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Original Article

The Relationship Between Subarachnoid Hemorrhage Volume and Development of Cerebral Vasospasm

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Objective : The objective of this study is to verify the relationship between subarachnoid hemorrhage (SAH) volume (not Fisher grade) and development of cerebral vasospasm prospectively.

Methods : Patients who visited our hospital with a diffuse or localized thick subarachnoid blood clot seen on computed tomography (CT), taken within 48 hours after SAH and the aneurysm was confirmed by CT Angiogram (CTA) from March 2010 to July 2011 were enrolled in this study. CTA was checked at least twice after admission. Angiographic vasospasm (AVS) on CTA was defined as irregularity or narrowing of intracranial vessels on follow up CTA compared with initial CTA. Total intracranial hemorrhage (ICH) volume (subdural, SAH, intracerebral and intraventricular) was calculated and SAH volume (all supratentorial and infratentorial cisterns) was also calculated using the MIPAV software package.

Results : A total of 55 patients were included in our study. Thirty six patients did not show AVS on CTA or clinical deterioration (non vasospasm group: NVS). AVS without ischemic neurologic symptoms was observed in four patients and development of symptomatic vasospasm (SVS), defined as AVS with ischemic symptoms, was observed in 15 patients. SAH volume in SVS patients was statistically larger than that in NVS patients ($p < 0.05$). Total ICH volume in SVS patients was larger than that in NVS patients. However, the difference was not statistically significant.

Conclusion : Results of this study indicate an association of development of vasospasm with the SAH volume, not intracranial hemorrhage.

Keywords Subarachnoid hemorrhage, Hemorrhage volume, Vasospasm

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INTRODUCTION

Subarachnoid hemorrhage (SAH) from a ruptured intracranial aneurysm is a devastating disease with a high rate of mortality and morbidity.[1] Apart from the potentially disastrous effects of the initial hemorrhage and rebleeding from the ruptured aneurysm, cerebral vasospasm is a major contributor to death and disability after SAH.

Some risk factors associated with development of cerebral vasospasm have been reported.[6] Among those, a strong association of patients with higher Fisher grade on the initial computed tomography (CT) scan with development of a cerebral vasospasm has been demonstrated.[1)4)7)19)] However, the measurements used in the scale are increments displayed on printed CT scans, which have no relationship to the real clot thickness.[11] Therefore, volumetric analyses of blood in SAH patients are necessary and have been previously reported by some authors.[4)11)15)18)19)] However, pre-

vious studies did not show which component of intracranial hemorrhage (ICH), between total ICH volume and total SAH volume, was really associated with development of cerebral vasospasm. In addition, those studies were retrospective.

Therefore, the main goal of this prospective study is to verify the relationship between total ICH volume and SAH volume shown on the initial CT scan and development of cerebral vasospasm.

MATERIALS AND METHODS

Patient population

In this study, we enrolled patients who visited our hospital with a diffuse or localized thick subarachnoid blood clot on the initial CT scan taken within 48 hours after spontaneously ruptured aneurysmal SAH and were confirmed as having an aneurysm by CT angiogram (CTA) from March 2010 to July 2011. All of the patients were checked for brain CT scans soon after their arrival at the emergency room, as well as a follow-up brain CT after their operations. The follow-up CTA was checked at least twice (from four to nine days and ten days after SAH) after admission.

A total of 156 patients with aneurysmal SAH visited during this period. Patients were excluded from the study if: (1) they were comatose, (2) they were considered unlikely to survive for more than two weeks, (3) they were not checked in the follow-up CTA at least twice for angiographic vasospasm, (4) they were treated by coiling. A total of 101 patients were excluded from this study. Thus, 55 patients were enrolled for this analysis, and their demographic and clinical data were collected.

Definition of cerebral vasospasm

Angiographic vasospasm is defined as diffuse or focal narrowing of an artery compared to initially checked CTA without development of ischemic neurological symptoms. Symptomatic vasospasm is defined by the following combined clinical and radiological criteria: 1) clinical deterioration (confusion, disorientation, and/or decreasing the level of consciousness) within four to 12 days after SAH: 2) brain CT scan excluding other causes of neurological worsening such as intracranial hemorrhage, brain swelling, and hydrocephalus: 3) no evidence of electrolyte disturbance, seizures or hypoxia: 4) confirmation of vasospasm by CTA.[5)]

Vasospasm on CTA was defined as irregularity or narrowing of intracranial vessels on follow up CTA, compared with initial CTA. Maximum Intensity Projection (MIP) images were used for evaluation of vessels.

Clinical management

All patients were treated by surgical clipping of the aneurysmal sac without cisternal drainage. After surgical clipping of the ruptured aneurysmal sac, all patients were treated with prophylactic administration of intravenous fluids in order to maintain normovolemia, normotension and hemodilution with isotonic crystalloid as well as continuous intravenous injection of nimodipine for 0.5 μg/kg/min from day four to day 14 after SAH. Patients who showed symptomatic vasospasm were treated with hypertensive, hypervolemic, and hemodilution therapy (triple H therapy). If vasospasm symptoms persisted and more aggravated vasospasm was observed on follow-up CTA, balloon or pharmacological angioplasty was performed.

Classification of patients

Patients were divided into three groups according to existence of vasospasm: No vasospasm group (NVS), patients who did not experience vasospasm during the hospitalization period; Angiographic vasospasm group (AVS), patients who did not experience symptomatic vasospasm but angiographic vasospasm; Symptomatic vasospasm (SVS), patients who experienced clinical deterioration with evidence of angiographic vasospasm on CTA.

Volumetric quantification[4)]

Nonenhanced images in initial CT scan obtained

from selected patients were retrieved from the institution's digital archive system and stored on a SOMATOM Workstation (Sun Microsystems, Inc., Mountain View, CA). Each CT study comprised contiguous 5-mm-thick images obtained through the skull base and top of the head. Software-based volumetric quantification was performed on admission CT scans by a single examiner blinded to clinical information. MIPAV software package (Medical Image Processing, Analysis, and Visualization, version 5.2.1; National Institutes of Health) was used for analysis of CT scans. We used a CT number in the range of 50-80 Hounsfield units.

The SAH volume contained an interhemispheric fissure, both sylvian fissure, suprasellar cistern, bilateral basal sylvian cistern, interpeduncular, and ambient cistern.

Total ICH volume contained SAH volume plus subdural, intracerebral, and intraventricular hemorrhage volume.

Statistical analysis

Comparisons of demographic variables including age, sex, size and location of aneurysm among the groups were performed using χ^2 test and One-way analysis of variances. Values of $p < 0.05$ were considered significant. Statistical Package for the Social Sciences (SPSS) statistical package for Windows (version 19.0 : IBM, Chicago, IL) was used for all statistical analyses.

RESULTS

General characteristics of SAH patients and incidence of vasospasm:

Male to female ratio was 18:37. Mean age was 57.65 ± 3.9 years. Mean aneurysmal size was 5.5 ± 0.65. In 26 cases (47.2%), the aneurysm was located in the anterior communicating artery (AcomA), in 14 cases (25.5%), it was located in the middle cerebral artery (MCA), and, in 15 cases (27.3%), it was located in the internal carotid artery (ICA).

Thirty six patients neither showed AVS nor developed SVS. SVS was observed in 15 patients (AcomA aneurysm: ten cases, MCA aneurysm: three cases, ICA aneurysm: two cases), and development of AVS was observed in only four patients (AcomA aneurysm: one case, MCA aneurysm: three cases).

The relationship between intracranial hemorrhage volume and development of vasospasm

The calculated total intracranial hemorrhage volume of each group was 11.58 ml in NVS, 16.25 ml in AVS, and 22.27 ml in SVS. The calculated SAH volume in each group was 9.50 ml in NVS, 14.00 ml in AVS, and 17.67 ml in SVS.

In SAH volume, a statistically significant difference was only observed between NVS and SVS and no other intergroup difference (AVS-SVS and NVS-AVS) was found in post hoc analysis. ($p < 0.05$)

Age, sex, location of aneurysm, aneurysmal size, and total ICH volume were not associated with devel-

Table 1. General characteristics of the three study groups

	No vasospasm(NVS)	Angiographic vasospasm(AVS)	Symptomatic vasospasm(SVS)	*p* value*
Number	37	4	15	
Age(years)	56.11 ± 5.33	50.75 ± 13.77	63.20 ± 5.88	0.064
Sex(M:F)	13:24	3:1	2:12	0.145
Aneurysmal Size(mm)	5.64 ± 0.75	3.75 ± 1.52	5.67 ± 1.70	0.269
Location				
AcomA	15	1	10	
MCA	8	3	3	
ICA	13	0	2	
Total ICH volume	11.58 ± 3.12	16.25 ± 19.89	22.27 ± 7.25	0.07
SAH volume	9.50 ± 2.57	14.00 ± 18.28	17.67 ± 5.18	0.006

M = male; F = female; AcomA = anterior communicating artery; MCA = middle cerebral artery; ICA = internal carotid artery; ICH = intracranial hemorrhage; SAH = subarachnoid hemorrhage

opment of vasospasm (Table 1).

DISCUSSION

Cerebral vasospasm is a major contributor to death and disability after SAH. Poor clinical grade (related to more severe hemorrhage), age and cigarette smoking have been reported as independent risk factors for symptomatic vasospasm.[5)6)8)9)13)14)22)]

Among many risk factors for vasospasm, we focused on hemorrhage volume. Patients with higher Fisher grade on initial CT scan are known to have a strong association with development of cerebral vasospasm. However, it was qualitative because Fisher grade was based on the thickness of the hemorrhage clot at the subarachnoid space on CT scan.

Some quantitative trials have been reported in the literature.[1)4)5)11)14)] However, those trials had some limitations in the following respects. First, between total ICH volume and SAH volume, they did not show which one was really associated with development of cerebral vasospasm.[5)14)] Second, some studies only included patients with Fisher grade 3.[4)11)] Third, no study of a single modality treated group was conducted.

There is no consensus regarding the relationship of development of vasospasm depending on the treatment modality – endovascular coiling of the aneurysmal sac and surgical clipping of the aneurysmal neck for ruptured intracranial aneurysm. Therefore, in order to reduce the potential for selection bias, we studied patients who were treated only by surgical clipping regardless of the Fisher grade.

In order to check vasospasm, we used only CTA without using transcranial Doppler ultrasonography (TCD) and catheter angiography. It is obvious that checking of vasospasm using only CTA has some limitations: 1) There are some technical artifacts caused by contrast injection time and contrast dosage 2) CTA cannot detect mild vasospasm of distal arteries. However, TCD also cannot detect mild vasospasm of distal arteries. In addition, CTA is less expensive and less invasive than catheter angiography. Therefore, despite some limitations, CTA can be used as a reliable method to check vasospasm of cerebral vessel after aneurysmal SAH.[2)]

In volumetric analysis using CT scans, the setting of the CT number of the hemorrhage is very important. Previous study about Hounsfield Unit (HU) reported brain parenchyma (all gray and white matter) CT numbers ranging from 25-40 HU.[16)21)] Therefore, in our analysis, we adopted CT number of hemorrhage from 50-80 HU.

Reilly et al.[7)] studied the relationship between the SAH grade as classified on the Fisher grade, the initial clot volume, initial clot density, and percentage of clot cleared per day and development of vasospasm. They demonstrated that initial clot volume and percentage of clot cleared per day was a significant predictor of vasospasm, whereas Fisher grade and initial clot density were not.

Friedman et al.[4)] calculated subarachnoid hemorrhage volume in patients with Fisher Grade 3 aneurysmal SAH and investigated the relationship between SAH volume and the development delayed ischemic neurological deficit (DIND) caused by vasospasm. They concluded that a larger volume of SAH volume on an admission CT scan is highly associated with development of DIND.

Some authors[1)21)] have reported an association of intraventricular hemorrhage, especially hemorrhage in the lateral ventricle, with development of vasospasm. Therefore, we studied the relationship between total ICH volume and SAH volume and development of cerebral vasospasm. In our study, total ICH volume appeared to be associated with development of vasospasm. However, SAH volume had stronger relevance to development of angiographic and symptomatic vasospasm. A difference in mean value of SAH volume was observed between the two groups (angiographic vasospasm group and symptomatic vasospasm group), however, there was no statistical significance. We thought that this was due to the small number of cases of angiographic vasospasm.

We studied the relationship of incidence of vaso-

spasm and aneurysm location. In our study, AcomA area ruptured cases were largest in the general population and in the vasospasm group. However, no statistical relevance was found between incidence of vasospasm and aneurysm location.

All symptomatic vasospasms occurred within four to nine days after ictus. However, date of occurrence of vasospasm was not associated with SAH volume.

Some studies have reported an association of other factors - aneurysm size, age, etc. – with development of cerebral vasospasm.[6)20)] However, in our study, there was no association with development of cerebral vasospasm and those factors.

There are some limitations in our study. First, our study was a single center study. Second, the patient population enrolled in this study was too small for establishment of a cut-off volume. Third, the number of cases of angiographic vasospasm (only four cases) included in this study was too small.

CONCLUSION

In our study, development of symptomatic vasospasm was associated with SAH volume not total intracranial hemorrhage volume.

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