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Is There a Relationship Between the National Institutes of Health Stroke Scale Scores and Magnetic Resonance Volumetric Measurements in Acute Stroke?

Akut İnmede National Institutes of Health Stroke Scale Scores ile Manyetik Rezonans Volumetrik Ölçüm Arasında İlişki Var mıdır?

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Abstract

Objective: In this study, we determined the relationship between the volumetric measurement value detected in the acute infarct area by diffusion magnetic resonance imaging (MRI) and the National Institutes of Health Stroke Scale (NIHSS).

Methods: This is a cohort study comparing the relationship between volumetric volume measured by diffusion MRI and NIHSS in patients with a definite diagnosis of stroke. Between February 2014 and February 2015, 99 patients over the age 18 and 57 healthy controls who applied within the first 72 h after the onset of acute stroke symptoms were included. Inclusion criteria of the patients; patients with ischemic stroke admitted to the hospital within 72 h of symptom onset, patients with MRI (including DWI) within 72 h of symptom onset are patients with an NIHSS score obtained just before MRI. DWI lesion volumes were measured on the image of the maximum contrast (ie, the DWI with the highest b-value) between the lesion and normal brain regions.

Results: The results of the volumetric measurement values determined in the patient group; left MCA 40.6%, right MCA 31.7%, left ACA 2%, right ACA 2%, left PCA 9.9%, right PCA 8.9%, left cerebellar 7.9%, right cerebellar 6%, 9, left PICA 5%, right PICA 5%, thalamooperferator 2%, AICA 2%, lacunar 2%. A statistically significant correlation was found between the NIHSS score and volumetric measurements ($p<0.005$).

Conclusion: Segmenting penumbra and infarct core regions based on PWI and DWI, and making volumetric measurements are important in determining immediate and future risks in acute stroke patients.

Keywords: Acute ischemic stroke, MRI volumetric measurement, NIHSS score

Öz

Amaç: Bu çalışmada, difüzyon manyetik rezonans görüntüleme (MRG) aracılığı ile akut infarkt alanında saptanılan volümetrik ölçüm değeri ile National Institutes of Health Stroke Scale (NIHSS) arasındaki ilişkiyi saptamayı amaçladık.

Yöntem: Bu çalışma, kesin inme tanısı olan hastalarda difüzyon MRG ile ölçülen volümetrik hacim ile NIHSS arasındaki ilişkinin kıyaslandığı kohort çalışmasıdır. Çalışmaya Şubat 2014 ile Şubat 2015 arasında akut inme semptomları başlangıcından sonra ilk 72 saat içerisinde başvuran 18 yaş üzeri 99 hasta ve 57 sağlıklı kontrol dahil edilmiştir. Hastaların çalışmaya dahil edilme kriterleri; semptomların başlamasından sonraki 72 saat içinde hastaneye başvuran

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Öz

iskemik inme, semptom başlangıcından sonraki 72 saat içinde MRG (DWI dahil) olan hastalar, MRG'den hemen önce elde edilen NIHSS skoru olan hastalardır. DWI lezyon hacimleri, lezyon ile normal beyin bölgeleri arasındaki maksimum kontrastın (yani en yüksek b değerine sahip DWI) görüntüsü üzerinde ölçüldü.

Bulgular: Hasta grubunda saptanan volümetrik ölçüm değerleri sonuçları; sol MCA %40,6, sağ MCA %31,7, sol ACA %2, sağ ACA %2, sol PCA %9,9, sağ PCA %8,9, sol serebellar %7,9, sağ serebellar %6,9, sol PİCA %5, sağ PİCA %5, talamoperferator %2, AİCA %2, lakuner %2'dir. Bu sonuçlara göre en sık sorun saptanan damar ve en büyük volümetrik ölçüm sol MCA'da saptanmıştır. NIHSS skoru ile volümetrik ölçümler arasında istatiksel olarak anlamlı ilişki saptanmıştır (p<0,005).

Sonuç: PWI ve DWI'ya dayalı olarak penumbra ve enfarktüs çekirdek bölgelerini segmentlere ayırmak, volümetrik ölçüm yapmak akut inme hastalarında anlık ve gelecekteki riskleri belirlemekte önemlidir.

Anahtar Kelimeler: Akut iskemik inme, MRG volümetrik ölçüm, NIHSS skoru

Introduction

Stroke is one of the leading causes of death and long-term disability worldwide. In 2013, the stroke prevalence was estimated to be 25.7 million worldwide with 6.5 million stroke-related deaths, which makes stroke the second leading cause of death after ischemic heart disease[1]. In the last few decades, it has become a great challenge to improve the outcome in acute ischemic stroke. The treatment options largely depend on the stage of the disease and findings that develop over time[2,3]. The intravenous recombinant tissue-plasminogen activator can be used within hours, while intra-arterial mechanical thrombectomy was found to be beneficial when used within 6 h after the onset of symptoms[4-7]. Recent clinical trials including EXTEND-IA[8], ESCAPE[9], SWIFT PRIME[10], MR CLEAN[11], DAWN[12] and DEFUSE[13] showed the efficacy of endovascular therapies; however, in the acute period, it is critical to select patients likely to benefit from reperfusion therapy in the care of patients with stroke.

Multi-modal magnetic resonance imaging (MRI) has emerged as a promising tool for the diagnosis of ischemic stroke and the selection of therapeutic strategies in the acute phase. Various imaging findings from MRI sequences can represent the instantaneous status of stroke at a given time point. Thus, MRI can be used to determine eligibility for reperfusion therapies and potential benefits by distinguishing viable tissue at risk and ischemic tissue[14,15].

In patients with acute ischemic stroke, the penumbra is considered target tissue for reperfusion therapies; however, it is at risk of irreversible infarction. Although the penumbra, surrounding the ischemic lesion, is at risk of progression to infarction if not reperfused, it may survive when reperfused[16].

In clinical practice, the availability of MRI allows predicting infarction site and size of penumbra. The volume of the infarction site can be estimated using diffusion-weighted images (DWI) while penumbra volume surrounding the infarction site can be estimated using cerebral blood profile from perfusion-weighted images (PWI). Thus, PWI-DWI mismatch on MRI imaging can aid in assessing potential risks and benefits of thrombolysis by providing information about recoverable tissue or age of ischemic lesion[17-19]. This requires identification and quantification of core infarction sites and penumbra. However, manual identification of the core infarction site and penumbra is time-consuming and labor-intensive. Previous studies have proposed some approaches to aid clinicians for estimation of core infarction site and penumbra[20-22]. most these algorithms rely on multi-modal MRI imaging, including PWI, DWI, clear diffusion coefficient (ADC), T1-weighted, T2-weighted and fluid-attenuation inversion recovery sequences[20]. A recent study reported a semi-automated lesion segmentation algorithm based solely on DWI.[21] In another study, an automated segmentation algorithm was reported; however, the algorithm requires a normal image sequence and was applied to lesions at the occipital lobe.[22]

In previous studies, it was found that a low National Institutes of Health Stroke Scale (NIHSS) score is associated with poor prognosis in acute stroke.

In this study, we determined the correlation between volumetric measurement of acute infarct site by diffusion-weighted MRI and NIHSS.

Materials and Methods

Study Design

This is a cohort study comparing infarct volume by diffusion-weighted MRI and NIHSS in patients with a definitive diagnosis of stroke.

Study Population

The study included 99 patients (aged ≥18 years) who presented within 72 h after the onset of acute stroke between February 2014 and 57 healthy controls. The inclusion criteria were acute ischemic stroke presented to the hospital within 72 h, the presence of MRI (including DWI) within 72 h after the onset of symptoms and available NIHSS score noted just before MRI imaging. The patients with symptoms and findings extending beyond 72 h (transient ischemic attack) and negative DWI were excluded. Additionally, patients with hemorrhagic stroke, vascular dementia, hypertensive encephalopathy, pregnant patients, breastfeeding patients and those with chronic renal disease, chronic liver disease, chronic heart failure and acute transient ischemic attack were excluded. In all patients, demographic characteristics, risk factors for stroke and time of stroke were prospectively recorded to Stroke Data Sheet. Additionally, the time of assessment in the hospital, NIHSS score at presentation (before imaging studies), time and type of imaging studies, treatment, anatomical localization of stroke and putative mechanisms of stroke was also recorded. The NIHSS score was recorded by a specialist accredited for NIHSS.

Throughout the study period, multimodal MRI (including DWI and PWI) was a routine component of assessment in patients with acute stroke, including unstable and irritable patients, unless MRI was contraindicated.

This study was approved by Necmettin Erbakan Univertisy Local Ethics Committee (approval no: 35, date: 07.02.2014). All patients and controls or their legal guardians gave written informed consent before participation.

Clinical Findings

In all patients, a comprehensive assessment including physical examination, neurological examination, history, and standard assessment for stroke was performed. In all patients diagnosed with stroke, NIHSS standard neurological and general assessment was performed[23]. In all stroke patients, a computed tomography scan was obtained immediately, while MRI was performed within 72 h. All patients were managed by an experienced neurologist. A standard questionnaire including history, risk factors for stroke, medication and previous stroke was completed in all control visits.

Magnetic Resonance Imaging and Analysis

All MRIs were obtained from a standard clinical MRI device using single-pulse echo-linear gradients. The standard imaging protocol includes DWI, sensitivity-weighted (T*) images, traditional spin-echo T1- and T2-weighted images and MRI angiography. In each ischemic area, penumbra area was calculated in the region of interest, which, then, multiplied by the thickness of the section to estimate the volume of the ischemic area. The DWI lesion volumes were measured on the image with maximum contrast between the lesion and normal brain regions (DWI image with highest b value). DWI lesion volumes were measured by an experienced, blinded observer in a duplex manner and mean values were used in the analysis. The measurements were performed by an experienced observer blinded to clinical scores and DWI lesion volumes. To obtain better prediction of the total volume of dysfunctional brain tissue, total lesion volume was defined to be larger than the DWI or PWI lesion volume in each patient, controlling cases with re-canalization before imaging. Figure 1 shows measurement of volumetric value. MRI imaging studies were conducted using a Siemens MRI device (MAGNETOM Symphony, A Tim System, 1.5T eco, 792MR37433, United States).

Statistical Analysis

All statistical analyses were performed using Statistical Package for the Social Sciences version 20.0 (IBM Corp., Armonk, NY, USA). Numerical data were tested for normal distribution. Wilcoxon sign test was used to assess paired groups while Kruskal-Wallis test was used to assess more than 2 independent groups. Mann-Whitney U test was used to assess 2 independent groups when needed. Pearson and Spearman's correlation tests were used for numerical variables. A p value <0.05 was considered statistically significant.

Results

Table 1 presents the demographic characteristics of the study group (n=99). The volumetric values in the study group were as follows: 40.6% in left MCA; 31.7% in right MCA; 2% in left ACA; 2% in right ACA; 9.9% in right PCA; 8.9% in right PCA; 7.9% in left cerebellar; 6.9% in right cerebellar; 5% in left PICA; 5% in right PICA; 2% in thalamoperforating artery; 2%

Table 1. Demographic and patient characteristics of the patients

Parameters	Patients (n=99)	p value
Age (years)	72.35±13.33	**0.001**
Gender (% male)	42/101 (45.5)	0.133

*p<0.05 considered important.

in AICA; and 2% in lacunar region. Based on these results, left MCA was the most commonly involved vessel with the largest volumetric value. Table 2 presents the volumetric values in the study group. Graphic 1 presents the distribution of the volumetric values. Thrombolytic treatment was administered to 9 patients in the emergency department with high NIHSS scores and large area involved in volumetric measurement.

Acute DWI Lesion Volume and NIHSS Score

There was a significant correlation between DWI lesion volume and NIHSS score for all cerebral lesions. It was found that volumetric values increased with increasing NIHSS score, indicating a positive correlation (r=0.290; p=0.004). Table 3 presents a comparison between the volumetric values and those of the NIHSS.

Table 2. Volumetric measurements in the study group

	n=99
Left MCA	41 (40.6%)
Right MCA	32 (31.7%)
Left ACA	2 (2%)
Right ACA	2 (2%)
Left PCA	10 (9.9%)
Right PCA	9 (8.9%)
Left serebellar arter	8 (7.9%)
Right serebellar arter	7 (6.9%)
Left PICA	5 (5%)
Right PICA	5 (5%)
Thalamooperforator artery	2 (2%)
AICA	2 (2%)
Lacunar	2 (2%)

MCA: A. cerebri media, ACA: A. cerebri anterior, PCA: A. cerebri posterior, PICA: A. cerebellaris posterior inferior, AICA: A. cerebellaris anterior inferior

Table 3. Comparison of NIHSS score and DWI volume

NIHSS	MRI volume	n	p value
0-5	6.26	31	0.004
6-10	19.44	19	0.001
11-15	45.21	12	0.000
16-20	44.81	8	0.000
>20	81,9	29	0.000

MRI volume: Magnetic resonance imaging volumetric measurement values (cm^3), NIHSS: National Institutes of Health Stroke Scale

Discussion

This study showed that acute DWI lesion volume was higher in patients with a low NIHSS score. These results were valid in patients who underwent imaging study within 72 h after the onset of stroke.

It is highly important to detect and measure the penumbra and infarction core in a rapid and automated manner to determine treatment strategies in patients with hyper-acute stroke where clinical and prognostic benefits are time-dependent. In this study, we determined whether volumes of penumbra and infarction core as measured by PWI and DWI, are correlated with NIHSS. To the best of our knowledge, there are a limited number of studies comparing NIHSS scores and volumetric values.

NIHSS is an important tool in clinical trials on stroke and an integral component of clinical practice for many neurologists treating patients with stroke. It was shown that NIHSS is a good marker for post-stroke outcome and is superior to simpler clinical stroke scales, while it was also shown that it is a strong predictor of efficiency of treatment in stroke[23,24]. It is known that the NIHSS assesses right and left motor functions as well as right and left cortical functions[25]. For tests directing assessing verbal functions, NIHSS can provide only a maximum score of 7 points (from 42) and 2 points for extinction and inattention (orientation: 2 points; commands: 2 points; aphasia: 3 points)[26].

In another study, no significant differences were detected in the relations between acute MRI lesion volumes and NIHSS scores other than patient subgroup with right hemisphere stroke and low NIHSS score[27]. In our study, no difference was detected in correlations between MRI lesion volumes and NIHSS in ischemic strokes on both sides, in agreement with the above-mentioned study. The lack of difference in these correlations may represent wide variations regarding acute lesion volume and clinical presentation across individuals with stroke. In the literature, there are several studies on the correlation between NIHSS score and DWI or perfusion volumes reported controversial results[28-31]. In our study, it was found that there was no significant difference in clinical scores between patients with similar lesion volumes in both hemispheres and that there was a significant correlation between NIHSS score and DWI or perfusion volume in agreement with these studies.

Unlike our results, in a previous study, it was reported that there were different clinical scores between hemispheres

despite similar lesion volumes[27]. This clinical variation can be associated with the different neuroanatomy of the lesion and the dynamic nature of the pathophysiology of acute stroke.

It was shown that DWI lesion volume is an independent predictor of functional outcome within 48 h after onset of stroke[32]. At the early stage of stroke, markers such as diffusion-perfusion mismatch and persistent vascular

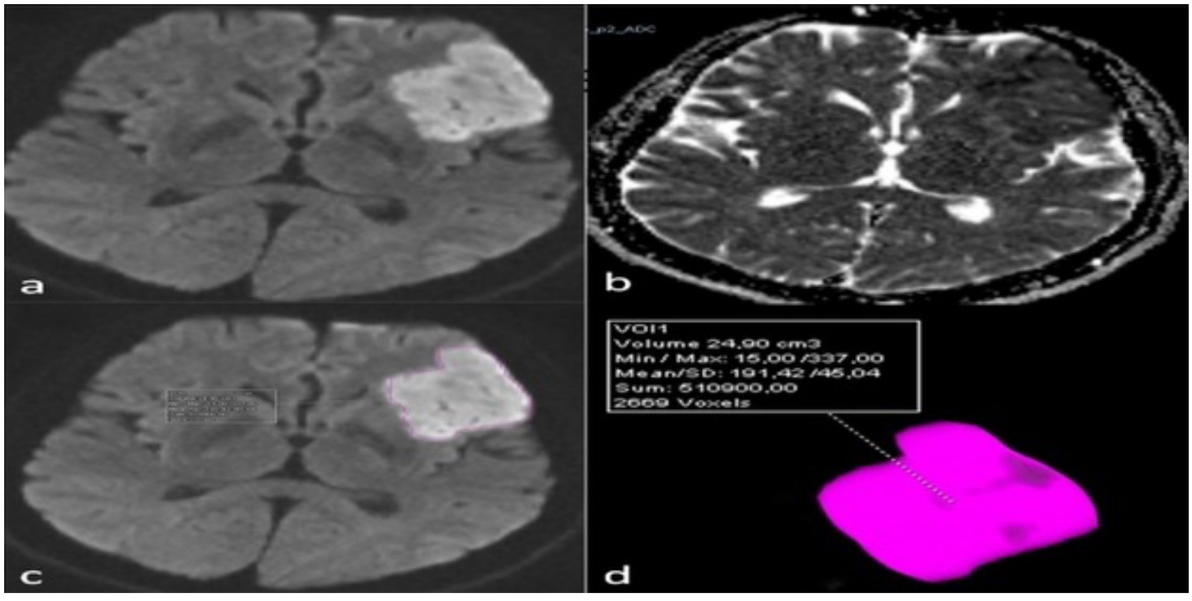
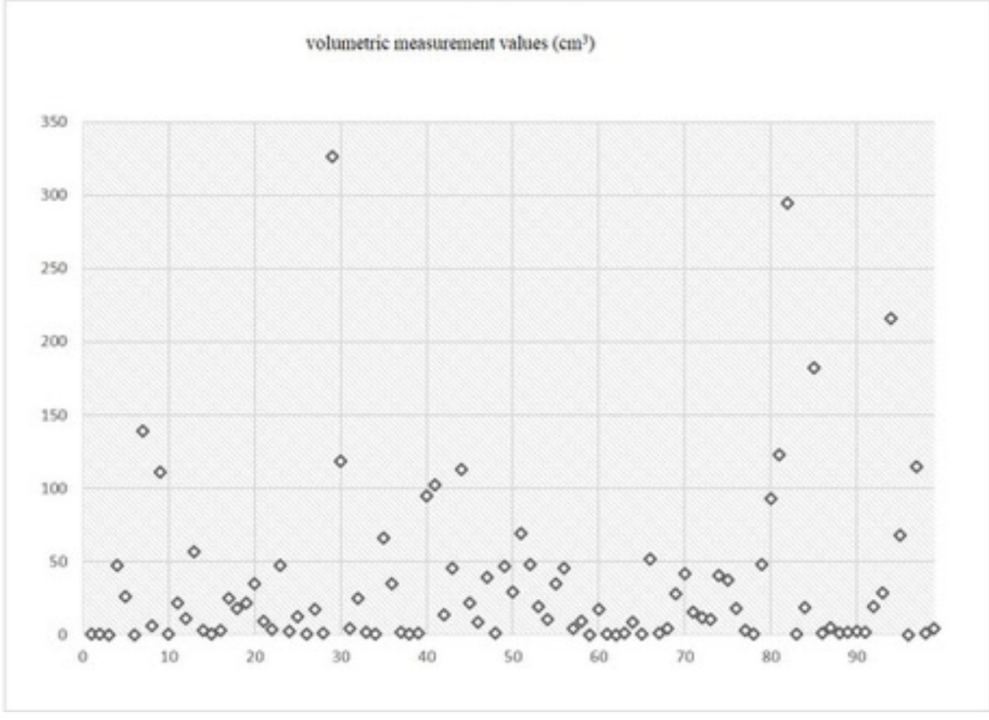


Figure 1. Obtaining the volumetric measurement value



Graphic 1. Distribution of volumetric measurement

occlusion can be additional markers for high risk of progression and adverse outcome[33,34].

Data provided by multimodal MRI can be helpful in identifying patients to be included in acute stroke protocols when clinical uncertainty is present, such as those in patients with right hemisphere syndromes related to small motor deficits. It is needed to review registries, including acute imaging findings and eligibility criteria prospectively.

Study Limitations

This study has some limitations including single-center design, the small sample size and shorter duration of follow-up. Additionally, there may be differences in time of symptom onset and time to presentation as there may be differences in access to emergency medicine services. Thus, volumetric measurements might be affected. In a study without such limitations, volumetric measurements can be a candidate for optimal marker for the prognosis of acute stroke.

Conclusion

In conclusion, segmentation and volumetric measurements of penumbra and infarction core based on PWI and DWI are important to determine current and future risks in patients with acute stroke. Thus, clinical information can be obtained in a more rapid and accurate manner, regarding thrombolysis. However, we think that the decision-making process for thrombolytic therapy can be more rapid based on the correlation between volumetric measurements and NIHSS score in patients with limitations in access to thrombectomy. This may provide a higher survival rate and long-term prognosis by early thrombolytic therapy in the emergency department. In conclusion, this method can be used and be helpful in the management of patients by decreasing the need for medical resources.

Ethics

Ethics Committee Approval: This study was approved by Necmettin Erbakan Univertisy Local Ethics Committee (approval no: 35, date: 07.02.2014).

Informed Consent: Consent form were obtained from the parents of the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.T., B.C., Concept: A.T., B.C., Design: A.T., B.C., Data Collection or Processing: A.T., B.C., Analysis or Interpretation: A.T., B.C., Literature Search: A.T., Writing: A.T.

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