants.

Among 953 participants, 69 (7.24%) had MCI and 884 (92.75%) participants had normal cognition. An L/M ratio PR AUC of 0.13 [Table 1] was obtained indicating that L/M ratio might have utility of differentiating MCI and Normal as compared to VLOM if further study is done with more confounders.

Hence, the modifications on VLOM ratio derived from ACE III-R can be explored in order to have a potential utility as a screening tool to identify people who may develop major neurocognitive impairment in the future. In our cohort, we demonstrate that VLOM ratios from ACE III-R when modified as L/M ratio might have good prediction accuracy

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Table 1: L/M ratio prediction evaluation for MCI versus healthy controls.

Metric	PR curve AUC
L/M ratio	0.13

MCI: Mild cognitive impairment, AUC: Area under the curve, PR: Precision recall

in differentiating between healthy controls versus MCI. However, further studies using ACE III-R are necessary to construct a better model with more confounders.

The significance of a simple clinical bedside tool which have the additional benefit of being able to be administered even by the non-clinical health care personnels such as VLOM ratio and L/M ratio cannot be overlooked. Hence the applications of VLOM ratios and its potential modifications in differentiating different cognitive states can be beneficial due to its simple nature of applicability and usability.

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Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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