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Effect of Early Aneurysm Surgery On Prognosis: Calm Down In A Hurry!

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ABSTRACT

This study investigates the effects of early surgery in aneurysmal subarachnoid hemorrhage (SAH) on the outcome and postoperative complications.
This retrospective study includes 250 patients who presented to a teaching hospital with SAH and underwent aneurysm clipping during a 10-year period. 212 patients (84.8%) underwent early, and 38 (15.2%) underwent late surgery. Presenting symptoms, clinical and neuroradiological findings, and outcomes were reviewed. The severity of SAH was assessed using the World Federation of Neurosurgical Societies (WFNS) SAH scale and Fisher's grading system. Glasgow Outcome Scale (GOS) was used for postoperative outcome measures.
Patients consisted of 142 (56.8%) females and 108 (43.2%) males with a mean age of 52.5 years and a female-to-male ratio of 1.3. The most common presenting symptoms were headache and vomiting (n=164; 65.6%). The incidence of SAH was highest in fall and spring, respectively. The patients were mostly classified as grade 1 on the WFNS SAH scale and as grade 2 on Fisher's scale. A significant correlation was found between WFNS and Fisher's grades and GOS. The majority of patients underwent early aneurysm surgery, and re-bleeding occurred in 4.3%. Mortality was 10.3%, and vasospasm-related morbidity and mortality occurred in 6% and 6.8% of the patients, respectively. 84.8% of patients had favorable outcomes, and 15.2% of patients had poor outcomes.
Results showed that early surgery led to reduced morbidity and mortality. Patients admitted with SAH should be promptly evaluated and undergo angiography. Subsequently, the aneurysm should be promptly excluded from circulation to prevent rebleeding, thus enabling the team to concentrate on managing other complications.

Key words: Subarachnoid hemorrhage, aneurysm, early surgery, vasospasm

Introduction

Subarachnoid hemorrhage is the extravasation of blood from the brain, cerebellum, and spinal cord into the subarachnoid space and is mainly caused by arterial and rarely by venous factors. SAH has an incidence of 10-16 per 100,000 population, which has also been reported to be 25, 16, and 16 per 100,000 population in Japan, Finland, and the USA, respectively (1,2).

Trauma is the most common cause of SAH, while aneurysm rupture is the cause of 80% of spontaneous SAH. The other causes of spontaneous SAH include arteriovenous malformation, hypertensive bleeding, hemorrhagic diathesis, and mycotic aneurysms caused by infections (1,3,4). Intracranial aneurysms are usually diagnosed after the onset of SAH. However, recent advances in diagnostic techniques have increased the prevalence of incidentally detected aneurysms. Although the mortality from SAH has slightly decreased over the last decade, aneurysmal SAH has a high mortality and morbidity rate, up to 50% and 15-20%, respectively. Moreover, only 25-35% of the patients show varying degrees of improvement (moderate-good) (1,2,5).

Re-bleeding is the most dreadful complication after aneurysmal SAH. However, this problem has been partially resolved with the increasingly widespread utilization of early surgery; hence, cerebral vasospasm has become the most critical complication of SAH in terms of mortality and morbidity. Fortunately, cerebral vasospasm can be

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treated more effectively after obliterating the aneurysm by early surgery. Moreover, the mortality and morbidity caused by SAH can be effectively reduced by taking appropriate measures to abate the effects of vasospasm in patients undergoing clipping of a ruptured aneurysm, particularly by close monitoring of the early signs of vasospasm and prompt management of suspected conditions. However, these measures can only be possible in patients who undergone early surgery (6,7).

In this retrospective study, we aimed to evaluate the outcomes of patients with aneurysmal SAH who undergone early surgery with regard to several parameters to discuss these outcomes in light of literature.

Materials and Methods

This study included a total of 250 patients who presented to Dr. Lutfi Kirdar Kartal Teaching and Research Hospital Department of Neurosurgery with aneurysmal SAH and underwent surgery between January 1999 and December 2009. The patients were divided into early and late intervention groups. Patient charts and video footage of the cases gathered from the operating microscope were retrospectively evaluated for each patient.

Patients that died before getting a definitive aneurysmal SAH diagnosis, patients with negative digital subtraction angiogram (DSA) findings, patients with multiple aneurysms, and patients with a history of endovascular surgery were excluded from the study.

The severity of SAH was assessed based on the WFNS SAH scale, and the amount of subarachnoid blood on CT was graded using Fisher's grading system.

The diagnosis of SAH was established based on the clinical presentation of the patient, evaluation of the cranial CT, and lumbar puncture findings in equivocal cases. Location, size, morphology and projection of the aneurysm were assessed with DSA. Additional findings including intraventricular hematoma (IVH), intracerebral hematoma (ICH), and hydrocephalus were evaluated in each patient from initial and serial CT imaging findings. In addition, age, sex, season of the patients' presentation, presenting symptoms, characteristics of the aneurysm, clinical and neurological findings, treatment approach, the timing of the definitive treatment, and treatment outcomes were reviewed.

Early aneurysm surgery within 72 h after the onset of SAH was performed in patients with WFNS grades 1 and 2 and also in patients with WFNS grade 3 and higher and a Fisher grade 4 that required emergency decompression as shown on cranial CT. The patient who was not suitable for early aneurysm surgery underwent late aneurysm surgery 10-14 days after the onset of SAH.

Postoperative neurological assessment of the patients was performed using GOS. The patients were followed up every 3 months in the first year and then every 12 months thereafter.

Data were analyzed using SPSS for Windows version 24.0 (International Business Machines Corporation, Armonk, NY, USA). GOS, WFNS, and Fisher Scale parameters were compared between the two groups. The two groups were compared using the Chi-square test, and a p-value of <0.05 was considered significant.

Results

The 250 patients included 142 (56.8%) females and 108 (43.2%) males with a female-to-male ratio of 1.3. Figures 1a and 1b present the age groups of the patients and the seasonal distribution of SAH, respectively.

Most common presenting symptoms were headache and vomiting (n=164; 65.6%), followed by vomiting and sudden loss of consciousness (n=58; 23.2%), speech impairment and cerebrovascular symptoms such as motor weakness (n=15; 6%), seizure (n=8; 3.2%), and ptosis and diplopia (n=5; 2%)

Of the 250 patients, 92 (36.8%) patients had no significant past medical history while the remaining 158 (63.2%) patients had a history of various comorbidities including hypertension (HT) (n=111; 70.2%), diabetes mellitus (DM) (n=22; 13.9%), cerebrovascular disease (CVD) (n=11; 6.9%) and coexistence of HT, DM, and CVD (n=14; 8.8%). Additionally, of these 158 patients, 132 (83.5%) patients had a history of smoking, 16 (10.1%) had a history of alcohol misuse, and 10 (6.3%) had a history of smoking and alcohol misuse.

The most common location of aneurysm was the anterior communicating artery (n=80; 32%), followed by the middle cerebral artery (n=72; 28.8%), posterior communicating artery (n=38; 15.2%), the internal carotid artery (n=33; 13.2%) and others (n=27; 10.8%). The aneurysm diameter was 0-10 mm in 189 (75.6%), 11 mm –

Table 1. Significant Correlation Between Fisher's and WFNS Grades (p <0.001)

		WFNS Grade				
Fisher Grade	n	1	2	3	4	5
1	29	27 (93.1%)	1 (3.45%)	1 (3.45%)	-	-
2	136	65 (47.8%)	67 (49.3%)	4 (2.9%)	-	-
3	52	11 (21.1%)	28 (53.8%)	11 (21.1%)	1 (2%)	1 (2%)
4	33	2 (6%)	4 (12.1%)	17 (51.5%)	9 (27.3%)	1 (3.1%)
Total	250	105	100	33	10	2

Table 2. Significant Correlation Between GOS Grades and WFNS Grades (p <0.001)

WFNS Grade	n	Good recovery (GOS 5)	Morbidity (GOS 2. 3. 4)	Mortality (GOS 1)
1	105	95 (90.5%)	8 (7.6%)	2 (1.9%)
2	100	61 (61%)	26 (26%)	13 (13%)
3	33	20 (60.6%)	8 (24.2%)	5 (15.2%)
4	10	3 (30%)	3 (30%)	4 (40%)
5	2	-	-	2 (100%)

Table 3. Significant Correlation Between GOS Grades and Fisher's Grades (p <0.001)

Fisher's Grade	n	Good recovery (GOS 5)	Morbidity (GOS 2. 3. 4)	Mortality (GOS 1)
1	29	28 (96.5%)	-	1 (3.5%)
2	136	111 (81.6%)	16 (11.8%)	9 (6.6%)
3	52	26 (50%)	18 (34.6%)	8 (15.4%)
4	33	14 (42.4%)	11 (33.3%)	8 (24.3%)
Total	250	179 (71.6%)	45 (18%)	26 (10.4%)

2.5 cm in 53 (21.2%), and >2.5 cm (giant aneurysm) in 8 (3.2%) patients.

Early aneurysm surgery was performed in 212 (84.4%) and, late aneurysm surgery was performed in 38 (15.2%) patients. Distributions of the patients respecting WFNS and Fisher scales are presented in Figures 1c and 1d, respectively. Moreover, there was a significant correlation between Fisher's and WFNS grades, which is presented in Table 1 (p <0.001).

Surgery was performed via a right pterional approach in 186 (74.4%), a left pterional approach in 29 (11.6%), a frontal (bifrontal, subfrontal) approach in 25 (10%), and a suboccipital approach in 10 (4%) patients. Aneurysm clipping was the most common surgical procedure applied in our patients (n=238; 95.2%), followed by carotid artery ligation (n=5; 2%), cauterization-bipolar remodeling of aneurysm (n=4; 1.6%), trapping of the parent vessel (n=2; 0.8%), and wrapping (coating) (n=1; 0.4%) (Figure 2).

Figure 3 presents the annual distribution of total mortality and prevalence of preoperative re-bleeding rates in our patients. Vasospasm-related morbidity and mortality occurred in 15 (6%) and 17 (6.8%) patients, respectively. As for the other complications, 11 (4.4%) patients had ICH and were operatively treated; 4 (1.6%) patients had EDH, of whom 3 patients underwent surgical treatment and 1 patient was followed up only; 8 (3.2%) patients developed hydrocephalus and received a ventriculoperitoneal (VP) shunt; 5 (2%) patients had meningitis and were treated by antibiotic therapy; 3 (1.2%) patients had SDH and were operatively treated, 2 (0.8%) patients had IVH and underwent external ventricular drainage; 2 (0.8%) patients showed signs of contusion and were followed up only.

In postoperative GOS grades, 26 (10.4%) patients had grade 1, 12 (4.8%) patients had grade 2, 17 (6.8%) patients had grade 3, 16 (6.4%) patients had grade 4, and 179 (71.6%) patients had grade 5 (Figure 1e). The correlations between the GOS grades and the WFNS and Fisher's grades are presented in Tables 2 and 3, respectively (p <0.001).

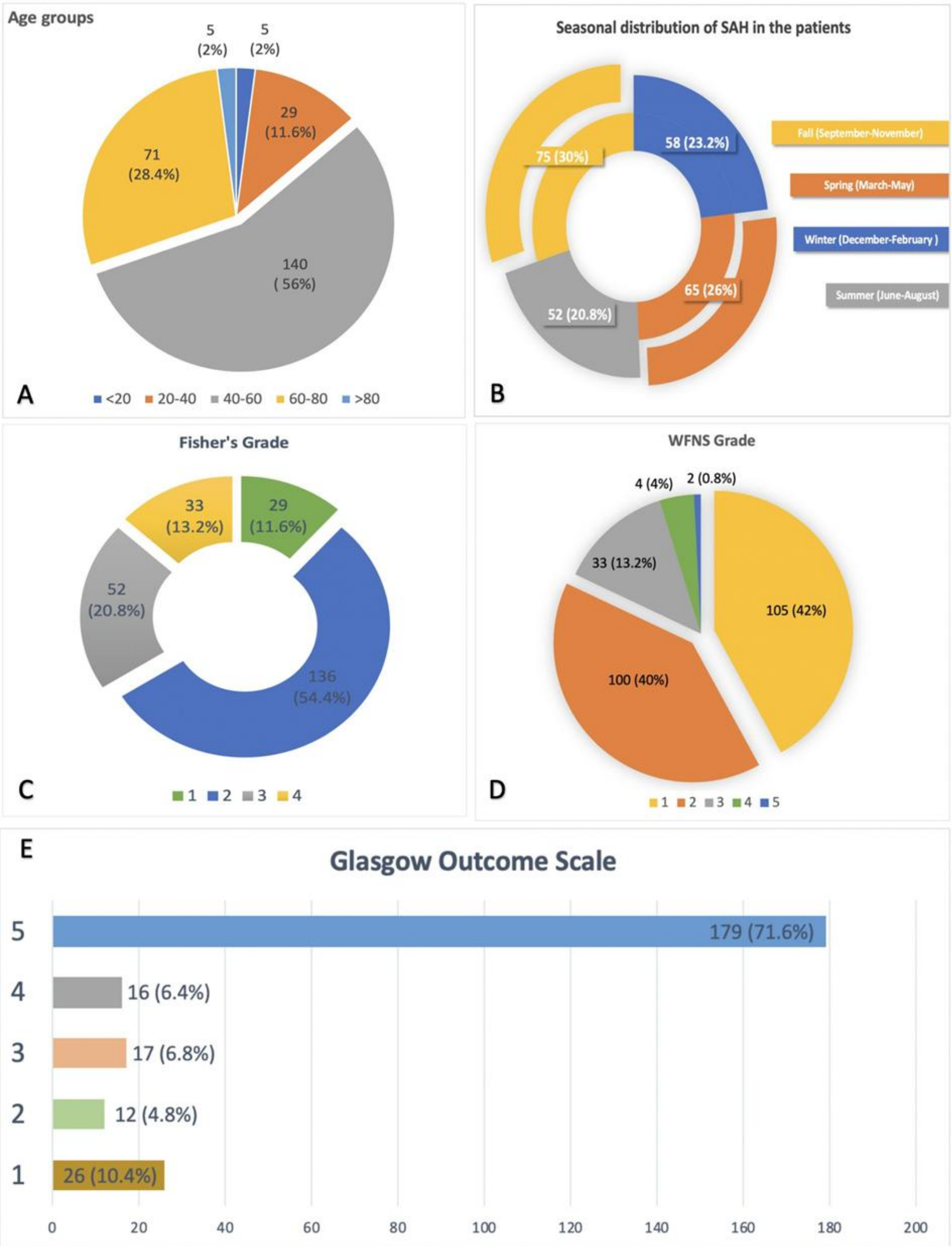

Fig. 1. a) Age groups, **b)** Seasonal distribution of SAH in the patients, **c)** Fisher's grading system of intracranial blood on CT in SAH patients, **d)** WFNS Grading System, **e)** Distribution of Glasgow Outcome Scale (GOS) grades

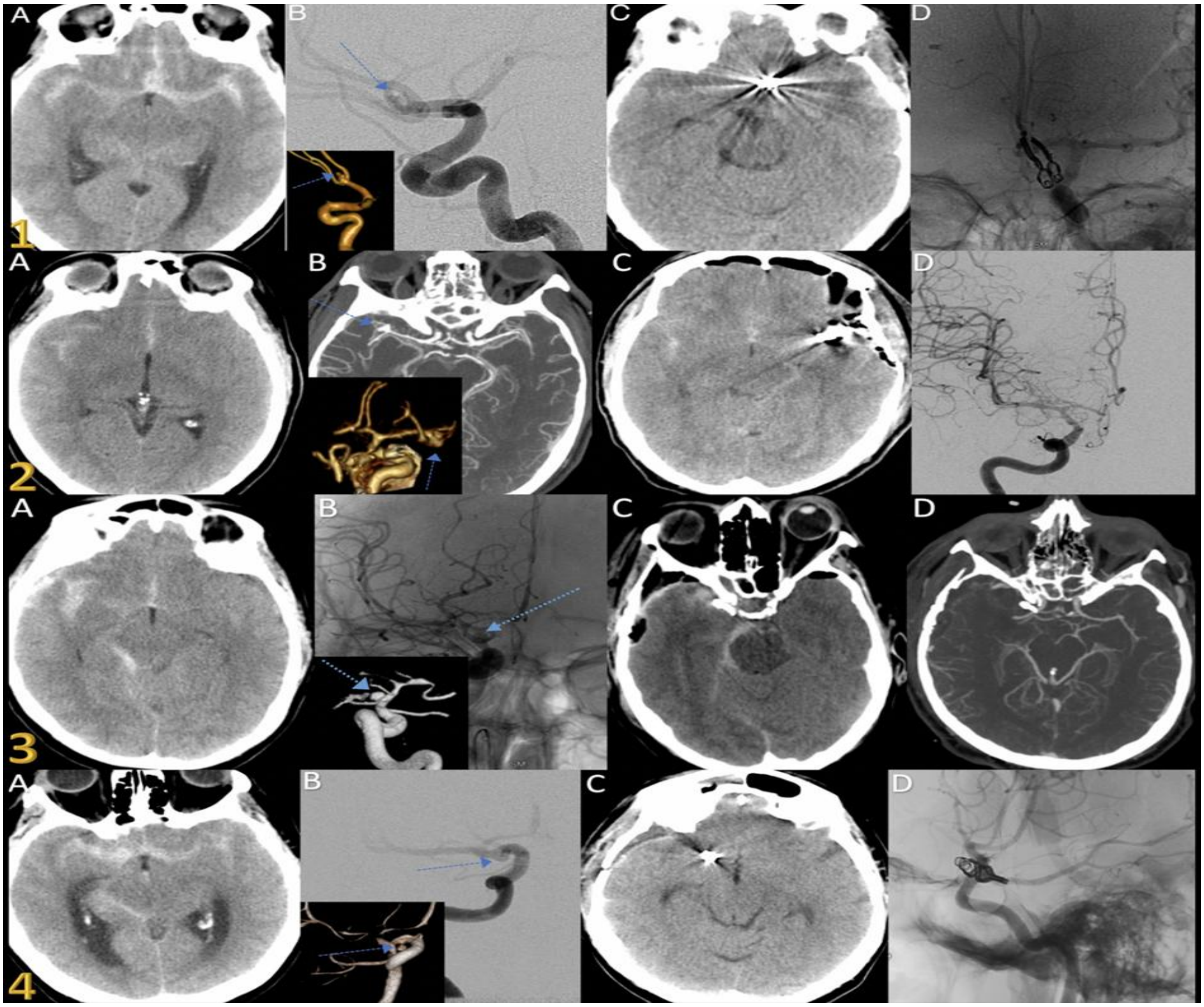

Fig. 2. 1- A) Preoperative axial CT shows SAH in lamina terminalis, interpedincular, interhemispheric and sylvian cistern. **B)** CT and Cerebral anjiogram shows a 3.5 mm lobulated anterior communicating artery aneurysm. C) Postoperative CT. **D)** Postop cerebral angiogram shows no residual aneurysm

2- A) Preoperative axial CT shows SAH in interhemispheric and sylvian cistern. **B)** Cerebral anjiogram shows a 9 mm middle cerebral artery aneurysm. **C)** Postoperative CT. **D)** Postop cerebral angiogram shows no residual aneurysm

3- A) Preoperative axial CT shows SAH in ambient, interhemispheric and sylvian cistern. **B)** Cerebral anjiogram shows a 3 mm posterior comminicating artery aneurysm. **C)** Postoperative CT. **D)** Postop CT angiogram shows no residual aneurysm

4- A) Preoperative axial CT shows SAH in ambient, lamina terminalis, interhemispheric and sylvian cistern. B) Cerebral anjiogram shows a 6 mm internal cerebral artery aneurysm. **C)** Postoperative CT. **D)** Postop cerebral angiogram shows no residual aneurysm

*Arrows display aneurysms

The mean time from surgery to hospital discharge was 13±3 days. The mean follow-up period was 6.9±1.1 years.

Discussion

In the present study, most of the patients underwent early aneurysm surgery, and the analysis of multiple factors revealed that early aneurysm surgery is more appropriate in patients with SAH (8-11).

In our study, the ages of the patients ranged between 18-83 years, the mean age was 52.5 years, and the highest incidence of SAH was seen in the fourth decade (56.1%). These findings were consistent with the literature data that suggest that the peak incidence of SAH is 40-60 years (4,12). Literature also suggests that the cumulative incidence of SAH is 1.5-2 times higher in females

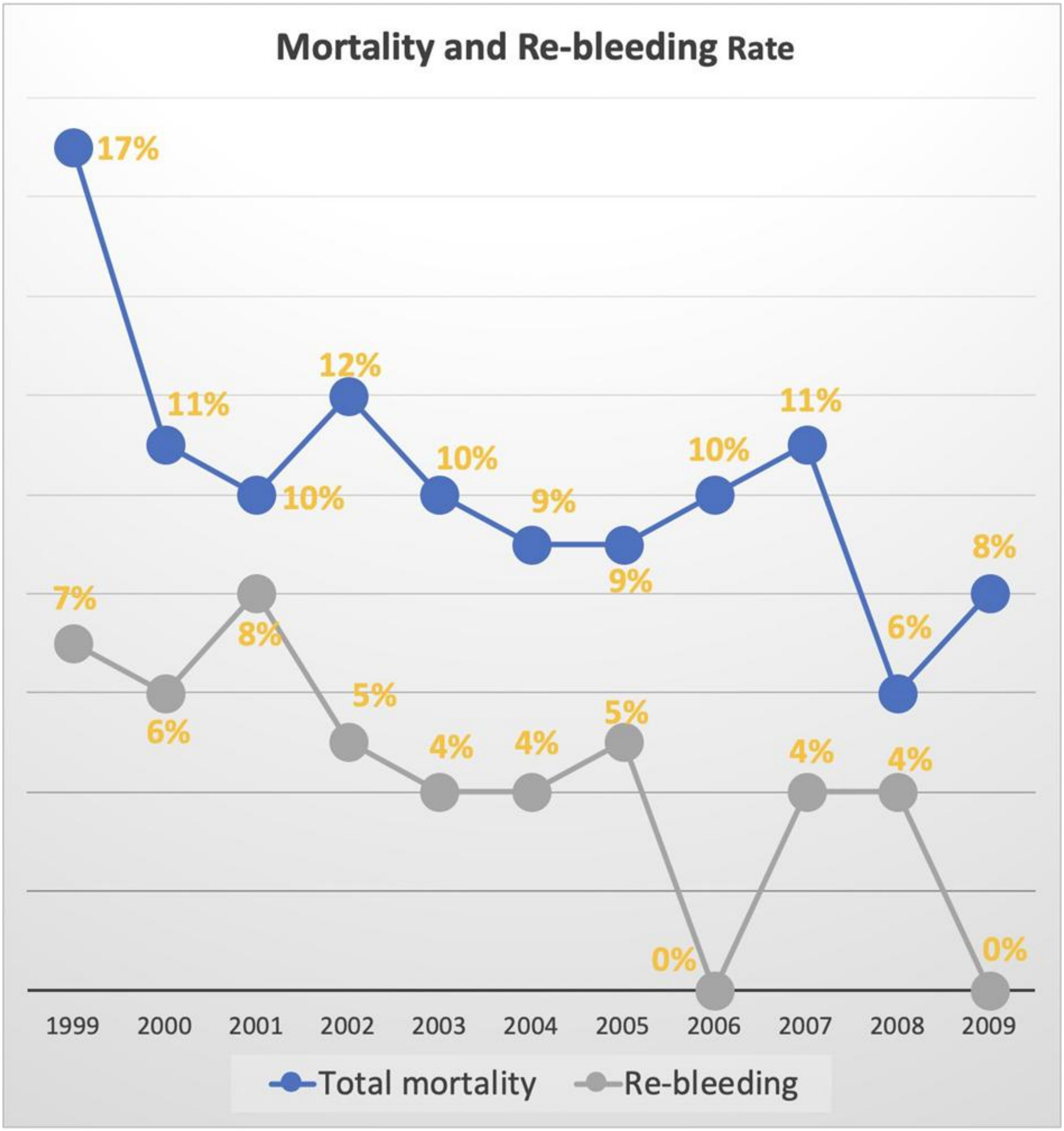

Fig. 3. Annual Distribution of Total Mortality and The Prevalence of Re-Bleeding

than in males (4,13,14). In our patients, however, the incidence of SAH was 1.3 times higher in women than in men.

There are several studies reporting on the seasonal variation of SAH, which suggest that SAH is mostly seen in the spring and fall seasons (15). Similarly, the incidence of SAH in our study was the highest in fall (30%), followed by spring (26%). The most common presenting symptom in patients with SAH is a sudden-onset severe headache which has been reported in 80% of the patients. This headache is considered to be caused by the enlargement of the aneurysmal dome or a minor leak of blood into the wall of the aneurysm(16,17). Similarly, the headache was also the most common presenting symptom in our patients (65.6%).

Smoking and/or alcohol misuse and preexisting comorbidities such as HT, DM, and CVD have been identified as risk factors of SAH(18,19). In our study, these factors were also found to be associated risk factors for aneurysmal SAH. Of the 250 patients, 92 (36.8%) patients had no significant history while the remaining 158

(63.2%) patients had a history of various clinical conditions including HT (n=111; 70.2%), DM (n=22; 13.9%), CVD (n=11; 6.9%) and coexistence of HT, DM, and CVD (n=14; 8.8%). Of these 158 patients, smoking was revealed to be a significant predisposing factor in 132 (83.5%) patients.

Cerebral angiography plays a crucial role in detection of intracranial aneurysms and their localizations and also in the surgical planning of the patients. In our study, a four-vessel DSA was performed on each patient and, the most common aneurysm location was ACoA (n=80; 32%). Similarly, literature data suggests that ACoA is the most common aneurysm location associated with SAH(20). Aneurysms with a maximum diameter of >2.5 cm are defined as giant aneurysms(21). Giant aneurysms have been shown to constitute 3-13% of intracranial aneurysms(22). In our study, giant aneurysms accounted for 3.2% of all aneurysms.

The incidence of IVH and ICH in SAH patients is reported as 17%(4). In our study, IVH and ICH were detected in 9.6% of the patients. Of the 250 patients, 15 patients had vasospasm-related neurological deficits such as aphasia and paresis. These deficits mainly were seen between postoperative days 1-4, and the patients were treated with medication.

In our study, patients with higher WFNS grades had a relatively worse prognosis. In a previous multicenter study, Kassel et al. (4). evaluated a cohort of 2,922 patients and reported that 14% of the patients died, and 69% of the patients were discharged with a good neurological status (GOS 5). Similarly, Osawa et al. (9) evaluated a cohort of 2,055 patients and revealed that 12.9% of the patients died and, 68.5% of the patients had a good neurological status. In our study, 10.3% of the patients died and, 71.6% of the patients were discharged with a good neurological status ($p < 0.001$). Moreover, it was also revealed that early aneurysm surgery is essential in such patients as it reduces blood loss, results in lower complication and mortality rates, and also leads to favorable neurological outcomes (8,10,11,23).

The importance of early surgical treatment of aneurysms has been confirmed by numerous studies (8,10,11,23,24). On the other hand, the direct effect of SAH, cerebral vasospasm and re-bleeding have been reported as the most significant causes of mortality and morbidity in patients with aneurysmal SAH (12,25). The primary goal of early aneurysm surgery is to prevent re-bleeding and to combat cerebral vasospasm. On the contrary, there are some opposing views reported in the literature. The International Cooperative Study indicated that there was no significant difference between early (0-3 days) and late (after 11 days) aneurysm surgery with regard to mortality, although the surgeries performed on the days 3-10 were associated with increased mortality (3,4,26). In our practice, we usually prefer early aneurysm surgery (within the first 72 hours) in patients with good-grade SAH (WFNS grade 1 and 2) and prefer late aneurysm surgery following patient recovery (after 10-14 days) in patients with poor-grade SAH (WFNS grade 3, 4, and 5). However, we also perform early aneurysm surgery in patients with poor-grade that have a poor clinical condition associated with hematoma.

Canbolat et al. evaluated 76 patients that underwent early aneurysm surgery and found a significant correlation between the WFNS and CT grades and also suggested that these grades were affecting the prognosis of the patients (8). In our patients, a significant correlation was found between the initial CT and WFNS grades and between the WFNS, CT grades and GOS grades ($p < 0.001$). Similarly, literature reviews indicate that the correlation between clinical grades and Fisher's grades has been reported in numerous studies. Accordingly, these grades are reliable parameters in the predicting prognosis in patients with aneurysmal SAH (27).

Re-bleeding and cerebral vasospasm are the most critical complications in patients with aneurysmal SAH and often occur within the first 24 hours and the first 6-8 days after SAH, respectively (3,17). Re-bleeding has a mortality of approximately 50% and can be prevented by excluding the aneurysm from circulation via early aneurysm surgery(3,17). The International Cooperative Study detected re-bleeding in 381 (11%) out of 3,521 patients and, the authors suggested that the highest risk of re-bleeding was seen within the first 24 hours (4%) (3). In our study, most of the patients underwent early aneurysm surgery and, re-bleeding occurred in 4.3% of the patients, which implies that the risk of re-bleeding is significantly reduced in patients undergoing early aneurysm surgery.

A previous study evaluated a cohort of 3521 patients that were admitted to the hospital within the first three days after the onset of aneurysmal SAH and underwent surgical treatment with no preference for surgical timing and, the authors reported that the incidences of vasospasm-related morbidity and mortality were 6.3% and 7.2%, respectively (3). Similarly, in our study, the incidences of vasospasm-related morbidity and mortality were 6.0% and 6.8%, respectively. Based on this finding, it is wise to consider that by preferring early aneurysm surgery, vasospasm can be combatted more effectively and, the vasospasm-related morbidity and mortality rates can also be reduced.

Early aneurysmal surgery is advocated since it eliminates the risk of re-bleeding, allows lavage to remove potentially spasmogenic agents from contact with vessels, and facilitates treatment of vasospasm, which peaks in incidence between days 6 and 8 after SAH by allowing induction of arterial hypertension and volume expansion without risking aneurysmal rebleeding. Nevertheless, this approach may pose challenges for surgery as the brain parenchyma is edematous, cisternal spaces are obliterated with blood, and the risk of iatrogenic injury during exposure is higher immediately after SAH. However, in late aneurysm surgery, the brain edema is relieved, subarachnoid blood is partially resorbed and, thus the parenchyma is less prone to injury during exposure. Although the surgical decision of a surgeon is affected by the physical conditions of the hospital, patients admitted to the hospital should be promptly evaluated with CT, and after the diagnosis of SAH, prompt angiography and obliteration of the aneurysm should be performed as to prevent re-bleeding and thereby focus on the treatment of vasospasm and other complications.

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