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

Etiyolojik Faktör Olarak Non-Valvuler Atriyal Fibrilasyon Saptanan İnme Hastalarında Beyin Damar Alanlarının İncelenmesi

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Abstract

It was aimed to investigate the cerebral vascular territories in stroke patients with NVAF as an etiologic factor. A total of 208 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's chi-square and Fisher's exact test were used for differences analysis. 53.8% (n=112) of the patients were male and 46.2% (n=96) were female. The mean age was 73.5. MCA was the most common site of vascular involvement in NVAF-dependent strokes. SCA and PCA followed MCA. Approximately 64% of the NVAF-related strokes were anterior circulation infarction (ACI) and 22% were posterior circulation infarct (PCI). 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 ACI and PCI in hypertension, cardiac history and diabetus mellitus factors ($p > 0.05$). 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.

Keywords: Brain Vessel, Ischemic Stroke, Non-Valvular Atrial Fibrillation

Öz

Bu çalışmada; non-valvuler atriyal fibrilasyon (NVAF) etyolojisine sahip inme hastalarında serebral vasküler bölgeleri araştırmak amaçlandı. Ocak 2015-Eylül 2016 tarihleri arasında hastanemize başvuran ve 55 yaşın üzerinde olan, tıbbi öykülerinde standart EKG veya Holter EKG kaydı bulunan veya NVAF tanısı konan ve iskemik serebrovaskuler hastalık teşhisi alan 208 hasta çalışmaya dahil edildi. Çalışmamız retrospektif verilerin bir analizi olarak tasarlanmıştır. Hastaların ayrıntılı öykü, fizik muayene ve elektrokardiyografi (EKG) değerlendirmeleri yapıldı. Bulguların tespitinde tanımlayıcı istatistikler kullanılmış ve t-testi, Pearson ki-kare ve Fisher'in kesin testi, farklılıklar analizi için kullanılmıştır. Hastaların %53.8'i (n=112) erkek, %46.2'si (n=96) kadındı. Yaş ortalaması 73.5 idi. Orta serebral arter (MCA), NVAF'ye bağlı inmelerde en sık vasküler tutulum alanıydı. Superior serebellar arter (SCA) ve posterior serebral arter (PCA), MCA'yı takip etti. NVAF ile ilişkili inmelerin yaklaşık %64'ü ön sirkülasyon enfarktüsü (ACI) ve %22'si arka sirkülasyon enfarktüsü (PCI) idi. Yaş ve geçmiş inme öyküsü faktörlerinde ACI lehine anlamlı bir fark vardı ($p <0.05$). Hipertansiyon, kardiyak öykü ve diabetüs mellitüs faktörlerinde ACI ve PCI arasında anlamlı fark yoktu ($p> 0.05$). Sonuç olarak, akut olarak ortaya çıkan enfarktlarda iskemiye uğrayan damar alanının ve bu damar alanı için etiyolojik faktörün tahmin edilebileceği vurgulanmıştır.

Anahtar Kelimeler: Beyin Damar Alanları, İskemik Serebrovaskuler Olay, Non-Valvuler Atriyal Fibrilasyon

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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 CHA2DS2-VASc 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.

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Material and Method

Our study was designed as a retrospective analysis of 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.

The CHADS2 score assigns 1 point for heart failure, hypertension, age ≥75 years, and diabetes mellitus and 2 points for prior stroke or transient ischaemic attackThe CHA2DS2-VASc score has been proposed as an improvement to the CHADS2 score specifically for risk discrimination of lower risk patients.7 Compared with the CHADS2 score, the CHA2DS2-VASc score includes three additional risk factors for ischaemic stroke: age 65–74 years, female sex, and vascular disease, the latter defined as previous myocardial infarction or peripheral arterial disease. 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 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).

Summary statistics were expressed as mean ± standard deviation, number of cases and percentage (%). Welch t-test was used to assess the age difference between anterior and posterior circulation infarction patients. To determine whether there is any significant association between two vascular territories (ACI, PCI) and Stroke History, Cardiac Disease History, HT and DM risk factors, Chi-square and Fisher's Exact tests were used. A p-value of < 0.05 was considered statistically significant. All statistical data analyses were performed using SPSS v22.

Results

A total of 208 patients participated in our study. Of these patients, 53.8% (n=112) were male and 46.2% (n=96) female. The mean age of the patients was 73.5 (±9.8). In addition, 44.2% (n=92) of patients had previous stroke, 92.3% had HT, 34.6% had DM, and 78.8% had a cardiac history (Figure 2).

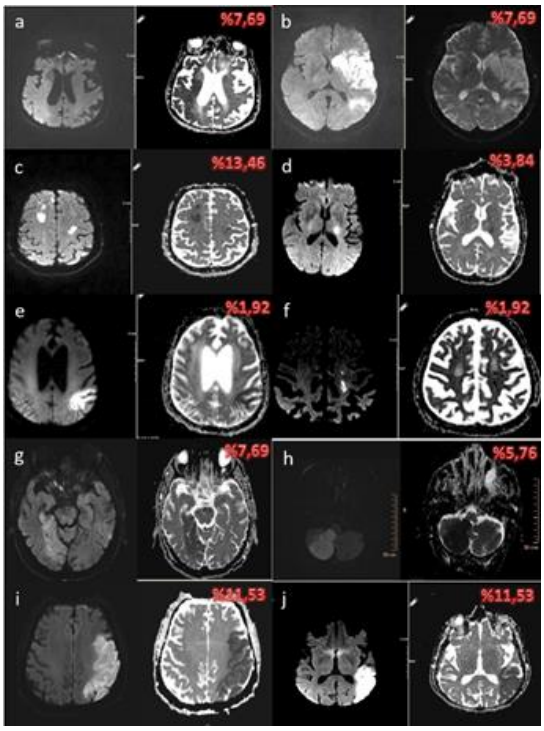

Figure 1. Vascular territories and Infarct Fractions a-Acute phase MCA Upper and Lower Division involvement (Deep Branch Protection) MRI Diffusion Sequence; b-Subacute period total MCA involvement (Upper + Lower and Deep Branches) MRI Diffusion Sequence; c-MRI Diffusion Sequence compatible with acute multiple infarct; d-MRI Diffusion Sequence Consistent with Acute Phase Subcortical Lacunar Infarct; e- MRI Diffusion Sequence compatible with Acute-Subacute period MCA-PCA common irrigation area; f-MRI Diffusion Sequence compatible with Acute-Subacute period MCA-MCA Deep branch common irrigation area; g-MRI Diffusion Sequence compatible with acute-subacute period PCA irrigation area; h- MRI Diffusion Sequence (including vertebral irrigation area) compatible with Acute-Subacute period PICA irrigation area; i- MRI Diffusion Sequence compatible with Acute-Subacute period MCA upper division irrigation area; j- MRI Diffusion Sequence compatible with Acute-Subacute period MCA subdivision irrigation area.

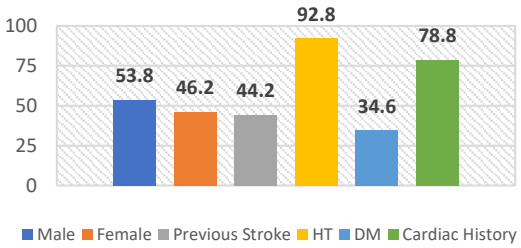

Figure 2. Ratio of risk factors to total number of patients (%)

As a result of the detailed evaluations made, the most common 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 28 patients had HT and cardiac history, and 16 patients had prior strokes.

Table 1. Vascular territories and demographic data

Cardioembolic Stroke	**M**	**F**	**n**	**n%**	**Age (Aver.)**	**% Previous Stroke**	**% HT**	**% DM**	**% Cardiac History**
Multiple Infarct	20	8	28	13.5	78	57	100	42	100
MCA-UD	12	12	24	11.5	73.3	83	100	66.6	100
MCA-AD	4	20	24	11.5	83	50	100		66.6
SCA	16	4	20	9.6	65	20	100	20	50
Total MCA + Deep Branch	8	8	16	7.7	79.5	75	75	0	75
Total MCA - Deep Branch	12	4	16	7.7	75	25	100	25	100
PCA	8	8	16	7.7	71	20	100	25	50
Cortical Border Zone	8	8	16	7.7	84	50	75	50	75
ACA	4	4	8	3.8	78	50	100	50	100
LSA		8	8	3.8	65	50	50	0	50
AchA		8	8	3.8	70.5	0	100	100	50
PICA	4	4	8	3.8	68	0	100	50	100
Subcortical Lak.	8		8	3.8	68	50	100	50	100
VA	4		4	1.9	61	0	0	100	100
Internal Border Zone	4		4	1.9	84	0	100	100	0
Total	**112**	**96**	**208**	**100**	**73.5**	**44.2**	**92**	**34.6**	**78.8**

M: Male, F: Female, n: Number of patients, n%: Percentage of patients

A total of 20 patients with border zone infarcts had an average age of 84 years and 16 patients had infarct cortical localization. All of the 8 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 (ACI) and 22% were posterior circulation infarction (PCI). The average age at ACI was 75 and 66 at PCI. The ratio of female to male in ACI was found to be 1.6, and this ratio was found to be 0.5 in PCI, and the difference was in favor of males. The stroke history in ACI was found to be 53% in all cases and 16% in PCI.

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

When Table-2 is examined; the factors of age and past stroke history were significantly different in favor of ACI (p=0.000, p=0.002). However, there was no significant difference between ACI and PCI in HT, cardiac history and DM factors (p=0.668, p=0.181, p=0.659).

Table 2. ACI and PCI comparison.

	ACI (n=134)	**PCI (n=46)**	**p**
The average age	75	66	**0.000**†
Female / Male Ratio	1.6	0.5	-
Previous Stroke History	%53	%16	**0.002**×
HT	%92	%91	0.668‡
Cardiac Disease History	%80	%66	0.181×
DM	%30	%33	0.659×

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

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, 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 NVAF 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 more than 40% of patients with ACA territory infarction received extensive evaluation, whereas only 8.5% of patients with vertebral artery territory infarction did. In our study, approximately 64% of the NVAF-related strokes were anterior circulation infarction (ACI) and 22% were posterior circulation infarction (PCI).

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. As a result of our study, MCA was found as the most frequent vessel involvement area in NVAF-related strokes, and similar with other studies.

In a study of Chung and colleagues, cardioembolism was the leading cause in superior cerebellar artery territory. AF was detected as the reason for 50% of SCA infarcts (5 of 10 patients) (1). In our study, the ratio of SCA is %9.6 and the second most affected vessel area.

ACA infarction is usually caused by cardioembolism in studies from Western countries (17). In a study of Chung and colleagues are similar and %3.6. The difference may reflect an ethnic difference (1).

We carried out this study with the aim of emphasizing the particular artery bed-related stroke that the NVAF, 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 (ACI) and 22% are posterior circulation infarction (PCI) 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 NVAF 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.

Ethics Committee Approval: Haydarpaşa Numune Research and Educational Hospital Ethics Committee Permission was obtained with the letter dated 24.04.2017 and numbered 41.

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