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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

LESION LOCALIZATION, ETIOLOGY AND DEMOGRAPHIC EVALUATION IN SPONTANEOUS CEREBRAL AND CERVICAL ARTERIES DISSECTION

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ABSTRACT

INTRODUCTION: Spontaneous carotid and vertebral artery dissection involves 1-2% of all ischemic stroke and 10-25% of stroke cases among young adults. The aim of our study was to identify the dissection cases and neurological symptoms and signs, to investigate the etiological risk factors, to reveal the vascular involvement and to evaluate the demographic characteristics and treatment practices particularly in young patients.
METHODS: A total of 53 cranio-cervical dissection patients who were hospitalized in our hospital between January 2010-July 2019 were examined retrospectively. Age, sex, risk factors, and trauma history in the last month, neurological symptoms and signs were noted. Cranial MRI, cranial and cervical MR-anjio, T1-weighed fat sat cervical MRI, DSA were applied for suspected patients.
RESULTS: Of the 53 patients with dissection, 23 were female and 30 were male. The mean age for vertebral artery dissection (VAD) was 40,8 and carotis artery dissection (CAD) was 42,2 years. Thirty patients were VAD, 23 patients were CAD. Four patients had bilateral carotid and one patient had bilateral vertebral artery dissection. In the subgroup analysis, 30 patients had extracranial, 23 had intracranial dissection. When risk factors were evaluated, cigarette smoking and hypertension were most common. Major or minor trauma story was observed in 41,5% of patients. Antiaggregant treatment was used in 88,6% of patients.
DISCUSSION AND CONCLUSION: In the present study, VAD was more common and can be different from the other studies in literature. Extracranial dissections were dominant and nearly 40% of all dissections had a history of minor or major trauma. Smoking and hypertension were the most common risk factors. It needs more patients with multi center study to understand the incidence of craniocervical dissections in Turkish population. Arterial dissection has to be considered in differential diagnosis in young stroke patients.
Keywords: Craniocervical dissection, carotis artery dissection, vertebral artery dissection.

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SPONTAN SEREBRAL VE SERVİKAL ARTER DİSEKSİYONUNDA LEZYON LOKALİZASYONU, ETİYOLOJİ VE DEMOGRAFİK İNCELEME

ÖZ

GİRİŞ ve AMAÇ: Spontan karotis ve vertebral arter diseksiyonu tüm iskemik inmelerin %1-2'sini, genç inme hastalarının ise %10-25'ini oluşturmaktadır. Bu çalışmada genç hastalarda diseksiyon vakalarını tanımlamak, nörolojik semptom ve bulgularını saptamak, demografik özelliklerini ortaya koymak, etyolojik risk faktörlerini araştırmak, damar tutulumu ve tedavi yöntemlerini incelemek amaçlanmıştır.

YÖNTEM ve GEREÇLER: Ocak 2012 -Temmuz 2019 tarihleri arasında hastanemiz nöroloji servisinde, kraniyo-servikal diseksiyon tanısı ile takip edilen toplam 53 hasta çalışmaya alındı. Demografik özellik olarak yaş, cinsiyet; risk faktörü, son 1 ay içinde travma öyküsü sorgulandı. Nörolojik semptom ve bulgular kayıt edildi. Diseksiyon tanısı düşünülen hastalara; kraniyal MRG, servikal/ kraniyal MR Anjio, yağ baskılı T1-ağırlıklı servikal MRG ve gerekli görülen hastalara DSA incelemesi yapıldı.

BULGULAR: Çalışmaya alınan 53 hastanın, 30'u erkek, 23'ü kadın hastadan oluşmaktaydı. Vertebral arter diseksiyonlarında (VAD) yaş ortalaması 40,8, karotis arter diseksiyonlarında (KAD) ise 43,3 olarak bulundu. Çalışmada 30 hastada VAD, 23 hastada KAD görüldü. Bilateral KAD 4 hastada, bilateral VAD 1 hastada tespit edildi. Ekstrakraniyal diseksiyon 30 hastada, intrakraniyal diseksiyon 23 hastada mevcuttu. Risk faktörlerine bakıldığında sigara ve hipertansiyon en sık rastlanan risk faktörüydü. Son 1 ay içinde geçirilmiş travma sorgulamasında hastaların %41,5'unda major ya da minor travma öyküsü vardı. Hastalarda %88,6 oranında antiagregan tedavi tercih edildi.

TARTIŞMA ve SONUÇ: Literatürde karotis arter diseksiyonlarının daha fazla olduğu bildirilmekle birlikte sınırlı sayıda hasta ile yaptığımız çalışmamızda vertebral arter diseksiyonu daha fazla bulunmuştur. Ekstrakraniyal diseksiyonlar çoğunlukta olup, tüm diseksiyonlar arasında %40 oranında minor ya da major travma öyküsüne rastlanmıştır. Sigara ve hipertansiyon en önemli risk faktörü olarak karşımıza çıkmaktadır. Ülkemizde hangi artere ilişkin diseksiyonların daha fazla olduğunu saptamak için çok merkezli çalışmalara ihtiyaç vardır. Genç inme ile gelen hastalarda diseksiyon ayırıcı tanıda akılda tutulmalıdır.

Anahtar Sözcükler: Kraniyoservikal diseksiyon, karotis arter diseksiyonu, vertebral arter diseksiyonu.

INTRODUCTION

Spontaneous carotid artery (CA) and vertebral artery (VA) dissection constitute 1-2% of all ischemic strokes and 10-25% of young stroke patients (1). The tear in the arterial wall can be subintimal or subadventitial. Subintimal dissections cause stenosis and subadventitial dissections lead to aneurysmatic dilatation (2,3).

Dissection can emerge as major or minor trauma or spontaneously (2). It is frequently thought to be spontaneous. The annual incidence is reported as 2.5-3:100.000 people in carotid artery dissections and 1-1.5:100.000 people in VA dissections (1). In large vessel cerebrovascular diseases, it ranks second after atherosclerosis (4). In the etiology, there are genetic, familial or hereditary disorders. Even though the majority of the spontaneous dissections are idiopathic, other underlying pathologies such as hypertension, atherosclerosis, fibromuscular dysplasia, Ehlers-Danlos syndrome, Marfan syndrome, osteogenesis imperfecta may accompany them (5).

It is stated that carotid artery dissections are more common compared to VA dissections.

Dissection may be in the intracranial or extracranial segment; however, it is known that the extracranial segments of both arteries are more affected (2).

While clinical symptomatology is observed compared to the existing affected vessel, non-invasive methods are more commonly used in diagnosis, but digital subtraction angiography (DSA) is the gold standard (6). In our present study, demographic data of the patients found to have cranio-cervical artery dissection within a cross-sectional timeframe, artery involvement area, methods used in diagnosis and treatment are discussed.

METHODS

The study was conducted in accordance with the Helsinki Declaration ethical standards and approved by the Marmara University Faculty of Medicine Clinical Studies Ethics Committee (Number: 09.2016.357, Date: 03.04.2016).

A total of 53 patients who were below the age of 60 and monitored with the diagnosis of cranio-

cervical dissection in the neurology department of our hospital between January 2012 and July 2019 were included in the study after informed consent was obtained.

The patients' age, gender, risk factor and history of trauma in the last one month were investigated. Neurological examinations of all the patients were carried out in detail, and their symptoms and findings were recorded. In line with the findings obtained from both the investigation and blood test results as a risk factor, hypertension, hyperlipidemia, diabetes, smoking, migraine history, presence of connective tissue diseases and oral contraceptive use in female patients were investigated.

Cranial MRI, cervical/cranial MR Angio or CT angio, fat-suppressed T1-weighted cervical MRI were applied to patients assumed to have dissection, and DSA examination was carried out on the patients for whom it was considered necessary. As a result of these imaging methods, the diagnosis of dissection was established in compliance with the characteristic neuroradiological findings.

5 segments of the carotid artery for carotid artery dissections are as follows: carotid bulbus, cervical segment, petrous segment, cavernous segment and supraclinoid segment. In the practical approach, carotid bulbus and cervical segment were classified to be extracranial and other segments to be intracranial. Similarly, V4 segment in the vertebral artery was noted as intracranial segment and other sections as extracranial segment.

Treatment method was stated as 1) thrombolytic therapy, 2) acetylsalicylic acid or clopidogrel 3) low-molecular-weight heparin (LMWH) 4) stent procedure.

Statistical method: Chi-square test was used for categorized data, Student's t test or Mann-Whitney U test was applied for numerical data. In this study, which was conducted on a limited number of patients, presence of no patients or presence of few patients would influence the statistical data in subgroup analyses; therefore, no statistical procedure was implemented in these analyses, and the values were stated numerically together with percentages. As the statistics program, Statistical Package for the Social Sciences (SPSS, version 17.0, Inc.; New York, USA) version was used. $p<0.05$ pointed at statistical significance.

RESULTS

Demographic characteristics: Of 53 patients, vertebral artery was detected in 30 (56.6%) patients and CA dissection in 23 (43.4%) patients. In respect of gender, there were 30 male and 23 female patients. The male/female ratio was 1.3. Male predominance was higher in vertebral artery dissections (2/1), however, in CA dissections, the rate was in favor of females; 13 females and 10 males. The number of extracranial dissections was higher in both genders (Table I).

When the patients with 30 VA dissections in total were grouped as intracranial and extracranial dissections, intracranial VA dissection was observed in 12 patients and extracranial VA dissection in 18 patients; 4 intracranial CA dissections and 19 extracranial CA dissections were detected in the cases with a total of 23 CA dissections (Figure I and II).

Table I. Demographic characteristics of the patients and risk factors.

	Vertebral Artery N=30 (56.6%)	Carotid Artery N= 23 (43.4%)
Mean age	40,8	43,3
Gender		
Female	10 (33,3%)	13 (56,6%)
Male	20 (66,7%)	10 (43,5%)
Risk Factors		
Hypertension	5 (17%)	7 (30,4%)
Hyperlipidemia	1 (3,3%)	4 (17,3%)
DM	2 (6,6%)	3 (13%)
Smoking	10 (33,3%)	5(21,7%)
Oral contraceptive	1 (3,3%)	1 (4,3%)
Migraine	4 (13,3%)	3 (13,0%)
Trauma	11 (36,6%)	11 (47,8%)

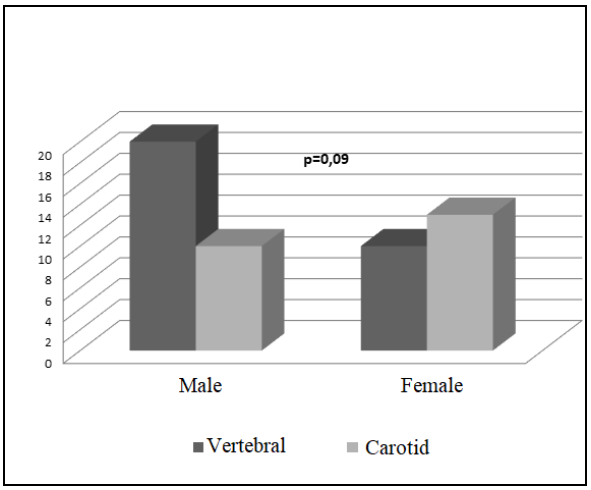

Figure I. Distribution of vertebral and carotid artery dissection patients by gender.

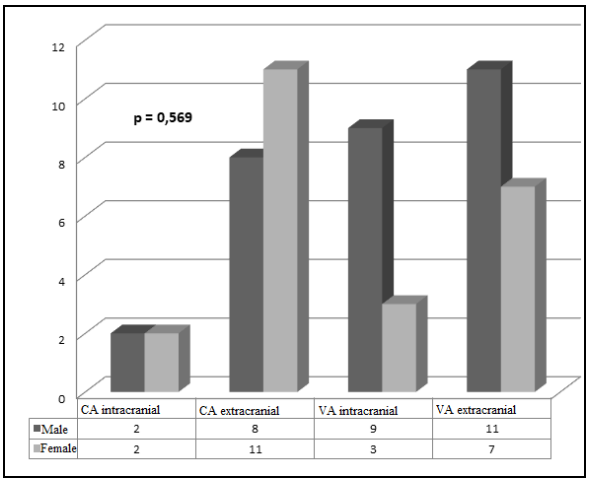

Figure II. Gender category according to intra- and extracranial involvement of vertebral and carotid artery dissection patients (CA: Carotid artery; VA: Vertebral artery).

The mean age was 40.8 in vertebral artery dissections and 43.3 in CA dissections. In VA dissections in women, no significant difference was observed between intracranial and extracranial dissections in terms of the mean age, however, female mean age was significantly higher in intracranial CA dissections (mean age: intracranial CA: 47, extracranial CA: 40) (Table I and II).

Table II. Demographic characteristics and risk factors according to intra- and extracranial nature of the dissection in vertebral and carotid artery dissections.

	Vertebral Artery N=30		Carotid Artery N=23	
Demographics	Intra	Ekstra	Intra	Ekstra
Number of patients	12	18	4	19
Gender				
Female	3	7	2	11
Male	9	11	2	8
Female mean age	38,33	38,5	47	40
Male mean age	39,77	43,36	34	43
Risk Factors				
Hypertension	2	3	2	5
Hyperlipidemia	0	1	1	3
DM	1	1	0	3
Smoking	6	4	0	5
Migraine	4	0	3	0
Oral contraceptive	0	1	0	1
Trauma	2	9	3	8

Bilateral dissection: Seen in 4 CA and 1 VA dissection patients.

Risk factors: Even though the number of patients was low when patients were distributed according to risk f actors, smoking was a more common risk factor in VA dissection and the history of hypertension in carotid artery dissections (Table I and II).

Trauma: 41.5% of the patients had a history of trauma, and the trauma history (32%) was higher extracranial dissections compared to intracranial dissections (9%). In their subgroup analyses, 9 of 18 patients with extracranial VA dissection and 8 of 19 patients with extracranial CA dissection had a history of trauma. Because minor trauma investigation was also performed, extracranial dissections had a very high rate, 41.5%, in our series (Table II), (Figure III).

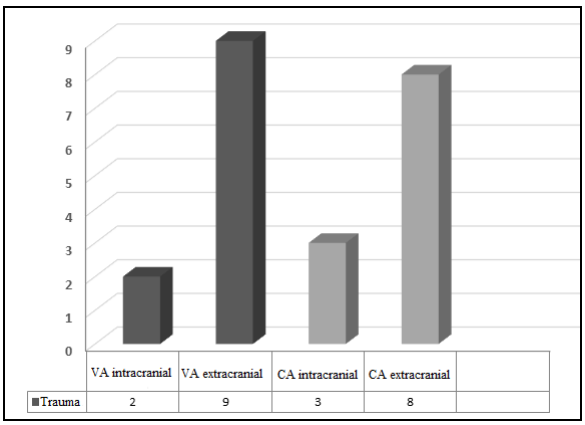

Figure III. History of trauma according to intra- and extracranial involvement of vertebral and carotid artery dissection patients (CA: Carotid artery; VA: Vertebral artery).

Clinical findings: Dizziness, nausea and head and neck pain in the posterior circulation dissections, and head and neck pain and hemiparesis in the anterior circulation dissections were among the leading findings (Table III).

Diagnostic method: Although, as the imaging methods, MR or CT angio, fat-suppressed MRI and DSA method, when deemed necessary, were used for the patients, the fat-suppressed T1-weighted cervical MRI method came to the fore as more frequently used method in the diagnosis in our center (Table III).

Lesion localization: Of 53 patients, acute infarction was detected by diffusion MR imaging in 48 patients, and their distribution indicated 20/23 patients in CA dissections and 28/30 patients in VA dissections. While the most frequent lesion resulting from CA dissections was observed in the middle cerebral artery irrigation area, the cerebellum was the most involved structure in VA dissections (Table IV).

Table III. Clinical symptomatology from vertebral artery and carotid artery dissections and diagnostic methods.

	Vertebral Artery N=30	Carotid Artery N=23
Clinical symptoms		
Head and neck pain	13	7
Hemiparesis	4	15
Dizziness, nausea	20	4
Symp related to vision	4	1
Loss of consciousness-seizures	0	2
Horner syndrome	0	1
Diagnostic methods		
MR angio	10	5
DSA	3	9
Fat-suppressed MRG	17	9
BT angio	1	0

Table IV. Presence of lesions in MRI and localization of these lesions.

	Vertebral Artery N=30	Carotid Artery N=23
Cranial MRI		
Lesion yes	28	20
Lrdion no	2	3
Lesion localization		
MCA	-	18
ACA	-	2
PCA	4	-
Brain stem	8	-
Cerebellum	19	-

Brain stem lesions: mesencephalon 1, pons 1, medulla 1

Treatment: Antiaggregant therapy was the most applied treatment in the patients, however, in patients with progressive symptoms, the Enoxaparin 2x0.6 mL or Enoxaparin 2x0.8 mL treatment was used as an alternative in extracranial dissections. One patient with carotid artery dissection and acute stroke was given t-pa treatment, but no hemorrhage developed in the patient (Table V). Stenting in VA was applied in 2 patients with VA dissection, and decompressive surgery was performed on 1 patient with large middle cerebral artery infarct.

Table V. Applied treatment methods.

	Total cerebral artery dissection	Vertebral artery	Carotid artery
T-pa	1	0	1
Aspirin or clopidogrel	47	27	20
DMAH 2X1	6	3	3
Warfarin in follow-up	1	1	0
Stent	2	2	0
Decompressive surgery	1	0	1

DISCUSSION AND CONCLUSION

Unlike many studies, VA dissection was detected in a higher number in our study, where the demographic, clinical and radiological findings of the patients below 60 years of age and diagnosed with dissection, who we monitored in the neurology clinic of our hospital between 2012 and 2019, and the treatment methods were evaluated (Table I). The dissection rate was higher in the extracranial segments of both carotid and vertebral arteries, and the trauma rate increased up to 41.5% as minor trauma was also included in the investigation.

Although different values are given in different publications, the annual incidence is reported to be 2.5-3: 100.000 in CA dissections and 1-1.5: 100.000 in VA dissections (1). This shows that the incidence rate of VA dissections is half of CA dissections, however, in some publications, this rate may drop to at least 1:3 or 1:4 (7,8). There are also a few studies showing that VA dissection is more common, as in our series.

In a community-based study covering 2006-2011 in Dijon, France, 16 of 27 patients were identified with VA dissection. In this study, the incidence was found as 1.21/100.000 for CA dissection and 1.87/100.000 for VA dissection (9).

In our country, Kaplan et al. (10) conducted a study to determine the poor prognosis in the dissection patients they monitored at İnönü University Hospital between 2000 and 2013; the number of patients with CA dissection was 28 (41.8%), and the number of patients with VA dissection was 39 (58.2%). In the study conducted by Yalciner et al. on 45 patients, the CA dissection was found in 20 (44%) patients and VA dissection in 25 (56%) patients, according to the DSA results. In our country, there are also publications in the form of case series for VA dissection (11,12). In these studies, the VA dissection rate is close to 56.6%, which we detected in our present series (Table I). Since there are no published multicenter national studies in our country, it cannot be concluded whether there are more VA dissections in Turkish society. There are also publications on VA dissection, especially in the Far East and Southeast Asian countries where yoga is common. In response to the study of von Babo et al. (13) on 1027 patients who presented the profile in the western countries, a large number of patients, "Multicenter Chinese Cervicocephalic artery

dissection study (CCADS): rationale and protocol for a multicenter prospective cohort study (14), which is planned to be completed in 2021 and includes the Chinese population and a larger number of patients, will have significance in terms of revealing the differences between the Asian race and the white race.

In the multicenter study of Switzerland and France stated above, the mean age was 46 in CA dissections whereas it was reported as 42 in VA dissections (11).

In our study, the mean age is 43 in extracranial CA dissections and 40 in VA dissections (Table I). Studies report that carotid artery dissections occur at advanced ages, and in our study, CA intracranial dissection was observed in female patients aged between 45-50 (Table I and II).

Spontaneous craniocervical dissections are more widely observed in the extracranial segments of the carotid and vertebral arteries (Table II). These parts are both close to the bone structures and the most mobile parts of the vessels (15). In our study, dissections in the extracranial segment were the most common and intracranial CADs were the least common dissections. Here, less mobility of the intracranial carotid artery was an important factor. While no gender difference is detected in extracranial dissections, intracranial VA dissections are frequently observed in the male gender (16,17). In our study, the number of female/male was found to be 18/19 in extracranial dissections, and no significant difference was found in respect of gender. In our series, the M/F ratio was found to be 3/1 in intracranial VA dissections, however, female predominance was observed in extracranial CA dissections. (11/8) (Figure I and II).

While the history of trauma is reported up to 35-40% in some publications, similarly, in our series, the history of trauma was more common in extracranial dissections, and the history of trauma was available in all the dissections by 41.5% (18) (Table I) (Figure III).

Bilateral dissections are rare and often occur in the extracranial segment. Bilateral involvement is stated to be more common in VA dissections in some publications and in CA dissections in other publications (13,19) whereas hypertension, smoking, trauma, genetic diseases and connective tissue diseases are given as the factors that trigger them. In our study, 4 CA and 1 VA have bilateral characteristics. 2 patients with bilateral dissections had a history of trauma, 2 patients had connective tissue diseases, and 1 patient had a history of hypertension (Table II).

In craniocervical dissections, clinical findings appear depending on which artery is involved. CA dissections are presented as ipsilateral head and neck pain, partial Horner syndrome, retinal ischemia and focal neurological deficit. Headache is not distinctive; it may be in the form of migraine or cluster headache (20). In VA dissections, acute pain in the occipital and cervical region, vertigo, and "dizziness" constitute clinical symptomatology. Even though subarachnoid hemorrhages (SAH) occur particularly in intracranial VA dissections, SAH was not detected in our current study (15) (Table III).

While hypertension and smoking stand out in our study as a risk factor (Table I), these risk factors gained significance in the study conducted by Konrad et al. (21).

In the diagnosis of the patients, the fat-suppressed MRI method has been the diagnostic method we have used the most frequently. AHA, ASA and IHS recommended MRA/fat-suppressed MRI examination as the best screening test (Table IV).

Studies have shown that IV thrombolysis can be performed in patients meeting the criteria of thrombolysis, and thrombolytic therapies had similar reliable results with stroke patients without dissection. The CADISS study revealed that antiaggregant and anticoagulant therapies did not present a statistically significant difference in terms of recurrent stroke (22). Endovascular and surgical treatment should be kept in mind in cases with recurrent dissection and clinical progress. In our study, antiplatelet therapy was given to 88.6% of our patients (Table V).

After diagnosis and treatment is initiated, it is necessary to monitor these patients every 3-6 months in general. The inclusion of no information about the prognosis of the patients and recurrent stroke in follow-up constitute the limitation of our study. In the long-term follow-up, the fact that patients visit the outpatient clinics less frequently and phone communication cannot be sustained mostly brings about this difficulty.

Although VA dissections are more widely observed in our study, it cannot be concluded whether there are more VA dissections in Turkish society since there are no published multicenter

national studies in our country. Skepticism and awareness are required in young ischemic stroke to recognize cranio-cervical artery dissections. Craniocervical artery dissection should be considered in the differential diagnosis and trauma should be investigated when young patients apply especially with the complaints of head and neck pain.

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Ethics

Ethics Committee Approval: The study was approved by the Marmara University Faculty of Medicine Clinical Studies Ethical Committe (Number: 09.2016.357, Date: 03.04.2016).

Informed Consent: Informed consent was obtained from all patients.

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Peer-review: Internally peer-reviewed.

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