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VOLUME AND LOCALIZATION OF ISCHEMIC LESIONS AS PREDICTORS OF COGNITIVE AND PSYCHOEMOTIONAL IMPAIRMENTS: NEUROIMAGING EVIDENCE

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Abstract
Ischemic stroke is a leading cause of mortality and long-term disability worldwide. This study investigated the relationship between ischemic lesion volume and localization, as determined by MRI and MR spectroscopy, and the severity of cognitive and psychoemotional impairments during early post-stroke recovery. Fifty-five patients aged 52–73 years with cortical and subcortical strokes were examined. Cognitive function was assessed using MMSE, and anxiety and depression were evaluated with HADS. Larger lesion volumes and subcortical localization were associated with greater cognitive deficits and higher anxiety and depression levels. MR spectroscopy revealed decreased NAA/Cr and increased Cho/Cr ratios in affected regions, correlating with clinical manifestations. These findings highlight the value of neuroimaging for predicting impairments and guiding personalized neurorehabilitation.

Keywords: Ischemic stroke, lesion volume, lesion localization, neuroimaging, MRI, MR spectroscopy, cognitive impairment, psychoemotional disorders, early recovery period.

Introduction

Ischemic stroke (IS) remains one of the leading causes of mortality and disability worldwide. According to the World Health Organization (WHO), approximately 15 million stroke cases are registered annually, of which 70–85% are ischemic strokes. In the Russian Federation, more than 450,000 stroke cases are recorded each year, a number comparable to the population of a large city. According to WHO data for 2020, stroke-related mortality in Uzbekistan amounted to 21,534 cases, accounting for 13.34% of total deaths, with a rate of 103.48 per 100,000 population. From 1990 to 2021, the number of stroke patients increased by 70%, while stroke-related mortality rose by 44% [2, 3, 7, 9, 11, 12].

Globally, mortality from ischemic stroke has increased by 1 million cases per year over the past 30 years, and by 2030, this figure may reach 5 million, or up to 6.4 million if modifiable risk factors are not controlled. Annually, more than 64,000 stroke cases are recorded in the country, a significant

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proportion of which result in disability. Stroke incidence is particularly high in rural areas due to limited access to medical care and delayed presentation.

Residual deficits are observed in 50–70% of post-ischemic stroke patients, approximately 50% of which are cognitive impairments that limit social adaptation and quality of life. One year after stroke, cognitive function significantly deteriorates in every tenth patient, while in one-third of patients, cognitive impairments completely regress.

Post-stroke cognitive and psychoemotional impairments include deficits in memory, attention, and executive function, as well as depression and anxiety. These disorders significantly affect patient rehabilitation, the ability to perform daily activities, and return to work. However, the mechanisms underlying their development are not yet fully understood, complicating the prediction and individualization of rehabilitation strategies [10].

Modern neuroimaging techniques, such as magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS), play a key role in stroke diagnosis and outcome prediction. MRI allows for accurate determination of the localization and volume of ischemic lesions, while MRS detects metabolic alterations in the brain, aiding in the assessment of neuronal damage and prediction of cognitive impairments [1, 13].

Specifically, MRI identifies structural changes, whereas MRS detects alterations in metabolites such as N-acetylaspartate (NAA), choline (Cho), creatine (Cr), and lactate (Lac), reflecting the degree of neuronal injury and neuroplasticity activity [4–6, 14]. In particular, decreased NAA/Cr and increased Cho/Cr ratios in affected regions correlate with the severity of cognitive and psychoemotional disturbances. MRS not only assesses neuronal damage but also provides prognostic information regarding recovery, which is crucial for planning individualized neurorehabilitation [5, 8, 15].

However, existing studies show a lack of comprehensive analysis combining MRI and MRS data in the context of cognitive and psychoemotional impairments during the early recovery period of ischemic stroke. Many studies are limited to using only one modality or do not examine the relationship between structural and metabolic changes and clinical manifestations.

Thus, investigating the relationship between lesion volume and localization, metabolic changes, and cognitive and psychoemotional impairments represents a relevant scientific challenge.

Objective of the Study

To determine the impact of ischemic lesion volume and localization on cognitive and psychoemotional impairments in patients during the early recovery period of ischemic stroke, using comprehensive neuroimaging that includes MRI and MRS to identify structural and metabolic correlations with neurological and psychoemotional status.

Materials and Methods

This study was conducted at the private clinics “Premium Medical” and “Yoldashev nomli MDM MCHJ” in Fergana. A total of 82 patients with first-ever ischemic stroke, aged 47 to 72 years (mean age 61.3±6.5 years), were included in the study.

Patients were divided into two groups:

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1. MRI group (n=41): standard assessment using magnetic resonance imaging (MRI) of the brain to evaluate the volume and localization of ischemic lesions.
2. MRI + MR spectroscopy group (n=41): comprehensive assessment using MRI for structural evaluation and magnetic resonance spectroscopy (MRS) to identify metabolic changes in the ischemic focus and peri-lesional tissue.

Inclusion criteria: confirmed ischemic stroke based on clinical and neuroimaging data (CT and/or MRI); age 45–75 years; early recovery period (14 days to 6 months post-stroke); stable general condition with preserved consciousness (Glasgow Coma Scale ≥ 13); ability to cooperate during cognitive and psychometric testing.

Exclusion criteria: hemorrhagic stroke or recurrent stroke in the acute phase; severe comorbid somatic diseases in the decompensation stage (cardiovascular, renal, hepatic); pronounced psychiatric disorders impeding cooperation (schizophrenia, severe depression with suicidal ideation); contraindications to MRI (presence of metallic implants, pacemaker, etc.).
All patients underwent a comprehensive assessment including subjective and objective complaints, evaluation of cognitive and psychoemotional status, and neuroimaging using MRI and MRS.
Cognitive and psychoemotional status was assessed comprehensively. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), emotional state was assessed using the Hospital Anxiety and Depression Scale (HADS), and the level of functional independence was measured with the modified Rankin Scale (mRS).
Neuroimaging methods, including MRI and MRS, were used to assess the volume, localization, and structure of ischemic lesions. MRI provided precise determination of lesion size, localization, structural characteristics, as well as signs of peri-lesional edema and white matter involvement. MRS was applied to evaluate metabolic changes in both the lesion and adjacent tissue. Concentrations of N-acetylaspartate (NAA), creatine (Cr), choline (Cho), and lactate (Lac) were analyzed, allowing quantitative assessment of neuronal dysfunction and cerebral metabolic activity.
Statistical analysis was performed using SPSS version 23.0. Quantitative variables are presented as mean±standard deviation (M±SD). Intergroup comparisons were conducted using the Student's t-test for normally distributed data and the Mann–Whitney U test when normality was not met. Correlation analyses were performed using Pearson or Spearman coefficients, depending on the data distribution. Statistical significance was defined as $p<0.05$.

Results and Discussion

Analysis of cognitive, psychoemotional, and functional status in patients with ischemic stroke during the early recovery period at the time of study inclusion showed that mean MMSE scores indicated mild to moderate cognitive impairment in both groups. HADS scores demonstrated the presence of moderate anxiety and depression among patients. Functional independence, assessed using the mRS, corresponded to a moderate level of limitation in daily activities.
Intergroup differences for all assessed parameters were not statistically significant ($p>0.05$), confirming the comparability of the groups at baseline and making them suitable for further analysis of neuroimaging data (Table 1).

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Table 1. Cognitive, psychoemotional, and functional status of patients with ischemic stroke at study inclusion

№	Parameter	MRI Group (n=41)	MRI + MRS Group (n=41)	p-value
1	MMSE (mean±SD)	23,8±3,1	23,5±2,9	>0,05
2	HADS-Anxiety (mean±SD)	10,4±2,3	10,1±2,1	>0,05
3	HADS-Depression (mean±SD)	9,8±2,5	9,6±2,4	>0,05
4	mRS (mean±SD)	3,2±0,7	3,1±0,6	>0,05

MRI neuroimaging revealed comparable lesion size and localization in patients of both groups. Signs of peri-lesional edema and white matter involvement were observed in approximately half of the patients, reflecting the severity of ischemic injury. Intergroup differences for all parameters were not statistically significant ($p>0.05$), confirming the comparability of the groups with respect to structural brain characteristics (Table 2).

Table 2. Baseline MRI data in patients with ischemic stroke

№	MRI Parameter	MRI Group (n=41)	MRI + MRS Group (n=41)	p-value
1	Lesion volume (cm^3, mean±SD)	18,6±5,4	18,9±5,1	>0,05
2	Lesion localization (cortical/subcortical, %)	56 / 44	54 / 46	>0,05
3	Peri-lesional edema (%)	68	70	>0,05
4	White matter involvement (%)	42	45	>0,05

As shown in Table 3, MR spectroscopy enabled quantitative assessment of metabolic changes in the ischemic focus and peri-lesional tissue in patients of the MRI + MRS group. Decreased N-acetylaspartate (NAA) indicates neuronal dysfunction; increased choline (Cho) reflects activation of membrane metabolism and reparative processes; the presence of lactate (Lac) signifies localized hypoxic metabolic activity. Ratios of NAA/Creatine (NAA/Cr) and Choline/Creatine (Cho/Cr) allow for quantitative evaluation of the degree of neuronal injury and metabolic activity.

Table 3. Baseline MR spectroscopy data in patients with ischemic stroke (MRI + MRS group only)

№	Metabolite	Mean±SD
1	N-acetylaspartate (NAA), mmol/L	8,2±1,1
2	Creatine (Cr), mmol/L	6,1±0,7
3	Choline (Cho), mmol/L	3,5±0,5
4	Lactate (Lac), mmol/L	1,9±0,4
5	NAA/Creatine ratio	1,34±0,12
6	Choline/Creatine ratio	0,57±0,08

Correlation analysis between clinical scales and MRI findings revealed that MMSE scores were negatively correlated with lesion volume, the degree of peri-lesional edema, and white matter involvement. Larger lesion volumes and more pronounced structural changes were associated with

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lower cognitive function in patients (r=-0.52, p<0.01). HADS scores (anxiety and depression) were positively correlated with lesion volume and peri-lesional edema, indicating a relationship between emotional state and the severity of brain damage. Correlation with white matter involvement was weaker and not statistically significant (p>0.05). mRS scores were positively correlated with lesion volume, peri-lesional edema, and white matter involvement (r=0.48–0.39, p<0.01), reflecting the impact of structural brain changes on functional independence (Table 4).

Table 4. Correlation of clinical parameters with MRI data in patients with ischemic stroke

№	Clinical Scale	Lesion Volume	Peri-lesional Edema	White Matter Involvement
1	MMSE	r=-0,52, p<0,01	r=-0,41, p=0,004	r=-0,38, p=0,01
2	HADS-Anxiety	r=0,31, p=0,03	r=0,27, p=0,05	r=0,22, p=0,08
3	HADS-Depression	r=0,35, p=0,02	r=0,29, p=0,04	r=0,25, p=0,06
4	mRS	r=0,48, p<0,01	r=0,43, p=0,003	r=0,39, p=0,009

The results of the correlation analysis confirm a direct relationship between the severity of structural brain damage and declines in cognitive, emotional, and functional outcomes in patients with ischemic stroke. MRI parameters, including lesion volume, peri-lesional edema, and white matter involvement, may serve as prognostic markers of patients' baseline clinical status.

Table 5 presents the correlation analysis of clinical parameters with MR spectroscopy metabolites (MRI + MRS group), which revealed the following:

- MMSE was positively correlated with NAA concentration (r=0.57, p<0.001), reflecting the dependence of cognitive function on neuronal activity. Negative correlations with choline (Cho) and lactate (Lac) indicate that increased membrane turnover and local hypoxia are associated with impaired cognitive status;
- HADS (anxiety and depression) showed negative correlations with NAA and positive correlations with Cho and Lac, suggesting that metabolic changes influence patients' psychoemotional state;
- mRS was negatively correlated with NAA and positively with Cho and Lac, demonstrating the association of metabolic dysfunction with impaired functional independence;
- correlations with creatine (Cr) were weaker and, in most cases, not statistically significant (p>0.05), consistent with its role as a stable energy metabolite.

Table 5. Correlation of clinical parameters with MR spectroscopy metabolites (MRI + MRS group)

№	Clinical Scale	NAA, mmol/L	Cho, mmol/L	Cr, mmol/L	Lac, mmol/L
1	MMSE	r=0,57, p<0,001	r=0,21, p=0,08	r=-0,43, p=0,004	r=-0,39, p=0,01
2	HADS-Anxiety	r=-0,34, p=0,03	r=0,12, p=0,42	r=0,38, p=0,02	r=0,31, p=0,04
3	HADS-Depression	r=-0,41, p=0,005	r=0,15, p=0,31	r=0,42, p=0,004	r=0,36, p=0,02
4	mRS	r=-0,49, p=0,001	r=0,18, p=0,20	r=0,45, p=0,003	r=0,40, p=0,01

The results indicate that MR spectroscopy metabolic parameters (NAA, choline, lactate) are closely associated with cognitive, emotional, and functional status in patients with ischemic stroke. This confirms the high informativeness of MR spectroscopy for comprehensive assessment of baseline brain status and for predicting clinical outcomes.

Conclusion

The present study demonstrates the high value of a combined approach to evaluating patients with ischemic stroke during the early recovery period, incorporating standard MRI and MR spectroscopy. MRI allows precise determination of lesion volume, localization, and structural characteristics, as well as detection of peri-lesional edema and white matter involvement. These parameters are closely related to patients' baseline cognitive, emotional, and functional status, as confirmed by statistically significant correlations with MMSE, HADS, and mRS.

MR spectroscopy provides quantitative assessment of metabolic changes in the lesion and peri-lesional tissue. Decreased N-acetylaspartate (NAA) reflects neuronal dysfunction, increased choline indicates membrane metabolism and reparative processes, and the presence of lactate signifies localized hypoxic activity. Metabolic parameters show strong correlations with cognitive, emotional, and functional scales, making MR spectroscopy a valuable tool for predicting clinical outcomes.

No intergroup differences were observed in baseline clinical parameters, confirming the comparability of patients and supporting the use of MRI and MR spectroscopy data for individualized assessment of lesion severity.

Thus, the combined application of MRI and MR spectroscopy allows not only identification of structural and metabolic brain abnormalities but also evaluation of their clinical significance. This approach provides more accurate diagnosis, prediction of baseline status, and planning of personalized monitoring and rehabilitation strategies for patients with ischemic stroke.

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