ORIGINAL ARTICLES

UDC: 616.831-005.1-06:159.95
DOI: https://doi.org/10.2298/VSP250225065B

Cognitive status and quality of life of post-stroke patients: evidence from Serbia

Kognitivni status i kvalitet života bolesnika nakon moždanog udara: dokazi iz Srbije

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Abstract

Background/Aim. Stroke is a major global health problem, and more than half of stroke patients suffer from cognitive impairments. The aim of this study was to assess the impact of secondary rehabilitation on cognitive status and to examine its correlation with quality of life in post-stroke patients. **Methods.** A total of 100 patients (average age 66.5 ± 7.3 years) participated in the study, of whom 50 were diagnosed with ischemic stroke (IS) and 50 with intracerebral hemorrhagic stroke (ICH). The Mini-Mental State Examination (MMSE) was utilized to assess cognitive status, while the European Quality of Life (EuroQol) 5-dimensional 3-level (EQ-5D-3L) questionnaire was employed to evaluate quality of life. **Results.** The MMSE test results showed significant differences at three months ($p = 0.037$) and six months ($p = 0.009$) of secondary rehabilitation compared to admission. For the EQ-5D-3L, significant differences were observed at the time of admission ($p < 0.001$), one month ($p = 0.001$), and six months ($p = 0.007$). In addition, the Wilcoxon signed-rank test showed a statistically significant improvement in both MMSE and EQ-5D-3L scores when comparing results from admission to those taken one month ($p < 0.001$), three months ($p < 0.001$), and six months ($p < 0.001$) after secondary rehabilitation for both IS and ICH. **Conclusion.** The results indicate a significant correlation between cognitive status and quality of life, measured at all four time points. Additionally, it was found that a longer duration of secondary rehabilitation leads to improved cognitive status and a higher quality of life for post-stroke patients.

Key words:
cognition disorders; hemorrhagic stroke; ischemic stroke; rehabilitation; quality of life.

Apstrakt

Uvod/Cilj. Moždani udar je veliki globalni zdravstveni problem i više od polovine bolesnika sa moždanim udarom pati od kognitivnih oštećenja. Cilj ove studije bio je da se proceni uticaj sekundarne rehabilitacije na kognitivni status i da se ispita njegova korelacija sa kvalitetom života kod bolesnika nakon moždanog udara. **Metode.** U studiji je učestvovalo ukupno 100 bolesnika (prosečne starosti 66,5 ± 7,3 godine), od kojih je 50 imalo dijagnozu ishemijskog moždanog udara (*ischemic stroke* – IS), a 50 je imalo dijagnozu intracerebralnog hemoragijskog moždanog udara (*intracerebral hemorrhagic stroke* – ICH). Test za procenu mentalnog stanja *Mini-Mental State Examination* (MMSE) korišćen je za procenu kognitivnog statusa, dok je Evropski upitnik za kvalitet života [*European Quality of Life* (*EuroQol*) *5-dimensional 3-level* – EQ-5D-3L] korišćen za procenu kvaliteta života. **Rezultati.** Rezultati MMSE testa pokazali su značajne razlike nakon tri meseca ($p = 0,037$) i šest meseci ($p = 0,009$) trajanja sekundarne rehabilitacije u odnosu na prijem. Za EQ-5D-3L, uočene su značajne razlike u vreme prijema ($p < 0,001$), nakon mesec dana ($p = 0,001$) i šest meseci ($p = 0,007$). Uz to, *Wilcoxon signed-rank test* pokazao je statistički značajno poboljšanje i MMSE i EQ-5D-3L skorova bolesnika i sa IS i sa ICH, kada se uporede rezultati prijema s onima uzetim mesec dana ($p < 0,001$), tri meseca ($p < 0,001$) i šest meseci ($p < 0,001$) nakon sekundarne rehabilitacije. **Zaključak.** Rezultati ukazuju da postoji značajna korelacija između kognitivnog statusa i kvaliteta života merenog u sva četiri momenta. Dodatno, utvrđeno je da duže trajanje sekundarne rehabilitacije dovodi do poboljšanja kognitivnog statusa i višeg kvaliteta života bolesnika nakon moždanog udara.

Ključne reči:
kognicija, poremećaji; moždani udar, hemoragijski; moždani udar, ishemijski; rehabilitacija; kvalitet života.

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Introduction

Acute, focal neurological impairment caused by vascular injury (hemorrhage, infarction) of the central nervous system is known as a stroke. Stroke represents a major and growing global health concern [1]. Stroke is the second leading cause of mortality worldwide and the third leading cause of death and disability combined. Only ten risk factors account for more than 90% of the total modifiable risk for stroke, and they may be responsible for nearly half of all stroke-related deaths. Countries with varying income levels exhibit differences in age-standardized rates of stroke disability and mortality that can be attributed to modifiable risk factors, with higher-income countries being less at risk than lower-income countries [2]. The World Health Organization states that lowering the risk of hypertension (high systolic blood pressure), high lipids, diabetes (high fasting plasma glucose), smoking, inactivity, poor diet, and abdominal obesity (high body mass index) are all effective ways to avoid stroke [3].

The two types of strokes are intracerebral hemorrhagic stroke (ICH) and ischemic stroke (IS) [4]. Differentiating the kind of stroke is important for patient care within a few days after the stroke, but early detection is essential for stroke patients to avoid complications and irreversible damage [5].

There are numerous detrimental effects of a stroke on a person's life. Stroke and cognitive impairment have been strongly associated in numerous studies. The cognitive impairments that stroke patients endure can have a significant effect on their independence, everyday functioning, and general well-being [6].

More than half of stroke patients suffer from cognitive impairments such as memory problems and intellectual disability [7].

Stroke imposes limitations on personal, social, and professional responsibilities, which significantly impacts quality of life (QoL). It also places several restrictions on sensorimotor, cognitive, and behavioral levels, which offers a serious obstacle to functional independence. Evaluating post-stroke patients' QoL is essential for forecasting the imposed illness load and assessing how well treatment is working [8].

The aim of this study was to examine how secondary rehabilitation affects cognitive status and whether there is a correlation between cognitive status and QoL in patients who survived IS and ICH.

Methods

Study design

This was a prospective observational study carried out at the Special Hospital for Progressive Muscular and Neuromuscular Diseases in Novi Pazar, Serbia, from November 1, 2021, to July 1, 2022, designed to evaluate the cognitive status and QoL of post-stroke patients over a six-month period.

The study was approved by the Ethics Committee of the Special Hospital for Progressive Muscular and Neuromuscular Diseases, Novi Pazar (No. 872, from October 20, 2021), and it adhered to the principles of the Declaration of Helsinki [9]. Prior to their recruitment in the study, written informed consent was obtained from each patient. They were also informed that they could withdraw from the study at any time without facing any repercussions. The identities of the participants were concealed in the study report, and all data collected from them were safeguarded, with access restricted solely to the research team.

The respondents were divided into two groups. The first group consisted of patients with IS, and the second group consisted of patients with ICH. Based on neurological examination, computed tomography, or magnetic resonance imaging results, data were gathered by evaluating and monitoring patients who had suffered a stroke. Patients who experienced their first-ever IS or ICH were included no earlier than one month following the acute stroke event, aligning with the start of secondary rehabilitation. Examinations were performed on patients upon admission, and one, three, and six months following secondary rehabilitation.

Study population

Out of the 100 patients who took part in the study, 50% suffered IS, and the other 50% experienced ICH.

Inclusion criteria for the study were as follows: patients 46 years old or above; patients with a National Institutes of Health Stroke Scale (NIHSS) score between 4 and 24; patients who experienced IS or ICH for the first time no earlier than one month after the start of follow-up; patients who could participate in the rehabilitation program; patients able to communicate; those who provided written consent to participate in the study.

The following were exclusion criteria from the study: patients aged below 46 years; an NIHSS score below 4 or above 24; a history of IS or ICH; patients unable to talk; patients reluctant to provide written consent; patients with certain additional neurological conditions that impacted their functional ability.

Measures and procedures

In this study, patients participated in a secondary rehabilitation program that included functional electrostimulation and motor training using kinesitherapy. The program was conducted five days a week. After vital parameters stabilized and with a doctor's approval, rehabilitation began. Individual evaluations and program adaptations were made for each patient. The majority received monitoring and examinations while undergoing treatment in the hospital for three to four weeks, followed by three to four weeks of outpatient care spread out over six months. Patients received psychological support because it is thought to be crucial for both patients and their families to learn to cope with stroke [10].

The total duration of secondary rehabilitation, including inpatient and outpatient care, was approximately six months, with the most intensive phase during the first three months. Psychological support included individual counseling sessions, psychoeducation about stroke recovery, stress management strategies, and emotional support provided both to patients and their families.

The validated Serbian version of the Mini-Mental State Examination (MMSE) instrument was used to assess the patient's cognitive status [11, 12]. The MMSE comprises multiple items assessing cognitive domains, with a maximum score of 30 points. It has eleven items that evaluate linguistic skills: word repetition, recall, orientation, focus, and computation. A score of 24 or higher is considered normal, a score between 19 and 23 is mild, between 10 and 18 is moderate, and a score below 9 represents significant cognitive impairment [11, 12]. To assess the QoL, the European Quality of Life (EuroQol) 5-dimensional 3-level (EQ-5D-3L) questionnaire was employed [13]. It was used in a validated version in the Serbian language that is also free for use in student non-commercial research. It assesses five domains: mobility, self-care, daily activities, pain/discomfort, and anxiety/depression, at three levels of severity (no problem, moderate problem, and severe problem) [13]. Sociodemographic and clinical data relevant to the study's findings were collected using a questionnaire designed specifically for this study.

Statistical analysis

This study used the Kolmogorov-Smirnov test to assess the normality of the data distribution. Statistical significance was evaluated using two-tailed tests at the 0.05 level. We compared the frequency of specific attribute feature groups using the Chi-square test. We employed the analysis of variance (ANOVA) test (non-parametric Friedman) to examine the variance difference before applying the Wilcoxon signed-rank test to ascertain differences in repeated measurements. To examine the relationship between MMSE and EQ-5D-3L, we used Spearman's rank correlation coefficient, as the data were not normally distributed. The delta value (Δ) represents the difference between the MMSE and EQ-5D-3L scores at one, three, and six months of secondary rehabilitation and at the patient's admission. The descriptive statistics are presented either as numbers (n) and frequency (%) or as mean ± standard deviation (SD). SPSS Statistics software (IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY, USA) was used to conduct the statistical analysis.

Results

The research sample consisted of 100 respondents with an average age of 66.5 ± 7.3 years, of whom 48 were male and 52 were female. Among all subjects, 50 had IS (27 men and 23 women), and 50 had ICH (21 men and 29 women). Of the total number, 71 patients had high blood pressure, 46 had high cholesterol, and 39 had diabetes mellitus. Other sociodemographic and clinical characteristics of the patients who participated in the study, which may be important for the outcome of the study, are shown in Table 1.

Descriptive statistical analysis revealed that the mean MMSE score at admission was 12.88 (SD = 9.4), increasing to 16.79 (SD = 9.3) after one month, 21.55 (SD = 8.5) after three months, and 23.34 (SD = 7.5) after six months of secondary rehabilitation. The Kolmogorov-Smirnov test indicated that the distribution of MMSE scores was mixed, necessitating the use of non-parametric tests. Statistically significant improvements in MMSE scores were observed at three months (p = 0.037) and six months (p = 0.009) compared to baseline.

Table 1

Sociodemographic and clinical characteristics of patients

Characteristics	Sample size (n = 100)
Monthly income	
below average	23 (23)
average	67 (67)
above average	10 (10)
Alcohol	
never used	63 (63)
currently using	3 (3)
previously used	34 (34)
Coffee	
never used	7 (7)
currently using	55 (55)
previously used	38 (38)
Cigarettes	
never used	40 (40)
currently using	24 (24)
previously used	36 (36)
Medicaments	
never used	9 (9)
currently using	81 (81)
previously used	10 (10)
Children	
yes	80 (80)
no	20 (20)
Marital status	
not married	11 (11)
married	58 (58)
divorced	11 (11)
widow/widower	20 (20)
Level of education	
primary school	36 (36)
high school	38 (38)
higher education	15 (15)
college	11 (11)
Employment status	
unemployed	20 (20)
employed	19 (19)
housewife	18 (18)
farmer	18 (18)
retired	25 (25)

n – number.

All values are given as numbers (percentages).

Regarding QoL assessed by the EQ-5D-3L, the mean score at admission was 6.2 (SD = 1.9), rising to 7.7 (SD = 2.2) after one month, 9.2 (SD = 2.4) after three months, and reaching 10.9 (SD = 2.4) at the six-month follow-up. Although non-parametric tests were applied due to the distribution of the data, only the three-month follow-up data met the criteria for normal distribution. Statistically significant differences in EQ-5D-3L scores were found at admission ($p < 0.001$), one month (p = 0.001), and six months (p = 0.007), indicating a steady improvement in patients' perceived QoL throughout the rehabilitation period.

MMSE domain values at admission and one, three, and six months after admission were shown to differ statistically significantly ($p < 0.001$) for patients with IS and ICH, according to the Friedman test (Table 2).

Subsequent analysis revealed that both IS and ICH showed statistically significant improvements in MMSE test scores in the Wilcoxon signed-rank test between admission and one ($p < 0.001$), three ($p < 0.001$), and six ($p < 0.001$) months after secondary rehabilitation. The EQ-5D-3L test improved statistically significantly between admission and one ($p < 0.001$), three ($p < 0.001$), and six ($p < 0.001$) months following secondary rehabilitation for both IS and ICH, according to the Wilcoxon signed-rank test (Table 3).

Table 2

Friedman test results for cognitive domains at multiple time points in patients with IS and ICH

MMSE domains	χ^2	*p*
Time orientation		
IS	59.19	< 0.001
ICH	64.45	< 0.001
Spatial orientation		
IS	60.27	< 0.001
ICH	58.03	< 0.001
Verbal memory		
IS	41.65	< 0.001
ICH	50.45	< 0.001
Attention		
IS	60.99	< 0.001
ICH	57.99	< 0.001
Memory recall		
IS	48.41	< 0.001
ICH	53.44	< 0.001
Naming		
IS	28.64	< 0.001
ICH	39.53	< 0.001
Repetition		
IS	30.51	< 0.001
ICH	34.44	< 0.001
Triple order		
IS	53.64	< 0.001
ICH	55.26	< 0.001
Following instructions		
IS	32.66	< 0.001
ICH	27.93	< 0.001
Writing		
IS	29.50	< 0.001
ICH	29.60	< 0.001
Crossing out		
IS	29.80	< 0.001
ICH	30.55	< 0.001

IS – ischemic stroke; ICH – intracerebral hemorrhagic stroke; MMSE – Mini-Mental State Examination.

Table 3

MMSE and EQ-5D-3L scores with changes over time for IS and ICH patients

Stroke type	MMSE (mean ± SD)	Δ MMSE	EQ-5D-3L (mean ± SD)	Δ EQ-5D-3L
IS				
admission	14.4 ± 8.6	-	7.5 ± 2.7	-
1 month	16.4 ± 7.6	2.0	9.4 ± 3.0	1.9
3 months	22.1 ± 6.9	5.6	11.0 ± 2.7	3.5
6 months	24.5 ± 5.1	2.5	11.7 ± 1.9	4.2
ICH				
admission	11.3 ± 7.2	-	5.8 ± 1.7	-
1 month	14.4 ± 6.9	3.1	7.9 ± 2.3	2.1
3 months	21.0 ± 6.8	6.6	9.7 ± 2.5	3.9
6 months	22.2 ± 6.0	1.1	10.9 ± 2.6	5.1

EQ-5D-3L – European Quality of Life 5-dimensional 3-level; SD – standard deviation.
For other abbreviations, see Table 2.

Table 4

Correlation analysis between MMSE and EQ-5D-3L for ischemic stroke

Parameter		EQ-5D-3L			
		admission	1 month	3 months	6 months
MMSE admission	CC	0.747	0.813	0.754	0.504
	p-value	< 0.001	< 0.001	< 0.001	0.010
1 month	CC	0.770	0.836	0.779	0.562
	p-value	< 0.001	< 0.001	< 0.001	0.003
3 months	CC	0.739	0.830	0.799	0.518
	p-value	< 0.001	< 0.001	< 0.001	0.008
6 months	CC	0.444	0.565	0.504	0.496
	p-value	0.026	0.003	< 0.001	0.012

CC – Spearman's correlation coefficient. For other abbreviations, see Tables 2 and 3.

Table 5

Correlation analysis between MMSE and EQ-5D-3L for intracerebral hemorrhagic stroke

Parameter		EQ-5D-3L			
		admission	1 month	3 months	6 months
MMSE					
admission	CC	0.412	0.788	0.791	0.632
	p-value	0.003	< 0.001	< 0.001	0.001
1 month	CC	0.407	0.772	0.794	0.637
	p-value	0.003	0.000	< 0.001	0.001
3 months	CC	0.397	0.794	0.805	0.665
	p-value	0.004	< 0.001	< 0.001	< 0.001
6 months	CC	0.245	0.637	0.610	0.595
	p-value	0.237	0.001	0.000	0.002

CC – Spearman's correlation coefficient. For other abbreviations, see Tables 2 and 3.

The correlation analysis's findings demonstrated a statistically significant association between the MMSE scale scores for both types of stroke and the QoL as assessed at each of the four points in time. There was a high to moderately strong positive correlation (Table 4).

Only in the case of ICH, there was no statistically significant association between EQ-5D-3L values at admission and MMSE scale values after six months (Table 5).

Discussion

Since it has been proven that patients face a series of mental changes after a stroke, we conducted this research with the aim of examining how secondary rehabilitation affects cognitive status and whether there is a correlation between cognitive status and QoL in a group of patients who survived IS and ICH [13].

Given that it has been proven that the ability of patients to communicate (verbally or non-verbally), follow, understand, and carry out orders is essential for a successful outcome of rehabilitation, only patients in whom this ability was preserved were included in our research. It is also important that the patient does not have major memory disorders or psychological changes [14]. Assessment of the impact of the duration of secondary rehabilitation on the cognitive status of our patients was performed using the MMSE instrument, since it represents the gold standard for examining cognitive impairment in hospitalized patients [7].

It was confirmed that the length of secondary rehabilitation significantly improves the cognitive status of stroke patients, with positive correlations between cognitive status and QoL. The MMSE test score at admission and later measurements indicates a positive effect on patients' mental states [15]. Taking this statement into account, and since the aforementioned results were related to the entire sample, the total score of the MMSE test in patients with IS and ICH was shown separately at all four measurement moments. It was observed that the values of the MMSE test increased significantly in both types of stroke, and those changes were statistically significant.

A study involving 218 stroke survivors found that post-stroke cognitive impairment affects 47.7% of participants, with nutrition and social interaction significantly promoting cognitive improvement. The study suggests that maintaining social interaction can lead to improved cognitive function and training effects [16].

Correlation analysis showed that in patients with IS, cognitive status was associated with QoL at all times of the examination. The study found a connection between ICH and secondary rehabilitation in patients at three examination points, but no connection after six months of rehabilitation. Recently published research results by Barbosa et al. [17] at the level of a one-year prospective cohort study of 391 patients with a first stroke, evaluated at the beginning, three, six, and twelve months after the stroke, proved that for a better QoL it is significant that the patients have a higher MMSE score and that the rehabilitation process lasts

as long as possible. These findings are consistent with the findings obtained in our research.

As we have already mentioned, patients with ICH exhibit more severe impairments and slightly lower scores than patients with IS. Therefore, we assume that this is why the results of the correlation analysis suggest that there is no relationship between MMSE scores and QoL after six months of rehabilitation. It has been proven that depression is often present in patients after stroke, and that its occurrence directly affects the QoL [18, 19]. According to research by Capo-Lugo et al. [20], in order to enhance functional recovery and QoL, patients who have had ICH should begin adopting rehabilitation treatments as soon as possible.

All types of stroke affect different aspects of QoL. A study by Katzan et al. [21] with 2,181 patients who had an IS, ICH, subarachnoid hemorrhage, or transient ischemic attack revealed that physical function, social role satisfaction, and executive function were the domains most impacted across all types of these events. This underscores the necessity of creating efficient interventions to enhance these health domains in survivors of these cerebrovascular events.

Research indicates that social interaction is a useful predictor of daily life activities in stroke survivors. It is assumed that this may be a consequence of the beneficial effect of training from good relationships with therapists. Good cognitive function has been shown to lead to better rehabilitation outcomes [22–24].

Certainly, stroke causes a number of mental changes and can sometimes cause serious cognitive impairments that patients face later [25]. Rehabilitation after a stroke requires interdisciplinary cooperation and should begin promptly. Decisions to discharge patients should be individual, and hospital stays should not hinder neurorehabilitation. Knowledge of common complications and early prevention can improve cognitive abilities [26].

As Dimunová et al. [27] demonstrated, through the joint engagement and action of the multidisciplinary team during rehabilitation, significant progress was also achieved in our case in terms of the recovery of patients' mental abilities.

The application of the MMSE scale has fewer limitations and requires minimal patient cooperation for a successful examination. Although the results of this test provide only a rough estimate, it is useful for assessing treatment effectiveness and cognitive status over time [28]. The values of the MMSE scale in our research were additionally analyzed in order to assess whether progress was achieved within all domains.

The analysis of the time orientation domain showed that patients' ability to state the date, year, and time was significantly improved compared to admission, in both IS and ICH patients. In our study, secondary rehabilitation also contributed to higher average values in the spatial orientation domain, underscoring its importance in both types of stroke.

In addition to the results obtained by Bo et al. [29], as well as the findings of our study demonstrating improvements in patients' mental state through exercise and cognitive training, Gamito et al. [30] recommend the use of a virtual reality-based game application incorporating attention and memory tasks, aiming to reduce costs, save time, and offer additional benefits. Within the verbal memory domain, the ability of patients to repeat three words is assessed, and in our sample, significant improvement was achieved over admission in both types of stroke. The study found significant improvements in attention and verbal memory domains at admission in both IS and ICH stroke patients, as well as notable gains in naming and repetition domains, compared to initial assessment.

The values of the three-step command domain, in which patients perform three given actions (following verbal instructions, writing, and crossing), were significantly different at admission in both IS and ICH patients. A recent study suggests that an individual's enriched life experiences, including education and occupation, provide a buffer against stroke-induced cognitive impairment and promote faster cognitive recovery after stroke. In addition, higher education minimizes long-term cognitive decline after stroke, especially in elderly patients [31].

It can be pointed out that clinical measures and secondary rehabilitation care are important predictors of the cognitive status and QoL of stroke survivors, regardless of the sociodemographic and clinical characteristics of the patients and the type of stroke. Our findings offer an evidence base to effectively address the problems that lie ahead while developing suitable ways to reduce disability among post-stroke patients.

In addition to rehabilitation, factors such as social support, mood disorders (especially post-stroke depression), socioeconomic status, and comorbidities such as diabetes or hypertension may also influence cognitive recovery and mental status over the six-month period [32]. These factors warrant further investigation in future studies.

It is clear that after a stroke event, cognitive status and QoL are impaired, and determining which domains are impacted is essential for making plans for future care. Including multiple QoL domains highlights the importance of holistic rehabilitation programs that integrate cognitive, psychosocial, physical, and pharmaceutical factors for stroke survivors [33].

Conclusion

According to our study results, secondary rehabilitation interventions have a substantial impact on stroke patients' cognitive status and quality of life. Six months of follow-up with multiple examinations (at one, three, and six months) showed that patients' cognitive status and quality of life improved when they participated in a secondary rehabilitation program that included cognitive training and psychological support, among other components. The key conclusions of this study are that cognitive status and quality of life are significantly correlated, and that a longer duration of secondary rehabilitation results in better outcomes in both cognitive function and quality of life after stroke.

Acknowledgment

Dr. Emir Biševac and Dr. Teodora Safiye wish to express their heartfelt gratitude to Dr. Elvis Mahmutović for his unwavering support, thoughtful encouragement, and expert guidance throughout their academic journey. His professionalism, integrity, and dedication have been a continuous source of inspiration. It is both a privilege and an honor to regard him not only as a collaborator but also as a true academic role model.

Conflict of interest

The authors declare no conflict of interest.

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Received on February 25, 2025
Revised on June 6, 2025
Revised on July 20, 2025
Accepted on August 6, 2025
Online First September 2025