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A Comparison of Different Cognitive Screening Instruments on Early Detection of Mild Cognitive Impairments in Post-Stroke Patients.

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Abstract: *Strokes pathology creating negative effects on brain structure producing both physical and cognitive impairments, the recovery of both are time sensitive. Early detection of cognitive impairment (CI) is crucial to augment recovery rate. Formal cognitive assessment often needs 2-4 hours, which may not be clinically available. There is a need of an efficient cognitive screening test as an aide for subsequent proper referral to neuropsychologists for a thorough neuropsychological assessment. The Mini mental state Examination (MMSE), The Montreal Cognitive assessment (MoCA) and the Addenbrooke's Cognitive Examination-Revised (ACE-R) are commonly used as screening tools for CI. Thisstudy aimed to compare the proportions of MCI determined by different cognitive screening instruments (CSI), identifying the most effective one. This was a cross-sectional study for stroke patients with age 55.81±3.03 years, and stroke duration 4.86±0.73 months. The proportion of MCI identified using MMSE, MoCA and ACE-R were 40%, 66% and 75%. This difference was statistically significant (chi-square test, p < 0. 05). The proportion of MCI identified in post-stroke patients was higher when using ACE-R and the MoCAin comparison to the MMSE,the ACE-R and The MoCAare recommended as an alternative in the early detection of MCI in post-stroke patients.*

Keywords- *Strokes,Cognitive impairment, MMSE,MoCA,ACE-R.*

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I. Introduction

Cognition is the capacity for and expression of knowledge. It represents an individual ability to gain and retain relevant information so that it can be applied in appropriate situations. Stroke is a pathology that causes alternation in conscious level and function, somatosensory dysfunctions, motor deficits, cognition, language and sleep disorders [1, 2, and 3]. Even though the stroke mortality rate has recently been decreased [4], the incidence of stroke and its consequent sequels of morbidity stay high [5]. Strokes lead to negative effects on brain structure and cognitive function [6]. The intervention in some of these effects is time sensitive , and therefore the longer a stroke goes untreated, the greater the possibility of permanent neurologic and cognitive dysfunction [7, 8]. The concept that stroke related repercussions are time sensitive does not apply to physical recovery only, but also applies to cognitive recovery [9]. Post-stroke vascular cognitive impairment (VCI) is a syndrome that rangedin severity from post-stroke vascular mild cognitive impairment (VaMCI) to dementia [10, 11]. It was mentioned that up to 92% of Stroke survivors is complicated in the early stages of recovery by cognitive impairment [12, 13]. Post-stroke VaMCI is identified by impairment in at least one cognitive domain with intact or mildly impaired instrumental activities of daily living [14]. More than half of patients with VCI (57%) are VaMCI [15, 16]. While 40% with non-disabling ischemic stroke had VaMCI [17]. Indeed, in patients with moderate neurologic recovery, cognitive impairment has recently been identified as the most persistent problem of stroke [18]. Furthermore, it is estimated that one quarter to one third of stroke patients can demonstrate dementia criteria within three months of experiencing stroke [19, 20], leading to an indirect health care costs, decreased participation in rehabilitation [21], reduced daily functional capabilities [22, 23], hospitalization and cognitive impairment [23, 24]. Then, the detection of patients with MCI, as early as possible, is crucial for the clinicians to developan appropriate treatment. This can help to recognize the patients' potentials and deficiencies, functional impairments and patient safety that could be affected by cognitive impairment [25]. It is not easy or practical to do a neuropsychological test battery early after stroke so brief CSI are required to identify patients who need further assessment. Canadian Stroke practice guidelines suggested that all patients with medically evident stroke should be screened for CI, as soon as is appropriate, and the patients who are

identified as having CI on the screening test should be referred for additional comprehensive cognitive evaluation [26, 27, 28]. A stroke patient with suspected CI [16, 26] should have a formal neuropsychological evaluation (including assessment of neglect, language, memory, emotional responsesandpraxis) [29]. Certainly; the cognitive state should be assessed periodically during rehabilitation, to ensure faster and greater recovery and reduced deficits in instrumental ADLs [30]. The clinical examination to CI should be short in time and covers multiple cognitive aspects. Attempts have been made to validate a brief CSI for the detection of MCI, Studies have determined that, there have been inconsistent findings about the discriminatory ability of the commonly used CSI for CI detection in stroke patients, either in the acute phase [31, 32], or at one year after stroke [33]. There are many CSIs used in clinical practice like; Mini-Mental State Examination (MMSE), The Montreal cognitive Assessment (MoCA) and the Addenbrooke's Cognitive Examination-Revised (ACE-R). The most widely used test is the Mini-Mental State Examination (MMSE) [34]. The MMSE was designed to detect dementia in community dwelling older adults. It is commonly used because it is quick and easy to administer and does not need any training or special equipment [35, 36]. The MMSE includes 11 questions that examinemultiple cognitive aspects,including orientation, memory, recalls, attention, registrations, orders understanding and execution,language andvisuo-construction. Patients require about 10 minutes to be scored byMMSE [37]. Researches confirmed that the MMSE value equal to 27or more is considered a normal cognitive stat, while suspect CI if the value falls between 22-26 and a confirmed CI stat if the value less than or equal to 21. However, the MMSE has limitations for patients with acute stroke [13]. Blake et al found the MMSE was only satisfactory in determining the presence of general CI, with good specificity (88%) and moderate sensitivity (62%) at an optimal cut-off of <24,consequently, MCI needs a more sensitive screening test to be identified [38].TheMoCA and the ACE-R are considered two of the best alternatives to the MMSE. The MoCAincludes 30 questions that are more complex than the MMSE and also administered in about 10-minutes. The MoCA include recalls of short-term memory and tests of visuo-spatial ability, executive function, attention, language, concentration, and orientation to place and time. MoCAmaximum score is 30, with a higher score indicating better cognition and scores below 26 suggest CI [39]. The MoCA is considered a short and reliable screening tool to detect MCI in elderly patients [40]. The MoCAhas a sensitivity 96% and a specificity 95% with a cut-off score of <23 in discovering CI [41]. The Addenbrooke's Cognitive Examination (ACE) [42] was developed in 1990 to act as a screening tool for detecting CI while also incorporating the Mini Mental State Examination [35]. The ACE was developed by extending the language, memory, and visuospatial abilities components of the MMSE and adding a verbal fluency component [42, 43]. ACE was designed to assess five cognitive domains; attention, memory, verbal fluency, language and visuospatial abilities. ACE was later revised in 2006 to improve sensitivity resulting in a new version named the Addenbrooke's Cognitive Examination Revised (ACE-R) [44]. ACE-R involves 19 items, takes 15-20 min to finish and 5 min to score, the maximum scores is 100, and a higher score indicates anormal cognitive abilities [44].

1.1 Aim of the study and hypothesis.

The aim of this study was to perform a comparison into the utility of cognitive screening instruments indetermining post-stroke MCI proportions using the MMSE, the MoCA and ACE-R. Also to compare the required times to administer the MMSE, MoCA and the ACE-R.It was hypothesizedthat there were no difference in the proportion of MCI detected using the MMSE, MoCA and the ACE-R. We suggest that this study will help the clinician in the early detection of MCI by using the most efficient scale for cognitive assessment.

II. Material and Methods

This cross-sectional study was carried out on the inpatient stroke rehabilitation unit, located in the neurology department in King Khalid Hospital,Tabuk City, Saudi Arabia. And also in AlkasrAleini hospital outpatient clinic, Cairo University Egypt.From May 2016 to October 2017. A total 100 stroke patients, aged 40-60 years [45], whom previously diagnosed as having stroke not more than 6 months duration [46, 47] were in this study.

2.1 Study Design: Cross-sectional study

2.2 Study Location: Carried out on the inpatient stroke rehabilitation unit located in the neurology department in King Khalid Hospital, Tabuk City, Saudi Arabia. And also in AlkasrAleini hospital outpatient clinic, Cairo University Egypt.

2.3 Study Duration: From May 2016 to October 2017.

2.4 Sample size: 100 stroke patients.

2.5 Sample size calculation: The sample size, considering confidence level of 95% and power of 80%, also we used similar studies to calculate sample size.

2.6 Subjects & selection method: The study populationwas recruited as being a stroke patients discharged from an inpatient stroke rehabilitation program located in the neurology department of King Khalid Hospital,Tabuk City, Saudi Arabia. Also recruited from AlkasrAleini hospital outpatient clinic, Cairo University Egypt, from May 2016 to October 2017.

2.7 Inclusion criteria:

1. Patients with stroke diagnosis and confirmed by the MRI and comprehensive neurological examinations.
2. Either sex
3. Stroke patients aged from 40-60 years,
4. Stroke duration not more than 6 months.

2.8 Exclusion criteria:

1. Patients had any history of previous traumatic brain injury;
2. Patients with recurrent stroke
3. Patients with other neurological disorders except for stroke
4. Patients who are deaf or blind.
5. Patients who aren't alert enough to complete the assessment.

2.9 Procedure methodology

Following each subject or their relatives reads and signs an informed consent, then, the patients were assessed by an experienced PT; demographic data were obtained including age, sex and duration of stroke. One hundred stroke patients form the study group. The outcome measures of cognitive examination were collected using the MMSE, the MoCA and the ACE-R, and were recorded across one or more days, within a maximum interval of seven days as the patient wish.

Evaluation environment was constant through the study. The analysis procedures were done to each patient by the same physiotherapist, a brief explanation about the protocol of evaluation was given to each patient.

The data collection was performed using: the MMSE, the MoCA and the ACE-R scales. Both MMSE and MoCA measures yield total scores out of 30. The published recommended limit to detect the presence of MCI is a score below 24 (18-24/30) on the MMSE [35] and below 26 on the MoCA, [48, 49] with higher scores indicating intact cognitive ability. The ACE-R Test scores of MCI participants are typically found to be in the range of 75-88/100 [50].

2.10 Statistical analysis

SPSS software ver. 21 (SPSS Inc., Chicago, IL, USA) utilized to analyze data.Descriptive statistics was used to describe the demographic data that were collected from the patients. A chi-square test used to compare the proportion of MCI detected in stroke patients using the MMSE, the MoCA and the ACE-R. Analysis of variance (ANOVA) was used to compare the time required to complete the different CAI. Spearman correlation test was used to find the correlation in between the CAI. The result was statistically significant if $P < 0.05$ with a 95% confidence interval (CI).

III. Result

The average age of the patients was 55.81±3.03years of age. The proportions of CI determined in the study group patients using the MMSE, the MoCA and the ACE-R were 40% and 66%, and 75%, respectively (Table 1). Using a chi-square test to compare the difference in proportion of MCI detected among the MMSE, the MoCA and the ACE-R the results showed that there were a significant difference as the two sided P-value < 0. 05 (Table 2). Using a chi-square test to compare the difference in proportion of MCI detected between the MMSE and the MoCA(Table 3) and between the MMSE and the ACE-R (Table 4) the result showed that there was a significant difference as the two sided P-value < 0. 05. In compare the proportion of MCI detected between the MoCA and the ACE-R (Table 5) a chi-square test reveals a non-significant difference P-value > 0. 05. The mean screening time for the MMSE, the MoCA and the ACE-R were 6.39±2.63, 10.41±2.87 and 18.85±2.06 respectively (Table 6). One way ANOVA reveals a significant difference in screening time among the MMSE, the MoCA and the ACE-R P-value < 0.05(Table 7) , Tukey-kraymer multiple comparison test reveals that there were a significant difference in screening time among the MMSE and the MoCA, the MMSE and the ACE-R, the MoCA and the ACE-R, P < 0.05(Table 8).Nonparametric Spearman correlation revealed

that there were a moderate correlation among the MMSE and the MoCA, the MMSE and the ACE-R, the MoCA and the ACE-R, r= 0.7616, 0.6765, 0.713 respectively and P-value < 0.05(Table 9).

Table no 1: Showcross tabulation cognitive impairment proportions values between the MMSE, the MoCA and the ACE-R.

Count				
		result		Total
		Impaired cognition	Normal cognition	
test	MMSE	40	60	100
	MoCA	66	34	100
	ACE-R	75	25	100
Total		181	119	300

Table no 2: Show Chi-Square Tests among the MMSE, the MoCA and the ACE-R.

	Value	df	Sig. (2-sided)
Chi-Square	27.606a	2	.000
Likelihood Ratio	27.706	2	.000
Linear-by-Linear Association	25.508	1	.000
N of Valid Cases	300		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 39.67.			
df degree of freedom			

Table no 3: ShowChi-Square Tests between the MMSE and the MoCA.

	Value	df	Sig. (2-sided)
Chi-Square	13.569a	1	.000
Continuity Correction	12.545	1	.000
Likelihood Ratio	13.729	1	.000
Linear-by-Linear Association	13.501	1	.000
N of Valid Cases	200		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 47.00.			
df degree of freedom			

Table no 4: Show Chi-Square Tests between the MMSE and the ACE-R.

	Value	df	Sig. (2-sided)
Chi-Square	25.064a	1	.000
Continuity Correction	23.652	1	.000
Likelihood Ratio	25.672	1	.000
Linear-by-Linear Association	24.939	1	.000
N of Valid Cases	200		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 42.50.			
df degree of freedom			

Table no 5: ShowChi-Square Tests between the MoCA and the ACE-R.

	Value	df	Sig. (2-sided)
Chi-Square	1.947a	1	.163
Continuity Correction	1.539	1	.215
Likelihood Ratio	1.953	1	.162
Linear-by-Linear Association	1.938	1	.164
N of Valid Cases	200		
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 29.50.			
df degree of freedom			

Table no 6: Show screening times for the MMSE, the MoCA and the ACE-R.

Test	Mean	Standard deviation	Minimum	Median	Maximum
The MMSE	6.39	± 2.63	4	6	14
The MoCA	10.41	± 2.87	5	10.5	19
The ACE-R	18.85	± 2.06	15	19	24

Table no 7: Show One-way Analysis of Variance (ANOVA) screening time for.

Source of variation	Degrees of freedom	Sum of squares	Mean square	F	P
Treatments (between columns)	2	7555.5	3777.8	582.94	0.0001
Residuals (within columns	294	1924.7	6.481		
Total	299	9480.3			

Table no 8: ShowTukey-kraymer multiple comparisons.

Comparison	Mean Difference	q	P value
Time MMSE vs time MoCA	-3.520	13.827	P<0.001
Time MMSE vs time ACE-R	-11.960	46.981	P<0.001
Time MoCAvs time ACE-R	-8.440	33.154	P<0.001

Table no 9: ShowSpearman correlation among the MMSE, the MoCA, and the ACE-R.

Test	95% confidence interval	r	* P value
MMSE vs. MoCA	0.6612 to 0.8351	0.7616	p < 0.00
MMSE vs. ACE-R	0.5495 to 0.7729	0.6765	p < 0.00
MoCA vs. ACE-R	0.5977 to 0.8003	0.7136	p < 0.00

* The two-tailed P value

IV. Discussion

It is neither practical nor feasible in clinical sittings to measure all cognitive domains in full detail. Instead, the physical therapist need a brief, quick, easy, and comprehensive CSI that can screen and detect MCI, this acts as a guide for subsequent referral and comprehensive examination.

Mini Mental State Examination (MMSE) is the most popular used test for detecting CI [35], but it has established limitations in finding out early dementia and in detecting multiple cognitive domains [48, 51].

The purpose of this study was to compare three CSI, the MMSE, the MoCA, and the ACE-R, to determine the most efficient CSI in the early detection of MCI, in terms of time efficiency and the ability to differentiate normal from patients suffer from MCI.

The average age of the subjects was 55.81±3.03 years old. The age range from 40-60 years can reduce the effect of the degenerative process and aging i.e. the geriatric population that may causecognitive impairment, consequently, the CI detected in our patients was expected to be aconsequenceof thestroke and not by degenerative process. This come in accordance with a survey performed by the Asian Neurologic Association (ANA), which declared that most stroke patients are between 45 and 64 years old(54.7%), while 33% are above 65years and 11.8% less than 45 years old [45].

This study includes a sample of patients with stroke onset from 3 months and up to 6 months, the average of stroke duration was 4.86±0.73 months [46, 47].

Indeed the comparison ofCSIsis difficult because each scale test different cognitive aspects and hasa different difficulty level. The MoCA [52] and the ACE-R [44, 53] are considered a more difficult form of MMSE. Today, the MMSE is the most popular scale used, even though many studies revealed that the MMSE has low sensitivity to find MCI and sometimes cannot detect it.Nys et al reported that the MMSE has a lower level of specificity (34%) but higher sensitivity (70%) [13].

Our results revealed that, the MoCA and the ACE-R had a higher ability to detect MCI in comparison with MMSE, with percentage of 66%, 75% in comparison with 40% respectively (p-value< 0.000). There was a non-significant difference in the ability to detect MCI using both the MoCA and the ACE-R, p-value = 0.214.

It comes in accordance to our results that the MMSE had a poor ability to detect MCI in stroke patients, this can be explained by; The MMSE scoring depends mainly on verbal items and has no measuresvisuospatial, executive function, or information retention [54]. The MMSE is less effective in determining CI in patients who have had a right hemisphere stroke rather than left hemisphere stroke [55]. The MMSE is designed to examine global cognitive functioning; it would not be sensitive to the focal deficits commonly found in stroke patients [56].The MMSE has items which considered too easy and concentrate on memory impairment. MCI can only be identified with more difficult tasks [57].The orientation totime and place itemsscored 10 from 30 points, consequently the MMSE is too focused on orientation which is not suitable for the stroke patients [57].

The MoCA and the ACE-R incorporate the MMSE items, but also have more complicated items to detect MCI. As the measurement of executive function, Semantic elements, tested by picture naming, this is known to be subtly impaired in MCI and many more cognitive domains [58, 59].This can add some benefits as decreasing the ceiling effect in compare withMMSE;improve the internal reliability, and provide a greater association to determine the functional status.Many researchers described that the direct comparison of the MMSE with other screening measures has indicated that the MMSE was less sensitive at discriminating between MCI and healthy elderly [60, 61, 62, and 63].

In a comparison of the MMSE and the MoCA, the MMSE had a sensitivity of 18% whereas the MoCA showed a sensitivity of 90% to identify MCI patients [48]. In a comparison of the MMSE and the ACE-R, Mioshi et al, found that the ACE-R addresses a broader range of cognitive impairments than the MMSE [44].

Our results agreed with Morris et al who explained that the ACE-R has recently been validated for use with acute stroke patients and it is a quick and easy to administer with minimal training. The ACE-R was more sensitive to identifying cognitive impairment in stroke patients than the MMSE [64]. The previously mentioned MMSE limitations was considered in the ACE-R, as the ACE-R includes the MMSE but also has measures of

executive function and offers assessment on five subscales (attention and orientation, memory, fluency, language, and visuospatial). The ACE-R has been established useful to detect impairment in attention,visuospatial and executive aspects of cognitive function in acute post-stroke patients [64]. Moreover, the ACE-R sub-scale (language)has afavorable level of sensitivity and specificity, to screen for aphasia in post-stroke patients[65].

Our results come in accordance with Nasreddine et al., who said that the MoCA screens for MCI and can be utilized to detect patients who complain of MCI and score within normal range of the MMSE. The MoCA is a 30-point test with more complicated items than the MMSE, which accounts for its increased level of sensitivity for patients in the early stages of CI [48]. Lestari et. Al. mentioned that the MoCAcan detectMCI in stroke patientsbetter thanthe MMSE[52]. This is almost similar to Toglia et al., who found that the proportions of CI detected in patients with sub-acute stroke using the MoCA and the MMSE were 89% and 63%, respectively [66]. Our results was in agreement with the study conducted by Pedlebury et al., which mentioned that more than half of the patients with a normal MMSE value (> 27), determined as CI patients and had abnormal results (< 26)when assessed with the MoCA.Pedlebury et al., mentioned that the MoCAcandetect CI more than MMSE as it investigates more cognitive aspects, which are not examined in the MMSE. Also they stated that the MMSE questions are too easy for the patients, and has a high ceiling effect [67].

Also, our results said that there was a significant difference in time needed to complete the screening for recognition of MCI, with the MMSE, the MoCA and the ACE-R, being 6.39±2.63, 10.41±2.87 and 18.85±2.06 minutes respectively $p<0.05$. Based on that time analysis, it was found that the MoCA and the ACE-R requires a much longer examination timewhen compared to the MMSE. This may be due tothe greater difficulty and the large number of questions in the MoCA and the ACE-Rthan in the MMSE.

The MoCA contains visuospatial/executivefunction, identification, attention, memory,language, abstraction, orientation components and delayed memory (18 differentitems). The ACE-R is a 100-item questionnaire that measures overall cognitive performance (attention, memory, language, fluency, and visuospatial skills). On the other hand, the MMSE only includes orientation, attention, registration, recall, calculation, and language components (11 different items). As well Aggarwal et al., results was similar to ours, theyfound that the MMSE require 7.4 minutes to be administered, while the time needed to administer the MoCA is 14.8 minutes [68]. Nasreddine et al. said that the time required to complete the MoCA is approximately 10 minutes to administer this brief, 30-point test [48].

Our results come in accordance with Samara et. al. who declared that the MoCA and the ACE-R may be more useful CSI taking only 10 and 15 minutes respectively. For comprehensiveness assessment covering primary domains of cognition to create a concise, initial clinical impression about a patient with MCI [69].

Our results also pointed out that there were a moderate correlation among the MMSE, the MoCA and the ACE-R using Spearman correlation, as follows; the MMSE and the MoCA, the MMSE and the ACE-R, the MoCA and the ACE-R,$r= 0.761,0.676$ and 0.713 respectively $P < 0.000$. This moderate correlation comes in agreement with many studies as Lestari et. al. who mentioned that there was a statistically significant moderate correlation between the MMSE and the MoCA values ($r = 0.671$; $p = 0.000$) [52]. YanHong et. al. who pointed out that there were significant correlations between the MMSE and the MoCA scores during the sub-acute stroke phase [70]. Emmanuelle et. al. mentioned that there was a very well correlated scores of the MoCA and the ACE-R with (MMSE), suggesting that these scales have good concordant validity[71]. Mattia et. al. pointed out that there was significant correlation between the ACE-R with the MoCA ($r = 0.612$, $p<0.05$) [72].

Coming from all these studies we can state that the MoCA and the ACE-R are global cognitive scales that can detect cognitive impairment, as well as the MMSE, which is the most-popularscale used recently. This moderate correlation among the MMSE, the MoCA and the ACE-R are explained by the partial overlap of the three scales. Those CSI may be a powerful global instruments to be used to discover MCI in patients with stroke.

V. Conclusion

We can say the MoCA and the ACE-R has been developed as a cognitive screening instruments to discover MCI. The proportion of MCI that can be early detected in post-stroke patients using the MoCA or the ACE-R was greater than the proportion that can be detected using the MMSE. Consequently, it is strongly suggested that the MoCA or the ACE-R can be used as an alternative to MMSE screening cognitive test for post stroke patients.

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