Original Article

Evaluation of Vascular Cognitive Impairment using the ICMR-Neuro Cognitive Tool Box (ICMR-NCTB) in a Stroke Cohort from India

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Abstract

Background and Purpose: Vascular cognitive impairment (VCI) presents with a spectrum of cognitive impairment due to stroke and poses a huge socioeconomic burden especially in low middle-income countries. There is a critical need for early recognition and identification of VCI patients. Therefore, we developed and validated culturally appropriate neuropsychological instruments, the ICMR-Neuro Cognitive Tool-Box (ICMR-NCTB) and Montreal Cognitive Assessment (MoCA) to diagnose vascular MCI and dementia in the Indian context. **Methods:** A total of 181 participants: 59 normal cognition, 25 stroke with normal cognition, 46 vascular MCI (VaMCI) and 51 vascular dementia (VaD) were recruited for the study. The ICMR-NCTB and MoCA were administered to patients with VCI and major cognitive domains were evaluated. **Results:** The ICMR-NCTB was found to have good internal reliability in VaMCI and VaD. The sensitivity of the ICMR-NCTB to detect VaMCI and VaD ranged from 70.8% to 72.9% and 75.9% to 79.7%, respectively, and the specificity for VaMCI and VaD ranged from 84.8% to 86.1% and 82.5% to 85.2%, respectively. The MoCA had excellent sensitivity and specificity to detect VaMCI and VaD at ideal cut-off scores. **Conclusion:** The ICMR-NCTB is a valid neuropsychological toolbox that can be used for comprehensive cognitive assessment and diagnosis of VCI in India. In addition, the Indian version of MoCA is more adept as a screening instrument to detect VCI due to its high sensitivity. The ICMR-NCTB will aid in early detection and management of many patients, thereby reducing the burden of vascular MCI and dementia in India.

Keywords: Cerebrovascular disorders, stroke, validation study, vascular cognitive impairment, vascular dementia, vascular mild cognitive impairment

Introduction

Vascular cognitive impairment (VCI) represents a range of cognitive impairment due to cerebrovascular disease and/or stroke to subclinical vascular brain injury.[1] VCI includes a wide spectrum of disorders from a severe form of vascular dementia (VaD) to milder forms of cognitive impairment referred to as vascular mild cognitive impairment (VaMCI).[2] VaD is the second common cause of late onset dementia and accounts for approximately 30% of dementia in low middle-income countries including India[3] and relatively lower prevalence of 15%-20% of dementia in developed countries.[4] The onset and severity of VCI is a variable depending on the clinical characteristics and stroke severity, with prevalence over one-third of severe strokes compared to only 8% of minor strokes[5] and 5% of transient ischemic attacks.[6] VCI is reversible in ≤20% of patients with stroke, with the highest rate of recovery seen shortly after stroke.[7] The reported absolute risk for dementia after stroke ranges from 7% in population-based studies to more than 40% in hospital-based studies.[6]

Various cognitive functions such as executive functioning, processing speed, delayed recall of word lists, and visuospatial functioning are impaired in patients with VCI.[8] Pattern of cognitive impairment depends on the type of vessel involved in stroke: small-vessel dementia commonly presents with executive dysfunction and large-vessel dementia presents with visuospatial and language dysfunction.[9] VCI can exert major influences on long-term occupational functioning, can adversely affect functional ability of an individual,[1] and is a strong predictor of death.[10] It poses a huge economic and social burden in developing countries.[11]

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Assessment of VCI requires valid neuropsychological protocols that are sensitive and reliable to specific cognitive deficits in the context of vascular etiologies. Considering the clinical importance of VCI, the National Institute for Neurological Disorders and Stroke and Canadian Stroke Network (NINDS-CSN) developed and validated the NINDS-CSN neuropsychological battery for early identification and diagnosis of VCI.[12] Currently, NINDS-CSN has been validated in Korean,[13] Mandarin,[14] French,[15] and Chinese[16] languages in stroke and transient ischemic attack patients. As vascular risk factors or diseases are modifiable and treatable,[17] early recognition and identification of VCI is of utmost importance in the management of these patients. Standardized cognitive test battery for the assessment of VCI in diverse sociodemographic and multilingual societies such as India will assist in predicting a response to rehabilitation and long-term occupational outcomes. Recently, the Indian Council of Medical Research-Neurocognitive Toolbox (ICMR-NCTB) was validated in five Indian languages for the diagnosis of dementia and MCI.[18,19] Considering the need for a culturally appropriate and validated battery for the assessment of VCI in the Indian context, the objectives of the present study were (1) to determine the utility of ICMR-NCTB to diagnose vascular MCI (VaMCI) and VaD in the Indian context; (2) to validate the ICMR-NCTB in age and education-matched VaMCI and VaD groups using a composite cut-off score; and (3) to validate Indian MoCA and establish its sensitivity and specificity to detect VaMCI and VaD.

Methods

The study was brought together by the ICMR-NCTB (ICMR-Neuro Cognitive Tool Box) consortium involving a large group of experts and specialists across India. The consortium collaborated toward adapting and developing a comprehensive cognitive test battery, the ICMR-NCTB, in five Indian languages (Hindi, Bengali, Telugu, Kannada, and Malayalam) that includes various tests and questionnaires assessing cognition, functional activities, behavior, and quality of life.[20]

In this cross-sectional study, participants were recruited from 2014 to 2017 to validate the ICMR-NCTB for diagnosis of stroke from different linguistic zones across India: All Indian Institute of Medical Sciences in Delhi, Apollo Gleneagles in Kolkata, Nizam's Institute of Medical Sciences in Hyderabad, National Institute of Mental Health and Neuro Science in Bangalore, Manipal Hospital in Bangalore, Jawaharlal Nehru Medical College in Belgaum, and Sree Chitra Tirunal Institute for Medical Science and Technology, Trivandrum.

Participants were recruited based on the following criteria: >40 years of age, willingness to participate, having no evidence of traumatic brain injury, infectious diseases, neurological diseases or neurodegenerative diseases, no history of serious medical or psychological problems, and no significant hearing or visual impairment that could interfere with cognitive assessment. Expert neurologists and neuropsychologists evaluated healthy participants and patients with detailed clinical history, physical examination, review of investigations, and neuropsychological testing: Clinical Dementia Rating scale (CDR),[21] Addenbrooke Cognitive Examination-III (ACE-III),[22] Rey Auditory Verbal Learning Test (RAVLT),[23] and Color Trails Test (CTT),[23] Participants were then classified into the following groups based on the uniform diagnostic process:

1. *Healthy controls*: All participants who scored normally on the ACE-III, CDR, RAVLT, and CTT and had no subjective cognitive complaints.
2. *Stroke with normal cognition*: Based on clinical evaluation and brain imaging (computed tomography and/or magnetic resonance imaging), all participants were diagnosed to have stroke and performed normally on the ACE-III, CDR, RAVLT, and CTT.
3. *Vascular MCI (VaMCI):* Those participants who have had a stroke and met the Internationlal Society for Vascular Behavioral and Cognitive Disorders (VASCOG) criteria.[24]
4. *Vascular dementia (VaD):* Those patients who have had a stroke and met the National Institute of Neurological Disorders and Stroke (NINDS) and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) criteria.[25]

A total of 181 participants were recruited: 59 participants with normal cognition, 25 stroke with normal cognition, 46 vascular MCI (VaMCI), and 51 VaD. The ICMR-NCTB was administered to all participants and major cognitive domains were evaluated: (a) *global cognitive function*: Montreal Cognitive Assessment (MoCA)[26]; (b) *attention-executive functions*: Trail Making Test A & B (TMT A & B)[27] and category fluency[18]; (c) *episodic memory*: Verbal Learning Test (VLT)–total learning, delayed recall, and recognition,[28] and Modified Taylor Complex Figure test - Delayed Recall (MTCF-DR)[29]; (d) *language*: Picture Naming Test (PNT);[18] and (e) *visuospatial skills*: Modified Taylor Complex Figure test–Copy (MTCF-Copy). Participants were also administered with the language use questionnaire to determine the testing language for each participant.[30] The process of the development and validation of the ICMR-NCTB across five languages, participant recruitment across centers, and sample size estimation has been reported previously.[20]

Statistical analysis

All statistical analyses were performed with the use of SPSS Statistics for Windows, version 16.0. Continuous data were expressed as mean and standard deviation (SD) and analyzed using analysis of variance to compare healthy controls, stroke with normal cognition, VaMCI, and VaD patients. If there was a significant difference on analysis of variance, the Bonferroni correction was used and Tukey post hoc test was done. The Chi-squared test was used to assess the categorical data. Internal consistency was measured using Cronbach's Alpha coefficient. To determine the external validity of

ICMR-NCTB, test scores were converted to standardized z-scores adjusting for stratified age and education bands in each language separately. The TMT time scores were multiplied by -1 after standardization. A composite score was calculated from the averaged z-score, based on which a valid cut-off point for classifying patients with VCI was established using receiver operating characteristic (ROC). The area under the curve (AUC) was developed to measure diagnostic power and to reflect the probability of a test to correctly identify patients with cognitive impairment. At an optimal cut-off point, the sensitivity and specificity were established. A value of $P < .05$ was considered as statistically significant.

Results

A total of 181 participants were recruited: 59 participants with normal cognition, 25 stroke with normal cognition, 46 VaMCI, and 51 VaD. Participants were matched for age and education across the four diagnostic groups. The mean age of healthy controls, stroke with normal cognition, VaMCI, and VaD were 63.66 ± 11.99 years, 57.48 ± 9.32 years, 61.37 ± 12.48 years, and 63.92 ± 11.17 years, respectively. The corresponding years of education were 11.75 ± 3.63, 13.80 ± 3.97, 12.00 ± 3.48, and 11.90 ± 3.23, respectively. The demographic characteristics of each diagnostic group are summarized in Table 1. The proportion of male participants were higher in stroke with normal cognition group (92.0%) than healthy controls (62.7%), VaMCI (82.6%), and VaD (74.5%). Of 181 participants, 141 were urban dwellers (77.95%). The gold standard cognitive and behavioral test scores of participants across the four diagnostic groups are presented in Table 2. The mean scores of ACE-III were significantly different across the diagnostic groups ($F_{3, 169} = 65.28$, $P < .001$). Among the patient groups, stroke with normal cognition scored higher ACE-III scores (mean = 89.93, SD = 5.88) and VaD patients scored the lowest (mean = 65.34, SD = 13.37). In post hoc analysis, the mean score of ACE-III was significantly different between healthy controls vs. VaMCI ($P < .001$); healthy controls vs. VaD ($P < .001$); stroke with normal cognition vs. VaMCI ($P < .001$); stroke with normal cognition vs. VaD ($P < .001$); and VaD vs. VaMCI ($P < .001$).

The mean scores, SD, and *P* values of cognitive tests of the ICMR-NCTB are detailed in Table 3. Healthy controls scored higher on all the ICMR-NCTB tests compared to other diagnostic groups. Among the four diagnostic groups, VaMCI and VaD patients took more time on the TMT A and B and scored lower on category fluency than healthy controls followed by stroke patients with normal cognition, indicating a significant impairment in their attention and executive functioning (*TMT A:* $F_{3, 164} = 13.42$, $P < .001$ *TMT B*: $F_{3,163} = 3.38$, $P = 0.020$ and *category fluency*: $F_{3,174} = 15.69$, $P < .001$). Similarly, patients with VaMCI and VaD performed poorly on VLT (total learning, delayed recall, and delayed recognition), PNT, and MTCF (copy and delayed recall) compared to healthy controls and stroke with normal cognition suggesting difficulties in episodic memory, language, and visuospatial abilities [*VLT (total learning, delayed recall and delayed recognition*:

Table 1: Demographic characteristics of controls, stroke with normal cognition, VaMCI, and VaD

	Controls (59)	Stroke with normal cognition (25)	VaMCI (46)	VaD (51)	*P*
Age	63.66 (11.99)	57.48 (9.32)	61.37 (12.48)	63.92 (11.17)	0.095
Education	11.75 (3.63)	13.80 (3.97)	12.00 (3.48)	11.90 (3.23)	0.091
Male	37 (62.7%)	23 (92.0%)	38 (82.6%)	38 (74.5%)	0.018
Urban	40 (67.8%)	19 (76.0%)	39 (84.8%)	43 (84.3%)	0.101
SES					
Upper	11 (18.6%)	5 (20.0%)	6 (13.0%)	7 (13.7%)	0.037
Upper Middle	29 (49.2%)	12 (48.0%)	23 (50.0%)	17 (33.3%)	
Middle	12 (20.3%)	6 (24.0%)	12 (26.1%)	19 (37.3%)	
Lower Middle	7 (11.9%)	2 (8.0%)	5 (10.9%)	7 (13.7%)	
Lower	-	-	-	1 (2.0%)	

VaMCI: Vascular Mild Cognitive Impairment; VaD: Vascular Dementia

Table 2: Cognitive and behavioural characteristics of controls, stroke with normal cognition, VaMCI, and VaD

	Controls (59)	Stroke with Normal Cognition (25)	VaMCI (46)	VaD (51)	*P*
ACE-III total	89.93 (5.88)	88.58 (6.81)	82.10 (9.51)	65.34 (13.37)	< 0.001
RAVLT DR	7.07 (2.96)	6.61 (3.06)	4.69 (3.50)	2.77 (2.95)	< 0.001
RAVLT HITS	14.17 (1.50)	12.39 (2.17)	12.66 (2.24)	9.68 (3.90)	< 0.001
HADS Anxiety	2.96 (3.09)	5.67 (5.29)	6.36 (4.13)	5.15 (4.04)	< 0.001
HADS Depression	2.74 (3.21)	4.57 (3.92)	6.56 (4.58)	5.83 (4.41)	< 0.001
IQCODE	2.96 (0.66)	2.73 (0.72)	3.10 (0.71)	3.01 (1.04)	0.546

VaMCI: Vascular Mild Cognitive Impairment; VaD: Vascular Dementia; ACE-III: Addenbrooke's Cognitive Examination-III; RAVLT DR: Rey Auditory Verbal Learning Test Delayed Recall; RAVLT HITS: Rey Auditory Verbal Learning Test ; HADS: Hospital Anxiety and Depression Scale; IQCODE: Informant Questionnaire on Cognitive Decline in the Elderly

$F_{3, 174} = 13.30$, $P < .001$); (*PNT*: $F_{3, 156} = 19.17$, $P < .001$); and *MTCF (copy and delayed recall*: $F_{3, 159} = 31.12$, $P < .001$)]. In post hoc analysis, it was found that the mean scores of all tests in ICMR-NCTB were significantly different between controls vs. VaMCI; controls vs. VaD; stroke with normal cognition vs. VaMCI; stroke with normal cognition vs. VaD; and VaD vs. VaMCI ($P < .001$) with the highest scores in healthy controls and low scores in VaD patients. There were no significant differences in the cognitive test scores between healthy control and stroke with normal cognition groups.

Internal consistency for overall data was found to be 0.925. The ICMR-NCTB had good internal reliability of >0.87 across all diagnostic groups [Table 4]. The ROC revealed that the ICMR-NCTB has a significant discriminating power between healthy controls, VaMCI, and VaD participants [Figure 1]. The AUC was relatively good for VaMCI (0.75) and VaD (0.82). The sensitivity of the ICMR-NCTB to detect VaMCI ranged from 70.8% to 72.9% and the specificity ranged from 84.8% to 86.1%. Similarly, to detect VaD patients, the ICMR-NCTB had a sensitivity ranging from 75.9% to 79.7% and a specificity ranging from 82.5% to 85.2%.

We also investigated the external validity of the MoCA (a global cognitive screening tool) separately using ROC. The internal reliability, AUC, sensitivity, and specificity of the MoCA to detect VaD and VaMCI is presented in Table 5. The MoCA has good discriminating power in distinguishing healthy controls from VaMCI (AUC = 0.86) and VaD (AUC = 0.90) [Figure 2]. The MoCA has a sensitivity of 92.27% and specificity of 69.70% in identifying VaMCI at an ideal cut-off point of 23 and a sensitivity and specificity of 95.6% and 72.3%, respectively, to detect VaD, at an ideal cut-off score of 21.

Discussion

The present study focuses on standardization of the ICMR-NCTB in diagnosing VCI in five Indian languages: Hindi, Bengali, Telugu, Kannada, and Malayalam, from rural and urban populations across India. A multidisciplinary expert team used cross-cultural adaptation principles to develop the ICMR-NCTB for the Indian context. The study determined validity of the ICMR-NCTB battery in VaMCI and VaD patients. The ICMR-NCTB is a valid battery in discriminating stroke patients with MCI and dementia from the stroke

Table 3: Neuropsychological test scores of controls, stroke with normal cognition, VaMCI, and VaD

	Controls (59)	Stroke with normal cognition (25)	VaMCI (46)	VaD (51)	*P*
Test for global cognitive function					
MoCA	25.94 (2.80)	24.91 (3.18)	22.61 (4.80)	16.42 (5.66)	< 0.001
Test for attention and executive function					
TMTA	73.43 (27.41)	83.04 (39.28)	104.81 (65.29)	171.10 (131.19)	< 0.001
TMTB	177.29 (66.91)	194.74 (85.58)	226.53 (108.03)	262.57 (217.65)	0.02
Category fluency- Animals	13.46 (3.61)	12.72 (5.88)	11.02 (4.98)	8.49 (4.90)	< 0.001
Test for episodic memory					
Verbal learning test - DR	4.52 (1.80)	3.92 (2.12)	2.82 (2.16)	2.14 (2.32)	< 0.001
Verbal learning test - TL	18.53 (3.20)	17.76 (4.48)	14.95 (4.73)	12.20 (5.36)	< 0.001
Verbal learning test - Recognition	18.90 (1.81)	17.88 (2.39)	18.55 (1.66)	17.10 (3.98)	0.004
MTCF DR	19.20 (7.31)	14.07 (7.71)	11.55 (6.35)	4.64 (5.63)	< 0.001
Test for language					
PNT	85.72 (5.41)	82.05 (5.79)	77.39 (14.56)	66.53 (18.21)	< 0.001
Test for visuo-spatial skills					
MTCF Copy	34.79 (1.62)	33.13 (3.66)	29.05 (9.45)	18.04 (13.72)	< 0.001

VaMCI: Vascular Mild Cognitive Impairment; VaD: Vascular Dementia; MoCA: Montreal Cognitive Assessment; TMT: Trail Making Test; DR: Delayed Recall; TL: Total Learning; MTCF: Modified Taylor Complex Figure; PNT: Picture Naming Test

Table 4: Internal reliability, AUC, optimal cut-off scores and the respective sensitivity and specificity of ICMR-NCTB to detect stroke with normal cognition, VaMCI, and VaD

Language	Internal Reliability (α)	AUC	z-score	Sensitivity	Specificity
Stroke with normal cognition	0.879	AUC=0.25, CI: [0.15, 0.44]	-	-	-
VaMCI	0.882	AUC=0.75, CI: [0.67,0.84]]	-0.750	70.8	86.1
			-0.723	71.5	85.3
			-0.719	72.9	84.8
VaD	0.889	AUC=0.82, CI: [0.75, 0.90]	-0.652	75.9	85.2
			-0.639	77.3	84.3
			-0.609	79.7	82.5

AUC: Area Under Curve; VaMCI: Vascular Mild Cognitive Impairment; VaD: Vascular Dementia

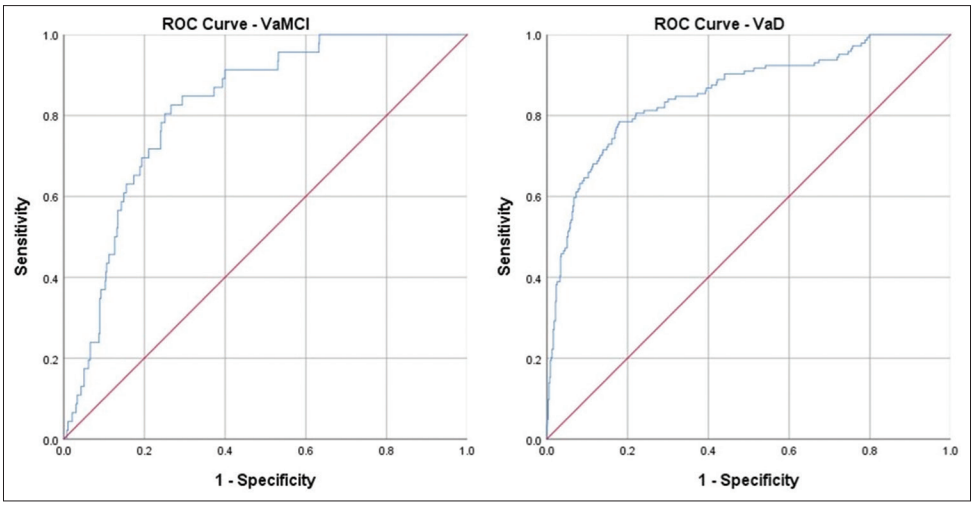

Figure 1: Area under curve of VaMCI and VaD for ICMR-NCTB

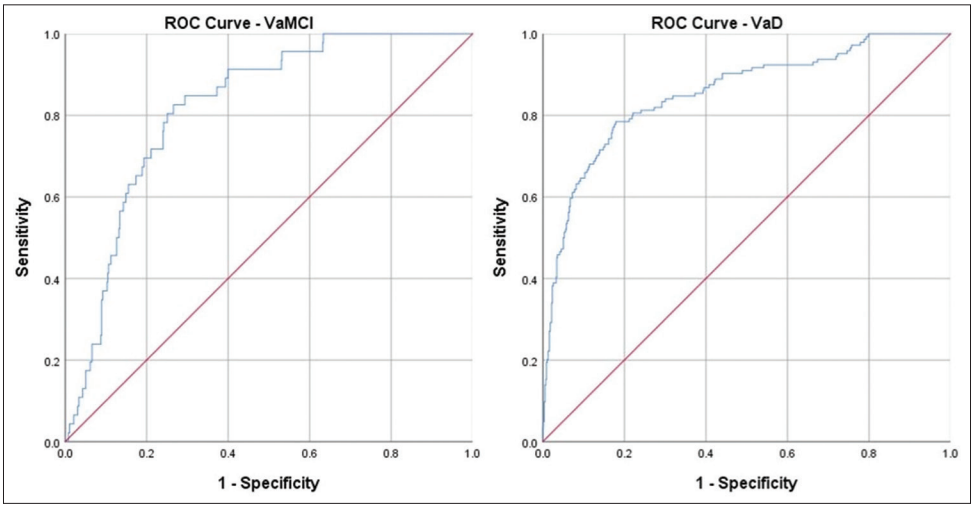

Figure 2: Area under curve of VaMCI and VaD for MoCA

Table 5: Internal reliability, AUC, optimal cut-off scores and the respective sensitivity and specificity of MoCA to detect Stroke with normal cognition, VaMCI, and VaD

Language	Internal Reliability (α)	AUC	Cut-off	Sensitivity	Specificity
Stroke with normal cognition	0.879	AUC=0.34, CI: [0.24, 0.44]	-	-	-
VaMCI	0.882	AUC=0.86, CI: [0.80, 0.94]	≤ 23	92.27	69.70
VaD	0.889	AUC=0.90, CI: [0.86, 0.95]	≤ 21	95.6	72.3

AUC: Area Under Curve; CI: Confidence Interval; MoCA: Montreal Cognitive Assessment; VaMCI: Vascular Mild Cognitive Impairment; VaD: Vascular Dementia

patients with normal cognition and healthy controls, with good reliability and internal consistency.

The development and validation of a comprehensive neurocognitive test battery to diagnose cognitive impairment in stroke patients was accomplished by studying a linguistically heterogenous cohort from various parts of India. The linguistic heterogeneity within the cohort could have led to variability in the performance of cognitive tests. As a result, a composite score was computed by converting the test scores to standardized z-scores in each language separately, adjusted for stratified age and education bands. After converting into z-score, age, education, and language-related variability were taken into account. The external validity of the ICMR-NCTB was determined by converting the test scores into standardized z-scores using ROC. The AUC was developed to assess the diagnostic power and corresponding sensitivity and specificity levels were established.

The sensitivity and specificity of the ICMR-NCTB to detect VaMCI ranged from 70.8% to 72.9% and 84.8% to 86.1%, respectively, and to detect VaD the sensitivity ranged from 75.9% to 79.7% and specificity from 82.5% to 85.2% with

good internal reliability of >0.87 across all diagnostic groups. The AUC for detecting VaMCI was 0.75 and 0.82 for VaD. The findings of the present study are consistent with previous VCI validation literature.[14,29] The Mandarin NINDS-VCI protocol distinguished between patients with VCI and healthy controls: the area under the ROC curve for the 60-minute protocol was 0.78 with sensitivity of 73.8% and specificity of 75.6%, whereas it was 0.80 for the 30-minute protocol, with 71.4% sensitivity and 68.3% specificity.[14] Similarly, the Chinese version of NINDS-CSN protocol detected stroke patients with VCI at good sensitivity and specificity levels (74% and 90%, respectively) with an AUC of 0.88 for the 60-minute protocol and 86% sensitivity and 76% specificity with an AUC of 0.88 for the 30-minute protocol. In addition, with area under the ROC of 0.77, the 60-minute version of Korean Vascular Cognitive Impairment Harmonization Standards neuropsychological procedure distinguished stroke patients from healthy controls.[31] Similar estimates of sensitivity and specificity were evident in our previous analysis of our MCI cohort.[19]

The study also demonstrated good external validity of the MoCA in differentiating stroke patients from healthy controls. For detecting VaMCI and VaD, the internal reliability of MoCA was >0.87 and AUC ranged from 0.86 to 0.90. The sensitivity and specificity of MoCA in detecting VaMCI was 92.27% and 69.70%, respectively, at an ideal cut-off point of 23 and with 95.6% sensitivity and 72.3% specificity in detecting VaD at an ideal cut-off point of 21. Godefroy *et al*. (2011)[32] investigated mild-to-moderate stroke patients and established a MoCA cut-off score of 24 for detecting VCI, with a sensitivity of 88% and specificity of 71%. As per Pendlebury *et al*. (2012),[26] a MoCA cut-off of 25 was generated with 82% sensitivity and 77% specificity to detect VCI in stroke patients. This establishes the relevance of MoCA as a useful screening instrument for VCI in the community, with the ICMR-NCTB useful as a diagnostic instrument for use in hospitals or in prospective cohort studies.

Major strengths of the study are: (i) this is a multicentric study conducted to develop and harmonize a neurocognitive battery for the diagnosis of VCI across five Indian languages; (ii) the study methodology included a standardized protocol for administering the ICMR-NCTB tests across centers; and (iii) the participants were recruited from major linguistic zones of India, which include the eastern, southern, and northern regions, and therefore, ICMR-NCTB could be employed uniformly in the Indian clinical contexts. There were some limitations in this study: (i) the study cohort was sociodemographically heterogeneous in terms of age and education; (ii) due to small sample size, validation of the ICMR-NCTB was conducted by combining five linguistic groups making individual language estimates of sensitivity and specificity difficult; and (iii) information about type and severity of stroke in patients were not available.

Conclusions

Our study is the first Indian multicentric study to examine the external validity, sensitivity, and specificity of ICMR-NCTB for comprehensive assessment of patients with VCI. These preliminary results have demonstrated that ICMR-NCTB in multiple languages can be used as a detailed assessment tool for the diagnosis of VaMCI and VaD as a validated instrument for cognitive evaluation and diagnosis of VCI in stroke survivors in India. The study also demonstrates the utility of MoCA as a valid screening instrument for poststroke cognitive impairment.

Ethical standards

The research procedures were explained to the participants and subjects were asked to provide a verbal and written informed consent. Study procedures were approved by the Research Ethics Committee at Nizam's Institute of Medical Sciences (the coordinating center) in Hyderabad for protection of human subjects and is as per guidelines of the Declaration of Helsinki. Approvals were also obtained from the participating centres (All India Institute of Medical Sciences Ethics Committee, Delhi; Institutional Ethics Committee, Apollo Gleneagles Hospital, Kolkata; Ethics Committee of Manipal Hospital, Bengaluru; and Institutional Ethics Committee, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Kerala).

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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