

Methods of cognitive status research in patients with glioblastoma

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Abstract

Introduction: Glioblastoma is a high-grade, aggressive central nervous system tumor with predominantly astrocytic differentiation, characterized by fast invasive growth into the surrounding brain parenchyma and aggressive clinical course. The short life expectancy of patients diagnosed with glioblastoma necessitates the need to maximize their quality of remaining life. One of the most common reasons for quality of life impairment in these patients is the cognitive deficit accompanying the disease. There is a lack of a unified and standardized method for the assessment of cognitive functions in these patients, which meets all the necessary criteria to be convenient and usable in the wide clinical practice.

Aim: The aim of the present study is to compare the Montreal cognitive assessment (MoCA) brief screening test with an extended neuropsychological examination to determine its applicability in patients diagnosed with glioblastoma.

Material and methods: The study includes 27 patients undergoing neurosurgical intervention for histologically proven IDH-wildtype glioblastoma in the Department of Neurosurgery, “St. Marina” University Hospital – a tertiary healthcare center, for the period January 2019 to December 2022. Preoperatively, patients were examined with the short MoCA screening test and an extended neuropsychological examination including the following subtests: Issac set test, Trail making test A and B, Luria test, Raven’s color matrices, Stroop test and Bender test.

Results: Of all the patients studied, those with a MoCA score below 26 points present at least one negative test of the extended neuropsychological examination. MoCA patients with scores of 26 or more do not demonstrate cognitive impairment in the extended neuropsychological impairment.

Conclusion: The obtained results support the claim that the MoCA short screening test is applicable for preoperative diagnosis of cognitive disorders in patients with glioblastoma. Due to the study’s small sample size, further research is needed to definitively prove this claim.

Key words: Montreal cognitive assessment test, cognitive functions, glioblastoma, IDH1 wild type

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Introduction

Glioblastoma is the most common primary brain tumor in adults. The life expectancy varies between twelve and sixteen months from the time of diagnosis.¹ The short life expectancy of these patients necessitates the need to maximize their quality of life. It has been proven that cognitive disorders are manifested in almost all patients diagnosed with a primary brain tumor during some of the stages of the disease development.² The existing cognitive deficit is directly related to the quality of life.³ The gold standard for the diagnosis of cognitive disorders is the extended neuropsychological examination, however it is not readily accepted as a routine neurosurgical clinical practice due to a number of disadvantages: long duration of the examination, requirement of an isolated space for implementation, the need for prior training and certification of the examiner or the presence of a clinical psychologist in the clinic, frequent false-negative results due to patient fatigue induced by the long duration of the study, and last but not least, not all tests are free and widely available. Various studies have been reported in the medical literature aiming to overcome these shortcomings by introducing brief screening methods to be used in the neurosurgical clinical practice, however all brief tests studied so far have been found to be insufficiently sensitive.

Materials and method

The present study is a single-center, prospective, comparative study of cognitive impairment in patients with glial tumors comparing the sensitivity of the brief MoCA screening method and the extended neuropsychological examination. Ethical approval was granted by the Committee on Scientific Ethics at Medical University – Varna „Prof. Dr. Paraskev Stoyanov”, Varna, Bulgaria.

For the period January 2019 to December 2022 year, all hospitalized patients for neurosurgical treatment, at the Department of Neurosurgery at the “St. Marina” University Hospital, a tertiary healthcare center, presenting with imaging and

clinical evidence suggestive of the presence of a glial tumor, were included in the study. All patients signed an informed consent and personal data protection form.

Initial exclusion criteria were patients previously subjected to central nervous system surgical intervention, previous cerebrovascular incident, preexisting neurocognitive deficit and history of trauma. Due to inconclusive and conflicting data on the influence of anxiety and depression on cognitive disorders, all patients with high levels of anxiety and depression are excluded from the study. Patients are preliminary screened for anxiety and depression by filling in a short questionnaire standardized for the Bulgarian population.

The study was conducted in two stages, within two consecutive days during the patients' preoperative period, in order to avoid false positive results due to patient fatigue and loss of concentration. Patient testing is performed solely by the principal investigator in order to place patients under the same conditions. The cognitive tests used to diagnose patients are: MoCA, Issac set test, Trail making test A and B, Luria's test, Raven's color matrices, Stroop test and Bender's test. The collected data from the preoperative cognitive tests was analyzed in a descriptive manner to depict the main characteristics of the sample, from the indicators included in the study. Central tendency measures such as arithmetic mean and non-parametric tests such as chi-square are used as the basis of the analysis in search of significant differences in the frequency representation of categorical values. Statistical significance in non-parametric tests was accepted at $p \leq 0.05$. All statistical tests were carried out using SPSS statistical software package.

Results

A total of 73 were initially screened. From the primary cohort, only 42 met the full inclusion criteria and based on their histopathology, 32 were diagnosed with a glial tumor, 27 of which with IDH-wild type glioblastoma. The

remaining patients with a different histological diagnosis (metastasis, abscess, astrocytoma) were retrospectively excluded from the study. From the IDH-wild type glioblastoma patients, n = 10 were female and n = 17 were male, aged 42–78 years old (mean age 60). In n = 13 patients the tumor was located in the left hemisphere, and in n = 14 – in the right hemisphere. (Fig. 1)

Fig. 1. Distribution of the glioblastomas by location

Location	Value	Glioblastoma
Frontal	№	5
	%	15.6%
Temporal	№	5
	%	15.6%
Parietal	№	3
	%	9.4%
Occipital	№	3
	%	9.4%
Parietooccipital	№	7
	%	21.9%
Frontoparietal	№	4
	%	12.5%
Temporooccipital	№	0
	%	0.0%
Frontotemporal	№	0
	%	0.0%
Total	№	27
	%	84.4%

Out of all 27 patients, two successfully passed the MoCA short screening test with a score greater than or equal to 26 points. No cognitive disorders were detected from those two patients when tested with the extended neuropsychological examination. The test includes: Issac set test, Trail making test A and B, Luria test, Raven’s color matrices, Stroop test and Bender’s test. (Fig. 2 and Fig. 3)

Fig. 2. MoCA test results

MoCA	Value	Glioblastoma
Not Passed	№	25
	%	78.1%
Passed	№	2
	%	6.3%
Total	№	27
	%	84.4%

Fig. 3. Advanced neuropsychological examination results

Test	result	№	%
ISSAC	Passed	2	100%
TMT-A	Passed	2	100%
TMT-B	Passed	2	100%
Luria	Passed with 8 points	1	50%
	Passed with 9 points	1	50%
Bender	Passed	2	100%
Raven	Above the average level for the age	2	100%
Stroop	Passed	2	100%

Of the remaining patients who did not pass the MoCA test, cognitive impairment is diagnosed according to at least one of the tests part of the extended neurocognitive examination. The most affected cognitive areas are: executive functions and memory, and the least affected are image-constructive abilities. The average total duration of the extended neuropsychological examination is 1 hour and 17 minutes. The shortest examination duration is 50 minutes and the longest examination is 2 hours and 45 minutes. The average duration of the MoCA examination is 15 minutes, and the examination do not last longer than 22 min. All of the tested patients evaluate the short MoCA screening test as not burdensome. Regarding the extended neuropsychological study, five of the test subjects report study-related exhaustion.



Discussion

MoCA has been established as a test for the study of cognitive functions in a number of neurological diseases.⁴ The test's sensitivity has been proven even in terms of detecting mild cognitive impairments.⁵ Regarding the applicability of the test in neuro-oncology, various studies are contradictory. A large part of the studies of the cognitive functions of patients with glial tumors were carried out only in the postoperative period, after removing the main cause of the cognitive deficit and after the superimposed influence of anesthesia and medication, which, in our opinion, is a prerequisite for inaccuracy in the final results.^{6,7} A small part of the studies that were carried out preoperatively were carried out in the period before 2021, before the introduction of the latest WHO classification of tumors of the CNS. This would retrospectively explain discrepancies in the results obtained, as it became clear that IDH-mutant astrocytomas and IDH wild-type glioblastomas have different behavior and prognosis. Due to the resulting heterogeneity of the examined patients in the studies before 2021 it can't be determined with certainty whether a given screening method for investigating cognitive deficits is appropriate for use in the diagnosis of glioblastoma. Some of the studies were carried out on the basis of a heterogeneous sample of tumors, whose clinical course and impact on cognition are difficult to compare, and the final conclusions may change when considering a specific tumor group in isolation.⁷

Conclusion

MoCA test showed no lapse in the diagnosis of cognitive impairment in patients with glioblastoma in the studied patient group. In terms of administration time, MoCA test showed a significant difference compared to the extended neuropsychological study and was better accepted by patients. This makes the test more convenient for application in daily neurosurgical practice compared to the advanced neuropsychological examination. Due to the small sample size of the present study, further research is needed to prove this claim.

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