RESEARCH PAPER

A Cross-Sectional Study in The Evaluation of Brain Ischemia by Magnetic Resonance Spectroscopy

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ABSTRACT

Introduction: Brain ischemia results in complex metabolic alterations preceding irreversible neuronal damage. Magnetic Resonance Spectroscopy (MRS) enables non-invasive evaluation of cerebral metabolites and provides additional biochemical information beyond conventional MRI in identifying infarct severity, tissue viability, and prognostic indicators in ischemic stroke.

Objectives: To evaluate metabolite abnormalities in ischemic infarct regions using MR Spectroscopy, determine preservation of N-acetylaspartate and elevation of lactate, estimate metabolite concentrations and ratios in infarct core and ischemic border regions, and assess their association with stroke severity and outcome.

Methods: This cross-sectional study included 94 patients with imaging-confirmed brain ischemia/infarction. MRI brain with T1WI, T2WI, DWI, and PRESS-144 multivoxel ^{1}H-MRS was performed. NAA, lactate, choline, creatine levels, and metabolite ratios were analysed using SPSS v17 and expressed as mean ± SD.

Results: Mean age was 58.3 ± 12 years, with male predominance (64.9%). MCA territory infarcts constituted 62.8% cases. Infarct core showed significantly reduced NAA and elevated lactate compared to ischemic border regions ($p=0.001$). NAA/Cr negatively correlated with NIHSS ($r=-0.61$), while lactate positively correlated ($r=+0.53$). NAA/Lactate ratio demonstrated highest prognostic accuracy (AUC 0.82).

Conclusion: MR Spectroscopy effectively identifies metabolic derangements in cerebral ischemia and differentiates infarct core from ischemic border tissue. Reduced NAA and elevated lactate are significant markers of neuronal injury and stroke severity. Metabolite ratios, particularly NAA/Lactate and NAA/Cr, provide valuable prognostic information in ischemic stroke evaluation.

Keywords: *Brain ischemia, Magnetic Resonance Spectroscopy, N-acetylaspartate, Lactate, Cerebral infarction, Metabolite ratios, Stroke prognosis, MRI brain.*
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INTRODUCTION

Brain ischemia occurs when blood supply to a part of the brain is reduced, leading to deficiency of oxygen and glucose in neuronal tissue. If this reduction persists, it may result in irreversible cellular injury and cerebral infarction. Ischemia remains an important cause of neurological disability because it can affect motor function, speech, cognition, consciousness, and long-term quality of life.[1] Routine magnetic resonance imaging is useful for detecting the site, extent, and stage of ischemic brain injury. Diffusion-weighted imaging and apparent diffusion coefficient mapping are especially helpful in acute ischemia. However, structural MRI mainly shows anatomical changes, while the biochemical status of ischemic tissue may require additional assessment.[2] Magnetic resonance spectroscopy is an advanced MRI-based technique that measures chemical metabolites within brain tissue. Unlike conventional MRI, which shows morphology, spectroscopy provides metabolic information from selected brain regions. This helps in understanding whether tissue has neuronal loss, membrane damage, anaerobic metabolism, or altered energy status.[3] The important metabolites assessed by proton magnetic resonance spectroscopy include N-acetyl aspartate, choline, creatine, lactate, and lipid peaks. N-acetyl aspartate is considered a neuronal marker, and its reduction suggests neuronal injury. Lactate indicates anaerobic metabolism, which is particularly relevant in ischemic conditions where oxygen delivery is reduced.[4] In brain ischemia, reduced oxygen supply shifts cellular metabolism from aerobic to anaerobic pathways, causing lactate accumulation. At the same time, neuronal injury may reduce N-acetyl aspartate levels. These changes can help identify the metabolic severity of ischemic damage, even when anatomical findings are not fully explanatory.[5] Magnetic resonance spectroscopy has been used in several neurological conditions to assess tissue metabolism and brain injury. Its clinical value has been highlighted in traumatic brain injury, where metabolite abnormalities reflect neuronal and cellular damage beyond routine imaging findings. This supports its wider use in neurological assessment.[6] Spectroscopy is also useful in differentiating ischemic lesions from other intracranial pathologies such as tumors. Brain gliomas commonly show increased choline due to cellular proliferation, whereas ischemic lesions more commonly show lactate elevation and reduced neuronal metabolites. Therefore, MRS can add diagnostic confidence when imaging findings overlap.[7]

MATERIALS & METHODS

Study design: Cross-sectional study

Place of study: A tertiary care hospital in a rural area of Tamil Nadu.

Study population: Patients with suspected brain ischaemia/infarct referred to the department of radiodiagnosis.

Sample size: 94

Inclusion criteria:

- All patients with symptoms of neurological deficit and imaging evidence of brain ischemia/infarct were subjected to Magnetic Resonance Spectroscopy.
- Both sexes.
- Patients of age between 20–80 years.

Exclusion criteria:

- Patients with known cerebral tumours.
- Patients with known metabolic encephalopathy.
- Patients with known infectious diseases.
- Patients with claustrophobia.

MRI Technique: Brain MRI with T1WI, T2WI, DWI, and PRESS-144 multivoxel ^{1}H-MRS evaluated infarct core and border regions by measuring NAA, creatine, choline, lactate concentrations, and metabolite ratios for pathological assessment.

Data analysis: Data were tabulated and graphically represented. Absolute metabolite values and ratios for infarct core and border regions were analysed using Microsoft Excel and SPSS v17, with results expressed as mean ± standard deviation.

RESULTS

The study included 94 patients with a mean age of 58.3 ± 12.0 years; 18 (19.1%) were aged ≤45 years, 43 (45.7%) were 46–60 years, and 33 (35.1%) were >60 years. Males were more common [61 (64.9%)] than females [33 (35.1%)]. Regarding education, 8 (8.5%) were illiterate, 27 (28.7%) had primary education, 33 (35.1%) had secondary education, and 26 (27.7%) were graduates or above. According to Modified Kuppuswamy SES, 6 (6.4%) belonged to the upper class, 18 (19.1%) upper-middle, 39 (41.5%) lower-middle, 21 (22.3%) upper-lower, and 10 (10.6%) lower class. Hypertension was present in 46 (48.9%) and diabetes mellitus in 28 (29.8%) patients, while the mean NIHSS score was 8.4 ± 4.1, suggesting moderate neurological deficit at presentation.

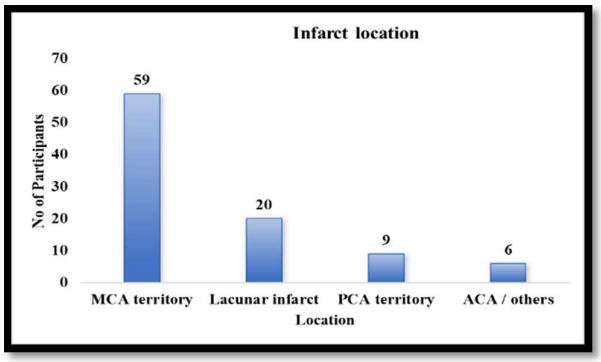

Figure 1: Distribution of infarct location among study participants, n = 94

Figure 1 Shows that Among the 94 patients, MCA territory infarcts were the most common location, observed in 59 (62.8%) patients, followed by lacunar infarcts in 20 (21.3%) patients. PCA territory infarcts were seen in 9 (9.6%) patients, while ACA/other territory infarcts were least common, accounting for 6 (6.4%) cases. This distribution shows predominant MCA involvement in the study population.

Table 1: Comparison of absolute metabolite levels between infarct core and ischemic border region

Metabolite	Infarct core Mean ± SD	Ischemic border Mean ± SD	Mean difference	p-value
NAA	6.20 ± 1.70	8.90 ± 1.60	−2.70	0.001
Creatine	4.90 ± 0.60	5.10 ± 0.50	−0.20	0.13
Lactate	2.38 ± 0.98	1.10 ± 0.50	1.28	0.001
Choline	2.79 ± 0.78	2.40 ± 0.70	0.39	0.001

In Table 1, The infarct core showed significantly lower NAA compared with the ischemic border region (6.20 ± 1.70 vs 8.90 ± 1.60; mean difference −2.70; p = 0.001), indicating greater neuronal injury in the core. Lactate was significantly higher in the core (2.38 ± 0.98 vs 1.10 ± 0.50; mean difference 1.28; p = 0.001), suggesting increased anaerobic metabolism. Choline was also significantly elevated in the core (2.79 ± 0.78 vs 2.40 ± 0.70; mean difference 0.39; p = 0.001), while creatine showed no significant difference (4.90 ± 0.60 vs 5.10 ± 0.50; mean difference −0.20; p = 0.13).

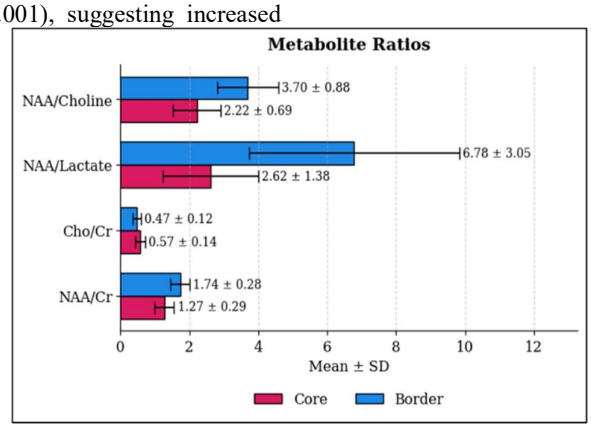

Figure 2: Comparison of metabolite ratios between infarct core and ischemic border region

Figure 2 Shows that infarct core showed a lower NAA/Cr ratio compared with the ischemic border region (1.27 ± 0.29 vs 1.74 ± 0.28), indicating reduced neuronal integrity in the core. The Cho/Cr ratio was higher in the core (0.57 ± 0.14 vs 0.47 ± 0.12), suggesting greater membrane turnover or cellular injury. The NAA/Lactate ratio was markedly reduced in the core (2.62 ± 1.38 vs 6.78 ± 3.05), reflecting increased anaerobic metabolism with neuronal loss. Similarly, the NAA/Choline ratio was lower in the core (2.22 ± 0.69 vs 3.70 ± 0.88), supporting more severe metabolic disturbance in the infarct core than in the ischemic border region.

Table 2: Lactate detection and lactate variation according to time from stroke onset

Parameter	Category / Predictor	Value	p-value
Lactate detection in core	**Present**	80/94 (85.1%)	—
Lactate detection in border	**Present**	49/94 (52.1%)	—

Lactate level by time from onset	**≤7 days**	3.08 ± 0.98	0.001
	8–28 days	1.90 ± 0.80	
	>28 days	1.00 ± 0.40	
Predictors of lactate presence	**NIHSS**	OR 1.18	0.003
	Early scan ≤7 days	OR 3.36	0.007

In Table 2, Lactate was detected more frequently in the infarct core [80/94 (85.1%)] than in the ischemic border region [49/94 (52.1%)], indicating greater anaerobic metabolism within the infarcted tissue. Lactate levels were highest when imaging was performed within ≤7 days of stroke onset (3.08 ± 0.98), decreased during 8–28 days (1.90 ± 0.80), and were lowest after >28 days (1.00 ± 0.40), with a statistically significant difference (p = 0.001). On predictor analysis, higher NIHSS score (OR 1.18; p = 0.003) and early scan within ≤7 days (OR 3.36; p = 0.007) were significantly associated with lactate presence, suggesting that lactate detection was more common in acute and clinically severe infarcts.

Table 3: Association of MRS metabolite parameters with stroke severity and clinical outcome, n = 94

Section	Variable / parameter	Category / comparison	Value / result	p-value
Stroke severity correlation	**NAA/Cr ratio in infarct core vs NIHSS**	Pearson correlation	r = −0.61	0.001
	Lactate level in infarct core vs NIHSS	Pearson correlation	r = +0.53	0.001
Clinical outcome distribution	**Favourable outcome**	mRS ≤2	59/94	62.80%
	Unfavourable outcome	mRS >2	35/94	37.20%
Association of NAA/Cr with outcome	**NAA/Cr <1.30**	Favourable outcome	14	0.001
		Unfavourable outcome	27	
	NAA/Cr ≥1.30	Favourable outcome	45	
		Unfavourable outcome	8	
Multivariate logistic regression for poor outcome	**Age**	Adjusted OR, 95% CI	1.20, 0.91–1.59	0.14
	NIHSS score	Adjusted OR, 95% CI	1.43, 1.22–1.66	<0.001
	NAA/Lactate ratio in infarct core	Adjusted OR, 95% CI	0.79, 0.67–0.93	0.005
ROC analysis for prediction of poor outcome	**NAA/Lactate ratio**	AUC, sensitivity, specificity	0.82, 78%, 76%	0.001
	NAA/Cr ratio	AUC, sensitivity, specificity	0.79, 72%, 74%	0.001
	Lactate level	AUC, sensitivity, specificity	0.75, 68%, 70%	0.002

In Table 3, Lower core NAA/Cr was significantly associated with higher NIHSS (r = −0.61; p = 0.001), while higher core lactate correlated positively with NIHSS (r = 0.53; p = 0.001). Favourable outcome (mRS ≤2) was seen in 59/94 (62.8%), while 35/94 (37.2%) had unfavourable outcome. NAA/Cr <1.30 was associated with more unfavourable outcomes (27 vs 14; p = 0.001). NIHSS (AOR 1.43; p <0.001) and core NAA/Lactate ratio (AOR 0.79; p = 0.005) independently predicted poor outcome.

DISCUSSION

In the present study, the mean age of participants was 58.3 ± 12.0 years, with the majority belonging to the 46–60 years age group (45.7%), and males constituted 64.9% of cases, indicating a higher burden of ischemic stroke among middle-aged and elderly men. Hypertension (48.9%) and diabetes mellitus (29.8%) were common comorbidities, while the mean NIHSS score was 8.4 ± 4.1, suggesting moderate stroke severity. MCA territory infarction was the predominant subtype (62.8%), followed by lacunar infarcts (21.3%). On MR spectroscopy, infarct

core regions demonstrated significantly reduced NAA levels (6.20 ± 1.70 vs 8.90 ± 1.60; p=0.001) and elevated lactate levels (2.38 ± 0.98 vs 1.10 ± 0.50; p=0.001) compared to ischemic border regions, reflecting neuronal loss and anaerobic metabolism. Choline was significantly elevated in the infarct core (2.79 ± 0.78 vs 2.40 ± 0.70; p=0.001), whereas creatine difference was statistically insignificant (p=0.13). These findings were comparable with Sassani et al. (2020).[8], who demonstrated metabolic dysfunction with reduced phosphocreatine and altered energy metabolism on MRS. Kwong and Ng (2019).[9] similarly reported significant neurological impairment among chronic stroke patients, while Damulina et al. (2020).[10] observed metabolite-related neurodegenerative changes correlating with disease progression. Infarct core regions demonstrated lower NAA/Cr (1.27 ± 0.29 vs 1.74 ± 0.28), lower NAA/Lactate (2.62 ± 1.38 vs 6.78 ± 3.05), and lower NAA/Choline ratios (2.22 ± 0.69 vs 3.70 ± 0.88) compared to ischemic border regions, whereas Cho/Cr ratio was elevated within the infarct core (0.57 ± 0.14 vs 0.47 ± 0.12), indicating severe neuronal dysfunction and altered membrane metabolism in established infarction. NAA/Cr ratio showed significant negative correlation with NIHSS score (r = −0.61; p=0.001), while lactate demonstrated positive correlation with stroke severity (r = +0.53; p=0.001). Patients with NAA/Cr <1.30 had predominantly unfavourable outcomes (27 vs 14; p=0.001). Multivariate analysis identified NIHSS score (OR 1.43, 95% CI: 1.22–1.66; p<0.001) and NAA/Lactate ratio (OR 0.79, 95% CI: 0.67–0.93; p=0.005) as significant predictors of poor outcome. ROC analysis showed highest predictive accuracy for NAA/Lactate ratio (AUC 0.82, sensitivity 78%, specificity 76%). These findings were comparable with Sassani et al. (2020).[8], who demonstrated significant metabolic derangements correlating with disability and functional impairment. Kwong and Ng (2019).[9] similarly reported strong association between neurological functional scores and mobility outcomes in chronic stroke. In contrast, Damulina et al. (2020).[10] evaluated neurodegenerative iron accumulation rather than ischemic metabolite ratios, although both studies highlighted imaging biomarkers associated with clinical progression.

CONCLUSION

The present study demonstrated that proton magnetic resonance spectroscopy is an effective adjunctive modality in evaluating cerebral ischemia and infarction by providing metabolic information beyond conventional MRI. Infarct core regions showed significantly reduced N-acetylaspartate and metabolite ratios, indicating neuronal loss and irreversible injury, while elevated lactate reflected anaerobic metabolism and tissue hypoxia. Ischemic border regions demonstrated relatively preserved metabolite levels, suggesting partial tissue viability. MCA territory infarcts were most common, with hypertension and diabetes mellitus identified as major associated risk factors. Metabolite ratios, particularly NAA/Lactate and NAA/Cr, showed significant correlation with stroke severity and functional outcome. Lower NAA/Cr ratios were associated with poor prognosis, and ROC analysis confirmed good predictive accuracy of spectroscopic parameters, supporting MR spectroscopy as a valuable prognostic biomarker in cerebral infarction.

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Ethical Approval: Obtained.

Consent: Written consent secured.

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