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Does Age Influence the Poor Prognosis after Aneurysmal SAH Surgery in Elderly Patients?

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Objective : The incidence of aneurysmal subarachnoid hemorrhage has been increasing. At the same time, surgical results for elderly patients are unsatisfactory and no guidelines of treatment are available. We carried out a study comparing variable factors and surgical results between young and old age groups to find ways to improve prognosis.

Methods : A retrospective study was carried out on 754 patients who were operated on between 1990 and 2004 by the same surgeon in our hospital. The patients were divided into seven groups according to age : 93 patients below 40 years of age (Group I), 419 patients aged 40~59 (Group II), 115 patients aged 60~64 (Group III), 82 patients aged 65~69 (Group IV), 28 patients aged 70~74 (Group V), 12 patients aged 75~79 (Group VI) and 5 patients over the age of 80 (Group VII). We then checked their medical history, Fisher's grade, Hunt-Hess grade, postoperative complications, and Glasgow Outcome Scale.

Results : Age was not a statistically significant factor among patients below 70 years of age (P value$\geq$0.05). But for those aged 70 and older, the age factor had a statistical value (P value$\leq$0.001). In addition, there was a close correlation between Hunt-Hess grade IV and V patients, and those with vasospasm, and hydrocephalus after surgery, with poor prognosis in elderly patients as well as young patients (P value$\leq$0.001).

Conclusion : Advanced age (under the age of 70) dose not precluded adequate surgical treatment in patient with AN SAH, and we should be also alert to preventable causes of delayed neurological deterioration for improving the outcome in all elderly groups.

KEY WORDS : Prognosis factors · SAH · Elderly patients.

Introduction

According to numerous reports, the incidence of aneurysmal subarachnoid hemorrhage(AN SAH) caused by the rupture of cerebral aneurysm is 1.5~2.5 cases per 100,000 persons in the young group. However, for those in the elderly group, it is 40~78 cases per 100,000 persons[2,4,25]. In Korea, information on the incidence of AN SAH related to age is insufficient. Nevertheless, similar to other findings published abroad, the incidence is believed to be higher among elderly patients.

The definition of a elderly population varies, and in the USA it is defined as those who have reached the retirement age of 65 and are entitled to Medicare. Nevertheless, studies on the classification standard for elderly patients based on actual prognosis, as well as factors influencing the prognosis, are insufficient.

Therefore, we conducted this study on AN SAH patients who underwent microscopical clipping of cerebral aneurysm to characterize the ages that actually mediate a serious effect on the prognosis, in other words, a statistically significant age factor, and to characterize other factors that may influence prognosis, to find a means of improving the postoperative outcome of elderly AN SAH patients.

Materials and Methods

Among 965 patients who were hospitalized for AN SAH in the Department of Neurosurgery at our hospital from 1990 to 2004 and underwent brain surgery (microsurgical clipping of cerebral aneurysm), we retrospectively examined and carried out comparative analysis of the medical records and radiological data of 754 patients operated on by the same surgeon and whose medical records were available for review.

For physical and neurological examination, the condition

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of patients at the time of admission was classified according to the Hunt and Hess clinical grading scale (H-H grade) and Fisher's grading scale (Fisher's grade). Patients' history prior to the illness was examined, and the proper surgery time was, in principle, early surgery except in patients with serious medical problems, in other words, in cases of acute myocardiac infarction, chronic renal failure, etc., and in instances that the patient's guardians refused surgery.

After surgery, development of complications such as hydrocephalus, vasospasm, etc. were assessed, hydrocephalus was diagnosed by brain CT, vasospasm was diagnosed by observing the clinical symptoms of patients, the relative Pulsality Index (PI) value on the Trans-Cranial Doppler(TCD) and Velocity of middle cerebral artery(Vm). A reading higher than 120cm/sec was diagnosed as vasospasm.

The final condition of the patient was evaluated 3 months after surgery, by the Glasgow outcome scale(GOS).

In addition, regarding factors that may have mediated an effect on the prognosis, their significance and causal relationship were analyzed by Chi-square and multi-variate logistic regression analysis.

The patients were divided into seven groups according to age : 93 patients below 40 years of age (Group I), 419 patients aged 40~59 (Group II), 115 patients aged 60~64 (Group III), 82 patients aged 65~69 (Group IV), 28 patients aged 70~74 (Group V), 12 patients aged 75~79 (Group VI) and 5 patients over the age of 80 (Group VII).

Table 1. Sex and age distribution in 754 patients

	39≥	40~59	60~64	65~69	70~74	75~79	80≤	Total
M/F	40/53	144/275	20/95	18/64	0/28	2/10	0/5	224/530
(%)	(43/57.0)	(34.4/65.6)	(17.4/82.6)	(22.0/78.0)	(0/100)	(16.7/83.3)	(0/100)	(29.7/70.3)
Total	93	419	115	82	28	12	5	754
(%)	(12.3)	(55.6)	(15.3)	(10.9)	(3.7)	(1.6)	(0.6)	(100)

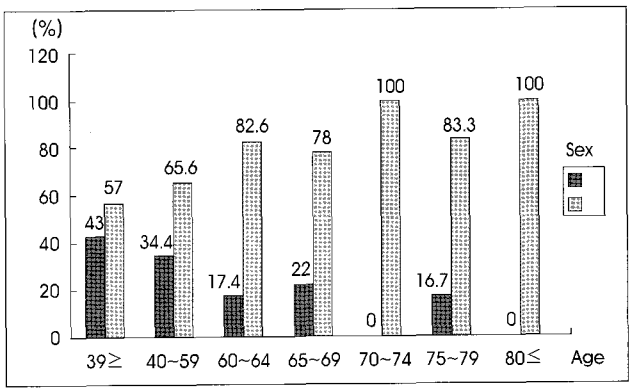

Fig. 1. Sex and age distribution in 754 patients.

Results

The sex and age distribution

Of 754 patients confirmed as those with cerebral aneurysm by 3D CTA, 3D DSA, or MRA, there were 224 males and 530 females. The male/female ratio was therefore 29.7%/70.3%. Most patients were in their forties, fifties and early sixties (Table 1, Fig. 1).

The past history of patients

In regard to the history of the study population, hypertension was most prevalent (157 cases, 20.8%). In addition, diabetes (73 cases, 9.7%), hepatic function impairment and other diverse conditions were noted (Table 2).

The Hunt Hess grade at the time of admission

At the time of admission, most patients were grade II (61.1%) and III (24.7 %) on the H-H grade. In addition, among patients

Table 2. Pre-existing medical conditions in 754 patients with AN SAH

Pre-existing medical conditions	No. of patients (%)							Total
	39≥	40~59	60~64	65~69	70~74	75~79	80≤	
HTN	11	86	19	24	10	5	2	157
	(11.8)	(20.5)	(16.5)	(29.3)	(35.7)	(41.6)	(40.0)	(20.8)
Cardiac Ds.	1	4	3	3	2	0	0	13
CVD	0	3	2	2	2	1	0	10
Pulmonary Ds.	0	3	6	7	5	4	3	28
DM	0	22	17	16	11	7	0	73
Renal Ds.	0	2	0	2	1	0	0	5
Hepatic Ds.	2	7	2	4	0	0	0	15

HTN ; Hypertension, Ds. ; Disease, CVD ; Cerebrovascular Disease, DM ; Diabetes Mellitus

Table 3. H-H grade of 754 patients

H-H grade	No. of patients (%)							Total
	39≥	40~59	60~64	65~69	70~74	75~79	80≤	
I	10	25	8	7	0	0	0	50
	(10.7)	(6.0)	(6.9)	(8.5)	(0)	(0)	(0)	(6.6)
II	53	294	58	37	11	7	1	461
	(57.0)	(70.2)	(50.4)	(45.1)	(39.3)	(58.3)	(20.0)	(61.1)
III	26	79	34	29	13	3	2	186
	(28.0)	(18.8)	(29.5)	(35.4)	(46.4)	(25.0)	(40.0)	(24.7)
IV	4	20	14	8	4	2	2	54
	(4.3)	(4.8)	(12.2)	(9.8)	(14.3)	(16.7)	(40.0)	(7.2)
V	0	1	1	1	0	0	0	3
	(0)	(0.2)	(0.9)	(1.2)	(0)	(0)	(0)	(0.4)
Total	93	419	115	82	28	12	5	754

in Groups III - VII (ie. those aged 60 or over), the percentage of those between 60 and 64 years of age with H-H grade III was 29.5%, between 65 years and 69 years of age it was 35.4%, between 70 years and 74 years of age it was 46.4%. As expected, the proportion of grade III patients increased with age. (Table 3, Fig. 2).

The Fisher's grade at the time of admission

The Fisher's grade at the time of admission, in the second decades to fourth decades was grade 2 or 3 in most cases, however, over 60 years of age, the proportion of grade 3 and 4 patients increased (Table 4, Fig. 3).

The prognosis of 754 patients

The Glasgow outcome scale(GOS) of all patients was examined 3 months after surgery. The rate of good recovery was 69.9% and the death rate was 6.8%. Among elderly patient groups, prognosis was poor overall, and the prognosis pattern worsened with the increase of age (Table 5, Fig. 4).

A good outcome on the GOS was the sum of good recovery(GR) and moderate disability(MD), while poor outcome was the sum of cases of severe disability(SD), vegetative state(V), and death(D). The proportion of SD, V, and D increased with the increase in patients' ages.

The analysis of factors that may influence the prognosis

In 754 patients, age, the H-H grade (good grades were Grades I, II, and III and poor grades were Grades IV and V), Fisher's grade (good grades were Grades 1 and 2, and poor grades were Grades 3 and 4), the presence of hydrocephalus and vasospasm, and the presence of hypertension were examined as factors that might influence the prognosis, and these factors were analyzed by chi-square.

The *p-values* of the age factor, the H-H grade, Fisher's grade, hydrocephalus, and vasospasm were found to be lower than 0.05 and were thus determined to be statistically significant to poor prognosis, while hypertension did not show any statistical significance with poor prognosis (Table 6).

Factors that may independently mediate an effect on poor prognosis

Regarding factors that may mediate an effect on poor prognosis, an odds ratio was obtained on the 754 patients by multivariate logistic regression analysis. In all patients, the 95% confidence interval(CI) of age factor(over 70 years of age), the

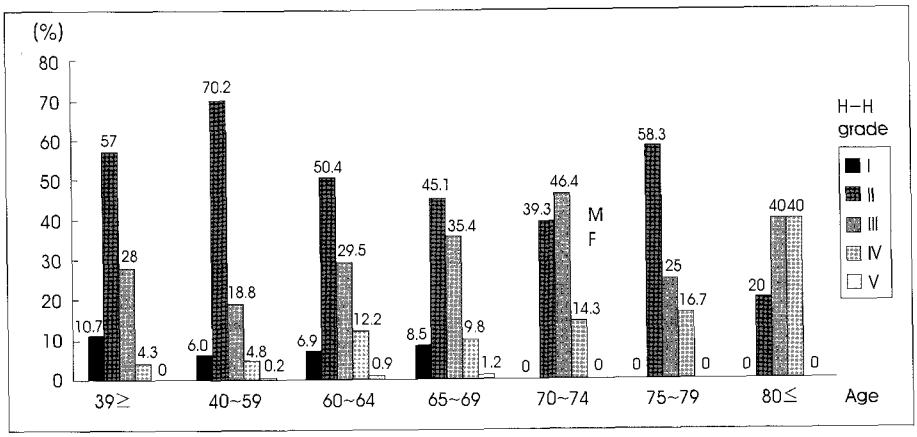

Fig. 2. H-H grade of 754 patients.

Table 4. Fisher's grade of 754 patients

Fisher's grade	No. of patients (%)							Total
	39≥	40~59	60~64	65~69	70~74	75~79	80≤	
1	5	15	7	7	1	0	0	35
	(5.4)	(3.6)	(6.1)	(8.5)	(3.6)	(0)	(0)	(4.6)
2	62	284	56	34	12	7	1	456
	(66.7)	(67.8)	(48.7)	(41.5)	(42.9)	(58.4)	(20.0)	(60.5)
3	22	91	37	32	9	4	2	197
	(23.6)	(21.7)	(32.2)	(39.0)	(32.1)	(33.3)	(40.0)	(26.1)
4	4	29	15	9	6	1	2	66
	(4.3)	(6.9)	(13.0)	(11.0)	(21.4)	(8.3)	(40.0)	(8.8)
Total	93	419	115	82	28	12	5	754

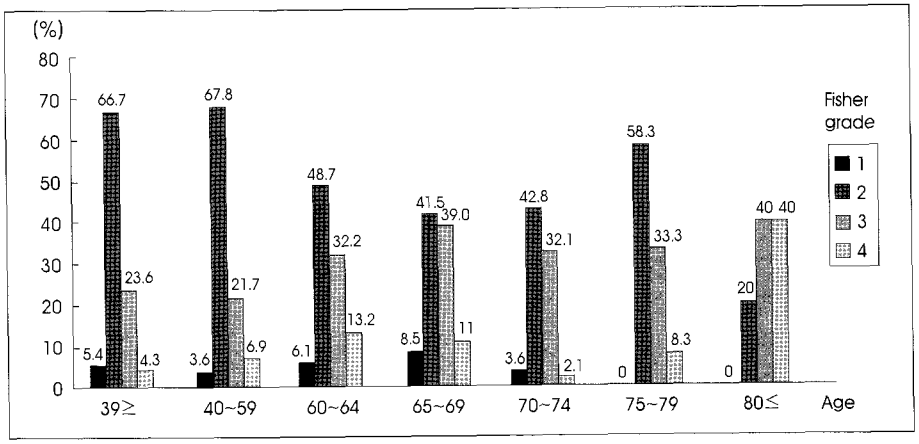

Fig. 3. Fisher's grade of 754 patients.

Table 5. Glasgow Outcome Scale of 754 patients

	No. of patients (%)							Total
	39≥	40~59	60~64	65~69	70~74	75~79	80≤	
GR	83	323	71	36	9	5	0	527
	(89.2)	(77.1)	(61.8)	(43.9)	(32.1)	(41.7)	(0)	(69.9)
MD	6	62	25	30	10	4	2	139
	(6.5)	(14.8)	(21.7)	(36.6)	(35.8)	(33.3)	(40.0)	(18.4)
SD	1	9	7	6	3	1	2	29
	(1.1)	(2.1)	(6.1)	(7.3)	(10.7)	(8.3)	(40.0)	(3.8)
V	0	2	2	2	2	0	0	8
	(0)	(0.5)	(1.7)	(2.4)	(7.1)	(0)	(0)	(1.1)
D	3	23	10	8	4	2	1	51
	(3.2)	(5.5)	(8.7)	(9.8)	(14.3)	(16.7)	(20.0)	(6.8)
Total	93	419	115	82	28	12	5	754

GOS : Glasgow Outcome Scale

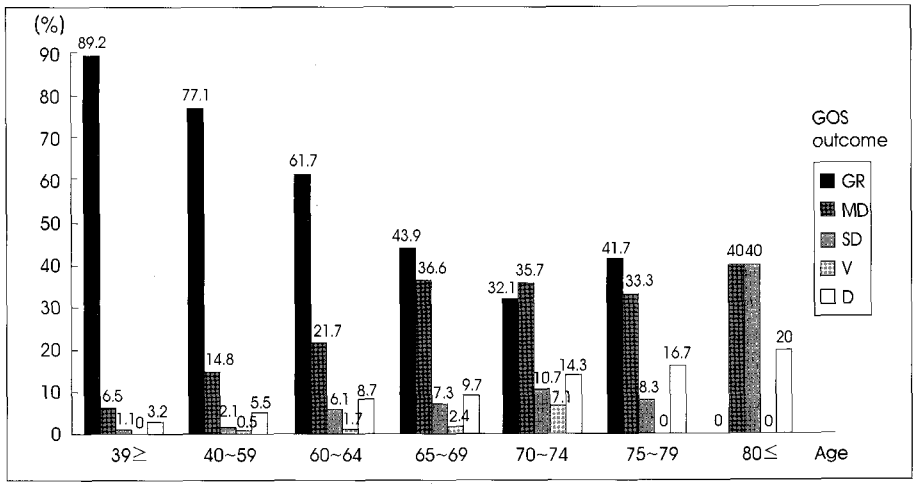

Fig. 4. Glasgow Outcome Scale of 754 patients.

Table 6. Causes of poor Glasgow Outcome Scale in 754 patients

		Good GOS	Poor GOS	*P-value*
Age	<60	474	38	
	60~64	96	19	
	65~69	66	16	< 0.001
	70~74	19	9	
	75≤	11	6	
H-H grade	I, II, III	627	70	< 0.001
	IV, V	39	18	
Fisher's grade	1, 2	451	40	< 0.001
	3, 4	216	47	
Vasospasm	−	516	51	< 0.001
	+	149	38	
Hydrocephalus	−	614	70	0.005
	+	47	23	
Pre-existing HTN	−	506	91	0.057
	+	136	21	

GOS : Glasgow Outcome Scale

poor H-H grade, postsurgical hydrocephalus, and the development of vasospasm did not contain 1, and thus they were observed to have a significant association with poor prognosis (Table 7).

Chi-square analysis revealed that the *p-value* of poor Fisher's grade was <0.001, and thus it was significant in the distribution of the incidence that may cause poor prognosis. Nevertheless, multi-variate logistic regression analysis results showed that its 95% CI contained 1, and thus a poor Fisher's grade did not independently contribute to poor prognosis.

Factors that may independently mediate an effect on poor prognosis in patients over 70 years of age

There were 45 patients in the over-70's patient groups where the confidence interval(CI) was over 1.0 statistically. It was examined whether the H-H grade, Fisher's grade, development of hydrocephalus, the presence of vasospasm, or the presence of the history of hypertension affected the prognosis, and an odds ratio was obtained by multi-variate logistic regression analysis. The 95% CI of the poor H-H grade as well as the development of hydrocephalus and vasospasm after surgery did not contain 1, and thus they were observed to be significantly associated with poor prognosis (Table 8).

Discussion

With a steady increase in the elderly proportion of the population, neurosurgeons are faced with increasing numbers of aged patients with AN SAH[11,20]. As a result of improvements in surgical and management techniques, the number of operations for AN SAH in elderly patients has increased, and good outcomes have been achieved in elderly patients[4,7,19,21,23]. However, unsatisfactory overall results have also been reported in elderly patients with AN SAH[10,11,14,24]. Lanzino et al.[14] concluded that age had a negative influence on the clinical outcome after AN SAH that was independent of other factors such as the clinical grade at admission, Fisher's grade, preexisting medical conditions, and the rebleeding rate. And other several studies have also found that the rate of poor outcomes after surgery for AN SAH increases with patient's age and that the risk of poor outcome is significantly increase

Table 7. Factors affecting poor outcome

		Odds Ratio (Relative Risk)	95% CI
Poor outcome (GOS)			
Age			
	60~64	1.79	0.94~3.39
	65~69	1.87	0.09~3.85
	70~74	2.72	1.04~7.09†
	75≤	4.67	1.56~13.89†
H-H Grade		2.51	1.47~4.29†
Hydrocephalus		1.93	1.93~3.64†
Vasospasm		1.83	1.02~2.84†
Fisher' s Grade		1.14	0.67~1.95
Pre-existing HTN		1.28	0.78~2.11

*Multi-variate logistic regression analysis, CI : Confidence Interval, †95% CI not contained 1 : factors independently contribute to poor prognosis

Table 8. Factors affecting poor outcome in 45 patients aged older than 70 years

	Odds Ratio (Relative Risk)	95% CI
Poor outcome (GOS)		
H-H Grade	2.64	1.56~4.49†
Hydrocephalus	1.93	1.93~3.64†
Vasospasm	1.88	1.14~3.10†
Fisher's Grade	1.2	0.72~2.07
Pre-existing HTN	1.045	0.29~3.85

*Multi-variate logistic regression analysis, CI : Confidence Interval, †95% CI not contained 1 : factors independently contribute to poor prognosis

in patients older than 60 years[13,24].

On the other hand, recent studies have reported that development of postoperative complications was not associated with age, and, to delay surgery or not to perform surgery due to age only, was not associated with poor prognosis[4,9,20,21]. Pinsker et al.[20] have insisted that advanced age dose not preclude successful surgery for ruptured aneurysm and most important factor for a good outcome was a good initial clinical status, though the majority of elderly patients presented with poor grades. And so, early surgical clipping and postoperative intensive care can attain a favorable outcome in a significant percentage of elderly patients[20]. Chung et al.[1,3] have also reported that in the analysis of the prognosis of 129 patients aged 70 or more, after surgery for AN SAH, the H-H grade 4 or 5 and Fisher's grade 3 or 4 at the time of admission were statistically significant factors with poor prognosis.

Like this, the question of whether increased age is a contraindication to surgery of AN SAH is still controversial. Therefore, we performed this retrospective study of 754 patients with AN SAH to define more clearly the relationships among age, baseline admission factors, and outcome in patients after AN SAH. Using a statistical model, we also tried to define the age limit after which rates of morbidity and mortality from SAH show a significant increase. In conclusion, we detected that age was not a statistically significant factor among patients below 70 years of age. But for those aged 70 and older, we observed that the age factor had a statistical value and might independently influence on poor prognosis.

As previously discussed, several factors contributing to an unfavorable outcome after AN SAH in elderly patients have been proposed[14], the primary brain damage and brain ischemia after AN SAH were more severe among elderly patients, the recovery ability after the primary damage and brain ischemia was markedly reduced, the incidence of rebleeding, hydrocephalus, and general complications in elderly patients was high, and morbidity due to diabetes, hypertension, etc. that may influence on AN SAH was also frequent[4,22]. And elderly patients were more likely to die or sustain a permanent neurological deficit from vasospasm. It is well known that cerebral blood flow(CBF) decreases with advancing age[17,18]. And elderly patients have a decreases cerebrovascular reserve. Additionally, SAH is also associated with impairment of the cerebrovascular reactivity (autoregulation) that normally prevents CBF from falling when cerebral perfusion pressure is reduced[8]. In such circumstances, elderly patients are more vulnerable because their CBF would have less far to fall before reaching the ischemic threshold. Additionally, in elderly patients, due to the overall cerebromalacia, the subarachnoid space and the cerebral ventricle are enlarged substantially, and with the increase of age, the ability to absorb the cerebrospinal fluid is limited greatly, therefore, in comparison with young age groups, hydrocephalus is developed more easily[4,22]. Actually, Ferch et al.[5] have reported that among AN SAH patients in their 80's and 90's who underwent surgery, hydrocephalus was developed in 44% of cases and thus the V-P (ventriculo-peritoneal) shunt was performed. Yoshioka et al.[27] have also reported that in the analysis of 576 AN SAH patients who underwent surgery, hydrocephalus was developed in 31% of the 289 cases that patients were in their fifties, 36% of the 69 patients between the age of 60 and 69, and 55% of the 118 patients aged 70 or older.

Recently, some authors have reported that there is no evidence for an age related contraindication of early AN SAH surgery[11,16] and there is convincing evidence that early surgery can be performed in elderly patients as safely as in younger patients[6,11,12,26]. There are several theoretical reasons that support early surgery in elderly patients[15] : the rebleeding rate increases with advancing age; elderly patients are more likely to experience intraventricular hemorrhage and acute hydrocephalus (both amenable to treatment with early intervention); and as previously discussed, elderly patients are at high risk for symptomatic vasospasm. When vasospasm occurs, it can be more aggressively treated with hyperdynamic therapy if the aneurysm has been secured. Although caution has to be exercised with patients over 70 years of age, there is convincing

evidence that early surgery can be performed in elderly patients as safely as in younger subjects[6,11,26]. For these reasons, Laidlaw et al.[12] pointed out that aggressive, early treatment is likely to benefit in elderly AN SAH patients, the potential benefit being greater for poor grade elderly patients. Our study showed that poor prognosis in elderly patients between 60 and 70 years of age, was significantly associated with only poor H-H grade, development of vasospasm, and hydrocephalus after surgery. We thought that in this group, age itself should not to be used as a criteria for denial of treatment and aggressive treatment should be carried out to improve the prognosis of AN SAH. And besides poor H-H grade, development of vasospasm, and hydrocephalus after surgery, age factor was strongly related to predict outcome in elderly patients over 70 years of age. Thus performing aggressive surgical treatment is a difficult decision, and so we suppose that the treatment plans should be decided according to the condition of patients in this group.

Conclusion

According to the postoperative analysis of 754 AN SAH patients at our hospital. Poor H-H grade, development of vasospasm, and hydrocephalus after surgery were significantly associated with poor prognosis among elderly patients as well as young patients. In patients under the age of 70, the age factor was not statistically significantly associated with poor prognosis. On the other hand, in patients over 70 years of age, age factor was a significant relationship with poor prognosis, in addition to the poor H-H grade, the development of hydrocephalus and symptomatic vasospasm. We suggest that advanced age (under the age of 70) dose not preclude adequate surgical treatment in patients with AN SAH and we should be also alert to preventable causes of delayed neurological deterioration for improving the outcome in all elderly groups.

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