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The Relationship Between Early Diffusion Weighted Imagining Lesion Patterns and Stroke Mechanisms at Atherosclerotic Diseases of Medial Cerebral Artery

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ABSTRACT

Objective: The underlying etiological reason in the process of stroke is the most important factor that determines the prognosis. In this study in atherosclerotic middle cerebral artery (MCA) disease and internal carotic artey (ICA) disease or cardioembolic (CE), research the stroke mechanism and compare to the described study findings in the literature making use of early diffusion-weighted imaging (DWI) (with in 48 hours) in acute stroke cases.

Methods: In this study, DWI lesion patterns taken with in the first 48 hours in 51 patients who due to acute stroke have been compared to stroke subtypes identified within the first week depending on magnetic ressonance angiography (MRA) results in order to determine the differences between lesion patterns. The DWI lesions have been identified as multiple or single lesions depending on the pattern in the literature. Single lesion have been identified as perforating artery infarcts (PAI), pial artery infarcts (PI), and border-zone infacts (BZI). Multiple lesions have been identified double or triple combinations of single lesions. Upon assesment with MRA, stroke subtypes have been identified as MCA dissease, ICA dissease and CE.

Results: Among 51 patients, 11 have been found to be in MCA disease group (21.6%), 25 in ICA disease group (49.1%), and 15 in CE group (29.4%). In the MCA disease group PAI (18.2%), PI (27.3%) and BZI (9.1%) have been detected. The rate of multiple lesions is 45%. Multiple lesion pattern has been detected as high in all three stroke groups (ICA 44%, CE 53%). No lesion pattern have been detected as significantly high in the MCA dissease group (p=0.753).

Conclusion: It is important that the stroke mechanism can be predicted in the early period for the treatment. This study concluded that the stroke mechanism cannot be predicted in the early satge relying on the lesion pattern characteristic at DWI.

Keywords: Middle cerebral artery ischemia, internal carotis artery disease, cardioembolism, diffusion-weighted magnetic resonance imaging, stroke etiology

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INTRODUCTION

Atherosclerotic occlusive disease of the middle cerebral artery (MCA) is an important cause of stroke. New studies and developments with magnetic resonance imaging (MRI) for lesion localization are being added day by day (1,2). Topographic distribution of lesion patterns in intracranial ischemia may provide an early clue in determining the etiology (3,4). Possible mechanisms of cerebral ischemia in MCA infarcts may be thrombosis resulting in complete occlusion, artery-to-artery embolism, hemodynamic insufficiency, local branch occlusion, and a combination of these factors (5). Diffusion-weighted imaging (DWI) is the most sensitive diagnostic method for detecting acute ischemic lesion (6). DWI has been used in many studies investigating the pathogenesis of ischemic stroke in patients with atherosclerotic MCA disease (5-7). Studies have shown that echoplanar imaging measurements with DWI are much more sensitive than conventional MRI (6). Studies examining the relationship between stroke mechanisms and lesion patterns are diverse (5,7-9). However, there are several limitations in these studies, such as the study being limited to a single lesion pattern, not allowing comparison with different stroke etiologies, or the time elapsed between the appearance of stroke findings and DWI application varies from study to study.

In a study conducted to reveal the differences between lesion patterns in atherosclerotic MCA disease and lesion patterns in internal carotid artery (ICA) disease or cardioembolic (CE) and to define the mechanism of stroke, perforating artery infarcts (PAI) were found as single lesions or lesions in association with pial artery and border-zone infarcts (BZI). It was determined that this was a specific lesion pattern for MCA disease, and distal embolization associated with local branch occlusion was a common stroke mechanism in MCA disease (10).

The aim of our study was to determine whether the lesion patterns seen on early DWI (within 48 hours) differed in atherosclerotic MCA disease, ICA disease or CE, which was determined according to the findings detected in magnetic resonance angiography (MRA) in patients with acute stroke and to investigate whether the DWI patterns gave an idea to predict the etiology and mechanism of acute, and to compare the findings with the literature.

METHODS

Patient Selection

This was a single-center, retrospective, observational study. Between January 2010 and June 2012, retrospective analyzes of 51 patients, 34 male and 17 female, out of 1200 patients who were admitted to the Neurology Clinic of University of Health Sciences Turkey, Taksim Training and Research Hospital with acute stroke and met the study criteria. Approval for this study was obtained from the Ethics Committee of Taksim Training and Research Hospital (decision no: 6, date: 03.04.2013).

Patients who underwent DWI within 48 hours of the onset of symptoms which confirmed the diagnosis of acute infarction, who had ischemic lesions in the unilateral MCA territory or border-zone and whose ischemic lesion was compatible with MCA disease, ICA disease, or CE were included in the study. Patients with multiple infarcts in areas outside of a single MCA territory (with MCA infarction or bilateral hemispheric lesions in other territories), stroke type other than MCA disease, ICA disease and CE (metastatic occlusion, etc.) and with concomitant ICA and MCA disease were excluded from the study (Figure 1).

Clinical data were obtained by examining patient files. The findings of the patients were clinically grouped into two classes

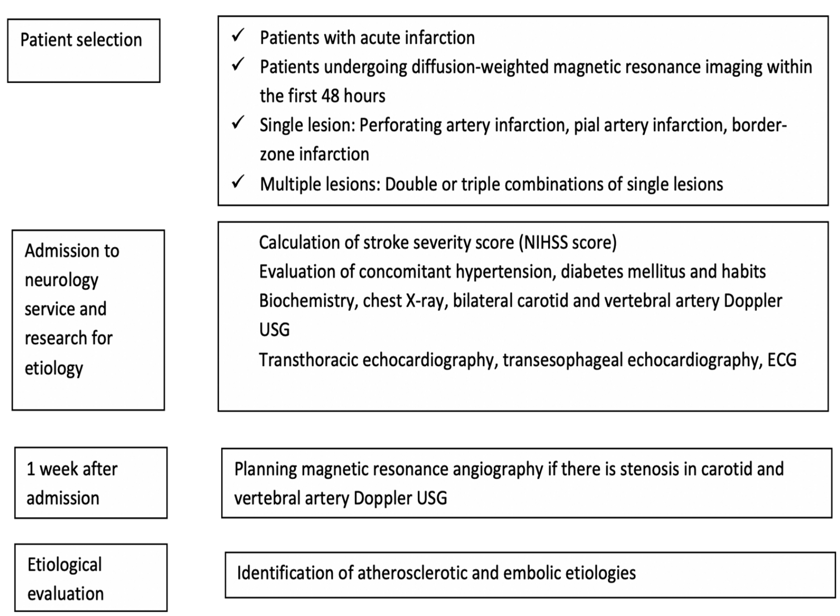

Figure 1. Flow-chart of the study

NIHSS: National Institutes of Health Stroke scale, ECG: electrocardiografi, USG: ultrasonography as lacunar syndromes (pure motor hemiparesis, pure sensorial stroke, sensory-motor hemiparesis, ataxic hemiparesis, dysarthria syndrome, dysarthria- clumsy hand syndrome) and non-lacunar syndromes (presence of cortical findings such as aphasia, neglect, gaze deviation, and changes in consciousness). The National Institutes of Health Stroke scale (NIHSS) was used for the numerical expression of stroke severity. In addition to MRI evaluation, patients' complaints at admission, clinical features, existing and accompanying diseases in their history, complete blood count, erythrocyte sedimentation rate, whole blood biochemistry, coagulation tests, electrocardiography (ECG), chest X-ray and urine test results were examined. Carotid and vertebral artery Doppler ultrasonography, transthoracic echocardiography, transesophageal echocardiography and 24-hour ECG follow-up were performed to investigate the etiology. As a result of these examinations, the risk factors, and etiologies of the patients in terms of stroke development were determined.

MRI was performed with a 1.5 tesla imaging device (Simens Avanto, Medical Systems) with echoplanar feature. 3800 ms repetition time (TR), 102 ms echo time (TE), matrix number 192-192, 5 mm slice thickness, 1.5 mm slice spacing, 21 axial slices, 240 mm image field, 0 and 1000 for DWIs. It was applied with a b value of 2 in s/mm^2. Those who showed an acute infarct pattern on DWI were transfered to the service for follow-up, examination, and treatment. Carotid-vertebral Doppler ultrasonography was performed in all patients. MRA examination was performed in the first week after admission to the service in patients with plaques that caused significant hemodynamic impairment in carotid-vertebral Doppler ultrasonography. Intracranial MRA with 3-dimensional TOF sequence was applied with 24 ms TR and ms TE 7 and 3-dimensional extracranial MRA with 20° flip angle, 159-159 matrix number and 240 mm field of view.

The topography of the ischemic lesion patterns on DWI of the patients was determined according to the vascular mapping published by Tatu et al. (11) in 1998. Vascular territories were determined as perforating, pial and border-zone. As PAI, striato-capsular infarcts and infarcts of perforating vessels of MCA were included. As pial infarcts (PI), infarcts in the territories of the superior and inferior cortical branches of the MCA were included. BZI were determined as infarcts in the anterior and posterior cortical border-zones and internal border-zone. Multiple DWI lesions were defined as hyperintense lesions observed in more than one vascular territory with no border neighborhood. According to Tatu's criteria, DWI lesions were small PAI (<2 cm in diameter), large PAI (>2 cm in diameter), PI, large region infarction, or BZI and multiple lesions (PAI and PI, PAI, PI and BZI, PAI and BZI, PI and PI, PI and BZI, and multiple BZI). PAIs smaller than 2 cm in diameter and PAIs larger than 2 cm in diameter were included in the PAI group. PI and BZI, which were seen as a single lesion, were divided into groups under the names of PI and BZI. The remaining combined patterns consisting of multiple lesions were included in a group called "combined multiple lesions" as the combination of single lesion patterns. Large MCA lesions, considered as a single lesion in the pattern literature, were also included in this last group as a combination of three single lesion patterns. The MRA findings of patients with MCA disease were considered in 3 grades: moderate stenosis (signal reduction greater than 50%), severe stenosis (image distal to MCA, but focal loss of signal) and complete occlusion.

Patients with 50% or more ipsilateral MCA stenosis or occlusion in MRA and no cause of CE or proximal to distal arterial embolism were defined as MCA disease. Patients with a stenosis or obstruction of 50% or more in the ipsilateral ICA and no evidence of MCA disease or a CE were included in the ICA disease group. Patients who had no atherosclerotic finding in cerebral vessels in MRA and who had embolic heart disease according to TOAST criteria were included in the CE group (11).

Statistical Analysis

The NCSS (Number Cruncher Statistical System) (Kaysville, Utah, USA) program was used for statistical analysis. Study data were presented using descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum). The conformity of the quantitative data to the normal distribution was tested with the Kolmogorov-Smirnov, Shapiro-Wilk test and graphical evaluations. Student's t-test was used for two-group comparisons of normally distributed quantitative data, and the Mann-Whitney U test was used for two-group comparisons of non-normally distributed quantitative data. Pearson chi-square test was used to compare qualitative data. The one-way analysis of variance and post-hoc Tukey test were used to reveal the difference between the groups. The significance level was accepted as $p<0.05$.

RESULTS

A total of 51 patients, 34 males (66.7%) and 17 females (33.3%), who were aged between 34 and 82 years, were included in the study. The mean age of men was 63.9±14.15 (range 34-80), and the mean age of women was 72.2±12.78 (range 38-82). MCA disease was found in 11 (21.6%) patients, ICA disease was found in 25 (49.0%), and CE was found in 15 (29.4%) patients. According to the presentation symptoms of the patients, clinical syndrome patterns were lacunar syndrome in 34 (66.7%) and non-lacunar syndrome in 17 (33.3%). In those with lacunar syndrome, the etiology was MCA disease in 9 (26.5%), ICA disease in 15 (44.1%), and CE in 10 (29.4%). Of the patients with MCA disease, 81% (9 patients) had lacunar syndrome. There were 15 (60%) patients who developed lacunar syndrome due to ICA disease. The rate of developing lacunar syndrome among patients with CE was 66.7%. In patients with non-lacunar syndrome, etiology was MCA disease in 2 (11.8%), ICA disease in 10 (58.8%), and CE in 5 (29.4%) patients. The rate of developing non-lacunar syndrome

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among patients with MCA disease was found to be 3.9%, while it was 19.6% in patients with ICA disease and 9.8% in patients with CE. The difference in the rates of developing lacunar syndrome or non-lacunar syndrome in different stroke types was evaluated with the chi-square test and no significant difference was found (p=0.441).

The mean NIHSS score calculated from the neurological findings of the patients at admission was 5.06±3.61 in patients with lacunar syndrome and 7.64±5.27 in those with non-lacunar syndrome and the difference was significant (p=0.045). The mean NIHSS score was 7.59±4.83 in patients with multiple lesions (22 patients), and 4.65±3.55 in patients with single lesion (29 patients), and the difference between the two groups was significant (p=0.016). The mean NIHSS score was 8.64±5.30 in patients with MCA disease, 4.60±3.18 in patients with ICA disease, and 6.13±4.66 in patients with CE. There was a significant difference between them [$F_{(20,50)}$=3.64, p=0.034]. With the post-hoc Tukey test, it was found that this difference stemmed from the difference between those with MCA disease and those with ICA disease.

Examples of lesion patterns by stroke subtype are shown in Figures 2, 3, 4, 5. No statistically significant difference was found between OSA disease, ICA disease and CE groups (p=0.753) (Table 1). Since the number of our patients was limited, PAI lesions smaller than 2 cm and PAI lesions larger than 2 cm were grouped under PAI lesion pattern, and lesion patterns consisting of various combinations of single lesions were grouped under multiple lesion patterns so that the groups could be compared (Table 1). There was no statistically significant difference in terms of lesion pattern between the different stroke subtypes (p=0.753).

Small or large PAI, PI or BZI single lesion patterns were detected in 29 (66.7%) patients. In 22 (33.3%) patients, it was observed that these lesion patterns formed multiple lesion patterns consisting of various combinations. There was no significant difference between different stroke subtypes in terms of developing a single or multiple lesion pattern (p=0.555) (Table 2) (The rates of multiple lesion pattern were 45.5% in the MCA disease group, 44.0% in the ICA group and 53.3% in the CE group). In the MCA disease group, the combination of PAI, PI and BZI (18.1%) and the combination of PAI and BZI (18.1%) were the most common multiple lesion patterns.

Diabetes mellitus (DM), one of the risk factors for stroke, was present in 1 (9.1%) of patients with MCA disease, 11 (44.0%) of patients with ICA disease, and 5 (29.9%) of patients with CE. There was no statistically significant difference between the types of stroke and DM coexistence (p=0.123). Hypertension (HT) was present in 5 (45.5%) of patients with MCA disease, 22 (88.0%) of patients with ICA disease and 9 (60.0%) of patients with CE. Association of HT was found to be significantly higher in the ICA disease group than in the other groups (p=0.020). There was a history of previous cerebrovascular disease (CVD) in 2 (18.2%) of patients with MCA disease, 4 (16.0%) of patients with ICA disease and 2 (13.3%) of patients with CE. There was no difference between stroke subtypes in terms of previous CVD history (p=0.943). Seventeen (33.3%) of the patients were smokers, and 4 (23.5%) of them were in the MCA disease group, 8 (47.1%) in the ICA disease group, and 5 (29.4%) in the CE group. There was no statistically significant difference between smoking and stroke subtypes (p=0.968).

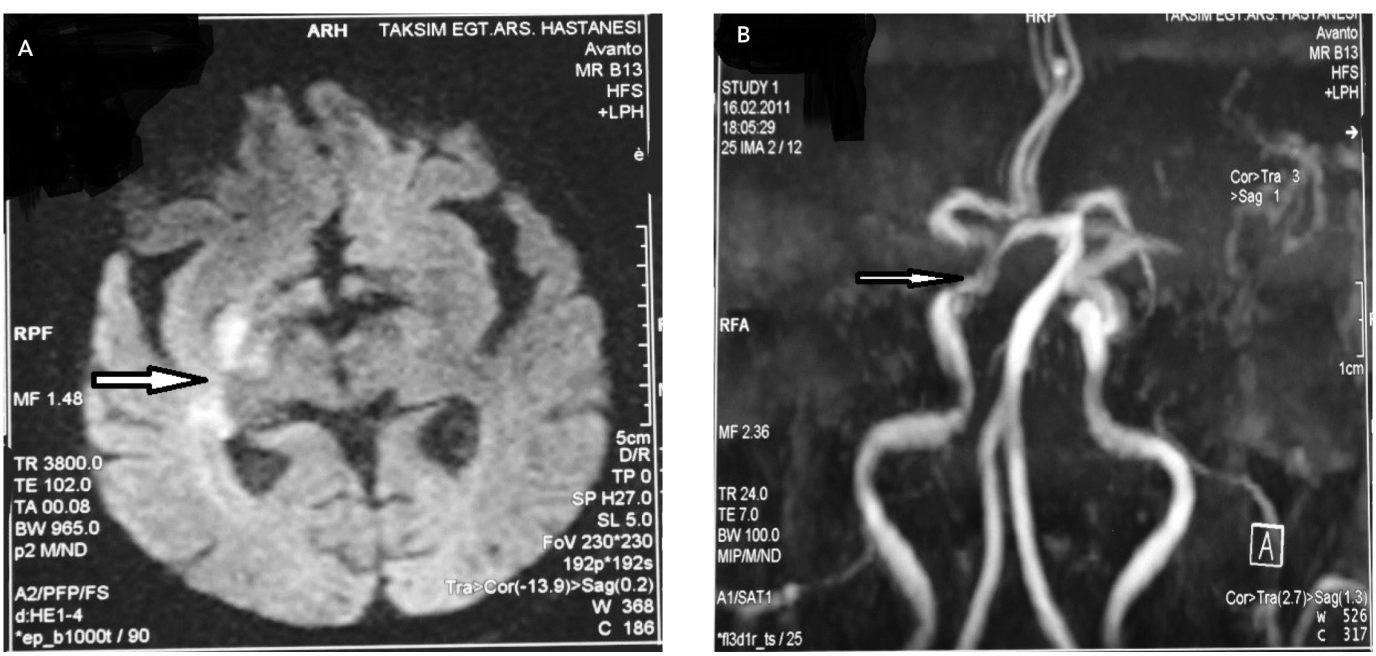

Figure 2. A) The lesion pattern of right perforating artery infarct in an 81-year-old patient with left hemiparesis and dysarthric speech. B) Magnetic resonance angiography image showing occlusion in the right middle cerebral artery

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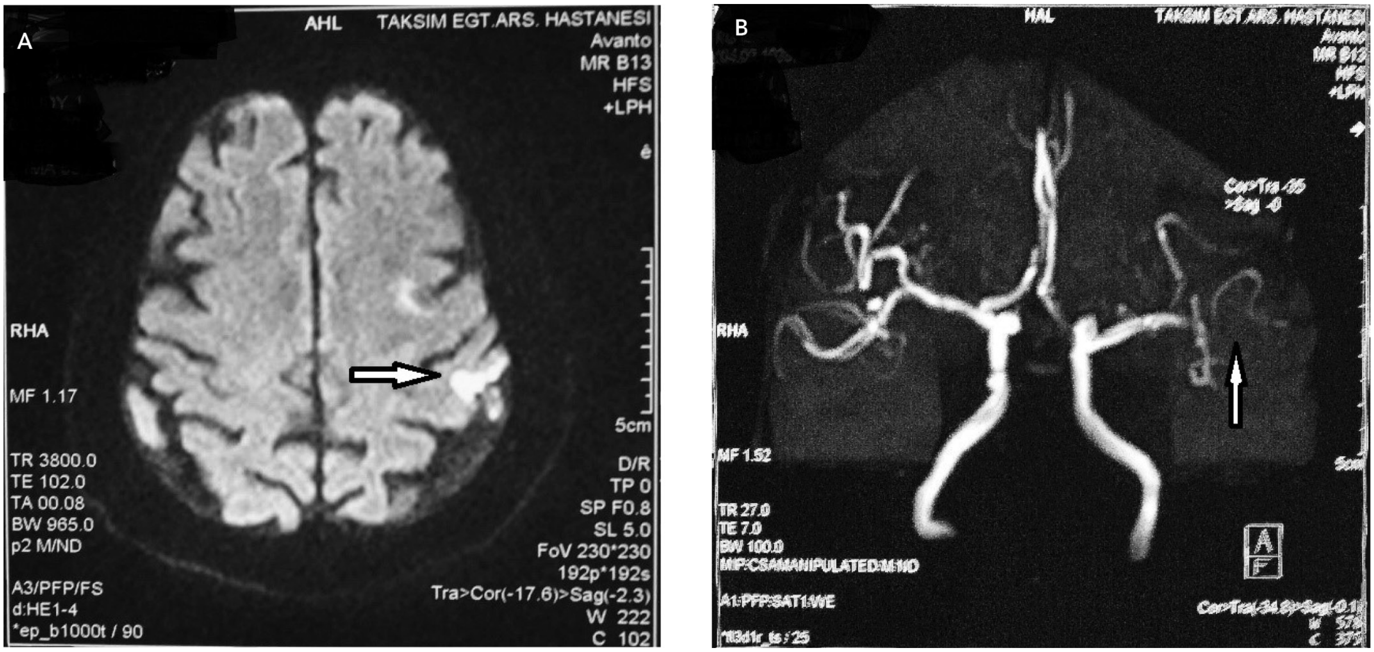

Figure 3. A) The lesion pattern of left pial infarct on diffusion weighted images of a 72-year-old patient with right hemiparesis. B) Cortical branch occlusion of the left middle cerebral artery on magnetic resonance angiography of the same patient

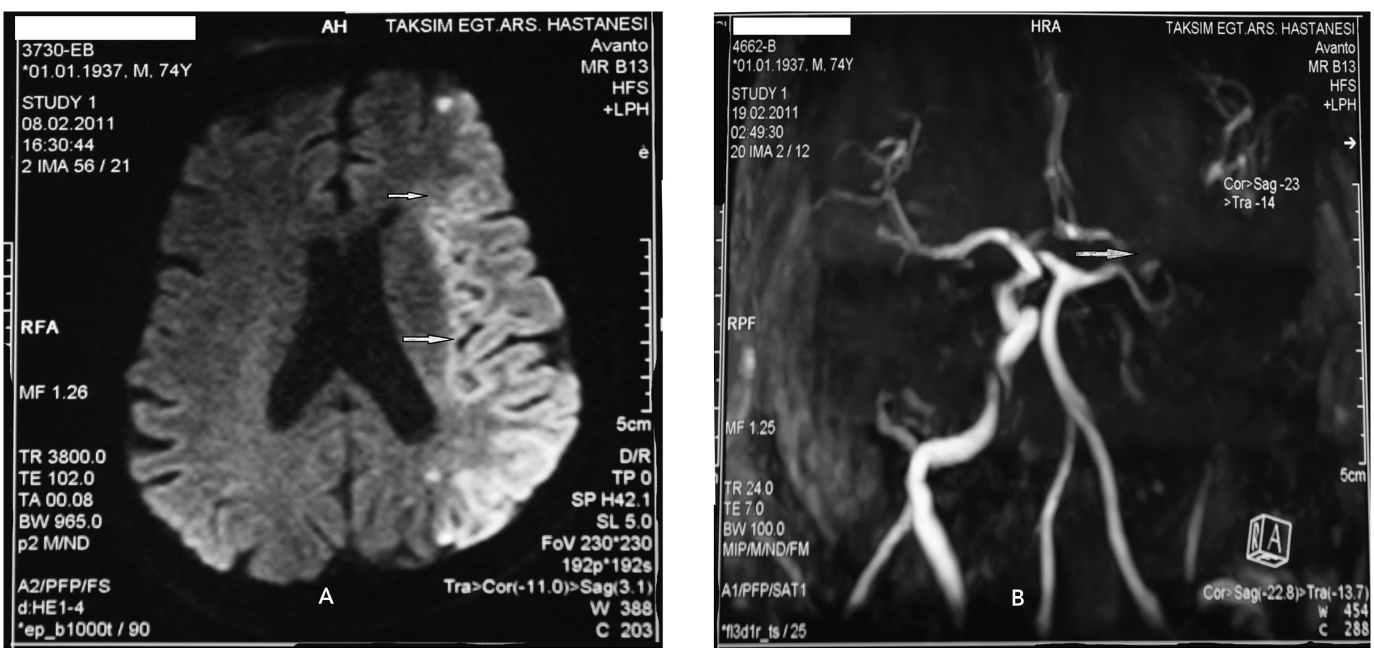

Figure 4. A) A 74-year-old patient presenting with motor aphasia and right hemiplegia has diffuse left middle cerebral artery infarction (a combination of perforating artery infarction, pial artery infarction, border-zone infarction patterns) on diffusion-weighted magnetic resonance imaging. B) There is a 70% stenosis in the left middle cerebral artery on magnetic resonance angiography of the same patient

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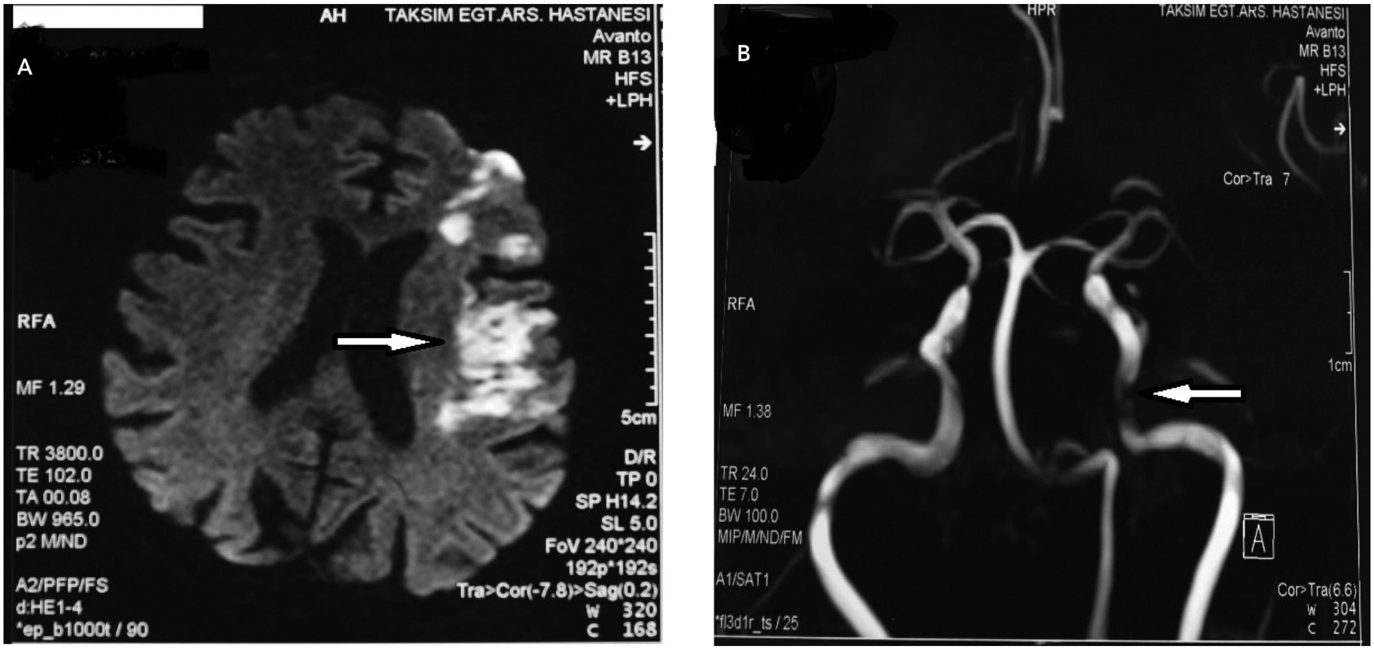

Figure 5. A) Combination of left perforating artery infarction, pial infarct and border-zone infarct lesion patterns in an 82-year-old patient with total aphasia and right hemiparesis. B) There is 50-60% stenosis in the left internal carotid artery in magnetic resonance angiography.

Table 1. Distribution of lesion patterns by stroke subtypes

Lesion pattern	Stroke type		
	MCA disease [n (%)]	ICA disease [n (%)]	CE [n (%)]
PAI	2 (18.2)	3 (12.0)	4 (26.7)
PI	3 (27.3)	9 (36.0)	3 (20.0)
BZI	1 (9.1)	2 (8.0)	0
Combined-multiple	5 (45.5)	11 (44.0)	8 (53.3)

MCA: middle cerebral artery, ICA: internal carotid artery, CE: cardioembolism, PAI: perforating artery infarct, PI: pial artery infarct, BZI: border-zone infarct

Table 2. Distribution of single or multiple lesions in different stroke subtypes

Number of lesions	Stroke type		
	MCA disease [n (%)]	ICA disease [n (%)]	CE [n (%)]
Single lesion	6 (54.5)	16 (64.0)	7 (46.7)
Multiple lesions	5 (45.5)	9 (36.0)	8 (53.3)

MCA: middle cerebral artery, ICA: internal carotid artery, CE: cardioembolism

DISCUSSION

In our study, the characteristics of the lesion patterns in atherosclerotic occlusive diseases of MCA were determined and compared with the findings in the literature. We did not detect a significant difference in the probability of developing multiple lesions in different stroke subtypes. Similarly, when stroke subtype and lesion pattern were compared, no difference was found between stroke subgroups. In a study involving 30 patients with acute MCA infarcts, the characteristics of the lesion (single or multiple lesion) and its pattern (whether the lesion was cortical or in the border-zone or in the territory of perforating artery) were defined using transcranial Doppler, DWI, and MRI. They found that the most common mechanism in MCA stenosis was a single penetrating artery infarction that caused a lacuna-like lesion, and that artery-to-artery embolization caused multiple small infarcts, especially in border-zone areas (5). However, in that study, the research was limited to a single lesion pattern, MCA ischemia

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was evaluated and no comparison with other stroke etiologies was made. In our study, different etiologies, embolic and atherosclerotic, were also evaluated. In a study comparing lesion patterns in DWI and MRA lesions, vessel stenosis was classified as moderate (50-70%) and severe (70-90%) narrowing (10). After determining the stroke subtypes as MCA disease, ICA disease and CE, these subtypes were compared with the lesion patterns. In that study, they found that the combination of PAI and PI, and PAI, PI and BZI were specific lesion patterns for the MCA disease group, and they claimed that the PI lesion pattern originating from MCA could be a marker for embolism (10). They pointed out that the high frequency of the combination of PAI, PI and BZI in MCA disease might suggest an interaction between hypoperfusion and embolism as a stroke mechanism in this group. PAI lesion pattern smaller than 2 cm was found in the second frequency in patients with MCA disease. They attributed this to MCA-induced atheroma occlusion of the perforating artery inlet or isolated lipohyalinosis of the penetrating artery. This pattern was not accompanied by cortical field infarcts and the occlusions were mostly moderate, which distracted from the idea of embolization. However, despite this support, the authors evaluated the stroke mechanism that created the PAI lesion pattern as not clarified (10).

Multiple lesion pattern was the most detected lesion pattern in all three subgroups of our patients. High rate of combination of PAI, PI, BZI was similar to the findings of the study of Lee et al. (10). However, this was not a high rate specific to the MCA disease group. Although the high rate of PI lesion pattern in our patients with ICA disease was remarkable (36%) and its relationship with embolization was considered, no statistically significant difference was found.

Various studies have investigated the relationship between lesion patterns and occlusion mechanisms, using DWI to investigate the pathogenesis of ischemic stroke in atherosclerotic MCA disease (7,8). In 920 patients, stenosis was examined using MRA, and the difference between lesion patterns in extracranial occlusions and lesion patterns in intracranial occlusions was determined. While deep perforating and internal BZI were mostly detected in MCA infarcts, superficial perforating and territorial infarcts were detected in ICA disease (8). The same group of researchers evaluated 850 patients with transient ischemic attack and stroke clinically and neuroradiologically and found that the MCA group developed more lacunar syndrome patterns than the ICA group. They reported that the occlusions in the ICA group mainly caused total anterior circulation infarcts, and they found that the mean NIHSS score of this group was higher when compared to the mean NIHSS score of the MCA group (9). In lacunar syndromes, when multiple lacunae in which single lesions were observed, it was emphasized that other etiologies should be investigated in addition. Occlusion of more than one vessel was associated with embolism, while multiple scattered lesions in one vascular area were associated with large vessel disease (12). In our study group, there was no difference in terms of developing lacunar and non-lacunar syndromes according to etiology, and NIHSS score was found to be higher in those in the MCA disease group.

The difference in the time elapsed between the appearance of stroke symptoms and performing DWI creates difficulties in comparing these studies. This period varies between 5-6 days and 2 weeks (5,7-9). The time elapsed between the appearance of stroke symptoms and performing DWI is important. In this regard, 99 patients with acute ischemic stroke were examined with DWI within 6 hours after the onset of symptoms, the examination was repeated within 1 week, the lesion patterns were compared. They stated that it was possible to detect recurrences with DWI and that the time of performing DWI would affect the lesion pattern (12). In the study in which patients with recurrent ischemic stroke were evaluated in the same year, it was revealed that the lesion pattern in DWI performed in the early period (less than 24 hours from the onset of stroke) was associated with the stroke subtypes in the classification determined according to TOAST criteria (12,13).

In our study, no significant difference was found in terms of lesion patterns in different stroke subtypes. There were also studies that found a significant relationship between DWI and stroke subtypes (14). In a study reported from Turkey, while specific DWI patterns were found to be associated with small vessel disease, no significant distinguishing DWI patterns were found for large artery atherosclerosis and CE. It has been emphasized that classical diagnostic methods such as echocardiography and doppler USG maintain their importance (3). Rapid planning of all examinations remains important in determining the etiology of stroke, and imaging alone cannot replace these examinations.

When different stroke subgroups were evaluated in terms of risk factors in our study, history of HT in the ICA disease group was found to be significantly higher than the other groups (88.8%). In the literature, the history of DM was found to be significantly higher in the ICA disease group compared to other groups (10). In our study, DM was seen as a risk factor for all stroke subgroups, and no difference was found between the groups in terms of DM. No significant difference was found between groups in terms of smoking rate. These results were found to be similar to the studies conducted in the Turkish population (3).

Study Limitations

Our study was conducted on 51 patients who met the inclusion criteria. Conducting it in a single center was effective in the small number of patients who met the inclusion criteria for the study. Being retrospective also caused unwanted data loss and limited patient recruitment. Another limitation of the study was that MRA examinations of the patients were not repeated. Demonstrating the functioning of the recanalization process in different types of strokes may be the subject of research in future studies. Since we did not perform repeat MRA, no interpretation could be made for recanalization during infarct development, and it was concluded that a prospective study would provide more information.

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CONCLUSION

Stroke is a condition of which prognosis is positively affected when it is intervened in the early period. Different stroke mechanisms require different treatment strategies. Therefore, it is important that the mechanism of stroke is predictable in the early period. Although this study concluded that the character of the lesion pattern and the mechanisms of stroke occurrence could not be predicted with DWI in the early period, it revealed the importance of repeating the same study with a larger number of patients in a multicenter manner in the light of the results of the studies in the literature.

Ethics Committee Approval: Approval for this study was obtained from the Ethics Committee of Taksim Training and Research Hospital (decision no: 6, date: 03.04.2013).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Author Contributions: Surgical and Medical Practices - K.U.; Concept - K.U., S.Ü.Ö., Ş.F.H.; Design - K.U., Ş.F.H.; Data Collection and/or Processing - K.U., S.Ü.Ö.; Analysis and/or Interpretation - K.U., Ş.F.H.; Literature Search - K.U., S.Ü.Ö.; Writing - K.U., S.Ü.Ö.

Conflict of Interest: The authors have no conflict of interest to declare.

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