# Factors Affecting on the Prognosis in Multiple Intracranial Aneurysms

Çoklu İntrakraniyal Anevrizmalarda Prognozda Etkili Faktörler

Tezcan ÇALIŞKAN 1 🕑, Mehmet Sabri GÜRBÜZ 2 🕑, Mehmet Onur YÜKSEL 3 ២, Mehmet Zafer BERKMAN 4 ២

1 Namık Kemal University, Medical Faculty, Department of Neurosurgery, Tekirdağ, Turkey

2 İstanbul Medeniyet University, Medical Faculty, Department of Neurosurgery, İstanbul, Turkey

3 Medipol University, Medical Faculty, Department of Neurosurgery, İstanbul, Turkey

4 Acıbadem Mehmet Ali Aydınlar, Medical Faculty, Department of Neurosurgery, İstanbul, Turkey

#### Abstract

Background: With improvements in diagnostic methods, the incidence of multiple intracranial aneurysms has increased up to 35%. Factors influential on outcome in multiple intracranial aneurysms are still debatable. We aimed to determine risk factors related to multiple intracranial aneurysms in patients admitted with subarachnoid hemorrhage caused by a ruptured intracranial aneurysm.

Material and Methods: This retrospective study was performed on 105 aneurysms of 48 patients diagnosed with multiple aneurysms using charts, records, and film archives among 250 patients admitted to Istanbul Haydarpaşa Numune Training and Research Hospital between January 2003-December 2009 who were examined and treated for subarachnoid hemorrhage. Age, gender, medical history, admission/surgery times, clinical features determined on neurological examination at admission (WFNS Score), amount of blood measured on cranial computed tomographic images (Fisher Score), number of aneurysms and systems to which they belonged, complications, and Glasgow outcome scale indicating the morbidity and mortality were recorded.

Results: The mean age was 52.75±14.02(4-90) years. The female/male ratio was 2.2. Most common clinical features were headache (83.7%), and hypertension (56.3%). The most common location was the middle cerebral artery, and aneurysm size was 2-6 mm (66.7%). The most common intervention was an early clipping of as many aneurysms as possible in one session (84.7%). Vasospasm and hydrocephalus were the most common complications (31.1%, 16.6%, respectively). No difference was present between early and late interventions regarding mortality. Glasgow outcome Scale was negatively correlated with Fisher score (r=-0.306), but not with WFNS score.

**Conclusions:** Age, amount of cisternal blood preoperatively, and postoperative vasospasm are risk factors for mortality, but not hypertension and postoperative hydrocephalus. WFNS Scoring system is not a reliable mortality predictor.

Key Words: Multiple intracranial aneurysms, Fisher score, Glasgow outcome scale, Subarachnoid hemorrhage, WFNS Score

#### Öz.

Amaç: Tanı yöntemlerindeki gelişmelerin sonucunda, multipl intrakraniyal anevrizma insidansı %35'e kadar yükselmiştir. Multipl intrakraniyal anevrizmalarda prognoz üzerinde etkili olan faktörler halen tartışmalıdır. Bu çalışmada, rüptüre olmuş intrakraniyal anevrizmanın neden olduğu subaraknoid kanama ile başvuran hastalarda MİA prognozu ile ilişkili faktörleri belirlemeyi amaçladık.

Materyal ve Metod: Bu retrospektif çalışma, Ocak 2003-Aralık 2009 tarihleri arasında İstanbul Haydarpaşa Numune Eğitim ve Araştırma Hastanesi'nde subaraknoid kanama nedeni ve anevrizma tanısı ile tetkik ve tedavi edilen 250 olgu arasında hasta çizelgeleri, kayıtları ve film arşivleri değerlendirilerek multipl anevrizma kriterlerine uyan 48 olgunun 105 anevrizması üzerinde gerçekleştirildi. Yaş, cinsiyet, tıbbi öykü, başvuru / cerrahi süreleri, başvurudaki nörolojik muayene bulgu değerlendirmesindeki özellikler (WFNS skoru), bilgisayarlı beyin tomografi görüntülerde ölçülen kan miktarı (Fisher Skoru), anevrizma sayısı ve ait oldukları sistemler, komplikasyonlar, morbidite ve mortaliteyi gösteren Glasgow sonuç skalası kaydedildi.

Bulgular: Yaş ortalaması 52,75 ± 14,02 (4-90) yıldı. Kadın / erkek oranı 2.2 idi. En sık görülen klinik özellikler baş ağrısı (% 83.7) ve hipertansiyon (% 56.3) olarak bulundu. En sık yerleşim yeri orta serebral arterdi ve anevrizma boyutu 2-6 mm (% 66.7) idi. En sık yapılan girişim tek seansta mümkün olduğunca çok anevrizmanın erken kliplenmesiydi (% 84.7). Vazospazm ve hidrosefali en sık görülen komplikasyonlardı (sırasıyla % 31.1 ve % 16.6). Erken ve geç girişim zamanları arasında mortalite açısından fark bulunmadı. Glasgow sonuç skalası skoru ile Fisher skorunun negatif korelasyonu olduğu bulundu (r = -0.306), ancak WFNS evresi ile korelasyon mevcut değildi.

Sonuç: Yaş, preoperatif sisternal kan miktarı ve postoperatif vazospazm mortalite için risk faktörleri olarak bulundu. Ancak hipertansiyon ve postoperatif hidrosefali risk faktörü değildi. WFNS skorlama sisteminin güvenilir bir mortalite belirleyicisi olmadığı sonucuna varıldı.

Anahtar Kelimeler: Çoklu intrakraniyal anevrizma, Fisher skoru, Glasgow sonuç skala, Subaraknoid kanama, WFNS evresi

#### Sorumlu Yazar / Corresponding Author

Dr. Tezcan ÇALIŞKAN, MD.

Namık Kemal University, Medical Faculty, Department of Neurosurgery, Tekirdağ, Turkey

Tel: +905057647387 E-mail: dtzcan\_07@hotmail.com

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# Introduction

The incidence of multiple intracranial aneurysms (MIA) was reported as 8-9%. However, with improvements in diagnostic methods, this rate increased to 15-35% in recent years with the introduction of 4-vessel cerebral angiography (1, 2). A meta-analysis study by Jabbarli et al. emphasized the discrepancy related to MIA incidence, varying within a range of 2-45% (3). Regarding surgical management of MIA, intervening in all aneurysms with a single craniotomy in a single session, if possible, is becoming increasingly common (4-8). Besides planning treatment in MIA, factors influential on the outcome are still debatable.

This study aimed to determine MIA-related risk factors in patients admitted with subarachnoid hemorrhage (SAH) caused by a ruptured intracranial aneurysm.

# Materials and Methods

In this retrospective study, 48 cases meeting MIA criteria among 250 cases treated for intracranial aneurysm and SAH at Istanbul Haydarpaşa Numune Training and Research Hospital between January 2003-December 2009 were investigated following the Hospital Ethics Committee's approval. The study was performed by assessing reviewing charts, records, and film archives of patients.

Age, gender, medical history and habits, family history of aneurysms, time of admission, neurological features at admission time, amount of blood measured on cranial computed tomographic (CCT) images, number of aneurysms and systems to which they belonged, time of surgery, and complications were investigated together with relationships of treatments and outcomes.

Neurological status was assessed and graded at admission by two scales. State of consciousness was assessed using the Glasgow Coma Scale (GCS), whereas the World Federation of Neurological Societies (WFNS) scale was used to evaluate findings on neurological examination. Fisher scale was used for classification of bleeding amount in admission CCT images of patients. The discharge status of patients were assessed according to the Glasgow Outcome Scale (GOS).

SAH was diagnosed by CCT and/or lumbar puncture (LP) in addition to medical history, physical and neurological examinations. In patients not presenting with hemorrhage, the diagnosis was made incidentally by magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA). All SAH patients were involved in medical treatment protocol determined according to their neurological and medical status, together with CCT, LP, and biochemical results at admission time. In appropriate cases, angiography was performed as soon as possible, and cases that an aneurysm was identified underwent early surgery.

### Statistical Analysis

NCSS (Number Cruncher Statistical System)-2007 and

PASS-2008 Statistical Software (Utah, USA) were used. In addition to descriptive statistical methods (mean, standard deviation), the Kruskal-Wallis test was used to compare non-normal parameters in quantitative data, and the Mann-Whitney-U test to determine the difference-causing group. Mann-Whitney-U test was used for inter-group comparisons regarding non-normally distributed parameters. Spearman's correlation analysis was performed for relationships among parameters. A P-value of less than 0.05 was considered significant.

# Results

Forty-eight patients meeting MIA criteria were identified among 250 patients with aneurysms diagnosed and treated at İstanbul Haydarpaşa Numune Training and Research Hospital between January 2003-December 2009(rate of MIA among all aneurysms was 19.2%). Distributions of patient age regarding age group and decade and distribution of patient gender were presented in Table 1.

 Table1. Demographic characteristics, clinical findings, comorbidities, and risk factors (n=48)

bidities, and risk factors (n=48)	-	
· · · · ·	n	%
Gender		
Male	15	31.3
Female	33	68.7
Age group (years)		
≤ 40	9	18.8
41-50	11	22.9
51-60	12	25.0
> 60	16	33.3
Age (decade-years)		
0-10	1	2.08
11-20	0	0
21-30	0	0
31-40	8	16.67
41-50	11	22.92
51-60	12	25.00
61-70	14	29.17
71-80	1	2.08
81-90	1	2.08
Clinical findings		
Headache	41	83.7
Nausea-vomiting	25	51.0
Nuchal rigidity	15	30.6
Seizure	3	6.1
Muscular weakness	5	10.2
Facial paralysis	3	6.1
Ptosis	1	2.0
Alterations of the state of con-	11	22.4
sciousness		
Miscellaneous	3	6.1
Comorbidities and risk factors		
Diabetes mellitus	1	2.1
Coronary artery disease	2	4.2
Hypertension	27	56.3
Polycystic kidney	3	6,3
Smoking history	17	35.4
Alcohol use	3	6.3
Goiter (operated)	3	6.3
Miscellaneous	6	12.5

The mean age was  $52.75 \pm 14.02(4-90)$  years. The highest number of cases belonged to 7<sup>th</sup> decade, with 29.17%(n=14). Nine(18.8%) cases were aged  $\leq 40$  years;

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there was only one pediatric patient (2.08%), and three patients in this age group were aged >30 years. Regarding gender distribution, 31.3%(n=15) of cases were male (mean age=45.20±14.97 years), and 68.7%(n=33) female (mean age=56.18±12.31 years).

Clinical (neurological) symptoms, signs, comorbidities, and risk factors retrieved from patient charts were shown in **Table 1**. The most common symptom was headache in 83.7% (n=41). Smoking was present in medical history in 35.4% (n=17). The two patients with PCKD (51-years-old male and 55-years-old female) were siblings, and their grandmother had PCKD also. The son of a 61-year-old male patient had undergone aneurysm surgery, a 50-year-old female patient had been operated on at our clinic in 1997 for an aneurysm of the anterior communicating artery (AcomA) and had been reoperated in 2004 for aneurysms of both the right middle cerebral (MCA) and anterior communicating arteries.

WFNS, Fisher, and GOS Scores of our patients were presented in Table 2. Of our MIA patients, 25 (52.08%) were scored as WFNS-1, 22 (45.8%) cases were Fisher-4, and 35 (72.9%) had a GOS score of 5.

Table 2. WFNS, Fisher, and GOS scores (n=48)	Table 2.	WFNS,	Fisher,	and GOS	scores	(n=48)
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	n	%	
WFNS Score			
1	25	52.08	
2	19	39.6	
3	2	4,2	
4	-	-	
5	2	4,2	
Fisher Score			
1	11	22.9	
2	3	6.3	
3	12	25.0	
4	22	45.8	
GOS Score			
1	7	14.6	
2	1	2.1	
3	3	6.3	
4	2	4.2	
5	35	72.9	
WENS: World Fode	aration of Neurologica	Societies	

WFNS: World Federation of Neurological Societies GOS: Glasgow Outcome Scale

Sizes of aneurysms according to Yaşargil's and conventional classifications, together with their locations, were presented in Table 3. A total of 105 aneurysms were identified in 48 patients. The most common aneurysm location was MCA (40.95%), followed by AcomA (19.04%) and internal carotid artery (ICA) (13.33%). Forty four (40.6%) aneurysms were located in the right hemisphere, 41 (39.6%) in the left hemisphere, and 20 (19.8%) in the midline region. 20 (41.6%) cases had ipsilateral localization of aneurysms, whereas 12 (25%) cases had contralateral localization. In 16 (33.3%) cases, a hemisphere and midline localization were present. According to Yaşargil's classification, 7 (6.7%) were <2 mm., 70 (66.7%) were 2-6 mm., 26 (24.8%) were 6-15 mm., one (0.9%) was 15-25 mm., and one (0.9%) was >25 mm. According to conventional aneurysm size classification, 98 (93.33%) aneurysms were <12 mm., six (5.7%) were 12-24 mm., and one (0.9%) was sized >24 mm.

Table 3. Distributions of the aneurysm sizes regarding Yaşargil's						
and	conventional	classifications,	together	with	their	loca-
tions(n=105)						

	n	%
Aneurysmal vessel		
Middle cerebral artery	43	40.95
Anterior communicating artery	20	19.04
Internal carotid artery	14	13.33
Posterior communicating artery	9	8.57
A <sub>2</sub>	7	6.66
A <sub>1</sub>	4	3.80
Posterior inferior cerebellar artery	2	1.90
Basilar artery	2	1.90
Superior cerebellar artery	2	1.90
Posterior cerebral artery	0	0
Vertebral artery	0	0
Size(mm) [Yaşargil's classification]		
< 2	7	6.7
2-6	70	66.7
6-15	26	24.8
15-25	1	0.9
25	1	0.9
Size(mm) [Conventional classification]		
< 12	98	93.3
12-24	6	5.7
> 24	1	0.9

Admission times, together with timing and types of performed interventions, were shown in Table 4. When the duration between symptom onset and hospital admission time was analyzed, it was determined that 41.7% (n=20) were admitted after four days. The average timing of intervention was 4.81 days and within the range of 1-28 days. Regarding timing of intervention, the early surgery was preferred in 54.2% (n=26). Clipping was performed in 84.7% (n=89) of 105 aneurysms.

**Table 4**. Distribution of admission times, together with the times and types of performed interventions in MIA patients

	n	%
Admission time (days, n=48)		
1	18	37.5
2-3	10	20.8
≥ 4	20	41.7
Intervention time (days, n=48)		
Early	26	54.2
Delayed-early	14	29.2
Delayed	8	16.7
Type of intervention		
Clipping(n=105)	89	84.7
Wrapping(n=105)	7	6.7
Embolization(n=105)	4	3.8
Trapping(n=105)	1	0.9
Ventriculoperitoneal Shunting(n=48)	5	10.4
External Ventricular Drain (n=48)	1	2.1

Complications were listed in Table 5. Vasospasm was present in 31.3% (n=15) of patients. HC and infarction were located at the second and third lines with rates of 16.6%

(n=8) and 12.5% (n=6), respectively. When we examined HC cases' CCT images, we determined the rate of Fisher-3 cases as 28.6% and of Fisher-4 as 42.9%. Eight patients developed hydrocephalus. Of these, hydrocephalus of three patients regressed with medical treatment and lumbar puncture. Ventriculoperitoneal shunt was inserted in five patients. HC, which was the second most common complication, was found to have no effect on mortality. This might be due to avoiding the factor's mortal effect with effective use of CCT in addition to close clinical pre and postoperative follow-up.

Table 5. Distribution of complications (n=48)

Complication	n	%
Vasospasm	15	31.3
Hydrocephalus	8	16.6
Late cerebral ischemia - Infarction	6	12.5
Disorders of state of consciousness	6	12.5
Psycho-organic syndrome	4	8.3
Intra-sylvian hematoma	3	6.3
Extradural hemorrhage	3	6.3
Bulging of the wound	3	6.3
Electrolyte imbalance	3	6.3
Subdural hematoma	2	4.2
Deep vein thrombosis	2	4.2
Confusion	1	2.1
Intraventricular hemorrhage	1	2.1
Infection of central nervous system	2	4.2
Cranial nerve paralysis	1	2.1
Pulmonary infection	1	2.1
Seizures	1	2.1
Rhinorrhea	1	2.1
Rebleeding	1	2.1

Fisher scores of 80% of cases in whom postoperative vasospasm had developed during their follow-up were 3 or 4. The outcome was GOS-1 in 13.3% (n=2) of cases with vasospasm. Late cerebral ischemia (LCI) occurred in 12.5% (n=6) of cases during follow-up. These cases were either Fisher-3 or 4, and the outcome was GOS-1 in 66.6% (n=4) of cases. When the timing of surgery in these four patients with GOS-1 outcome was analyzed, it was found that surgery was performed late-early (4-7 days) or late (>7 days), and infarction developed as a consequence of ischemia in three cases. Rebleeding was observed in one patient in the preoperative period, on the first day of hospitalization. Following surgery, the patient was discharged with a GOS of 5. No patient was observed to encounter postoperative rebleeding.

Mortality occurred in 14.6% (n=7) of cases. The mortality rate was 11.5% in the early surgery group, 21.4% in the late-early surgery group, and 12.5% in the delayed surgery group. No significant differences were present among the groups with different intervention timings regarding mortality (p=0.688).

Distributions of admission time and Fisher score regarding WFNS score were shown in Table 6. A significant correlation was present between the time to presentation to the hospital and the WFNS score (p<0.05). With delay in admission, reduction of WFNS score was determined (r: -

0.301; p:0.038; p<0.05). A significant positive correlation at the level of 31% was present between Fisher and WFNS scores (p<0.05).

Table 6. Distributions of admission time and Fisher score regarding WFNS Score (n=48)

		WFNS score						
	1	2	3	4	5			
	n (%)	n(%)	n(%)	n(%)	n(%)			
Admissi	ion time (days)							
1	6(%12.5)	10(%20.8)	0	0	2(%4.2)			
2-3	5(%10,4)	5(%10,4)	0	0	0			
≥4	14(%29,2)	4(%8,3)	2(%4,2)	0	0			
Fisher s	core							
1	9(%18.8)	1(%2.1)	0	0	1(%2.1)			
2	1(%2.1)	2(%4.2)	0	0	0			
3	6(%12.5)	6(%12.5)	0	0	0			
4	9(%18.8)	10(%20.8)	2(%4.2)	0	1(%2.1)			

WFNS: World Federation of Neurological Societies

The distributions of age, admission time, and Fisher Score regarding GOS score were shown in Table 7. A significant negative correlation at the level of 27.9% was present between age and GOS score (p=0.048). Significant differences were present among GOS scores according to admission time (p=0.037). As the result of binary comparisons performed to determine which group caused the difference, it was found that GOS scores of patients admitted on the 4<sup>th</sup>-day or later were significantly higher than those of patients presenting on the second or third day (p=0.012). No significant relationship was present between the WFNS and GOS scores (p>0.05). Timing of surgical intervention had no significant relationships with WFNS (p<0.05), Fisher (p<0.05), and GOS (p<0.05) scores. There was a significant negative correlation at the level of 30.6% between Fisher and GOS scores (p<0.01).

 
 Table 7. Distributions of age, admission time, and Fisher Score
 regarding GOS score (n=48)

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			GOS score			
	1	2	3	4	5	
	n(%)	n(%)	n(%)	n(%)	n(%)	
Age (ye	ears)					
<40	1(%2.1)	0	0	0	8(%16.7)	
41-50	1(%2.1)	0	0	1(%2.1)	9(%18.8)	
51-60	2(%4.2)	0	0	0	10(%20.8)	
>61	3(%6.3)	1(%2.1)	3(%6.3)	1(%2.1)	8(%16.7)	
Admiss	sion time (da	ys)				
1	2(%4.2)	1(%2.1)	2(%4.2)	1(%2.1)	12(%25)	
2-3	4(%8.3)	0	1(%2.1)	0	5(%10.4)	
≥4	1(%2.1)	0	0	1(%2.1)	18(%37.5)	
Fisher	score					
1	0	1(%2.1)	0	0	10(%20.8)	
2	0	0	0	1(%2.1)	2(%4.2)	
3	1(%2.1)	0	1(%2.1)	0	10(%20.8)	
4	6(%12.5)	0	2(%4.2)	1(%2.1)	13(%27.1)	

GOS: Glasgow Outcome Scale

### Discussion

We determined that age, the amount of cisternal blood in the preoperative period, and the presence of vasospasm were risk factors, whereas neither hypertension nor hydrocephalus were risk factors for outcome in MIA. The MIA/all

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aneurysms ratio was reported as 15-35%; however, this incidence has slightly increased with the addition of autopsy series (1, 2, 9, 10). In our study, the MIA/all aneurysms ratio was 19.2%, which was consistent with the literature.

In our series, female/male ratio was 2.2/1 with a female dominance similar to the literature (11-13). Defillo et al. reported a 1.39-fold increased incidence of MIA in females (14). In the study of Inagawa including 126 cases, 69% of MIA cases were females (15). Although the cause of increased MIA incidence in females has not been fully understood, hormonal factors such as the absence of estrogen's protective effect in postmenopausal women have been proposed.

More than 60% of patients reported by Yaşargil (7) and Nehls et al. (16) were in their fifth or sixth decades. Kaminogo et al. stated in their study on 361 cases with MIA that the highest MIA incidence was in the age group of 40-59 years, with a rate of 67% (11). In our study, the ratios of patients within 5th-6th-decades were slightly lower than the studies by Yaşargil and Nehls et al. It was reported that 0.5-4.6% of all intracranial aneurysms belonged to pediatric patients, and MIA incidence in the pediatric age group relatively increased when a family history of immune deficiency disorder was present (11, 17, 18). Regarding the pediatric age group, our study was consistent with the literature, having only one patient (2.08%); on the other hand, that single pediatric patient had no family history of an immune deficiency disorder.

Kassell et al. (19) determined that the mortality rate was 7%, and full recovery occurred in 86% of the patients in the 18-29 age group, whereas in patients aged >70 years, the mortality rate increased to 49%, and the full recovery rate decreased to 26%. The significant negative correlation between age and GOS score in our study showed that mortality and morbidity rates increased with increasing age, which was consistent with the study by Kassell et al. Various studies have reported an increased MIA incidence when hypertension, smoking, autosomal dominant PCKD, and a cerebrovascular disorder in family history were present (3, 9, 20, 21). In our series, hypertension and smoking were present with a high incidence, and PCKD was identified in three patients.

HT has been suggested to be influential on patients' outcome in SAH due to aneurysm, either single or multiple. On the other hand in the study by Kaminogo et al., no difference was reported between MIA patients and those with a single aneurysm regarding the effect of HT on the outcome (11). In our study, HT had no significant effect on patient outcomes in MIA.

Kaminogo et al. reported that the most common MIA location was MCA in males and ICA in females (11). Unlike the study of Kaminogo et al., MCA was the most common location of MIA in females and males in our study. Sheehan et al.(22), in their study on 897 SAH cases, reported the incidence of hydrocephalus as 25.9%, and Kassell et al.(19) reported this ratio as 15%. The hydrocephalus rate of 16.6% in our study was similar to Kassell's results, but lower than that of Sheehan's. Tomlinson stated that severe ischemic findings were present in 40% of patients who died, whereas, in 40% of the patients, ischemic findings were less severe (23). During follow-up of our patients, 12.5% (n=6) developed infarction due to LCI.

Mizoi et al. (5), in their study on 372 MIA cases, reported the morbidity and morbidity rates as 14-19% and 8%, respectively; however, in the same study, the mortality rate increased to 27% in MIA of vertebrobasilar system. MIA's mortality rate was 2% in Yaşargil's series (7), and 7.3% in Suzuki's series. In our study, mortality occurred in 7 patients (14.6%).

Solomon et al. (24) stated that, during acute phase of SAH, neurological findings were associated with the amount of bleeding, which was effective in the development of vasospasm and LCI. Inagawa (25) reported that as the amount of blood at admission CCT increases, the clinical stage gets poorer also. Our findings were similar to the findings of these two studies.

In our study, a significant result was the effect of admission time on the outcome. When the patient was admitted on the 4th-day or later following the symptom onset, the patient outcome worsened. Rosengart et al. stated that the time from ictus (onset of SAH) to hospital admission had not affected the outcome (26). Controversially, Weyhenmeyer et al. reported that the overall distance to a tertiary medical referral center was strongly effective on prognosis and complications (27). Our study was consistent with Weyhenmeyer's study.

The amount of cisternal blood in admission CCT has been related to mortality and morbidity (19, 28). Kassell et al. reported that GOS score was negatively affected by the amount of cisternal blood at admission CCT and considered a prognostic factor (19). In our study, we determined such a negative effect of Fisher's score on the GOS score, consistent with the study of Kassell et al.

Tapaninaho et al. (29) reported that the amount of blood on CCT images was effective on hydrocephalus development, and in cases with a severe amount of cisternal blood, hydrocephalus developed with a rate of 16%. Also, they showed associations between preoperative grade, hydrocephalus, and a requirement for shunting procedure; a shunting procedure was performed with a rate of 10-18% in Fisher-3 and Fisher-4 cases. In our study, more than 60% of patients with hydrocephalus were either Fisher-3 or 4, and a shunting procedure was performed with a rate similar to Tapaninaho et al.'s result. Since no relationship was present between the timing of surgical intervention and hydrocephalus in our study, we think that, besides cli-

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nical follow-up, CCT follow-up is crucial for monitoring enlargement of ventricles and treatment planning, independent from MIA surgery.

A direct relationship between the amount of cisternal blood and vasospasm was shown in the classification made by Fisher et al.(30), and vasospasm was most common in stage-3 cases. Harrod et al.(31) analyzed the medical literature between 1966 and 2005 to determine the risk factors for vasospasm developing after aneurysmal SAH and reported that an increased amount of cisternal blood was the common feature. Most of the cases belonging to either Fisher-3(20%-3 cases) or Fisher-4(60%-9 cases) groups in our study showed a relationship between vasospasm development and the amount of cisternal blood. Additionally, 13.3%(2 cases) of the cases who developed vasospasm had GOS-1 outcome. These two cases revealed that vasospasm was a significantly effective factor regarding mortality.

Kassell et al.(4) stated that early surgery enabled better mechanical cleaning of blood collected in subarachnoid space and, with the release of arachnoid adhesions, provided cleaning of arteries by the cerebrospinal fluid; moreover, these were important for safe use of hypervolemic, hypertensive, anticoagulant treatments. In his study investigating the effect of clot-cleaning through early surgery on vasospasm(25), Inagawa stated that early surgery had no difference than late surgery regarding angiographic vasospasm. However, clinically symptomatic vasospasm was present in 18% of cases who had undergone early surgical intervention, whereas 44% of cases in whom surgery was delayed had clinical manifestations of vasospasm.

Rinne et al. stated that since a more significant number of vascular structures were required to be manipulated if all aneurysms were targeted, especially in the presence of intraoperative complications, worse outcomes were observed(2). Thus, in MIA, all or the highest possible number of aneurysms should be treated, and this has been our treatment protocol. In our clinic, early surgery is preferred in patients with aneurysmal SAH to avoid recurrent bleeding and infarction because of vasospasm during the waiting period. When MIA is diagnosed, our preference is to close all aneurysms in a single session, if possible. A high WFNS score and hydrocephalus development not necessarily leading to a worse outcome in our study can be explained by administering effective preoperative and postoperative follow-up with CCT in SAH's clinical management and aneurysm surgery.

In conclusion, this study led us to suggest that age, the amount of cisternal blood in the preoperative period, and postoperatively developing vasospasm and infarction are risk factors for mortality, but not hypertension and postoperatively developing hydrocephalus. Besides, the WFNS Scoring system is not a reliable predictor of mortality. *Ethical Approval:* All procedures performed in studies involving human participants followed the institutional research committee's ethical standards (February 2011 Decision number: 62977267-903.99) and the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

**Conflict of Interest:** All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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### References

**1.** Ellamushi HE, Grieve JP, Jager HR, Kitchen ND. Risk factors for the formation of multiple intracranial aneurysms. J Neurosurg. 2001;94(5):728-732.

**2**. Rinne J, Hernesniemi J, Puranen M, Saari T. Multiple intracranial aneurysms in a defined population: prospective angiographic and clinical study. Neurosurgery. 1994;35(5):803-808.

**3.** Jabbarli R, Dinger TF, Darkwah Oppong M, Pierscianek D, Dammann P, Wrede KH, et al. Risk Factors for and Clinical Consequences of Multiple Intracranial Aneurysms: A Systematic Review and Meta-Analysis. Stroke. 2018;49(4):848-855.

**4**. Kassell NF, Torner JC, Jane JA, Haley EC, Jr., Adams HP. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 2: Surgical results. J Neurosurg. 1990;73(1):37-47.

5. Mizoi K, Suzuki J, Yoshimoto T. Surgical treatment of multiple aneurysms. Review of experience with 372 cases. Acta Neurochir (Wien). 1989;96(1-2):8-14.

**6**. Rinne J, Hernesniemi J, Niskanen M, Vapalahti M. Management outcome for multiple intracranial aneurysms. Neurosurgery. 1995;36(1):31-37; discussion 37-38.

7. Yaşargil MG. Multiple Aneurysms. In: Yaşargil MG, editor. Microneurosurgery: II Clinical Considerations, Surgery of the intracranial aneurysms and results. 2. Stuttgart: George Thieme Verlag; 1984. p. 305-328.

8. Yaşargil MG. Pathological Considerations. In: Yaşargil MG, editor. Microneurosurgery: I Microsurgical Anatomy of the Basal Cisterns and Vessels of the Brain; Diagnostic Studies, General Operative Techniques and Pathological Considerations of the Intracranial Aneurysms. 1. Stuttgart: George Thieme Verlag; 1984. p. 279-349.

**9**. Juvela S. Risk factors for multiple intracranial aneurysms. Stroke. 2000;31(2):392-397.

**10**. Inagawa T. Multiple intracranial aneurysms in elderly patients. Acta Neurochir (Wien). 1990;106(3-4):119-126.

**11.** Kaminogo M, Yonekura M, Shibata S. Incidence and outcome of multiple intracranial aneurysms in a defined population. Stroke. 2003;34(1):16-21.

**12.** Wachter D, Kreitschmann-Andermahr I, Gilsbach JM, Rohde V. Early surgery of multiple versus single aneurysms after subarachnoid hemorrhage: an increased risk for cerebral vasospasm? J Neurosurg. 2011;114(4):935-941.

**13**. Oh K, Lim YC. Single-session Coil Embolization of Multiple Intracranial Aneurysms. J Cerebrovasc Endovasc Neurosurg. 2013;15(3):184-190.

14. Defillo A, Qureshi MH, Nussbaum ES. Are Multiple Intracranial Aneurysms, More Than 5 At One Time, Almost Exclusively A Female Disease? A Clinical Series and Literature Review. J Neurol Stroke. 2014;1(4):24-29.

**15**. Inagawa T. Surgical treatment of multiple intracranial aneurysms. Acta Neurochir (Wien). 1991;108(1-2):22-29.

**16**. Nehls DG, Flom RA, Carter LP, Spetzler RF. Multiple intracranial aneurysms: determining the site of rupture. J Neurosurg. 1985;63(3):342-348.

**17**. Fogelholm R, Hernesniemi J, Vapalahti M. Impact of early surgery on outcome after aneurysmal subarachnoid hemorrhage. A population-based study. Stroke. 1993;24(11):1649-1654.

**18**. Wang R, Zhang D, Zhao J, Wang S, Zhao Y, Niu H. A comparative study of 43 patients with mirror-like intracranial aneurysms: risk factors, treatment, and prognosis. Neuropsychiatr Dis Treat. 2014;10:2231-2237.

**19.** Kassell NF, Torner JC, Haley EC, Jr., Jane JA, Adams HP, Kongable GL. The International Cooperative Study on the Timing of Aneurysms Surgery. Part I: Overall management results. J Neurosurg. 1990;73:18-37.

**20.** Schievink WI. Genetics of intracranial aneurysms. Neurosurgery. 1997;40(4):651-662; discussion 662-653.

**21**. Jiang H, Weng YX, Zhu Y, Shen J, Pan JW, Zhan RY. Patient and aneurysm characteristics associated with rupture risk of multiple intracranial aneurysms in the anterior circulation system. Acta Neurochir (Wien). 2016;158(7):1367-1375.

**22**. Sheehan JP, Polin RS, Sheehan JM, Baskaya MK, Kassell NF. Factors associated with hydrocephalus after aneurysmal subarachnoid hemorrhage. Neurosurgery. 1999;45(5):1120-1127; discussion 1127-1128.

**23**. Tomlinson BE. Ischaemic lesions of the cerebral hemispheres following rupture of intracranial aneurysms. 1. Descriptions of the ischaemic lesions. Newcastle Med J. 1966;29:81-84.

**24**. Solomon RA, Onesti ST, Klebanoff L. Relationship between the timing of aneurysm surgery and the development of delayed cerebral ischemia. J Neurosurg. 1991;75(1):56-61.

**25**. Inagawa T. Effect of early operation on cerebral vasospasm. Surg Neurol. 1990;33(4):239-246.

**26**. Rosengart AJ, Schultheiss KE, Tolentino J, Macdonald RL. Prognostic factors for outcome in patients with aneurysmal subarachnoid hemorrhage. Stroke. 2007;38(8):2315-2321.

**27**. Weyhenmeyer J, Guandique CF, Leibold A, Lehnert S, Parish J, Han W, et al. Effects of distance and transport method on intervention and mortality in aneurysmal subarachnoid hemorrhage. J Neurosurg. 2018;128(2):490-498.

**28**. Lanzino G, Kassell NF, Germanson TP, Kongable GL, Truskowski LL, Torner JC, et al. Age and outcome after aneurysmal subarachnoid hemorrhage: why do older patients fare worse? J Neurosurg. 1996;85(3):410-418.

**29**. Tapaninaho A, Hernesniemi J, Vapalahti M, Niskanen M, Kari A, Luukkonen M, et al. Shunt-dependent hydrocephalus after subarachnoid haemorrhage and aneurysm surgery: timing of surgery is not a risk factor. Acta Neurochir (Wien). 1993;123(3-4):118-124.

**30.** Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery. 1980;6(1):1-9.

**31**. Harrod CG, Bendok BR, Batjer HH. Prediction of cerebral vasospasm in patients presenting with aneurysmal subarachnoid hemorrhage: a review. Neurosurgery. 2005;56(4):633-654.