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Original article

Reprint

Functional prognosis of acute ischemic stroke patients from their neuropsychological features

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Abstract:
The objective was to evaluate the relationship between the patient neuropsychological condition and recovery of his/her motor activity disorder due to acute cerebrovascular accident.
Materials and Methods. The study involved 103 patients with ischemic stroke in the pools of middle and anterior cerebral arteries. We carried out clinical and neurological assessments of the patient condition, and conducted neuropsychological testing via Beck Hopelessness Scale (BHS), Montreal Cognitive Assessment (MoCA), SF-36, and Visual Analog Scale (VAS). The examination was performed on three occasions: during the acute phase of cerebral circulatory disorders, after two weeks and within the range of 24-36 months. After the long-term follow-up, all patients were distributed among two groups: with a favorable outcome and with unfavorable outcome. We attempted to identify the most typical values of above-mentioned scales for each group.
Results. The general physical health (GPhH) indicators based on the results of SF-36 (p=0.007), BHS (p=0.003 and 0.002), and VAS (p=0.025), collected after acute ischemic stroke, were prognostically significant. In both groups, the most important indicators for the stroke prognosis were MoCA (p=0.038), BHS (p=0.009) and SF-36 (GPH) (p=0.002), regardless of the stroke phase.
Conclusion. The connection between the patient neuropsychological condition and restoring the motor functions after the stroke was revealed. The investigated questionnaires can be included in the multivariate forecast model of the stroke prognosis among other criteria for the outcome of this disease.

Keywords: ischemic stroke, neuropsychological test, stroke prognosis, rehabilitation.

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Introduction

The psychological state of a person has a direct impact on his/her physical condition and on the functioning of all internal organs on the whole. Health disorders affect the psychological state of an individual, and vice versa. This becomes especially noticeable in case of serious diseases, such as an acute cerebrovascular accident (ACVA), also known as 'stroke'. Experiencing major manifestations of damage to the nervous system, characteristic of stroke (pronounced disorders of a motor, sensory, coordination, and speech-related nature, to name a few), a sick person suffers morally as well. The inability to perform habitual actions, smaller social activity, worries of being a burden for relatives, and fear of a permanent disability impose serious moral suffering on a patient [1].

Medical psychologists, who are part of a multidisciplinary team of rehabilitation specialists for the patients who experienced stroke, often diagnose depression, cognitive impairment, other emotional and personality disorders, and reduced quality of life in such patients. Correction and treatment of psychological disorders caused by ACVA are among important factors of successful motor function restoration in a patient after the stroke. Numerous scientific studies confirmed this fact. For example, in research conducted in Yekaterinburg in 2013 on 72 patients, I.A. Charikova et al. discovered a relationship between the severity of stroke and the intensity of the stress reaction and depression. The authors found the signs of severe depression in patients who underwent ACVA. A connection was revealed between the severity of emotional and volitional disorders and neurological manifestations, and a continuous process has been described when ischemic stroke was accompanied by stress, leading to the emergence of depression. The latter, in turn, impeded the restoration of impaired functions and hampered successful rehabilitation [2].

Emotional disorders under focal changes in the brain were described in detail by such clinicians as A.R. Luria, T.A. Dobrokhotova, E.D. Chomskaya, and others. Many authors conducted scientific research in this specific field and concluded that the state of emotions and mental functions depended on the brain lesion localization, along with initial

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personality characteristics, age, gender, and premorbid state [3-5]. Cognitive disorders very often accompany ACVA, being its consequence, which is manifested by a decrease in attention, memory, and mental capacity. It was shown that cognitive disorders, manifested by a decrease in memory, mental capacity for work, intelligence, and attention, are among the frequent effects of stroke. It is the state of cognitive abilities that often affect the course and prognosis of the disease [6]. According to available published sources, one third of patients with cerebral vascular diseases were diagnosed with the so-called 'vascular depression' [7].

The quality of life also changes in a patient after ACVA. The dynamics of indicators can be observed in different phases of the disease. According to I.L. Gureeva et al., patients with ACVA had a bias in assessing their quality of life as average normal precisely because of their reduced critical thinking and cognitive impairment, which did not allow them perceiving the full severity of the stroke consequences [8].

The mentioned studies in the field of neuropsychology confirmed the relevance of an in-depth research on neuropsychological characteristics of patients in the acute phase of ischemic stroke. The question remains open, whether the indicators of questionnaires, evaluating the levels of depression, along with cognitive functions, quality of life, and other factors, are the markers of the ACVA outcome. Can they be used as criteria reflecting the prognosis of the disease? Is there a relationship between them and the motor function recovery in patients with hemiparesis caused by ischemic stroke? Efforts of medical psychologists and psychiatrists regarding the rehabilitation of patients after the stroke is important, since their competent analysis of mental activity improves the quality of treatment and recovery of the entire human body [9].

Objective: to identify the relationship between the patient neuropsychological condition and recovery of his/her motor activity disorder, developed as a result of ACVA.

Materials and Methods

The study was carried out at the regional vascular center of Samara Oblast Clinical Hospital at Samara State Medical University of the Russian Federation Ministry of Healthcare. All procedures were performed in accordance with the standards of the tripartite Agreement on Good Clinical Practice, the ethical principles of the Declaration of Helsinki by the World Medical Association (Seoul, 2008), and the current legislation of the Russian Federation (research protocol No. 147 of October 22, 2014, Samara State Medical University). All patients signed written informed consent to participate in the study.

Of all patients admitted to the primary vascular department in 2015-2016, 103 individuals took part in the study: 66 men (64.1%) and 37 women (35.9%). Their age ranged from 39 to 88 years old. All subjects were diagnosed with ischemic stroke in the carotid system and central hemiparesis. The enrollment of patients in the study was performed taking into account the inclusion and exclusion criteria.

The inclusion criteria encompassed the following: verified diagnosis of ACVA (ischemic type); acute and subacute phases of stroke; presence of neurological symptoms in the form of central hemiparesis (1-3 points on Zacharias motor deficit scale); 2–20 points on the NIHSS (National Institutes of Health Stroke Scale); 2–4 points on Rankin scale; Rivermead Mobility Index of 1 to 9 points; specified type of ischemic stroke; localization of the ischemic focus in the internal carotid artery basin; ≤ 3 days from the stroke onset; informed consent of the patient or his/her relatives to participate in the study; lack of exclusion criteria.

The exclusion criteria incorporated the history of stroke with persistent motor deficit; hemorrhagic stroke with subarachnoid hemorrhage; ischemic stroke in the vertebrobasilar basin; speech disorders in the form of pronounced aphasia; severe general somatic condition of the patient (renal and/or hepatic failure, etc.); impaired consciousness (sensu Glasgow Coma Scale); psychomotor agitation; dislocation of the midbrain; hemispheric stroke; mental disorders in the premorbid period, including dementia; contraindications for brain computed tomography.

In all patients, the predominant symptom was impaired motor function in their limbs. In the first hours of treatment, patients underwent examination in accordance with the standards of medical care for patients with stroke: collection of clinical and anamnestic data, physical examination with assessment of neurological and general somatic statuses, Doppler ultrasound of brachiocephalic blood vessels, transcranial Doppler blood flow mapping, computed tomography of the brain, laboratory biochemical blood tests, hemostasis assessment, electrocardiography, and general urine test.

Extensive neuropsychological examination included the following components: assessment of the depression level sensu Beck Hopelessness Scale (BHS), evaluation of the cognitive functions sensu Montreal Cognitive Assessment Scale (MoCA), calculation of the quality-of-life index from the Short-Form 36 Health Status Questionnaire (SF-36) and the Visual Analog Scale (VAS). Such examination was conducted three times: in the acute period of stroke, at discharge (after 14 days) and on an outpatient basis (after 24-36 months).

Beck Depression Inventory is a questionnaire authored by A.T. Beck et al. (1961). The scale (BHS), based on that questionnaire, consists of 21 multiple choice questions with 4-5 options of an answer. Questions reflect the symptoms and manifestations of depression, and are indicative its different severity levels. According to the test results, it is possible to determine the presence and level of depression: 0-13 points designate the normal patient condition in terms of depression (i.e., none whatsoever); 14-19 points indicate mild depression; 20-28 points imply moderate depression; 29-63 points suggest severe depression [10].

Montreal Cognitive Assessment Scale, MoCA, has been in use since 1996. It is a rapid screening test for cognitive impairment. The results are evaluated in points: 26-30 points suggest the norm; lower score indicates the presence of cognitive impairment [11].

The SF-36 questionnaire, Medical Outcomes Study 36-item Short-Form Health Survey, developed in 1992, is often used to subjectively assess the quality of life. It consists of eight health categories. As a result, two major blocks are formed: general physical health (GPhH) and general psychological health (GPsH). We used these indicators in our study.

Visual Analog Scale, VAS, invented by Huskisson E.S. (1974), is conventionally employed to subjectively assess the pain experienced by the patient [12]. Patients are asked to assess their overall health status at the time of the survey on a 100 mm scale, where 0 is the worst health condition and 100 is the best one. Using a ruler, the score is determined by measuring the distance (mm) between the leftmost anchor on

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the 10 cm line and the patient's mark, thereby providing a range of scores from 0–100. Accordingly, based on the scores, the quality of life can be assessed as high (75-100 mm), slightly reduced (45-74 mm), moderately reduced (5-44 mm), or low (0-4 mm).

In addition to these tests, the patient clinical condition was monitored with an emphasis on the dynamics of hemiparesis. At the outpatient stage of follow-up (24-36 months after stroke), all patients were distributed among two groups: with a favorable outcome and unfavorable outcome, based on the recovery of the motor function in the arm and leg, lost in the course of the stroke. Those patients, whose strength in the paretic limbs increased on a five-point Zacharias motor deficit scale, the number of points on the NIHSS and Rankin scales decreased, whereas number of points according to the Rivermead and Fugl-Meyer questionnaires increased, were allocated to the group with positive dynamics. Accordingly, remaining patients were assigned to the group without positive dynamics. A retrospective comparison was made of how the results of questionnaires, reflecting the emotional and cognitive state of patients, correlate with the recovery of their motor function after stroke. The regularities in distribution of the results sensu listed scales in two groups of patients were assessed.

The statistical analysis was performed using Microsoft Excel and Statistica 12.0 software. The critical level of significance in the course of testing statistical hypotheses was assumed at the value of p=0.05. Pearson's chi-squared test was employed to analyze the normality of the distribution of samples. Quantitative features with a normal distribution of their values were presented as M (SD), where M is the arithmetic mean and SD is the standard deviation. The description of quantitative traits, the distribution of which was different from normal, was presented in the form of Me (Q1; Q3), where Me is the median, Q1 and Q3 are the first and the third quartiles, respectively. Frequencies and relative frequencies were indicated to describe qualitative features. For normally distributed populations, the comparison of independent samples was carried out using Student's unpaired t-test, whereas for dependent samples, Student's paired two-sample t-test was conducted. For populations with non-normal distribution, the comparison of independent samples was carried out using the Mann-Whitney U test, while dependent samples were subjected to Wilcoxon signed-rank test.

When analyzing contingency tables to investigate the relationship between the questionnaires' scores (the level of depression, cognitive impairment, assessment of the quality of life) and the corresponding group of patients, as well as to establish the fact of the statistical significance of differences in these biomedical indicators, we used Pearson's chi-squared test (if the frequencies in groups were at least 5), or Fisher's exact test (if the frequency in at least one subgroup was smaller than 5).

Results

The mean stroke severity score in the first 3-4 days of ACVA was 7.32 (4.07) points sensu NIHSS, 3.27 (0.98) points on Rankin scale, and 5.45 (3.73) points on Rivermead scale. The mean value of motor deficit sensu Fugl-Meyer scale was 60.07 (20.89) points. The median NIHSS score for the entire sample was 7 points (8 in the group with a favorable outcome vs. 6 in the group with unfavorable outcome).

Prior to analyzing the SF-36 scale data, all measured values of GPhH and GPsH indicators at both first and last patient examinations were checked for normality. Normal distribution of the sample was revealed on both occasions.

Patients rated their quality of life in the GPhH category in the chronic period of stroke at 41.76 (14.36) points; the average valued of the GPsH block was 44.99 (13.86) points. In the group of patients with a favorable outcome, the average GPhH score of 49.9 (8.97) points was higher than in the group with negative dynamics: 36.03 (10.83) points. Calculation of the Mann-Whitney U criterion and T statistic showed that the results of the SF-36 questionnaire (GPhH: p=0.396); GPsH: p=0.558) in the acute period of the disease did not have statistical significance for the prognosis of stroke in both groups of patients. At the third (outpatient) stage of patient examination, the GPhH indicator was statistically significant in terms of stroke prognosis (p=0.007), while GPsH was not (p=0.565).

The results of the SF-36 questionnaire were compared in dynamics (in acute vs. chronic stroke phases) in both patient groups (favorable vs. unfavorable outcomes). We were determining how much the quality of life has changed in a patient from a particular group. In the group with a favorable outcome, the difference between the quality-of-life levels at the onset of the disease and after 24-36 months, according to patients' opinions, was significant in terms of GPhH values (p<0.001): 37.71 vs. 43.64 points. As for GPsH, no significant difference was detected (p=0.313).

In the group with an unfavorable outcome, neither GPhH (p=0.388) nor GPsH (p=0.271) significantly differed in the acute phase vs. chronic phase of stroke. The values of these indicators did not have statistically significant dynamics.

For the entire sample, the difference in the GPhH values over time was significant (p=0.002), in contrast to GPsH (p=0.716). According to the patient survey results, physical health values increased from 36.32 points to 40.82 points.

To identify prognostically important signs influencing the outcome of ACVA, Beck Depression Inventory was conducted, and the results of BHS were analyzed.

The median level of depression for the entire sample was 2 (moderate); 1st quartile was represented by the level 1 (mild); 3rd quartile corresponded to level 3 (severe) both at the acute phase of stroke and at its chronic phase (i.e., during the outpatient stage of the study). Descriptive statistics for BHS data can be viewed presented in *Tables 1* and *2*.

Calculation, using the final number of points after passing the Beck test, resulted in no statistically significant relationships, revealed between the indicators of depression in groups 1 and 2 in the first three days of illness (p=0.273). However, such relationship was observed at the outpatient stage (p=0.003). For these calculations, Mann-Whitney U test was used.

Table 1. Depression levels sensu Beck Hopelessness Scale in the study groups (in points)

Statistic	Entire sample		Group 1		Group 2	
	1st visit	3rd visit	1st visit	3rd visit	1st visit	3rd visit
Me	2	2	2	2	3	3
Q1	1	1	1	1	1	2
Q3	3	3	3	3	3	3

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Table 2. Overall score on the Beck Hopelessness Scale in the study groups (in points)

Statistic	Entire sample		Group 1		Group 2	
	1st visit	3rd visit	1st visit	3rd visit	1st visit	3rd visit
Me	7	7	6	7	8	9
Q1	3	3	2	3	4	5
Q3	10	11	10	9	12	14

The Wilcoxon signed-rank T-test was used to compare the results BHS in each group of patients, interviewed in the acute phase of stroke vs. its chronic phase (i.e., after 24-36 months). The most pronounced statistically significant differences, when comparing the results of BHS, collected in different phases of stroke, were found across the entire sample (p=0.009) and in the group with an unfavorable outcome (p<0.001). In all patients, the severity of depression in the entire sample did not decline over time from the onset of the disease and remained equal to 7 points. In the group with negative dynamics of the motor activity, the median of BHS value increased from 8 to 9 points. In the group with a positive outcome, there was no statistically significant difference among the results of the questionnaire (p=0.294).

The observation results differ insignificantly when taking into account the severity of depression: from mild (1) to severe (3). No statistically significant relationships between depression values in the first vs. second groups were found during the study in the acute phase (i.e., first three days) (p=0.584), but such relationship occurred at the third phase (outpatient stage) (p=0.002). For these calculations, the Mann-Whitney test was employed.

As far as Wilcoxon statistic concerned, no statistically significant difference was found among the examination results in the acute vs. chronic phase of stroke for the entire sample (p=0.686); however, separately for each group, we observed significant trends: in the group with an unfavorable outcome, the degree of depression remained at the same level – severe depression (grade 3, p=0.018); in the group with a positive outcome of stroke, depression also remained stable at the moderate level (grade 2, p=0.018).

The results of the MoCA scale were analyzed. *Table 3* presents the descriptive statistics for those.

No statistically significant relationships were found between the values of the cognitive impairment scale in groups 1 vs. 2, based on interviewed patients both in the first three days (p=0.643) and several months after the onset of stroke (p=0.391). For these calculations, the Mann-Whitney test was used.

According to the Wilcoxon test, statistically significant differences between the obtained scores of the questionnaire for assessing cognitive functions in the first days after stroke and after 2-3 years were found in the group with an unfavorable outcome (p=0.023) and in the entire sample (p=0.038). For the entire sample, the level of cognitive impairment on the MoCA scale did not deteriorate and remained equal to 19 points (the median) throughout all observation period. The median MoCA values in the group with negative dynamics of paresis decreased from 20 to 19 points, which indicated a decline in the level of cognitive abilities. There was no significant difference in the scores on the MoCA scale in the group with a favorable outcome (p=0.937) during the survey on the first visit vs. the third visit.

Of interest are the results obtained in the course of analyzing the VAS scale values (*Table 4*).

he VAS results at the first visit in both groups of patients were not statistically significant in terms of stroke prognosis (p=0.929). Subjective assessment of his/her health by the subjects in the chronic phase revealed the statistical significance of this scale in terms of the disease outcome (p=0.025).

Comparison of the VAS results in dynamics in each group separately showed that in the group of patients with a favorable outcome, this indicator had a statistically significant difference in the scores on this scale in the acute vs. chronic phase of ACVA (p=0.016). At the onset of the disease, patients from the group with a favorable outcome assessed their health by a median of 50 points, while after improvement of their motor functions in the affected limbs, this score increased to a median of 60 points. The subjective assessment of their health increased over time. In the group with an unfavorable outcome (p=0.315), as well as in the entire sample (p=0.536), VAS values did not differ statistically significantly, in terms of health level scale, at different visits.

For clarity, the results for all questionnaires are summarized in *Table 5*.

Table 3. Overall scores on the Montreal Cognitive Assessment scale in the study groups (in points)

Statistic	Entire sample		Group 1		Group 2	
	1st visit	3rd visit	1st visit	3rd visit	1st visit	3rd visit
Me	19	19	19	20	20	19
Q1	15	14	15	14	14	14
Q3	22	23	24	23	21	21

Table 4. Overall scores on the Visual Analog Scale in the study groups (in points)

Statistic	Entire sample		Group 1		Group 2	
	1st visit	3rd visit	1st visit	3rd visit	1st visit	3rd visit
Me	50	50	50	60	55	50
Q1	47	40	50	50	39	38
Q3	70	80	70	80	70	80

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Table 5. Statistical significance of the results of neuropsychological questionnaires versus acute cerebrovascular accident phase or outcome (based on Chi-squared test)

Indicators	Acute phase of stroke	Long-term recovery phase of stroke (24-36 months)	Group with favorable outcome	Group with unfavorable outcome	Entire sample
SF-36 (GPhH)	0.396	0.007	0.003	0.388	0.002
SF-36 (GPsH)	0.558	0.565	0.313	0.271	0.716
BHS (overall score)	0.273	0.003	0.294	0.001	0.009
BHS (degree)	0.584	0.002	0.018	0.018	0.686
MoCA	0.643	0.391	0.937	0.023	0.038
VAS	0.929	0.025	0.016	0.315	0.536

Stroke – acute cerebrovascular accident; GPhH – general physical health; GPsH – general psychological health; MoCA – Montreal Cognitive Assessment scale; VAS – Visual Analog Scale, quality of life indicator sensu the SF-36 questionnaire.

Discussion

In our study group, the results obtained on various scales, such as the National Institutes of Health Stroke Scale, modified Rankin Scale for measuring the degree of disability, Rivermead Mobility Index (RMI) as a hierarchical mobility scale, and Fugl-Meyer Assessment scale of sensorimotor function, indicated that the patients in our sample had moderate hemiparesis and retained an ability of self-care. Deliberately, the study did not involve patients with aggravated motor disorders, paresis, or requiring an assistance of others to care about themselves.

The obtained mean values of the scale for assessing the quality of life were below the norm. For a person who has suffered from stroke with the development of a motor deficit, it was a natural and quite expected phenomenon: to assess their quality of life, taking into account their capability of self-care, availability of the social sphere, communication with others, along with other limitations. Patients, whose movement disorders became less pronounced over time, have assessed their condition more objectively (which reflected itself in the GPhH scale results), compared with the group where hemiparesis did not regress. There were no statistically significant differences between groups in the results of the quality-of-life scale in the acute phase of stroke. In the long-term recovery period of ACVA, the statistical significance of GPhH values among the groups of patients with an already known prognosis (favorable or unfavorable) was revealed.

Common to all investigated questionnaires (SF-36, BHS, MoCA and VAS) was the following: when assessing the quality of life, the level of depression and the level of cognitive functions in the first days after the onset of stroke, the obtained results did not have statistically significant relationships with the physical condition of the patient in the long run. In the acute phase of ACVA, each test alone could nor reliably predict the prognosis of the motor function recovery in a particular patient. These results make sense, because ischemic stroke actually reduces the quality of life due to motor limitations, deteriorates the emotional state and affects cognitive functions. All of the above are especially pronounced in the acute phase of the disease. This finding is confirmed by the data of many other studies. There is evidence in the literature that the clinical picture in a patient with a neurological disease is often accompanied by depression, a low quality of life score, and cognitive impairment [13]. Investigation of the relationship between depression and vascular diseases of the brain has been actively pursued since the 1970s. There is evidence that one out of three patients, who underwent stroke, develops depression [14, 15].

Our study demonstrated that the results of the questionnaires, reflecting the neuropsychological condition of patients in the chronic phase of stroke (BHS, VAS, SF-36) differed significantly between the groups of patients with satisfactory and unsatisfactory recovery of their motor functions: i.e., the scores obtained on all scales after 24-36 months after ACVA clearly correlated with the outcomes of motor function recovery in patients after stroke.

The exception was the MoCA scale. The scores obtained on that scale indicated that their use for ischemic stroke prognosis was not informative both in the acute and chronic phases.

Of interest are the results of identifying statistically important criteria in each study group. For the entire sample, such markers, according to our data, include GPhH, number of points on BHS, and MoCA score. For the group with a favorable outcome, objective indicators reflecting the course and outcome of the disease could be: GPhH value, the severity of depression sensu Beck and self-assessed health level sensu VAS. For patients who did not show positive dynamics in their motor function recovery in the long run, the prognosis of the disease was reflected to a greater extent by the number of points and the severity of depression on BHS, and by the MoCA result. Summarizing, we propose that the most likely criteria that may indicate a particular outcome of ischemic stroke are the data obtained from the Beck Depression Inventory.

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Conclusion

The results of our study have revealed a connection between the patient neuropsychological condition and recovery of his/her motor activity disorder, developed as a consequence of ACVA. Our data highlighted the following prognostically significant indicators: GPhH (sensu the SF-36 questionnaire), VAS, and BHS, given that their scores were measured after the acute phase of the stroke. The most significant criteria for predicting the outcome of the disease in each study group were identified: the most likely markers of a favorable or unfavorable course of the disease in terms of motor function recovery were the score of BHS questionnaire, GPhH (SF36), and MoCA scale score. Overall, due to the heterogeneity of our results, each of these tests alone, conducted in the acute phase of ACVA, could not predict the degree of the motor function recovery in a particular patient; however, they could be included in a multivariate prognosis model, along with a number of other criteria.

Investigation of a patient's neuropsychological status plays an important role in predicting the long-term prognosis of stroke, since it allows assessing the preservation of cognitive processes and the state of the emotional and volitional domains. Based on such data, a neuropsychological correction program is designed. Using such program in the rehabilitation of patients who underwent ACVA is crucial for developing a systemic integrated approach, along with an individual approach to designing a patient's rehabilitation program in order to ensure its higher efficacy.

Conflict of interest. The study did not have external funding. The authors take full responsibility their manuscript and its publication. All authors participated in the concept development, collection and statistical data processing, article structuring, and manuscript preparation. All authors are familiar with the final edited version of the manuscript. No conflicts of interest are declared by the authors.

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