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Research Paper

Sensitivity, Specificity, and Cut-off Point of the Mini-Mental State Examination in Patients With Mild Traumatic Brain Injury

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ABSTRACT

Background and Aim: Most patients suffering from traumatic brain injury (TBI) are those with mild injuries (mTBI). However, due to the absence of symptoms in brain imaging until long after the injury, the manifestations of cognitive impairments remain undiagnosed. Therefore, cognitive screening is considered a key measure in these patients. One of the common screening tools for evaluating cognitive impairments is the mini-mental state examination (MMSE) test. The present study aimed to determine the cut-off point, sensitivity, and specificity of the MMSE test in mTBI patients.

Methods and Materials/Patients: In this observational and cross-sectional-analytical study, the statistical population included all patients with mTBI who were injured in the 1st half of 2022. The case group included 79 mTBI patients admitted to the trauma, neurosurgery, and intensive care unit (ICU) departments of Poursina Hospital in Rasht City, Iran, in the 1st half of 2022, who had been referred to the same hospital and Velayat specialized clinic for rehabilitation and re-visit, and the control group included 79 normal healthy individuals. Both groups were cognitively evaluated by the MMSE test on two occasions with an average time interval of 2-3 weeks.

Results: The results of the discriminant analysis showed a cut-off point of 27 to 28 as the probable point of cognitive impairment. Also, to identify the cognitive impairment in mTBI patients, this test reported low sensitivity of 0.43-0.58 and a moderate specificity of 0.69-0.80 in two tests.

Conclusion: In screening for possible mild cognitive impairment in mTBI patients, the MMSE is relatively useful and should not be used solely to replace a comprehensive neuropsychological evaluation with diagnostic purposes.

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Highlights

- The cut-off point of 27 to 28 is used to determine the probability of mild cognitive impairment.
- The mini-mental state examination (MMSE) test has low sensitivity and moderate specificity in diagnosing cognitive impairment in the population of mild traumatic brain injury (mTBI) patients.
- The MMSE test cannot be used as an alternative to a comprehensive neuropsychological assessment for diagnostic purposes.

Plain Language Summary

Annually, about 69 million people worldwide suffer from traumatic brain injury (TBI) due to different reasons. This type of injury has various social, emotional, and especially cognitive consequences, affecting performance and quality of life. In terms of severity, TBI is divided into three categories, severe, moderate, and mild, of which 80%-90% are mild. Unlike the other two categories, in mild TBI patients, the consequences of head trauma may remain undiagnosed long after the injury. For this purpose, using a tool to identify cognitive impairments in this population is required. Therefore, in this study, the mini-mental state examination (MMSE), one of the most common and up-to-date tools to identify cognitive impairments, was used. The results showed that scoring 27 to 28 out of a total score of 30 indicates the possibility of cognitive impairment. Also, in this test, the ability to correctly diagnose cases with and without cognitive impairments is 43%-58% and 80%-69%, respectively. Hence, it can be used to identify mild cognitive impairments, but not as the only tool in comprehensive diagnosis and evaluation.

1. Introduction

Traumatic brain injury (TBI) is one of the most important health concerns and cognitive problems worldwide and is considered the leading cause of mortality and disability in people under 40 years of age [1]. TBI is estimated to annually affect about 69 million cases and impose a heavy burden on patients and their families [2, 3]. Moreover, this disorder is considered one of the five main causes of death and the main cause of disability in young people in Iran [4].

According to the current diagnostic protocols, patients with mild TBI (mTBI) constitute the highest proportion of patients with TBI at 80%-90% [5]. However, only a small number of mTBI patients have relevant or suspicious pathological signs, and approximately 50% of them have cognitive problems that take longer than 1 month or even up to 1 year to be diagnosed. Therefore, a large number of these patients receive no medical intervention [6] and due to the impossibility of detecting minor changes in the structure and function of the brain, their low cognitive performance is attributed to problems existing before the injury [7]. Hence, diagnosis can be one of the most challenging and valuable aspects of clinical neurologic care for these patients [1].

Therefore, by emphasizing the understanding of subtle differences caused by mTBI, completing a clinical evaluation, the impact of TBI on cognition, the importance of assessing cognitive disorders related to TBI, and the necessity to use cognitive screening tools that lead to facilitating optimal medical decision-making, facilitate individualized, and targeted therapeutic intervention, has globally attracted the attention of researchers in this field in the last two decades [8-10].

Mini-mental status examination (MMSE) is one of the most common tools for assessing the severity and progress of various cognitive impairments [11]. Due to its translatability to other languages, high reliability, and easy use in clinical and educational settings have been considered [12]. Briefly, this test evaluates several cognitive domains, including attention, calculation, recall, language, orientation, and short-term memory [11]. Moreover, the total time required to implement it is 5-10 minutes [11], which has made it an efficient, fast, and standardized screening tool for grading patients [13]. Although the MMSE is one of the most up-to-date and common tools for rapid cognitive assessment [12], the variable time required to perform it in different groups [14] and the interaction of age and education level [15] limit its use, especially in the initial screening of cognitive impairments in society.

Numerous clinical tests are used to confirm the presence or absence of disease or to proceed with the diagnosis process. Ideally, such tests can correctly identify all patients with this disease (sensitivity) and similarly identify all disease-free people (specificity) [12]. Different studies with different cut-off points have reported the sensitivity and specificity of this test to be 97%-13% and 100%-60%, respectively [16-18].

In this regard, little evidence has supported the usefulness of MMSE in the assessment of cognitive deficits. To date, no study has conclusively proven the clinical utility of MMSE in diagnosing cognitive impairment in mTBI patients. Now the question arises whether this tool can be used to estimate mTBI patients and provide a specific cut-off point for the cognitive deficits of these patients. Therefore, the present study aimed to use MMSE for rapid assessment of cognitive status in mTBI patients and to determine its sensitivity and specificity.

2. Methods and Materials/Patients

The statistical population of this study included all mTBI patients in Rasht City, the capital of Guilan Province in the north of Iran, who were injured in the 1st half of 2022. In this cross-sectional-analytical, the consecutive sampling method was utilized to select the samples. In estimating the sensitivity and specificity of the MMSE test, the F test family in G*Power version 3.1.9.6 was used to determine the required sample size [19]. The internal mechanisms of discriminant analysis and one-way multivariate analysis of variance (test of general effects) are the same. Therefore, the total sample size was 158 participants, of whom 79 had mTBI and were admitted to the trauma, neurosurgery, and ICU departments of Poursina hospital in Rasht City in the 1st half of 2022 and referred to the same hospital, as well as the Velayat specialized clinic for rehabilitation and revisit (case group). The control group included 79 normal healthy individuals who were matched with the patients in terms of age and job status that were selected from patients' companions and their families. This study was approved by the Biomedical Research Ethics Committee of Guilan University (Code: IR.GUILAN.REC.1400.038).

The inclusion criteria included an age range of 18-65 years, a Glasgow Coma scale (GCS) score of 13-15, any memory loss for events immediately before or after the accident for <24 hour, loss of consciousness (LOC) for <30 minutes, and changes in mental status at the time of the accident (confusion, bewilderment, etc.). The exclusion criteria included any serious mental/neurological disorders before TBI (e.g. schizophrenia, dementia, epilepsy, and Parkinson's based on clinical interviews with patients and their companions), clinical manifestations appeared >48 hours after the initial trauma (according to medical records), multiple and major traumas (fractured knee or chest, ruptured spleen, etc.), being unable to respond, and being unwilling to participate for any reason. After selecting the samples, the reasons and methods of conducting the study were explained to the patients and their families or companions. Then they were assured that their information will remain confidential and their non-participation will not affect the treatment process. After obtaining informed consent from the patients or their families and collecting demographic information, the mental status examination questionnaire was completed by mTBI patients during the interview.

Study tools

Neurological Assessment Questionnaire: This questionnaire includes the consciousness level of the patient since entering the hospital using the Glasgow Coma scale (GCS), Glasgow outcome scale (GOS), the type of skull fracture according to the radiographic images of the skull, hemispheres damage, the location of brain injury, type of local or diffuse brain damage according to computerized tomography (CT)-scan, and the presence of physical trauma with TBI.

Researcher-Made Questionnaire Related to Demographic and Hospital Information: This questionnaire includes information about age, gender, marital status, level of education, cause of TBI, job position before and after TBI, and length of hospitalization, which was completed by patients at the time of admission.

Mini-Mental State Examination (MMSE): MMSE test is a paper-and-pencil questionnaire with five cognitive items of temporal and spatial orientation, processing speed, attention and calculation, recall, and verbal memory with a total score of 30, which can be completed in 5-10 minutes. Scores of 0-10, 11-26, and 27-30 indicate severe, moderate and mild, and no cognitive impairment, respectively [20]. Based on Cronbach's alpha coefficient, the reliability of this test in patients with traumatic brain injury has been reported as 0.74 [21]. Also, Seyyedian et al. [22] showed with a confidence interval of 95% that MMSE can distinguish the cognitive performance of two groups of patients with dementia and normal individuals, and based on Cronbach's alpha coefficient, they reported its internal reliability of 0.81.

Glasgow Coma Scale: Glasgow Coma scale is used to assess the level of consciousness, verbal response, and motor response. The patients' overall score on this scale is calculated between 3 and 15. On the other hand, GCS scores of <8, 9-12, and >12 indicate severe, moderate, and mild traumatic injuries, respectively. Teasdale [23] reported favorable reliability for the Glasgow Coma scale. Also, in the Iranian sample of TBI patients, internal consistency based on Cronbach's alpha coefficient for this criterion was reported to be 0.82 [24].

Data analysis

In this study, descriptive statistics indicators such as frequency, frequency percentage, Mean±SD, were used to describe the data. In addition, the output of the discriminant analysis technique was used to determine the sensitivity and specificity, and cut-off point of the questionnaire. SPSS software version 26 was also used for statistical processing.

3. Results

Out of 158 participants in the present study, 79 were mTBI patients and 79 were normal individuals matched in terms of age and job status. Table 1 shows the demographic information of the two groups. Also, Table 2 summarizes the frequency and frequency percentage of background, clinical, and neuroimaging information of mTBI patients.

Table 1. Demographic characteristics of two groups of patients with mild traumatic brain injury (mTBI) and control group

Variables		No. (%)		Statistic	df	P
		mTBI (n=79)	Non-TBI (n=79)			
Age (y)		38.79(1.63)	40.96(1.57)	0.955	156	0.341
Sex	Females	7(8.9)	18(22.8)	0.139	156	0.016
	Males	72(91.1)	61(77.2)			
Marriage	Single	33(41.8)	17(21.5)	3.30	156	0.001
	Married	45(57.0)	56(70.9)			
	Divorced	1(1.3)	3(3.8)			
	Death of spouse	0(0)	3(3.8)			
Education	Low literacy	4(5.1)	1(1.3)	2.238	156	0.027
	Elementary	11(13.9)	10(12.7)			
	Middle school	26(32.9)	20(25.3)			
	High school	28(35.4)	28(35.4)			
	University	10(12.7)	20(25.3)			
Job	Unemployed	9(11.4)	5(6.3)	1.481	156	0.141
	Worker	2(2.5)	6(7.6)			
	Driver, servicer, housewife, farmer, student	39(49.4)	35(44.3)			
	Craftsman, repairman, foreman, University student	23(29.1)	18(22.8)			
	Manager, clerk, employee, seller	5(6.3)	10(12.7)			
	Professional, proficiency	1(1.3)	5(6.3)			

Abbreviations: mTBI: Mild traumatic brain injury.

Table 2. Demographic and clinical characteristics of patients with mild traumatic brain injury (mBTI)

Value		No. (%)
Job (after trauma)	Unemployed	11(13.9)
	Worker	2(2.5)
	Driver, servicer, housewife, farmer, student	38(48.1)
	Craftsman, repairman, foreman, University student	22(27.8)
	Manager, clerk, employee, seller	5(6.3)
	Professional, proficiency	1(1.3)
Cause of trauma	Car accident	18(22.8)
	Motorcycle accident	27(34.2)
	Pedestrian accident	5(6.3)
	Hit objects	2(2.5)
	Falling down	3(3.8)
	Conflict	8(10.1)
	Drop off	16(20.3)
Brain fracture	None	61(77.2)
	Linear	14(17.7)
	Depressed fracture	3(3.8)
	Basal fracture	1(1.3)
Brain injury direction	None	23(29.1)
	Right hemisphere	22(27.8)
	Left hemisphere	27(34.2)
	Bilateral injury	7(8.9)
Damaged area of brain	None	15(19.0)
	Forehead lobe	25(31.6)
	Temporal lobe	18(22.8)
	Parietal lobe	8(10.1)
	Combination	13(16.5)
Type of trauma	Focal	79(100)
	Diffuse	0(0)
Type of focal trauma	None	7(8.9)
	Cerebral contusion	16(20.3)
	EDH	19(24.1)
	SDH	6(7.6)
	SAH	7(8.9)
	ICH	3(3.8)
	Combination	21(26.6)

EDH: Epidural hematoma; SDH: Subdural hematoma; SAH: Subarachnoid hemorrhage; ICH: Intracerebral hemorrhage.

Table 3 shows the Mean±SD of the total score of the MMSE subscales in the two groups at two times (with an interval of 2-3 weeks after the trauma). The results of the Student's t-test showed a significant difference in the scores of MMSE subscales (P<0.05) except for the Processing Speed subscale in the 1st evaluation time (P=0.157). The cognitive performance of the control group was much better than the case group.

Discriminant analysis was performed to determine the sensitivity and specificity of MMSE in differentiating mTBI patients from normal individuals in terms of cognitive status, and its results are shown in Table 4.

Among the 79 patients, after the test in the 1st round, 34 real patients (true positive) and 45 falsely healthy (false negative) were diagnosed. Also, in the 2nd round,

Table 3. Comparison of the average of total scores and MMSE subscales between the two groups of patients with mild traumatic brain injury (mTBI) and control group in two times of the test

Subscale			Mean±SD	t	df	P
Orientation	Time 1	TBI	9.37±1.112	4.376	156	0.000
		Non-TBI	9.94±0.316			
	Time 2	TBI	9.68±0.689	3.458	156	0.001
		Non-TBI	9.96±0.192			
Speed processing	Time 1	TBI	2.97±0.158	1.423	156	0.157
		Non-TBI	3.00±0.000			
	Time 2	TBI	2.94±0.220	2.040	156	0.043
		Non-TBI	3.00±0.000			
Attention-calculation	Time 1	TBI	3.50±1.142	5.381	156	0.000
		Non-TBI	4.37±0.881			
	Time 2	TBI	3.84±1.075	3.140	156	0.002
		Non-TBI	4.35±0.947			
Recall	Time 1	TBI	2.77±0.451	4.111	156	0.000
		Non-TBI	2.98±0.112			
	Time 2	TBI	2.70±0.457	4.537	156	0.000
		Non-TBI	2.96±0.192			
Verbal memory	Time 1	TBI	7.26±1.247	4.396	156	0.000
		Non-TBI	8.11±1.176			
	Time 2	TBI	7.59±0.954	3.704	156	0.000
		Non-TBI	8.20±1.102			
Total	Time 1	TBI	25.89±2.902	6.215	156	0.000
		Non-TBI	28.43±2.164			
	Time 2	TBI	26.78±2.146	5.007	156	0.000
		Non-TBI	28.48±2.111			

TBI: Traumatic brain injury.

Table 4. Sensitivity and specificity of Mini-Mental State Examination (MMSE)

Time	Observed Membership	Predicted Membership		Sensitivity	Specificity
		TBI	Non-TBI		
1st	TBI	34	45	0.43	0.80
	Non-TBI	15	64		
	Overall classification accuracy	62%			
2nd	TBI	46	33	0.58	0.69
	Non-TBI	24	55		
	Overall classification accuracy	63.9%			

Abbreviations: TBI: Traumatic brain injury.

46 participants were diagnosed as real patients (true positive) and 33 participants were diagnosed as falsely healthy (false negative). Therefore, as shown in Table 4, the sensitivity of MMSE in the 1st and 2nd rounds was determined as 0.43 and 0.58, respectively. In addition, among normal individuals, after performing the test in the 1st round, 15 false patients (false positive) and 64 normal participants (true negative) were diagnosed. Also, in the 2nd test, among the healthy group, 24 participants (false positive) and 55 participants (true negative) were diagnosed as false patients and real healthy, respectively. Therefore, as shown in Table 4, the specificity of MMSE in the 1st and 2nd tests was 0.80 and 0.69, respectively. Also, the overall classification accuracy for this test was calculated as 62% and 63.9% in the 1st and 2nd rounds, respectively. It means that 62% of the participants were correctly classified into two groups, and the rest (38%) was incorrectly classified.

Cut-off point

In the 1st round of assessments, the cut-off point of MMSE with the discriminant analysis was calculated as 27.13, and obtaining a score between 27/28 and below in the MMSE test indicated that mTBI patients with possible cognitive impairment could be distinguished from normal participants without mTBI. Also, in the 2nd round of the MMSE cut-off point was calculated as 27.61 with discriminant analysis, and obtaining a score between 27 and 28 or below in the MMSE test indicated that mTBI patients with possible cognitive impairment could be distinguished from normal participants without mTBI. According to the findings obtained from the MMSE cut-off point at two times, the optimal cut-off point of this test for distinguishing patients with mTBI from normal participants was 27 to 28 in terms of cognitive status.

4. Discussion

Today, with improved levels of clinical treatment, more TBI patients can survive. However, their residual functional disorders seriously affect their prognosis and functional independence and impose a heavy burden on patients and their families [3]. Compared to the normal group, mTBI patients showed poorer performance in general cognitive ability, attention, processing speed, naming, short-term memory, and executive functions. The results from this study are consistent with previous studies that have reported significant cognitive deficits in mTBI patients, mainly related to episodic memory [25, 26]. In addition, during the 11-month follow-up, mTBI patients showed poorer performance in attention, memory, language, and executive functions [26]. These studies support the findings of the present study by providing evidence of impairment in several cognitive domains in mTBI patients.

Cognitive disorders are one of the leading causes of TBI-related disabilities that have detrimental effects on rehabilitation outcomes [9]. Despite the apparent conflicts and limitations in its accuracy and capability [27], the MMSE has been globally considered one of the most widely used cognitive screening tests for more than 40 years [12]. Most cognitive tests are influenced by age and education, and MMSE is no exception to these conditions [15]. So that patients with higher education levels may be more familiar with the tasks in it and thus show less deterioration in cognitive performance levels. Another significant limitation of this test is the time required to complete it. Since the MMSE is relatively easy to complete and takes about 5-10 minutes to complete [11], it can help clinicians to diagnose the presence or absence of a problem. However, while healthy individu-

als without cognitive impairment can complete it in 5-8 minutes, it often takes over 15 minutes in patients with cognitive impairment [14].

The results of this study introduce a cut-off point of 27 to 28 with 95% confidence level to distinguish mTBI patients with possible cognitive impairment from normal subjects without mTBI. According to this finding, previous studies have shown the range of scores of 27-30, 26-21, 20-11, and 0-10 for healthy and normal subjects, and people with mild, moderate, and severe cognitive defects, respectively [20]. More recent research has reported the MMSE cut-off point for identifying mild cognitive impairment in TBI patients to be 28.5 [28], which is almost consistent with the findings of the present study.

According to the results of sensitivity and specificity in this study, it is recommended that the MMSE test cannot be used as an alternative to a comprehensive neuropsychological assessment with a diagnostic purpose. Consistent with the present study, previous studies have shown that MMSE has low sensitivity in diagnosing mild cognitive impairment [17, 18]. In a study, the sensitivity of MMSE in diagnosing mild cognitive impairment with a cut-off point of 24 was about 0.6, but the specificity was >0.96 [27]. Also, in the study conducted by Tsai et al. [29] on patients with mild cognitive impairment, the sensitivity of the MMSE test at cut-off points of 24 and 20 was 0.88 and 0.79, and the specificity was 0.74 and 0.08, respectively.

On the other hand, patients attending clinics are often those who complain of memory and are sometimes referred from primary health care centers. Therefore, a comprehensive neuropsychological assessment provides more insight into the deficits that occur in general and specific cognitive functions [30]. Since MMSE has high specificity and low sensitivity to identify mild cognitive disorders [16], diagnosis of cognitive deficits is not recommended, especially in low-prevalence diseases, in which tests with high sensitivity and low specificity are more desirable to prevent the misdiagnosis of patients or healthy cases.

5. Conclusion

A score of 27/28 and below can indicate mTBI patients with possible cognitive impairment. The sensitivity and specificity results of this tool are significantly different from the optimal diagnostic values (90%), which may cause a substantial classification error. Nevertheless, the MMSE is somehow useful in excluding definite cases of cognitive impairment and free of cognitive impairment in screening possible cases of mild cognitive impairment. By using the MMSE to eliminate the need for a broader neuropsychological evaluation, physicians can speed up the clinical evaluation process to diagnose cognitive deficits.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Biomedical Research Ethics Committee of Guilan University (Code: IR.GUILAN.REC.1400.038).

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Authors' contributions

Conception and design: Maryam Jafroudi and Sajjad Rezaei; Data Collection: Maryam Jafroudi, Zoheir Reihanian and Shahrokh Yousefzadeh-Chabok; Data analysis and interpretation, drafting and revising the article and final approval: All authors.

Conflict of interest

The authors declared no conflict of interest.

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