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Clinical Article

Aneurysmal Subarachnoid Hemorrhage in Third and Fourth Decades of Life

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Objective : The aim of this study was to compare clinical characteristics of ruptured aneurysms in young adults, of the third and fourth decades of life, and to compare several clinical characteristics affecting the outcome of patients.
Methods : We retrospectively investigated 1459 patients who underwent surgery and endovascular treatment for ruptured cerebral aneurysms from June 1992 to December 2010 and compared clinical characteristics. We also reviewed pre-existing medical conditions and perioperative complications.
Results : Among 1459 patients, there were 21 patients (1.44%) in the third decade and 104 patients (7.13%) in the fourth decade of life. Within two age groups, 88 (70.4%) were male and 37 (29.6%) were female, a ratio of 2.37 : 1. In both groups, we observed the anterior cerebral artery (ACA) aneurysm with the most frequency (p=0.028). In general, favorable outcome was achieved in both age groups (90.5% and 81.7%, respectively). An initial univariate analysis showed Hunt-Hess grade, Fisher grade, location of aneurysm, and rebleeding significantly associated with outcome after aneurysm rupture. Further, multivariate analysis demonstrated that only Hunt-Hess grade (grade 4-5) was a risk factor for the outcome (odds ratio=9.730, 95% confidence interval 2.069-45.756, p=0.004).
Conclusion : The incidence of subarachnoid hemorrhage (SAH) was higher in the male population of the third and fourth decades of life. Aneurysms on the ACA were most frequently occurred in both age groups and the outcome of aneurysmal SAH among the third and fourth decades was favorable. Multivariate analysis revealed that high Hunt-Hess grade was a risk factor for patient's outcome.

Key Words : Aneurysm · Subarachnoid hemorrhage · Young adult.

INTRODUCTION

Subarachnoid hemorrhage (SAH) accounts for 10% of stoke and 20% of hemorrhage stroke, with an incidence of 10 in 100000 each year[15]. Aneurysmal SAH in patients younger than 40 years of age is uncommon[11,33]. However, its incidence in young adults has recently increased[31]. Although the etiologic and prognostic features that characterize SAH in the middle aged and elderly may not apply to young adults. We undertook a study of a series of young adult patients who were surgically and endovascularly treated for ruptured cerebral aneurysms. We compared the clinical features between patients in the third and fourth decades of life with published reports and compared several clinical characteristics affecting the outcome in patients. In addition, risk factors for unfavorable outcome were also assessed.

MATERIALS AND METHODS

Patients and methods

We retrospectively reviewed the medical records of 1652 patients with SAH who were treated from June 1992 to December 2010. Among those 1652 patients, 1459 patients were treated for ruptured aneurysms. Patients with unruptured, traumatic, and mycotic aneurysms were excluded from this study. The analysis focused on young adult patients aged from 20 to 39 years of age. We compared those in the third decade of life with those in the fourth decade, while comparing several clinical characteristics, including sex, Hunt-Hess grade, Fisher grade, size, location of aneurysm, multiplicity and outcome. We also reviewed pre-existing medical conditions (previous history of hypertension) and perioperative complications (rebleeding, vasospasm). The locations of aneurysm were classified into four

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groups : internal carotid artery (ICA), anterior cerebral artery (ACA), middle cerebral artery (MCA) and vertebrobasilar artery (VBA). Aneurysms were also divided into three groups based on their diameters : small (<10 mm), large (10-25 mm), and giant (>25 mm). The patient's outcome at discharge was categorized according to the Glasgow Outcome Scale (GOS), as a favorable outcome (good recovery and moderate disability) or an unfavorable outcome (severe disability, vegetative state and death). We compared several clinical characteristics affecting the outcome of the enrolled patients, including sex, age, previous history of hypertension, Hunt-Hess grade, Fisher grade, size, location and multiplicity of aneurysm, rebleeding and lastly, vasospasm.

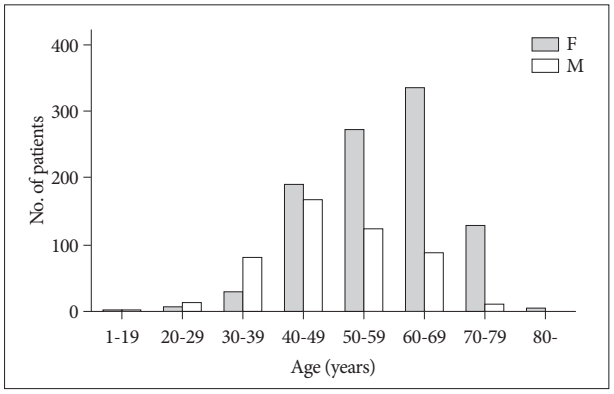

Fig. 1. Bar graph showing the age and sex distributions of 1459 patients who were surgically and endovascularly treated for aneurysmal subarachnoid hemorrhage.

Statistical analysis

All data are presented as a mean value±standard deviation. Differences between patient's groups were tested via univatiate analysis using t-test, chi-square test, or Mann-Whitney U test, as appropriate. Logistic regression was used to derive odds ratios (OR) for multilevel categorical variables. Multivariate models were adjusted for age, gender, hypertension or not, Hunt-Hess grade, Fisher grade, size and location of aneurysm, multiplicity, rebleeding, and vasospasm. All analyses were performed using Predictive Analytics SoftWare Statistics 18.0. A 2-tailed probability value of <0.05 was considered to be statistically significant.

Table 1. Characteristics of patients and aneurysms in young adults in the third and fourth decades of life who were surgically and endovascularly treated for aneurysmal subarachnoid hemorrhage

Clinical characteristics	No. of patients (%)		*p*-value
	Third decade	Fourth decade	
Male	14 (66.7)	74 (71.2)	0.681*
Previous history of hypertension	2 (9.5)	22 (21.2)	0.217*
Hunt-Hess grade			0.491*
1	4 (19.0)	26 (25.0)	
2	11 (52.4)	35 (33.7)	
3	1 (4.8)	14 (13.5)	
4	3 (14.3)	21 (20.2)	
5	2 (9.5)	8 (7.7)	
Fisher grade			0.504*
1	3 (14.3)	7 (6.7)	
2	6 (28.6)	25 (24.0)	
3	4 (19.0)	33 (31.7)	
4	8 (38.1)	39 (37.5)	
Size of aneurysm			0.834*
Small	17 (81.0)	87 (83.7)	
Large	4 (19.0)	16 (15.4)	
Giant	0 (0)	1 (1.0)	
Location of aneurysm			0.028†
ICA	6 (28.6)	17 (16.3)	
ACA	12 (57.1)	48 (46.2)	
MCA	3 (14.3)	30 (28.8)	
VBA	0 (0)	9 (8.7)	
Multiplicity	2 (9.5)	14 (13.5)	0.622*
Rebleeding	5 (23.8)	12 (11.5)	0.135*
Vasospasm	3 (14.3)	20 (19.2)	0.594*
Favorable outcome	19 (90.5)	85 (81.7)	0.328*

*Chi-square test, †Mann-Whitney U-test. ICA : internal carotid artery, ACA : anterior cerebral artery, MCA : middle cerebral artery, VBA : vertebrobasilar artery

RESULTS

From June 1992 to December 2010, 1459 patients were surgically and endovascularly treated for aneurysmal SAH. From which, 973 were female and 486 were male. The age and sex distributions of the patients with aneurysmal SAH are shown in Fig. 1. The mean age of the patients was 54.9±11.6 years (ranged from 14 to 86). The mean age of the female patients (58.0±10.7) was higher than that of the male patients (48.9±11.1). Among the 1459 patients, there were 21 patients (1.44%) in the third decade of life [20-29 years (26.3±2.7)] and 104 patients (7.13%) in the fourth decade of life [30-39 years (35.5±2.9)]. Within the third and fourth decade age group, 88 (70.4%) were male and 37 (29.6%) were female, a ratio of 2.37 : 1 (p=0.001). Mean follow up rate in two age groups was 41 months (ranged from 0 to 206) and 30-day mortality after ictus was 12.8%.

The age, Hunt-Hess grade, Fisher grade, size of aneurysm, rebleeding, vasospasm and outcomes did not differ significantly between the two age groups. And the distribution of ruptured aneurysms did not also significantly different between the two age groups. Aneurysms on the ACA and ICA were prevalent in

the third decade and aneurysms on the ACA and MCA were prevalent in the fourth decade of life. In particular, ACA aneurysms occurred with the greatest frequency in both age groups (57.1% in third decade and 45.8% in fourth decade) (p=0.028) (Table 1).

Favorable outcome rate for third and fourth decade were 90.5% and 81.7%, respectively (Table 2). An initial univariate analysis showed Hunt-Hess grade, Fisher grade, location of aneurysm, and rebleeding which significantly associated with outcome after aneurysm rupture (Table 2). A multiple logistic regression analysis demonstrated that only high Hunt-Hess grade (grade 4-5) was a risk factor for outcome, with an adjusted OR of 9.730 and confidence interval between 2.069 and 45.756 (p=0.004) (Table 3).

DISCUSSION

Aneurysmal SAH among young adults is rare[1,30]. Sixty percent of aneurysms are diagnosed in patients between 40 and 60 years of age, with 10 to 20% found in patients younger than 40 years of age[1]. Previously, it was reported that the prevalence of aneurysmal SAH in young adults ranged from 5.3% to 18.4%[4,9,11,17,22]. In our study, the prevalence was 8.57% (125/1459), which was not significantly different from the previous studies.

In general, it has long recognized that cerebral aneurysm occur more frequently in females than in males[10,16,25]. It has been reported that aneurysms in infants and children have different distributions from those seen in adults[2,11]. Further, a male predominance in young children with SAH has been reported in previous studies[3,9,19,20,33]. In our study, male dominance was observed during both the third and fourth decades of life and the incidence of female aneurysmal SAH progressively increases with age. In contrast, some authors have reported that incidence is higher in female young adults[11,17]. This discrepancy may reflect the fact that intracranial aneurysm formation and growth is associated with multiple factors in young adults[22].

Aneurysms on the ACA and ICA were prevalent in the third decade and aneurysms on the ACA and MCA were prevalent in the fourth decade of life. Especially, ACA aneurysms were most frequent in these age groups in our study. Previous authors[8,19,20,23] have noted that a vast majority of ruptured aneurysms in children and adolescents occur in the anterior circulation, especially in the ICA. The ICA has a blood flow much greater than the anterior communicating artery and MCA. Such flow may exert intense hemodynamic stress on the

Table 2. Clinical characteristics of patients with aneurysmal subarachnoid hemorrhage by outcome

Clinical characteristics	No. of patients (%)		p-value
	Favorable outcome	Unfavorable outcome	
Sex			0.524*
Male	72 (69.2)	16 (76.2)	
Female	32 (30.8)	5 (23.8)	
Decade			0.328*
Third	19 (18.3)	2 (9.5)	
Fourth	85 (81.7)	19 (90.5)	
Previous history of hypertension	18 (17.3)	6 (28.6)	0.232*
Hunt-Hess grade			0.000*
1	28 (26.9)	2 (9.5)	
2	46 (44.2)	0 (0)	
3	12 (11.5)	3 (14.3)	
4	14 (13.5)	10 (47.6)	
5	4 (3.8)	6 (28.6)	
Fisher grade			0.001*
1	10 (9.6)	0 (0)	
2	29 (27.9)	2 (9.5)	
3	34 (32.7)	3 (14.3)	
4	31 (29.8)	16 (76.2)	
Size of aneurysm			0.073*
Small	88 (84.6)	16 (76.2)	
Large	16 (15.4)	4 (19.0)	
Giant	0 (0)	1 (4.8)	
Location of aneurysm			0.031*
ICA	18 (17.3)	5 (23.8)	
ACA	55 (52.9)	5 (23.8)	
MCA	26 (25.0)	7 (33.3)	
VBA	5 (4.8)	4 (19.0)	
Multiplicity	14 (13.5)	19 (90.5)	0.622*
Rebleeding	10 (9.6)	7 (33.3)	0.004*
Vasospasm	16 (15.4)	7 (33.3)	0.053*

*Chi-square test. ICA : internal carotid artery, ACA : anterior cerebral artery, MCA : middle cerebral artery, VBA : vertebrobasilar artery

Table 3. Multivariate Logistic Regression Model results

Clinical characteristics	p-value	Adjusted OR	95% confidence interval	
			Lower	Upper
Hunt-Hess grade (grade 4-5)	0.004	9.730	2.069	45.756
Fisher grade	0.483	1.398	0.547	3.572
Size	0.531	1.038	0.923	1.168
Location	0.580	0.821	0.407	1.653
Rebleeding	0.529	1.546	0.399	5.996

OR : odds ratio

arterial walls and thus, result in the formation of an aneurysm and rupture. Controversy exists concerning whether there is a difference in the location of ruptured aneurysms among different age groups[14,28]. Although the causes of these differences in the location of ruptured aneurysms between childhood and young adults are uncertain, there is one hypothesis. Padget[21] proposed that in the anterior circulation, the development of the ICA is followed by that of the ACA and eventually, by that of the MCA. Thus, it is possible that a fragile, congenital portion of the ICA may develop into an aneurysm due to hemodynamic stress. Further, the development of an ACA aneurysm may take a longer time than the time for an ICA lesion to grow. We agree with this hypothesis, but further studies and investigations about the causes of these differences in the location of ruptured aneurysms among different age groups are needed in the future.

The mortality rate for SAH in the 1966 cooperative Study on Intracranial Aneurysms was 50% at 29 days[27] and 33% in a recent analysis of in-hospital deaths among SAH patients admitted through an emergency department[6]. In a population-based study by Broderick et al.[2], the 30-day mortality rate among all patients who suffered SAH was 45%, with the majority of deaths occurring in the first days after SAH. The most important determinants of 30-day survival have been previously elucidated as initial neurological status and age[18]. Outcome is reported to be poor in female patients. In addition, old age is also reported to be a strong predictor of poor outcome[5,7,26]. Outcomes of aneurysmal SAH among young adults are generally favorable[11,12,33]. Outcome results from previous studies were compatible with our results. Among 125 patients, 104 (83.2%) had a GOS better than 3 (90.5% in third decade and 81.7% in fourth decade). Further, when perioperative complications (rebleeding, vasospasm) did not occur, patient's outcome was more favorable. Chang et al.[4] reported that young patients usually present with a good neurological status and thus, have lower incidences of intraventricular hemorrhage, hydrocephalus, symptomatic vasospasm, and other underlying medical problems. Therefore, these young patients have a relatively good outcome.

Location of aneurysm is associated with mortality. The mortality at 6 months in conservatively treated patients was 34% to 39% after rupture of an anterior circulation aneurysm. Mortality at 6 months in patients with multiple aneurysm approached 50% and was higher in those with aneurysm arising from the posterior circulation, 61%[32]. Schievink et al.[29] reported that survival was greatly dependent on the location of the aneurysm and the prognosis of ruptured posterior circulation aneurysm is poor. In our study, aneurysms arising from VBA had more unfavorable outcome (p=0.031).

In addition to aneurysm location, clinical grade on admission is also associated with mortality. Winn et al.[32] reported that clinical grade on admission and mortality during the first 6 months after the initial hemorrhage showed a strong statistical correlated. This association was subsequently confirmed in a study by Phillips et al.[24] and more recently by Lagares et al.[13]. In our study, when Hunt-Hess grade was low, Fisher grade was low, and thereby, patient's outcome was more favorable. In addition, multivariate analysis demonstrated that only high Hunt-Hess grade (grade 4-5) showed a risk factor for outcome [OR, 9.730 (confidence interval, 2.069 to 45.756)]. Thus, level of consciousness following SAH strongly influenced patient's outcome.

The limitation of this study is being a retrospective review and patient's data were collected from only one institution. A large prospective multicenter study about aneurysmal SAH of young adult will be necessary in the future.

CONCLUSION

The incidence of SAH was higher in the male population in the third and fourth decades of life. Aneurysms on the ACA were most frequent in these age groups. Outcome of aneurysmal SAH among the third and fourth decades was favorable. Multivariate analysis revealed that high Hunt-Hess grade was a risk factor for patient's outcome.

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