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ORIGINAL ARTICLE **ARAŞTIRMA YAZISI**

DEMOGRAPHIC AND CLINICAL FEATURES OF SUBARACHNOID HEMORRHAGES WITH AND WITHOUT CEREBRAL ANEURYSM

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ABSTRACT

INTRODUCTION: Patients who have subarachnoid hemorrhage due to aneurysm rupture differ from patients suffering spontaneous nonaneurysmal subarachnoid hemorrhage (SAH) in the aspects of clinical features.
METHODS: We investigated retrospectively the demographic and clinical features of our patients with aneurysmal and nonaneurysmal SAH. The characteristics of the aneurysms including localization and size, and their relation with the severity of the hemorrhage by Fisher score were also evaluated.
RESULTS: Our study included 205 SAH patients who were divided into two groups: aneurysmal (n: 130) and nonaneurysmal (n: 75). The demographic characteristics, comorbidities, drug usage and clinical profiles of patients showed no difference. World Federation of Neurological Surgeons (WFNS) SAH grading (4.02±1.44 vs. 2.84±1.34, p= 0.00) and Fisher scores (2.78±0.97 vs. 2.25±0.85, p= 0.00) were found higher in aneurysmal SAH and the anterior communicating artery was the most common site of the aneurysms (n: 41, 20%). The size, diameter, neck and diameter-neck ratio of aneurysm had no effect on the severity of hemorrhage. In patients with hypertension, WFNS and Fisher scores were higher than in nonhypertensives.
DISCUSSION and CONCLUSION: We found higher WFNS and Fisher scores in aneurysmal SAH, and also in patients with accompanying hypertension. Most ruptured aneurysms were detected in the anterior communicating artery. The location and size of the ruptured aneurysm had no effect on bleeding severity.
Keywords: Cerebral aneurysm, subarachnoid hemorrhage, vascular neurology, nonaneurysmal, cerebral hemorrhage.

SEREBRAL ANEVRİZMAYLA BİRLİKTE OLAN VE OLMAYAN SUBARAKNOİD KANAMALARIN DEMOGRAFİK VE KLİNİK ÖZELLİKLERİ

ÖZET

GİRİŞ ve AMAÇ: Anevrizma rüptürüne bağlı subaraknoid kanaması (SAK) olan hastalar spontan nonanevrizmal SAK hastalarından klinik özellikleri ile ayrılırlar.
YÖNTEM ve GEREÇLER: Anevrizmal ve nonanevrizmal SAK hastalarımızın demografik ve klinik özelliklerini retrospektif olarak inceledik. Anevrizmaların lokalizasyon, boyut özellikleri, boyun, çap-boyun oranı ve kanama şiddeti açısından Fisher skoru ile ilişkisi de aynı zamanda değerlendirildi.
BULGULAR: Çalışmamızda 205 SAK hastası iki gruba ayrılarak yer aldı: anevrizmal (n: 130) ve nonanevrizmal (n: 75). Demografik özellikler, komorbidite, ilaç kullanımı ve hastaların klinik profilleri farklılık göstermedi. WFNS (4.02±1.44 vs. 2.84±1.34, p= 0.00) ve Fisher skorları (2.78±0.97 vs. 2.25±0.85, p= 0.00) anverizmal SAK'ta daha yüksek saptandı ve anterior kommunikan arter en sık anevrizma lokalizasyonunun olduğu yerdi (n: 41, 20%). Anevrizma boyutu, çap, boyun, çap-boyun oranının kanama şiddeti üzerine bir etkisi yoktu. Hipertansiyonu olan hastalarda WFNS ve Fisher skorları nonhipertansiflere göre daha yüksek elde edildi.
TARTIŞMA ve SONUÇ: Anevrizmal SAK ve ayrıca komorbid hipertansiyonu olan hastalarda bağımsız olarak daha yüksek WFNS ve Fisher skorları bulduk. En sık rüptüre anevrizmalar anterior kommunikan arterde lokalize idi. Rüptüre anevrizmanın yeri ve boyutunun kanama şiddeti üzerine bir etkisi yoktu.
Anahtar Sözcükler: Serebral anevrizma, subaraknoid kanama, vasküler nöroloji, nonanevrizmal, serebral hemoraji.

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INTRODUCTION

Subarachnoid hemorrhage (SAH) with or without an intracranial aneurysm is a serious health problem with a high case fatality. Aneurysmal SAH accounts for approximately 5% of all strokes (1), and aneurysm rupture is the cause of 85% of spontaneous SAH cases. Although there are novel strategies and advances in management, ruptured cerebral aneurysms still carry high mortality (30-50%) (2). The clinical presentation of cerebral aneurysms may be complex and multifactorial. Before deciding on the treatment modality there is a need to clarify the aneurysm's characteristics and its relation with SAH. The location, size and morphology of the aneurysm and the patient's age, previous medical history and comorbid pathologies may affect the severity of hemorrhage as well as the clinical outcome.

In up to 20 % of patients with SAH, no bleeding source can be identified despite neuroradiological investigations (3). In such patients, the clinic is much better than aneurysmal SAH, with a low risk of rebleeding (4). However, there is a need of more data about SAH with negative angiography. The clinical difference between such patients and aneurysmal SAH would provide clinicians with a broader view of SAH.

In this study, we investigated the demographic and clinical features of our patients with aneurysmal and nonaneurysmal SAH. Additionally, the characteristics of the aneurysms including localization and size and their relation with the severity of the hemorrhage were also evaluated.

MATERIAL AND METHODS

This is a retrospective study of 205 patients with SAH who were admitted to the Departments of Neurology and Neurosurgery between December 2013 and February 2016. The patients were diagnosed as having SAH according to noninvasive neuroimaging studies including computed tomography (CT), magnetic resonance imaging (MRI), CT angiography and MR angiography. All subjects had neurological examinations by a neurosurgeon or a neurologist.
The cerebral DSA procedures were performed in the angiography suite by an endovascular specialist within 2-48 hours (mean 6.5±0.96h). Selective catheterization of the internal and external carotid arteries, vertebral, or subclavian arteries was usually performed. Patients with hemorrhagic diathesis, renal insufficiency and contrast allergy were excluded since cerebral DSA could not be performed. Demographic data, comorbid diseases (hypertention (HT), diabetes mellitus (DM), cardiac disease, hyperlipidemia, peripheric vascular disease, thyroid and renal diseases) and previous antiaggregant and anticoagulant medication were recorded. Patients with SAH due to trauma or uncontrolled hypertension, hematologic diseases including coagulopathy, thrompocytopenia. Only 7 patients were under warfarin treatment with INR values between 2-2.5. The cerebral aneurysms were divided into six subgroups according to their localizations including anterior communicating (AComA), middle cerebral (MCA), internal carotid (ICA) and anterior cerebral arteries (ACA), posterior circulation aneurysms, and multiple aneurysms. The size of the aneurysm was also measured using the largest diameter measurement based on the long or perpendicular axis on the cerebral angiogram. The diameter, neck, and diameter-neck ratio of the cerebral aneurysms were also calculated. The patients were analyzed according to their World Federation of Neurosurgery Scale (WFNS) and Fisher scores.

The study was approved by the local ethics committee of our university.

Statistical Analyses

All statistical analyses were performed with SPSS 16.0 for Windows (SPSS Inc., Chicago, IL). Group comparisons were performed with Student's t-test for normally distributed continuous variables or Mann-Whitney U test for other continuous variables. Multiple mean comparisons were analyzed by one-way ANOVA, and $p<0.05$ was considered statistically significant.

RESULTS

A total of 205 patients (107 females and 98 males) with SAH and with a mean age of 58.38±10.91 (20-85) years were included in the study. The patients were divided into two groups: aneurysmal (group 1, n:130) and nonaneurysmal SAH (group 2, n:75). The demographic characteristics and the clinical profiles of patients are shown in Table 1. Both groups were also compared for comorbidities and drug usage, but no difference was found (Table 1). The only

Table 1. The demographic and clinical data of the patients with subarachnoid haemorrhage.

		SAH with aneurysm (n:130) (%)	SAH without aneurysm (n:75) (%)	p
Age		58.54±10.2	58.10±12.11	>0.05
Gender male		66 (50.76)	38 (50.7)	>0.05
Comorbid disease	HT	70 (53.8)	37 (49.3)	>0.05
	DM	32 (24.6)	14 (18.7)	>0.05
	Cardiac disease	12 (9.2)	4 (5.3)	>0.05
	Hyperlipidemia	13 (10)	10 (13.3)	>0.05
	Peripheric vascular disease	7 (5.4)	3 (4)	>0.05
	Thyroid pathology	11 (8.5)	6 (8)	>0.05
	Renal disease	6 (4.6)	6 (8)	>0.05
Drug usage	Acetylsalicylic acid	34 (26.2)	14 (18.7)	>0.05
	Clopidogrel	20 (15.4)	9 (12)	
	Coumadin	4 (3)	3(4)	
WFNS		4.02±1.44	2.84±1.34	0.0
Fisher score		2.78±0.97	2.25±0.85	0.0

SAH: subarachnoid hemorrhage, HT: hypertension, DM: diabetes mellitus, WFNS: World Federation of Neurosurgery Scale, NS: not significant

statistical significance was detected in the severity of hemorrhage according to WFNS (4.02±1.44 vs. 2.84±1.34, p=0.00) and Fisher scores (2.78±0.97 vs. 2.25±0.85, p=0.00).

The cerebral aneurysms were evaluated according to their localizations and evaluated in six subgroups. Most of them occurred in anterior communicating artery (AComA). (n:41, 20%). The others were located as follows: middle cerebral artery (MCA) (n:30, 14.6%), internal carotid artery (ICA) (n:30, 14.6%), anterior cerebral artery (ACA) (n:4, 2%), posterior circulation aneurysms (n:12, 5.9%) and multiple aneurysms (n:13, 6.3%). There were no significant differences between these six subgroups with respect to the size, neck and diameter-neck ratio of the aneurysms. However, when we compared the severity of SAH, we found that patients with posterior circulation aneurysms had lower WFNS and Fisher scores (Table 2).

Table 2. The localisation of cerebral aneurysms causing subarachnoid hemorrhages and their effects on disease severity.

	AComA (n:41)(%)	MCA (n:30) (%)	ICA (n:30) (%)	Multiple aneurysm (n:13) (%)	Posterior circulation (n:12) (%)	ACA (n:4) (%)	p
Age	57.41±9.8	58.8±10.4	60.1±8.7	57.0±10.5	58.8±15.12	60.7±6.65	>0.05
Gender male	21(51.2)	14(46.7)	16 (53.3)	6 (46.1)	5 (41.6)	4 (50)	>0.05
Diameter (mm)	12.5±4.05	11.26±3.75	9.9±3.8	13.8±7.9	10.10±2.3	11.2±2.7	>0.05
Neck (mm)	4.47±1.77	4.16±1.07	3.7±1.28	4.06±1.52	3.24±0.89	3.15±0.28	>0.05
Diameter/neck ratio	3.02±1.11	2.83±1.06	2.9±1.28	3.5±1.59	3.17±0.59	3.6±1.09	>0.05
WFNS	3.9±1.38	4.33±1.49	4.2±1.37	4.15±1.51	2.75±1.35	4.25±0.95	0.00
Fisher score	2.9±0.94	2.9±0.99	2.8±0.89	2.69±1.03	1.8±0.83	2.7±0.5	0.00

WFNS: World Federation of Neurosurgery Scale

The cerebral aneurysms were also divided into three groups according to their sizes. Most of the cerebral aneurysms were in the diameter range of 7-12 mm (n:72, 55.4%), followed by >13 mm (n:48, 36.9%) and <7mm (n:10, 7.7%). The diameter, neck and diameter-neck ratio of the cerebral aneurysms of these three groups were compared but no statistically significancy was found. Although WFNS and Fisher scores seemed to be higher in patients with cerebral aneurysms of >13mm this did not show any statistical difference (Table 2 and 3).

Medical comorbidities, antiaggregant and anticoagulant usage were also compared between aneurysmal and nonaneurysmal SAH groups and no significant difference was found (Table 1). However, in patients with hypertension, WFNS (3.97±1.38 vs. 3.34±1.4, p=0.006) and Fisher (2.8±1.01 vs. 2.43±0.89, p=0.007) scores were higher than in nonhypertensives.

Table 3. Clinical features of cerebral aneurysm subgroups.

	Diameter			
	<7mm (n:10) (%)	**7-12mm (n:72) (%)**	**>13mm (n:48) (%)**	**p**
Age	51.4±11.2	59.5±10.1	58.6±9.71	>0.05
Gender male	5 (50)	37 (51.3)	24 (50)	>0.05
WFNS	4±1.69	3.83±1.36	4.31±1.15	>0.05
Fisher score	2.8±1.03	2.7±0.89	2.89±1.07	>0.05

WFNS: World Federation of Neurosurgery Scale.

DISCUSSION

In this study, the demographic and clinical differences between aneurysmal and nonaneurysmal SAH were investigated. We found more severe hemorrhages in the aspects of and WFNS and Fisher scores in patients with SAH due to aneurysm rupture. It has been previously shown that patients with nonaneurysmal SAH have a better prognosis than those with aneurysm related SAH (5). The results of our study also confirm other reports (6-8). Cerebral aneurysm which is associated with vascular may worsen the amount of bleeding. Therefore, aneurysmal cases have more blood, which is associated with worse clinical status with higher WFNS and Fisher scores.

We found no significant difference between groups in terms of age, gender, comorbid diseases and drug usage. The mean age of our patients (58.38±10.91) was similar to that in the current literature (5, 9). No significant difference of gender was found between aneurysmal and non-aneurysmal SAHs in our study (10). However, in the literature there are conflicting data about gender distribution. Although non aneurysmal SAH was found to be more common in males (5, 11), there are also studies suggesting higher prevalence in females (12, 13). Nevertheless gender do not influence the disease severity, similar with our findings.

The localization of the aneurysms were also analysed in this study. Most of the ruptured aneurysms were located at AComA (31.5%) and secondly MCA (23.07%) and ICA (23.07%). The diameter and diameter-neck ratio of aneurysms didn't differ according to the localization. We also found that WFNS and Fisher scores were lower in SAH patients with posterior circulation aneurysms. In the study of Kozba including 402 aneurysmal SAH patients, most of the ruptured aneurysms were originated from AcomA (38.5%). The second most common site was MCA with a percentage of 37.8%, which is higher than our findings (14). Concomitant with the literature, aneurysms located at AComA and MCA are most likely to bleed (14-16).

Although it is well known that perimesencephalic SAH is mainly non-aneurysmal and associated with favorable prognosis (17), one third of perimesencephalic SAHs are caused by the rupture of a posterior circulation aneurysm (18). Fisher CT clot burden, and ruptured aneurysm location and diameter were found to be weak prognostic factors for the clinical outcome of SAH. In our study we also found that aneurysms of anterior circulation had similar WFNS and Fisher scores. On the other hand patients having SAH due to the rupture of an aneurysm located in the posterior circulation (n:12, 5.9%) had lower WFNS and Fisher scores. This may be the result of low number of our patients.

It has been also indicated that intracranial aneurysm size may be a primary determinant of rupture probability (19). The critical sizes are

reported to be 4-10mm. Unruptured small aneurysms (<10mm) were shown to have good prognosis without surgical treatment (16,20). In patients with unruptured intracranial aneurysms of less than 7 mm in diameter the rupture rate (about 0.1% per year) was reported as lower than that of larger aneurysms (21). Although aneurysm diameter has commonly been analyzed as a categorical predictor, different threshold values have been applied in different studies (22-24), and therefore comparison of reported results is difficult. In this study, patients were analyzed according to aneurysm diameter in three subgroups (<7mm, 7-12mm, >13mm). Most of our patients had aneurysms with a diameter of >7mm (92.3%). The most common aneurysm size was between 7 and 12mm (55.38%). Small aneurysms have a low risk of bleeding. In this study, symptomatic aneurysm with a diameter of <7mm could be find only in 8% of our patients which is concominant with literature (21).

No significant difference of WFNS and Fisher scores reflecting disease severity were found between these three groups. Additionally, there were no statistical differences of aneurysm diameter or diameter-neck ratio according to the localization. Although in the literature aneurysms in the anterior choroidal artery and the pericallosal artery tended to have a smaller size, our data showed no difference (15).

Our data was suggesting an independent association between premorbid hypertension and outcome. It has been reported that previously diagnosed hypertension increased the risk of SAH (25). In another study, it was shown that cerebral arteries from hypertensive rats are more susceptible to the vasosplastic effects of SAH than those from normal rats (26), which may also affect the clinic. In hemorrhage the pressure around the bleeding site rises until it equals arterial pressure, then the bleeding site clots. In comorbid hypertensive SAH patients, it is difficult to control arterial pressure. Additionally, the impact of the bleeding increases the pressure across the intracranial space above mean arterial pressure, temporarily impeding cerebral perfusion pressure (6).

Our study has several limitations. The two groups did not have the same number of subjects. We included mainly aneurysmal SAH patients and it was not possible to perform comparison of perimesencephalic nonaneurysmal SAH because of the small study group. Secondly, the calculations of aneurysms were made in the initial cerebral angiography and it was not possible to evaluate the effect of vasospasm. It would be much better to compare mortality, long term results of morbidity with modified Rankin scale between SAH patients with and without aneurysm.

In conclusion, the demographic and clinical data of SAH in our region was evaluated and our findings were concominant with the literature. WFNS and Fisher scores were found to be higher in aneurysmal SAH, and also in patients with comorbid hypertension. Ruptured aneurysm localization diameter, neck and diameter-neck ratio of aneurysm have no effect on bleeding severity in our study. The most ruptured aneurysms were detected in AComA. Although patients with posterior cerebral aneurysm had better clinics, because of the small number of them, it was difficult to make a comment on this.

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