MMSE and MoCA

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Objective: Primary care clinicians in Asia employed the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) to aid dementia diagnosis post-stroke. Recent studies questioned their clinical utility in stroke settings for relying on verbal abilities and education level, as well as lack of consideration for aphasia and neglect. We aimed to review the clinical utility of the MMSE and MoCA for stroke patients in Asia and provide recommendations for clinical practice.

Keywords: stroke ; cognitive impairments

1. Introduction

The risk of dementia in the first year after stroke is 50% greater than in the general population [1] and about 40% of stroke patients will present with mild cognitive impairments [2]. The MMSE (Mini-Mental State Examination) [3] and MoCA (Montreal Cognitive Assessment) [4] are the most used screening tools for cognitive impairments after stroke [5]. Both screening tests were originally designed to screen for dementia and mild cognitive impairments (MCIs). The diagnostic criteria for these conditions are based on the cognitive presentation of Alzheimer's disease (AD), where memory deficits are prominent [6][7]. However, unlike AD, stroke patients show more salient frontal/executive deficits, e.g., attention and cognitive flexibility [8][9]. The term vascular cognitive impairments (VCIs) was proposed to represent a continuum of cognitive deficits of vascular etiology [7] including post-stroke dementia (PSD) [10], thereby delineating it from AD.

The different cognitive profiles of AD and stroke suggest that the MMSE and MoCA may not be useful in stroke settings, as they do not consider impairments intrinsic to stroke, i.e., aphasia, neglect, and apraxia [5][11][12][13][14][15]. For instance, both tests place a high load on verbal abilities, which can be problematic for aphasic patients in areas where language is required to perform well [16][17]. In contrast, stroke patients who retain their language abilities, such as those with right ischemic lesion, might give a false impression of normal cognition [18]. The MMSE seems to fare worse than the MoCA in detecting post-stroke cognitive impairments (PSCIs) due to its reliance on language [19]. For example, performance on calculation and attention in the MMSE varies across Asian countries [20], possibly because some languages have a higher phonological load for number processing [21].

In addition to the inherent limitations of the MMSE and MoCA, it is also critical to select a valid cutoff score for PSCI due to its influence on detection accuracy. Many studies have found the cutoff of 26 in the MoCA [4] to be inadequate in addressing cognitive impairments in stroke settings. Rather, optimal values were shown to range from 19 to 27, conditional on whether screening was conducted in the acute or chronic phase of stroke [22][23]. Preliminary evidence in Asia suggests that the MoCA is more sensitive than the MMSE in predicting cognitive deficits after stroke [24][25][26][27]. However, only a few studies maintained methodological rigor in examining the optimal clinical cutoff for stroke patients. For example, education stratification in receiver operating characteristics (ROCs) was rarely applied [14]. This has a significant clinical impact, as many Asian studies report inadequate detection accuracy using the one additional point recommendation for the MoCA for patients with <12 years of education [28][29][30][31]. Furthermore, it is uncertain which cutoffs should be used in societies with greater educational disparities [32][33][34]. In brief, increasing evidence reveals that sociocultural considerations are indispensable in interpreting the results of the MMSE and MoCA.

The brief and broad nature of the MMSE and MoCA render them practical and popular in clinical settings, particularly in developing countries in Asia where resources are limited. It is commonplace that only patients showing prominent functional impairments are referred for further neuropsychological evaluation. However, such services are often inaccessible to underserved groups in the community (e.g., poor health, low income, rural areas). Thus, accurate detection for PSCI is crucial while patients are in the hospital. Is it possible to balance the limitations of the MMSE and MoCA with practicality for the benefit of both patients and clinicians? This question is worthy of exploration due to the 5–15% higher prevalence of dementia due to stroke in Asia than in North America and Europe [35]. Although cognitive screening is part of stroke care protocol, whether the MMSE and MoCA are clinically useful in Asia remains unclear.

The aim of this review is to compare the sensitivity and specificity of the MMSE and MoCA in Asia. Based on this, recommendations for future practice and research will be outlined. While there are other cognitive tests currently available—e.g., ACE-III (Addenbrooke's Cognitive Examination 3rd Edition) [36] and the IQCODE (Informant Questionnaire for Cognitive Decline in the Elderly) [37]—this review focused on the MMSE and MoCA because (1) ACE-III was designed to differentiate AD and frontotemporal dementia, (2) the IQCODE is an informant-based structured questionnaire—as opposed to the MMSE and MoCA, which directly measure the patient's cognitive function—and (3) the MMSE and MoCA remain the most well-known cognitive tests across multidisciplinary settings in Asia. Sensitivity and specificity were chosen as indices of detection accuracy because they are not dependent on the prevalence of PSCI in the population.

2. MMSE and MoCA

The search yielded 1306 records. After removing duplicates, 846 articles remained, and were screened by title and abstracts. Following this, 810 were excluded due to geographical locations, sample (e.g., dementia, Parkinson's disease, brain injury), non-cognitive outcomes (e.g., functional ability), review papers, randomized controlled trials, or neuroimaging studies. This resulted in 48 articles for further full-text evaluation, of which 11 articles met the inclusion criteria and were included in this review; 7 of these studies were conducted in China, 3 in Singapore, and 1 in Korea. The National Institute of Neurological Disorders and Stroke–Canadian Stroke Network 5-Minute Protocol (NINDS-CSN 5) [38] was included as it consists of the original subtests in the MoCA, i.e., five-word memory task, six-item orientation, and one-letter phonemic fluency. Moreover, two of the three studies examining the NINDS-CNS 5-Minute reported ≥200 participants [39][40].

2.1. Detection Accuracy of the MMSE and MoCA

Four studies that compared the MMSE and MoCA showed equivalent sensitivity and specificity to identify PSCI [41][42][43][44]. However, only two studies [41][43] met the detection accuracy standard of 80% sensitivity and 60% specificity, as suggested by Stolwyk et al. [14]. In the work of Dong et al. [42], there was a substantial difference in sensitivity between the optimal (MMSE = 61%, MoCA = 69%) and recommended (MMSE = 71%, MoCA = 78%) cutoff scores. Detection accuracy improved after a processing speed test was added in the ROC analysis (sensitivity = 97–98%, specificity = 76–78%). Likewise, Zhu et al. [44] reported poor sensitivity for both tests (MMSE = 68%, MoCA = 64%). Studies that found equivalent detection accuracy for the MMSE and MoCA also recruited older patients (see **Table 1**). Out of the nine studies that examined the MoCA, six reported adequate sensitivity (78–97%) and specificity (64–90%). Only one study showed poor specificity [45], attributable to the ceiling effect among patients with higher education levels. Two [40][46] of the three studies that examined the NINDS-CNS 5 demonstrated adequate sensitivity (82–92%) and specificity (67–68%). Another study showed fair SE (70%) but good SP (82%) [39].

Table 1. Summary of studies and covariates categorized by tests.

Study	Disease	Language	Study Design	Sample Size	Age	Education	NIHSS	Time Since Stroke	Cutoffs	Sensitivity (95% CI)	Specificity (95% CI)	PPV (%)	NPV (%)
MMSE													
Dong 2012	VCI	Preference	Prospective	239	67.9 *	5.7 *	1 to 4	3 days	≤25/26	0.88 (0.77, 0.95)	0.66 (0.59, 0.73)	47	94
Dong 2014	VCI	Preference	Prospective	400	64.3 *	6.3 *	0 to 1	2.4–3.4 months	≤26	0.71 (0.64, 0.77)	0.81 (0.74, 0.87)	84	67
Shen 2016	VCI-ND	Mandarin	Case–control	104	70.6 *	8.7	3.16	≤14 days	≤27/28	0.82 (0.70, 0.90)	0.78 (0.62, 0.89)	82	78
Zhu 2020	VCI	Mandarin	Prospective	229	63.8	6*	1	≤14 days	≤27	0.68 (0.58, 0.77)	0.82 (0.74, 0.88)	71	23
MoCA													
Dong 2012	VCI	Preference	Prospective	239	67.9 *	5.7 *	1 to 4	3 days	≤21/22	0.88 (0.77, 0.95)	0.64 (0.57, 0.71)	45	94
Tu 2013	VCI-ND, VD	Changsha	Case–control	470	69.4–73.2	6.3–8.1 *	?	≥3 months?	≤26/27	0.96 (0.91, 0.99)	0.76 (0.69, 0.82)	86	93
Wu 2013	VCI-ND	Mandarin	Case-control	206	68.1	8.65	?	Acute?	22/23	0.97 (0.91, 0.99)	0.47 (0.37, 0.57)	N/A	N/A

MMSE													
Study	Disease	Language	Study Design	Sample Size	Age	Education	NIHSS	Time Since Stroke	Cutoffs	Sensitivity (95% CI)	Specificity (95% CI)	PPV (%)	NPV (%)
Dong 2014	VCI	Preference	Prospective	400	64.3 *	6.3 *	0 to 1	2.4–3.4 months	≤23	0.78 (0.71, 0.83)	0.80 (0.72, 0.86)	84	72
Dong 2016	VCI-ND	Preference	Prospective	291	68.4 *	5.5*	1 to 4	2.6–4 days	≤20/21	0.83 (0.78, 0.88)	0.80 (0.68, 0.90)	50	95
Shen 2016	VCI-ND	Mandarin	Case–control	104	70.6 *	8.7	3.16	≤14 days	≤23/24	0.87 (0.75, 0.94)	0.76 (0.60, 0.87)	86	75
Zuo 2016	VCI	Mandarin	Case–control	102	58.3 *	Level *	1	10 days	≤22/23	0.85 (0.73, 0.93)	0.88 (0.74, 0.96)	91	80
Liao 2021	VCI	Mandarin	Case–control	316	61.1 *	Level *	2	6 months	≤24	0.63 (0.56, 0.70)	0.71 (0.63, 0.79)	74	60
Zhu 2020	VCI	Changsha	Prospective	229	63.8	6 *	1	≤14 days	≤21	0.64 (0.54, 0.74)	0.90 (0.83, 0.94)	N/A	N/A
NINDS-CNS 5													
Chen 2015	VCI	Mandarin	Case–control	80	62.9	7.2 *	2	10 months	24	0.92 (0.79, 0.98)	0.68 (0.52, 0.82)	73	90
Dong 2016	VCI-ND	Preference	Prospective	291	68.4 *	5.5 *	1 to 4	2.6–4 days	≤7/8	0.70 (0.64, 0.76)	0.82 (0.70, 0.91)	49	92
Lim 2017	VD	Korean	Prospective	308	69.1 *	Level	5	3 months	≤6/7	0.82 (0.69, 0.91)	0.67 (0.61, 0.73)	33	95
Wei 2020	VCI	Mandarin	Case–control	2989	63	Level	1.16	1–2 months	≤10	0.91 (0.89,0.92)	0.63 (0.60, 0.65)	71	87

* Significant differences between comparison groups; VCI: vascular cognitive impairment; VCI-ND: vascular cognitive impairment, no dementia; VD: vascular dementia; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; NINDS-CNS 5: The National Institute of Neurological Disorders and Stroke–Canadian Stroke Network 5-Minute Protocol; NIHSS: National Institutes of Health Stroke Scale.

Qualitatively, studies showing adequate sensitivity and specificity had several characteristics: (1) shorter time interval between stroke and screening (i.e., ≤4 days), (2) older patients, and (3) lower dropout rates in prospective cohort designs (<30%).

2.2. Covariates

Although the MMSE and MoCA both appear adequate for detecting PSCI, there are several covariates to consider.

2.2.1. Education

Many studies (82%) reported significantly lower education in patients with PSCI. Despite the considerable education weightage on PSCI, only two studies stratified patients according to education in the ROC analysis[40][45]. The 12-year education cutoff for MoCA was found to be inadequate[47]; instead, a 6-year or primary education level cutoff better fit the Asian population[31][40][41][42][44][45]. Over half of the studies included in the review raised concerns over education's effect on MoCA scores (see **Table 2**).

Table 2. Methods for education adjustment across studies.

MMSE				
Study	Adjusted	Additional One Point	Method	Notes
Dong 2012	Yes	< primary level education	Regression	Cutoff scores did not differ between patients with lower (≤6 years) and higher educational levels
Dong 2014	Yes	< primary level education	ROC analysis	Cited lack of education stratification for cutoff as study limitation
Shen 2016	No	<12 years		Due to small sample size
Zhu 2020	Yes	<6 years	ROC analysis	
MoCA				
Dong 2012	Yes	< primary level education	ROC analysis	Cutoff scores did not differ between patients with lower (≤6 years) and higher educational levels
Tu 2013	No			Regression analysis showed education's effect

MMSE				
Study	**Adjusted**	**Additional One Point**	**Method**	**Notes**
Wu 2013	Yes	<12 years	Cutoff scores stratified by education level	Not education-adjusted MoCA ≤ 22/23 Education ≤ 6 years MoCA ≤ 15 Education 6–12 years MoCA ≤ 22 Education > 12 years MoCA ≤ 23
Dong 2014	Yes	< primary level education	ROC analysis	Cited lack of education stratification for cutoff as study limitation
Dong 2016	Yes	< primary level education	ROC analysis	Education-adjustment did not affect cutoff scores
Shen 2016	No	<12 years		Cutoff scores not adjusted for education
Zuo 2016	No	<12 years		Authors recommended education-adjusted cutoff scores for future studies
Liao 2020	No	<12 years		Authors recommended education-adjusted cutoff scores for future studies
Zhu 2020	Yes	<6 years	ROC analysis	MoCA is more suitable for educated individuals
NINDS-CNS 5				
Chen 2015	Yes	Not applicable	Analysis of variance	Cutoff scores not adjusted for education
Dong 2016	Yes	Not applicable	ROC analysis	Education-adjustment did not affect cutoff scores
Lim 2017	Yes	Not applicable	Logistic regression	Categorized education as ≤6 years vs. >6 years

MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; NINDS-CNS 5: The National Institute of Neurological Disorders and Stroke–Canadian Stroke Network 5-Minute Protocol; ROC: receiving operating characteristic.

2.2.2. Age

Eighty percent of the studies that reported inadequate sensitivity and specificity for the MMSE and MoCA recruited younger stroke patients (61–64 years old). In comparison, studies that reported adequate sensitivity and specificity recruited older patients (68–73 years old). Overall, 73% of studies showed that patients with poorer cognitive outcomes were significantly older.

2.2.3. Stroke Characteristics

Seven studies (64%) recruited patients with mild stroke or TIA, and eight studies (73%) excluded patients with aphasia. Less than half of the studies reported stroke location [39][41][42][44][47], and only one study reported stroke lateralization [44]. Only two studies did not report stroke severity [31][45], i.e., using the NIHSS (National Institutes of Health Stroke Scale) [48]. The remaining studies reported

3. Current Insights on MMSE

While the MMSE and MoCA are widely used in stroke settings in Asia, this is the first review to address concerns about the psychometric properties of both tools for Asian stroke patients. An optimal cutoff score has the best trade-off between SE (true positive) and SP (true negative). However, to pool together the sensitivity and specificity of the MMSE and MoCA for a single cutoff score for the Asian population would undermine the diversity of cultures, ethnicities, and languages; the paucity of high-quality studies in other parts of Asia further deters this.

Studies that directly compared the MMSE and MoCA found them to be equivalent in detecting PSCI, but at varying accuracy levels. In other words, despite their equivalence, some studies found both screening tests to be inadequate for stroke patients [42][44]. These studies reported large sample sizes (*N* = 229–400), over 50% dropout rate at follow-up, and younger patients. The extent to which these factors are statistically significant remained a question because of the limited number of studies (N = 4); nevertheless, high dropout rate can erroneously estimate PSCI, e.g., in aging studies, dropouts were prevalent among individuals with worse white matter integrity [49][50]. In a study by Dong et al. [42], sensitivity improved by approximately 20% after a visuomotor processing speed test was added in the ROC analysis. This aligns with recent studies suggesting visual processing speed as an underlying cognitive function that affects performance in other cognitive domains in neurocognitive disorders [51][52]. Further evidence is warranted in Asia to determine whether the addition of a visual processing speed task can improve the detection accuracy of the MMSE and MoCA in stroke settings.

On the other hand, the MoCA generally showed adequate sensitivity and specificity for stroke patients. A closer examination of the findings supports the importance of education stratification in ROC analysis [53]. For example, many cognitive tasks in the MoCA (e.g., executive, memory, abstraction) were inadequate for stroke patients with higher education [45]. This can partly explain the poor specificity (47%) reported. It was postulated that some tasks in the MoCA are easy for patients with higher levels of education, risking an underestimation of PSCI. Arguably, a recent study in Israel found that the MoCA was difficult even for healthy and highly educated older adults [54]. In contrast, a floor effect was reported for stroke patients with lower education, suggesting that the test items in MoCA are too difficult for this group [44]. Similar findings have been reported in previous studies [7][22][55][56][57]. In this light, what may potentially contribute to the observed limitations? While sociocultural differences and stroke characteristics must be acknowledged, it is difficult to ignore the limitation of global cognitive screening tests—using a universal cutoff score to identify cognitive deficits. Recent evidence points towards domain-specific screening tests that minimize verbal requirements and emphasize clinical utility, e.g., informing clinicians of potential rehabilitative targets [11].

The studies that found adequate sensitivity also reported older patient samples, concurrent with epidemiological studies showing poorer cognitive outcomes after stroke with increasing age [1][56][58]. It is plausible that the MMSE and MoCA appear capable of accurate detection when results merely reflect a sociodemographic artefact. However, the age factor can also be intertwined with education, e.g., it was not mandatory for older individuals to obtain a formal education in past decades in developing countries [59].

One way to accommodate the aforementioned challenges is to provide normative data stratified by age and education, but this is financially demanding and time-consuming for developing countries to achieve. It may be feasible to pool data across Asia to provide appropriate age- and education-based cutoff scores. It may also be relevant to supplement the MoCA with additional cognitive tests, e.g., for processing speed [42][60]. Nevertheless, concern arises regarding qualification and skills, as administering additional cognitive tests means enlisting the expertise of neuropsychologists. Misinterpretation of results and liability due to misreporting can prove to be counterproductive. A possible alternative is to minimize the use of single cutoff scores and shift towards domain-specific scores, as increasing evidence shows that this provides a more sensitive measure for PSCI [12][61][57]. Clinicians are recommended to adjust cutoff scores for the MoCA based on education level, i.e., an additional 1 point for <6 years. Previous studies in Singapore and China further support this recommendation [28][45]. More studies are warranted to determine whether these recommendations improve detection accuracy for PSCI. For instance, illiteracy can be a potential confounding factor in community settings [55].

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