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Manuscript

Title:

Investigation of Brain Vascular Territories in Stroke Patients Detected Non-Valve Atrial Fibrillation as an Etiological Factor

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Abstract

Objective: It was aimed to investigate the cerebral vascular territories in stroke patients with NVAF as an etiologic factor.

Material and Methods: A total of 104 patients who were referred to our hospital between January 2015 and September 2016, who were over 55 years of age, identified or documented as having a standard ECG or Holter ECG record on their medical history, and diagnosed with stroke were included. Our study was designed as a retrospective analysis of prospective data. Detailed history, physical examination and electrocardiography (ECG) evaluations of the patients were performed. Descriptive statistics were used in the detection of findings, and t-test, Pearson-square test and Fisher's exact test were used for differences analysis.

Results: 53.8% (N = 56) of the patients were male and 46.2% (N = 48) were female. The mean age was 73.5. MCA was the most common site of vascular involvement in NVAF-dependent strokes. In MCA vascular territory, ischemic infarcts were detected most frequently in the upper and lower divisions. SCA and PCA followed MCA. Approximately 64% of the NVAF-related strokes were anterior circulation infarction (ASE) and 22% were posterior circulation infarct (PSE). There was a significant difference in age and past stroke history factors in favor of ASE ($p<0.05$). There was no significant difference between ASE and PSE in HT, cardiac history and DM factors ($p>0.05$).

Conclusion: It was emphasized that the area of the vessel that underwent ischemia in the acutely displayed infarcts and the etiological factor for this vessel area could be predicted.

Key words: Brain vessel, ischemic stroke, non-valvular atrial fibrillation

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Introduction

Non-valvular atrial fibrillation (NVAF) is an independent risk factor for ischemic stroke and cardioembolic causes account for close to 20% of all ischemic stroke (1). Studies indicate that the first stroke in the presence of atrial fibrillation (AF) is twice as fatal as in the absence of AF, and the risk of recurrent stroke is higher in survivors. The prevalence of AF in people over 65 years old is 5%. The annual risk of stroke in patients with AF is determined by the CAHDVAS2C score. This rate is significantly increased with age, accompanying comorbid diseases and especially stroke history.

Heart-borne emboli is the reason in two-thirds of patients with AF and ischemic stroke. When the etiologic factor is NVAF in ischemic stroke, the superiority of anticoagulant therapy is demonstrated in the preservation. Therefore, NVAF is an important etiologic factor for ischemic stroke in terms of treatment and prognosis (2). In this study, it was aimed to investigate the cerebral vascular territories in stroke patients who have non-valvular atrial fibrillation as an etiologic factor and it is aimed to emphasize the importance of stroke in patients with AF.

Material and Methods

Our study was designed as a retrospective analysis of prospective data. The patient population was determined to be over 55 years old, who applied to [the name of the hospital will be indicated after the referee evaluations] Education Research Hospital Neurology Department between January 2015 and September 2016. A detailed history, physical examination and electrocardiography (ECG) evaluations of 104 patients were performed.

Patients who were identified or documented as having AF case in their medical history, standard ECG or Holter ECG record and who received a stroke diagnosis were included in the study. Stroke diagnosis were admitted with clinical evaluations in patients whose symptoms lasted longer than 24 hours. It was also accepted that only the ischemic region formed in the brain by MRI diffusion was shown. The demographic characteristics of all patients were adjusted with the CHADS VASC scores recommended for use in the European Society of Cardiology (ESC) guidelines for atrial fibrillation published in 2010.

Risk factors for CHADS VASC score were age, gender, past infarction, diabetes mellitus (DM), hypertension (HT) and cardiac history. As cardiac history; coronary artery disease, past myocardial infarction, coronary artery bypass graft, and congestive heart failure were accepted. In addition, cranial vascular territories were confirmed with MRI diffusion at least

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once. Fetal posterior cerebral arteries were excluded from the study and vessel areas were classified based on the relevant literature (3).

These vessels were defined as anterior cerebral artery (ACA), middle cerebral artery (MCA), lenticulostriate artery (LSA), anterior choroidal artery (AchA), posterior cerebral artery (PCA), vertebral artery (VA), posterior inferior cerebellar artery (PICA) and superior cerebellar artery (SCA). MCA was classified as total MCA, MCA upper division, MCA lower division, total MCA with deep branches and malign MCA with deep branches affected by infarct areas. Border zone infarcts and subcortical lacunar infarcts were classified separately. Patients with infarcts in more than one vascular territory at the same time were identified as multiple infarcts (Figure 1). Descriptive statistics were used in the detection of findings, and t-test, Pearson-square test and Fisher's exact test were used for differences analysis. This study was conducted with the ethical approval of HNEH-KAEK-2017/406 number and dated 24.04.2017 issued by the Haydarpasa Numune Research And Education Hospital Ethical committee.

Results

A total of 104 patients participated in our study. Of these patients, 53.8% (N = 56) were male and 46.2% (N = 48) female. The mean age of the patients was 73.5. In addition, 44.2% (N = 46) of patients had previous stroke, 92.3% had HT, 34.6% had DM, and 78.8% had a cardiac history (Figure 2).

As a result of the detailed evaluations made, the most common venous occlusion area was determined as MCA in the strokes due to NVAF. In MCA vascular territory, ischemic infarcts were detected most commonly in upper and lower divisions. SCA and PCA followed MCA.

The most important risk factor for multiple infarcts was age and the rate was 13.5%. All of the seven patients had HT and cardiac history, and 5 patients had prior strokes.

A total of 10 patients with border zone infarcts had an average age of 84 years and 8 patients had infarct cortical localization. Four of the 4 patients with subcortical lacunar infarcts had HT history. Findings obtained as a result of our study are given in Table-1.

Approximately 64% of the NVAF-related strokes were anterior circulation infarction (ASE) and 22% were posterior circulation infarction (PSE). The average age at ASE was 75 and 66 at PSE. The ratio of female to male in ASE was found to be 1.6, and this ratio was found to be 0.5 in PSE, and the difference was in favor of males. The stroke history in ASE was found to be 53% in all cases and 16% in PSE.

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While the rate of all patients with HT risk factor in their background was 92% in ASE and 91% in PSE, these rates for DM were identified 30% for ASE and 33% for PSE. The rate of all patients with cardiac disease history was found 80% in ASE and 66% in PSE. While female gender is preliminary for strokes formed in the ASE areas, there is male dominance in PSE. While previous stroke history was frequent in ASE strokes, mean age in PSE strokes was found younger than ASE (Table-2).

When Table-2 is examined; the factors of age and past stroke history were significantly different in favor of ASE ($p<0.05$). However, there was no significant difference between ASE and PSE in HT, cardiac history and DM factors ($p>0.05$).

Discussion

Atrial fibrillation is a known cardiac risk factor (2). Studies have shown that strokes which develop in AF patients may be 2 times more mortal than non-AF patients (14,15). Especially with the increase of the CHADVASC score, the risk of stroke in patients with AF is increasing. It is suggested to fight with AF in all diagnosis and treatment guidelines for the prevention of major strokes and mortality and morbidity that may develop. New-generation anticoagulant agents have also been used in combination with warfarin, a vitamin K antagonist, to combat AF (16).

Stroke may develop in patients with NWAF despite proper antithrombotic treatment. Emboli originating from the left appendage is most often responsible for these patients' infarctions (10). There are larger particulate emboli in patients with AF compared to emboli that develop secondary to carotid disease and are more prevalent as transient ischemic attack (TIA). They cause large ischemic strokes (11). In addition to causing massive strokes, silent cerebral infarction and TIA can also be seen (12,13).

In a study of Chung and colleagues with 2702 stroke patients, 15.6% of all strokes were associated with AF and the most common vessel area was MCA. AF was detected as the reason for 50% of SCA infarcts (5 of 10 patients) (1). In the evaluation of 1000 patients who underwent their first stroke in the Lausanne stroke registry study, MCA was the most common vessel of heart embolization (5). In the Besancon stroke registry, prospective recordings of 2500 disease were also recorded, MCA is the most common embolization vessel (6). Rovira et al. [7] also found similar findings in their studies of stroke involvement and stroke mechanisms. The work of Stecco et al. (8) and Paciaroni (9) confirm all these studies.

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Conclusion

We carried out this study with the aim of emphasizing the particular artery bed-related stroke that the NWAF, which can cause great strokes, could develop. We also noted that stroke is a disease that needs to be taken precautions.

As a result of our study, MCA was found as the most frequent vessel involvement area in NVAF-related strokes, and SCA and PCA followed. In addition, about 64% of strokes with NVAF are anterior circulation infarction (ASE) and 22% are posterior circulation infarction (PSE) in our study.

Considering that some of the developed strokes are disabling strokes, the importance of prognosis in AF treatment is once again revealed in our study. In particular, left hemisphere MCA infarcts lead to right hemiparesis and limits the quality of life due to motor and sensory aphasia. The most common vessel associated with NWAF is MCA, which is consistent with the literature. However, the restrictive factors of our study were the lack of comparable studies, being single-centered and retrospective, having a small number of patients and reflecting a certain population.

In our study, it was predicted to determine the area of the vessel that underwent ischemia in the acutely displayed infarcts. It was also predicted that the etiological factor for this area of the vessel can be estimated. We think that further elaboration of these vascular territories and a more detailed examination of risk factors may give us more information about the etiology. Currently available classifications do not fully demonstrate the etiology of stroke and cause recurrent strokes (4). Therefore, the vascular area and proper treatment options need to be improved.

Acknowledgments:

The acknowledgment will be made after the referee evaluations.

Conflict of Interest:

There is no conflict of interest in the study.

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237 **Table and Legends**

238 Table 1. Vascular fields and demographic data

Cardioembolic Stroke	M	F	N	N%	Age (Aver.)	Previous Stroke	HT	DM	Cardiac History
MULTIPLE INFARCT	10	4	14	13.5	78	8	14	6	14
MCA-UD	6	6	12	11.5	73.3	10	12	8	12
MCA-AD	2	10	12	11.5	83	6	12		8
SCA	8	2	10	9.6	65	2	10	2	6
TOTAL MCA + DEEP BRANCH	4	4	8	7.7	79.5	6	6		6
TOTAL MCA - DEEP BRANCH	6	2	8	7.7	75	2	8	2	8
PCA	4	4	8	7.7	71	2	8	2	4
CORTICAL BORDER ZONE	4	4	8	7.7	84	4	6	4	6
ACA	2	2	4	3.8	78	2	4	2	4
LSA		4	4	3.8	65	2	2		2
AchA		4	4	3.8	70.5		4	4	2
PICA	2	2	4	3.8	68		4	2	4
SUBCORTICAL LAK.	4		4	3.8	68	2	4		4
VA	2		2	1.9	61			2	2
INTERNAL BORDER ZONE	2		2	1.9	84		2	2	
Total	**56**	**48**	**104**	**100**	**73.5**	**46**	**96**	**36**	**82**

239 M: Male, F: Female, N: Number of Patients, N%: Percentage of Patients

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242 Table 2. ASE and PSE Comparison

	ASE (N=67)	PSE (N=23)	p
The average age	75	66	**0.000**[†]

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Female / Male Ratio	1.6	0.5	-
Previous Stroke History	%53	%16	**0.002**ˣ
HT	%92	%91	0.668‡
Cardiac Disease History	%80	%66	0.181ˣ
DM	%30	%33	0.659ˣ

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249 †: t-test result, ˣ: chi-square result, ‡: Fisher's Exact Test result

250 **Figures and Legends**

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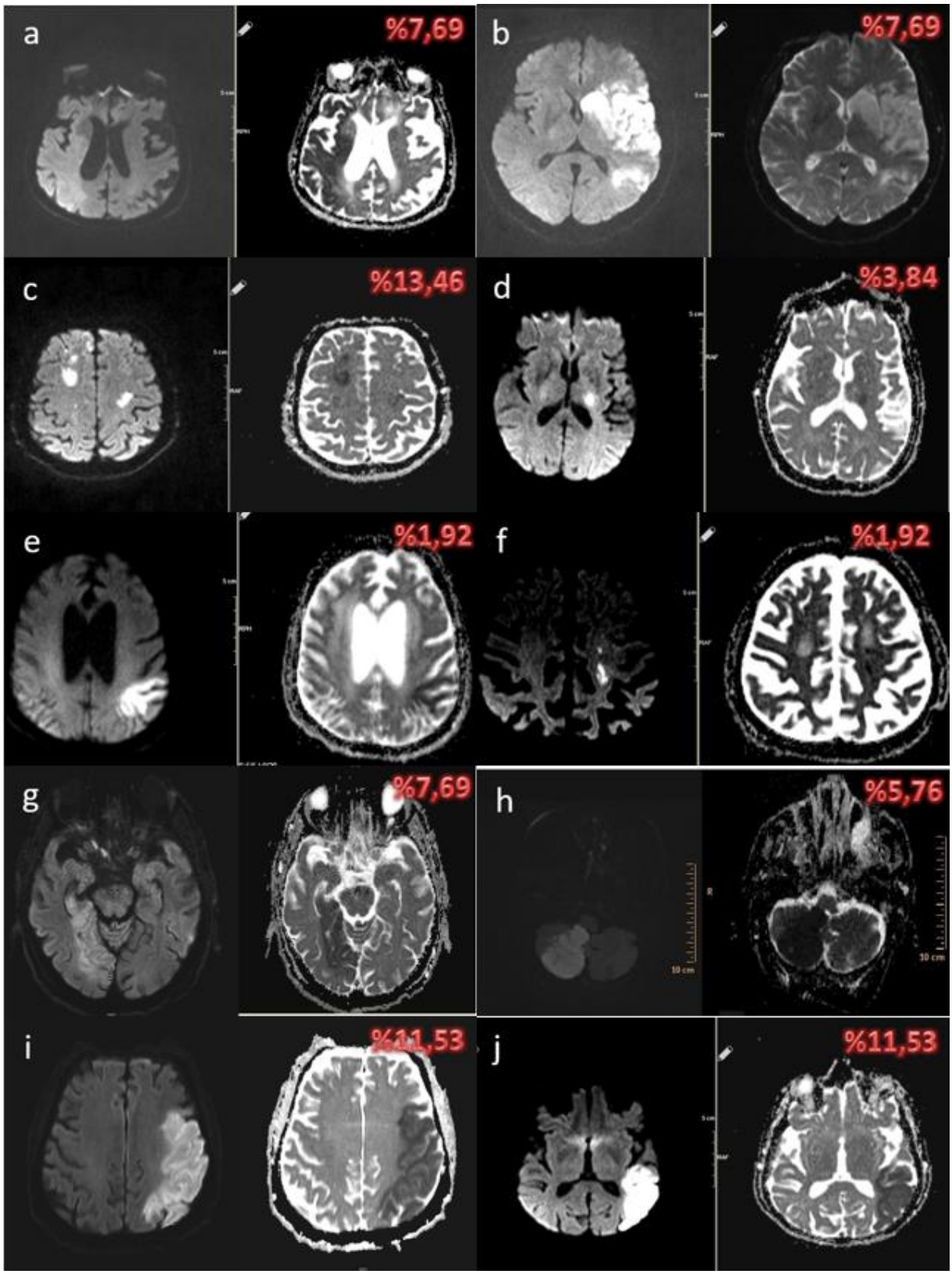

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253 Figure 1. Vascular territories and Infarct Fractions

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254 a-Acute phase MCA Upper and Lower Division involvement (Deep Branch Protection) MRI
255 Diffusion Sequence

256 b-Subacute period total MCA involvement (Upper + Lower and Deep Branches) MRI
257 Diffusion Sequence

258 c-MRI Diffusion Sequence compatible with acute multiple infarct

259 d-MRI Diffusion Sequence Consistent with Acute Phase Subcortical Lacunar Infarct

260 e- MRI Diffusion Sequence compatible with Acute-Subacute period MCA-PCA common
261 irrigation area

262 f- MRI Diffusion Sequence compatible with Acute-Subacute period MCA-MCA Deep branch
263 common irrigation area

264 g-MRI Diffusion Sequence compatible with acute-subacute period PCA irrigation area

265 h- MRI Diffusion Sequence (including vertebral irrigation area) compatible with Acute-
266 Subacute period PICA irrigation area

267 i- MRI Diffusion Sequence compatible with Acute-Subacute period MCA upper division
268 irrigation area

269 j- MRI Diffusion Sequence compatible with Acute-Subacute period MCA subdivision
270 irrigation area

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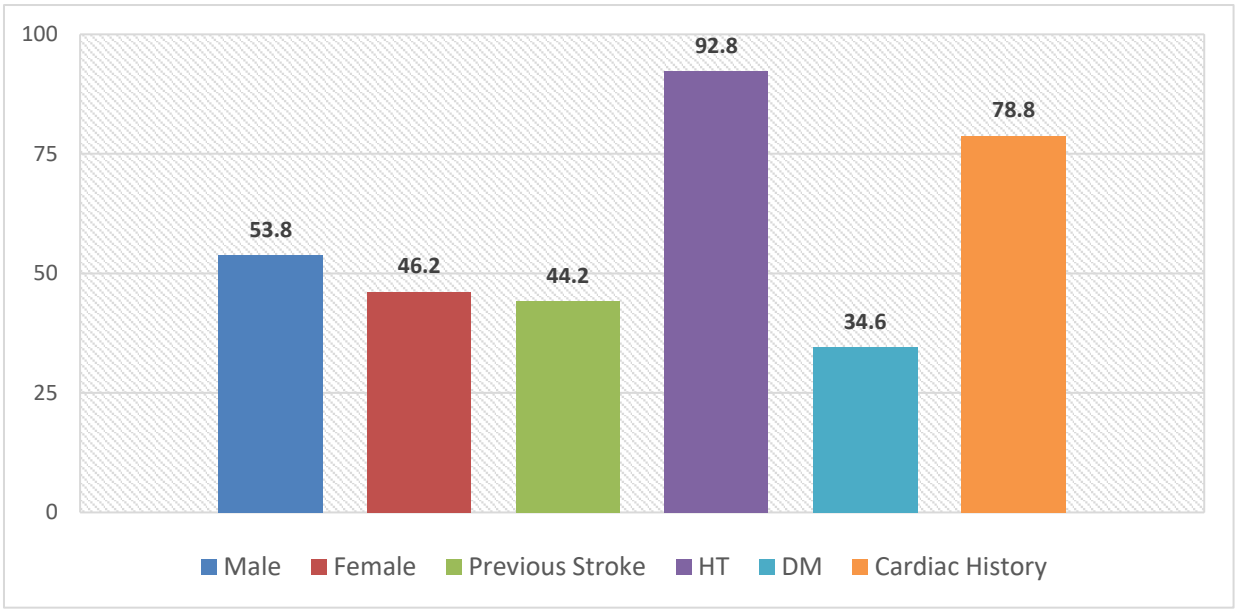

Figure 2. Ratio of Risk Factors to Total Number of Patients (%)