Size Ratio: A Morphological Factor Predictive of the Rupture of Cerebral Aneurysm?

Meihua Li, Zhiqun Jiang, Huiqiang Yu, Tao Hong

ABSTRACT: ***Background:*** Determining factors predictive of the natural risk of rupture of cerebral aneurysms is difficult. We studied morphological factors associated with rupture in a study model of patients with mirror location intracranial aneurysms, one aneurysm that had ruptured and one that had not, each patient served as their own control attempting to eliminate confounding variables. ***Methods:*** We collected five one-dimensional measurements and four two-dimensional indices from three-dimensional rotational digital subtraction angiography images of patients in the proposed study model and explored their correlation with aneurysm rupture. Parameters were analyzed with a paired Student's t test for significance and significant parameters were further examined by multivariate conditional logistic regression analysis. ***Results:*** Fifty-two patients with 52 pairs of intracranial aneurysms in a mirror location were studied. The maximum perpendicular height, neck diameter, maximum width, maximum height, aspect ratio, size ratio, and bottleneck factor were significantly associated with ruptured aneurysms on bivariate analysis. A logistic regression analysis showed that only size ratio,which was defined as the ratio of the maximal height to parent artery average diameter, is independently correlated with ruptured intracranial aneurysms. ***Conclusions:*** In a case-control study of patients with mirror location intracranial aneurysms, size ratio was identified as the unique morphological factor associate with the rupture of cerebral aneurysms.

RÉSUMÉ: Rapport de taille : un facteur morphologique de prédiction de la rupture d'un anévrisme cérébral? ***Contexte :*** Il est difficile de déterminer les facteurs de prédiction du risque naturel de rupture des anévrismes cérébraux. Afin de tenter d'éliminer les variables confondantes, nous avons étudié les facteurs morphologiques associés à leur rupture chez des patients porteurs d'anévrismes intracrâniens symétriques, en miroir, dont un anévrisme qui s'était rompu et l'autre non, et chaque patient était son propre témoin. ***Méthode :*** Nous avons recueilli 5 mesures unidimensionnelles et 4 indices bidimensionnels d'images angiographiques par soustraction digitale rotatoire 3D chez ces patients et nous avons examiné leur corrélation à la rupture d'anévrismes. Les données pairées ont été analysés au moyen du test de student et les paramètres dont la valeur statistique était significative ont été examinés par une analyse de régression logistique conditionnelle multivariée. ***Résultats :*** Cinquante-deux patients porteurs de 52 paires d'anévrismes intracrâniens localisés en miroir ont été étudiés. À l'analyse bivariée, la hauteur perpendiculaire maximale, le diamètre du col, la largeur maximale, la hauteur maximale, le rapport hauteur/largeur, le rapport de taille et le facteur goulot d'étranglement étaient associés de façon significative à la rupture des anévrisme. Une analyse de régression logistique a montré que seulement le rapport de taille défini comme étant le rapport de la hauteur maximale au diamètre moyen de l'artère hôte était corrélé de façon indépendante à la rupture des anévrismes intracrâniens. ***Conclusions :*** Dans cette étude cas-témoin de patients porteurs d'anévrismes intracrâniens symétriques, en miroir, le rapport de taille a été identifié comme étant le seul facteur morphologique associé à la rupture des anévrismes cérébraux.

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Intracranial aneurysms are common. The overall frequency in the general population ranges from 0.2% to 9% (mean frequency, about 5%) in autopsy studies.[1,2] However, despite their common occurrence, only 1% of all intracranial aneurysms actually rupture.[2] Recent advances in noninvasive neuroimaging technologies, such as magnetic resonance angiography and three-dimensional computed tomography (CT), have increased the likelihood of detecting an unruptured intracranial aneurysm. The treatment of asymptomatic unruptured intracranial aneurysms has been the subject of a great deal of debate in the neurosurgical community. Therefore, it is very important to be able to predict accurately the status of an aneurysm so that neurosurgeons can target interventions to those with the greatest risk of rupture.

Aneurysm location, size[3,4] and morphology[5-7] are well-recognized risk factors in predicting aneurysm rupture. Other factors,[5,8] such as cigarette smoking, familial preponderance, hypertension, female sex, connective tissue disorder, aneurysm growth rate, and presence of multiple intracranial aneurysms are also believed to be important risk factors associated with subarachnoidal hemorrhage (SAH). However, there is little consensus regarding a threshold value at which to treat these aneurysms. These previous rupture risk studies[3-13] had many

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critical drawbacks, in which ruptured aneurysms in a cohort of patients were compared with unruptured aneurysms in a separate cohort of patients. This allows for significant confounding variables between the two different cohorts of patients. Therefore,it is difficult to eliminate confounding variables in studying the rupture risk of aneurysms. Consequently, the comparison would be less distinct than the actual situation. There has been no available information regarding a decisive factor associated with aneurysm rupture.

In the current study, we have chosen to study patients with mirror location intracranial aneurysms in which a control unruptured aneurysm was present in each patient - an ideal study model, in which the differences between ruptured and unruptured aneurysms are limited to morphological variables such as size, shape, and aneurysm-to- parent vessel size ratio. To our knowledge, this represents the first attempt at verifying purely morphological parameters of aneurysm and its parent vessel for rupture risk assessment in a separate cohort of patients with mirror location intracranial aneurysms.

Methods and Materials

We reviewed a clinical database of Department of Neurosurgery, the first affiliated hospital of Nanchang University (Nanchang, China) from January 2008 through April 2012 for patients with mirror location cerebral aneurysms, of which one aneurysm had ruptured and the other had not ruptured. The ruptured aneurysm was identified at the time of surgery by direct observation and correlated with the hemorrhage pattern on CT scan. All patients underwent three-dimensional (3D) digital subtraction angiography (DSA). All 3D images were collected and examined for suitability to be included in the study. We could only include cases in which the rotational angiographic images were of sufficient quality for accurate segmentation and reconstruction. Two investigators (JZ and HT), who did not have knowledge of the aneurysm-related clinical results, reviewed all imaging studies in a blinded fashion and performed the measurements. Approval for the collection and review of data was obtained from the Institutional Review Board at Nanchang University.

The 3D angiography images were obtained with a Toshiba Infinix VFi/BP frontal C-arm system (Toshiba America Medical Systems, Inc., Tustin, CA), 3D reconstruction in surface-triangulation format and isolation of the region of interest (intracranial aneurysm (IA) plus adjacent vessels) were performed using in-house software based on the open-source Visualization Tool Kit libraries. The 3D intracranial aneurysms and parent vessel geometries were analyzed to provide the various morphology parameters.

We investigated nine morphology parameters (Figure) adapted from parameters that have previously been described for cerebral aneurysms[5,9,11,12,14]. The following one-dimensional measurements were collected: 1. the maximum perpendicular height of the intracranial aneurysm (H), 2. neck diameter (Dneck), 3. maximum width (Dmax width), 4. the maximum height (Hmax): The maximum height is not the maximum perpendicular height (H). Rather, it is the maximum (not necessarily perpendicular) distance from the centroid of the aneurysm neck to any point on the aneurysm dome. 5. parent artery average diameter (DV) was obtained by measuring two representative vessel cross sections upstream of the aneurysm (D1 at the proximal neck and D2 at 1.5 × D1 upstream), calculating the local diameters in the same way as the neck

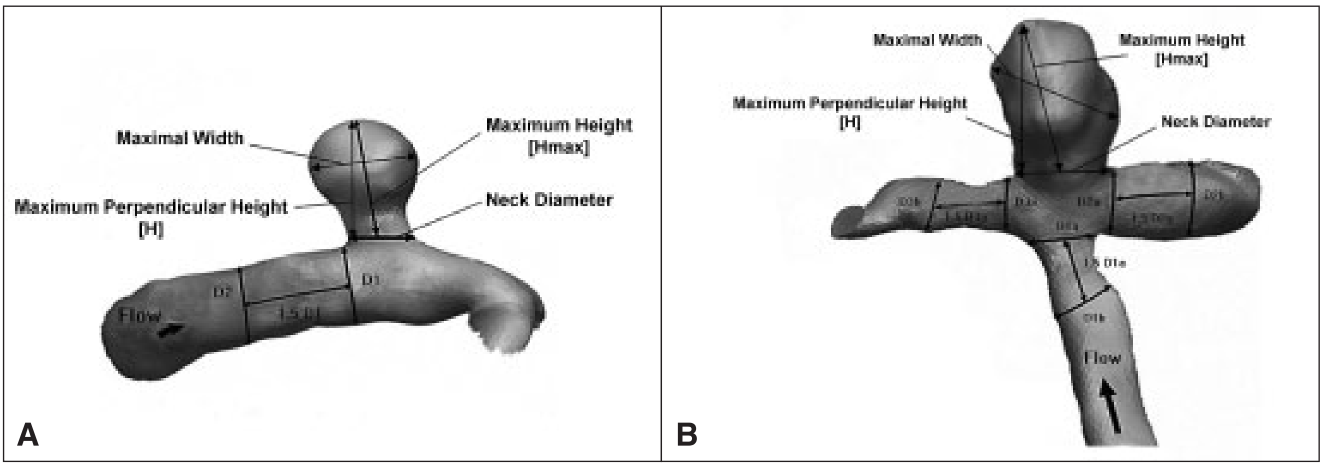

Figure: *Definition of aneurysmal morphology parameters for sidewall intracranial aneurysm (IA) (A) and terminal intracranial aneurysm (B). Five one-dimensional measurements were collected: 1. the maximum perpendicular height of the intracranial aneurysm (H), 2. neck diameter (Dneck), 3. maximum width (Dmax width), 4. the maximum height (Hmax), 5. parent artery average diameter (D_V),which was obtained by measuring two representative vessel cross sections upstream of the aneurysm (D1 at the proximal neck and D2 at 1.5 × D1 upstream), calculating the local diameters in the same way as the neck diameter, and taking their average value. The D_V for sidewall intracranial aneurysm was defined as $(D_1+D_2)/2$ (Figure 1A); The D_V for terminal intracranial aneurysm was defined as $(D_{v1}+D_{v2}+D_{v3})/3$ (Figure 1B). Then the following two-dimensional indices were calculated: 1. aspect ratio (AR), which was defined as the ratio of the maximum perpendicular height to neck diameter (H/Dneck); 2. size ratio (SR), which incorporates the geometries of the IA and its parent vessel and was defined as SR = Hmax / D_V; 3. bottleneck factor (Dmax width / Dneck); 4. height–width ratio (H/Dmax width).*

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diameter, and taking their average value[15]. We calculated the following two-dimensional indices: 1. aspect ratio (AR),which was defined as the ratio of the maximum perpendicular height to neck diameter (H/Dneck); 2. size ratio (SR),which incorporates the geometries of the IA and its parent vessel and was defined as SR = Hmax / DV; 3. bottleneck factor (Dmax width / Dneck); 4.height–width ratio (H/Dmax width).

Statistical analysis

The analysis was done with the Statistical Package for Social Sciences (SPSS) version 15 for Windows (SPSS Inc., Chicago, IL). Bivariate statistics were calculated with ruptured status as the dependent variable. A paired Student's t test was performed for each aneurysm parameter to assess the statistical significance of the observed difference between the means of ruptured and unruptured groups. P values from the t test were calculated, a p value of less than 0.05 was considered significant. The parameters found to be significant in the t test were further analyzed using multivariate conditional logistic regression to identify those parameters that retained significance when accounting for all relevant variables. Before performing the regression, each of the variables was scaled to span a range from 0 to 10, thereby ensuring that a unit increase in the parameter corresponds to 10% of its observed range. This makes the odds ratios obtained for the variables easily comparable. At each regression step, the analysis yields a model for the odds of rupture, which was reported with the P values, the odds ratios, and the 95% confidence intervals. The final equation for the odds of rupture contains only those parameters that are significant after the model has been adjusted for correlations between parameters.

Results

From January 2008 through April 2012, 52 patients with 52 pair of intracranial aneurysms in mirror location, of which one aneurysm had ruptured and its mirror location aneurysm had not ruptured, were included in this study. The sample comprised 18 males and 34 females, (i.e., a 1.9:1 ratio of females to males). The mean patient age was 56.3 years (yr) (range, 18-72 yr). The location of aneurysms included 33 pairs of posterior communicate artery aneurysms, 14 pairs of middle cerebral artery aneurysms, four pairs of aneurysms of supraclinoidal segment of internal carotid artery, and one pair of aneurysms of anterior cerebral artery. Thirty-three ruptured aneurysms were located in the left side and 19 in the right side.

Table 1 summerizes the aneurysm measurements of the ruptured and unruptured intracranial aneurysms. From the paired Student's t test, significant differences were found between ruptured and unruptured means for H, Dneck, Hmax, AR, SR and bottleneck factor; Dmax width, Dv and height-width ratio means were not significantly different. Multivariate conditional logistic regression analysis was performed on H, Dneck, Hmax, AR, SR and bottleneck factor, only SR was left as independently significant parameter for IA rupture risk (p=0.027; odds ratio, 1.49; 95% confidence interval, 0.83~2.66). For every step of the regression, the P values, the odds ratios, and 95% confidence intervals are listed in Table 2.

Discussion

The natural history and risk factors for rupture of cerebral aneurysms have been studied extensively.[4,9,14,16-22] However, the results are not always consistent. Multicentre prospective studies from the International Study of Unruptured Intracranial Aneurysms (ISUIA) suggested that small unruptured intracranial aneurysm could be regarded as having little chance of rupture, and treatment should seldom be recommended for such small unruptured intracranial aneurysms.[20,22,23] However, another interesting fact is that aneurysms may develop more quickly than expected[16] and rupture in the early period during their expansion phase, even though they are quite small in diameter.

Demonstrating an association between aneurysm shape and risk of aneurysm rupture is difficult, because these need to be

Table 1: Aneurysm morphological parameter measurement

Morphological parameter measurement	Unruptured (n=52)，mean±SD	ruptured（n=52), mean±SD	t test p value
H	3.45±1.97	5.35±3.49	0.017
Dneck	3.36±1.47	4.14±2.03	0.028
Dmax width	4.00±1.7	5.16±2.69	0.067
Hmax	4.14±2.85	6.37±4.66	0.037
Dv	2.88±0.59	2.98±0.90	0.542
AR	1.05±0.42	1.36±0.58	0.023
Height-width ratio	0.90±0.41	1.09±0.43	0.581
Bottleneck factor	1.21±0.26	1.25±0.28	0.0462
SR	1.46±1.09	2.13±1.28	0.014

SD, standard deviation; Dmax width, maximal width; Dneck, neck diameter; H, maximum perpendicular height; Hmax, the maximum heigh; DV, parent artery average diameter; AR, aspect ratio; SR, size ratio

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Table 2: Results from the multivariate conditional logistic regression analysis for intracranial aneurysms

Step and indices	P value	Odds ratio	95% confidence interval
1			
H	0.103	1.79	0.814–3.29
Dneck	0.624	0.608	0.114–3.16
Hmax	0.261	2.21	0.946-3.17
AR	0.08	2.11	1.37-3.09
SR	0.04	1.44	0.87-2.77
bottleneck factor	0.317	0.92	0.693–1.21
2			
H	0.16	1.81	0.839–3.52
Hmax	0.3	1.71	0.924–3.08
AR	0.1	2.15	1.27-3.03
SR	0.024	1.42	0.90-2.74
bottleneck factor	0.147	0.9	0.682–1.19
3			
H	0.172	1.68	0.812–3.04
AR	0.09	2.01	1.22-3.04
SR	0.028	1.40	0.90-2.88
bottleneck factor	0.33	0.79	0.608–1.06
4			
H	0.462	1.73	0.823–3.22
AR	0.12	2.13	1.39-3.11
SR	0.023	1.50	0.88-2.81
5			
AR	0.31	1.51	1.08–2.11
SR	0.024	1.48	0.86-2.73
6			
SR	0.027	1.49	0.83-2.66

H, maximum perpendicular height ; Dneck, neck diameter; Hmax, the maximum heigh; AR, aspect ratio; SR, size ratio

studied in comparison to proper control aneurysms, which are expected not to rupture. Possible patient-level disease related factors such as history of smoking, history of hypertension, or even genetic predisposition are almost impossible to control or eliminate. Recently, intracranial aneurysm rupture risk assessment was studied on patients with multiple intracranial aneurysms.[5,9] However, in these studies,[5,9] the location of aneurysm may allow for significant confounding variable even if ruptured aneurysms were compared with unruptured aneurysms in the same patients. Our study represents a useful way to assess purely morphological metrics of intracranial aneurysm that may correlate with intracranial aneurysm rupture. By studying patients with mirror location cerebral aneurysms, with one ruptured and one unruptured, each aneurysm has a mirror location control aneurysm. The specific morphology characteristics of the ruptured aneurysms can be compared directly with those of the unruptured aneurysms at their mirror image sites. In other words, in a particular patient, why did one of their aneurysms rupture and not their mirror location one?

Many quantified one-, two-, and three-dimensional geometric indices to characterize aneurysm size and shape have been described.[5,11,12] We adapted some of these indices in this study but did not use the three-dimensional indices (isoperimetric ratio and convexity ratio)[5,11] for the purpose of simplicity. Our goal was to identify purely morphology parameters that could be easily and quickly investigated without the need for sophisticated computer manipulations. Simple parameters that could be calculated in the office setting would be most helpful to the clinician in evaluating the risk of aneurysm rupture.

Recently, several studies have indicated that intracranial aneurysm size, location and shape may be a primary determinant of rupture probability.[5,9,11,12,14] From the above studies, it appears that the influence of IA location on rupture risk is at least partly related to the relationship between IA size and parent vessel diameter. However, the classification of aneurysms into categories solely on the basis of the "general" location (i.e., parent vessel name) is somewhat qualitative and cannot capture local variations in IA and vessel geometry. For example, the middle cerebral artery consists of several segments, each having a distinct geometry. Additionally, from individual to individual, the vessel diameters may vary significantly. To resolve this dilemma, we related aneurysm geometry to the local vessel geometry via the SR. Instead of comparing the absolute sizes of aneurysms in different locations, the SR compares their sizes in a manner that accounts for the local parent artery diameter. In our study, we have tested five one-dimension and four two-dimension morphological parameters for correlation with the rupture of intracranial aneurysms; only SR is independently correlated with ruptured intracranial aneurysms. Size ratio takes into account not only the aneurysm size itself but also the local vessel caliber and incorporates it into a quantifiable parameter and indirectly accounts for the effect of intracranial aneurysm location on rupture. The fact that intracranial aneurysms rupture most often on the anterior communicating artery and least on the internal carotid artery may be at least partly accounted for by the parameter SR. For example, a 4-mm aneurysm on the anterior communicating artery (average diameter, 2 mm) has a large SR of 2.0 (high rupture risk), but the same size aneurysm on the internal carotid artery (average diameter, 4 mm) has an SR of only 1.0 (low rupture risk).

The majority of ruptured aneurysms in our study, although slightly larger than unruptured ones, are much smaller than the 7 mm threshold that the ISUIA registry has proposed.[22] Data from prospective ISUIA study showed a risk of rupture of 0.52% for aneurysms 7 to 12 mm in diameter of the anterior circulation and 2.9% for aneurysms located posterior circulation in same size category.[22] Size is assumed to be one of the most important determinants for future rupture. However, there are many differences in size determinations among studies and investigators. Recently, one study[3] reported a mean height of 6.7 mm and an average width of 6.1 mm for ruptured aneurysms; another study[24] reported a mean diameter of all ruptured aneurysms was 6.28 ± 5.08 mm when measured with advanced 3D rotational angiography. These results indicate that the size of ruptured aneurysms are smaller than those of previous studies[5,11,22]. Some authors have suggested that aneurysms shrink after rupture. Wiebers et al[22] noted aneurysmal shrinkage after rupture, so the calculated size of ruptured aneurysms does not truly reflect their size before rupture. Recently, Raghavan et al[12] carried out a study to investigate this problem. They analyzed histologic findings for both ruptured and unruptured aneurysms and concluded that there was no histological evidence to suggest that aneurysms shrink after rupture. These findings support our results that even small aneurysms can rupture. However, our study was based on a comparatively small patient population, so bias error might have been large; this is related to the low prevalence rate of mirror location intracranial aneurysms.

Limitation of the study

The present study has several limitations. First, the study only concerns patients with mirror location aneurysms. Hence it is a narrow and biased sample. For example, lesion sites that frequently rupture, such as anterior communicating artery aneurysms, are under-represented in this series. Hence extrapolation to all patients with unruptured aneurysms is risky. Presentation with a rupture is taken as the 'cases' that will dictate what to do with patients who present with unruptured aneurysms, for whom a decision will have to be made. The appropriate study subjects should have been patients with unruptured mirror location aneurysms that present a rupture during follow-up. Secondly, the aneurysm morphology could have been affected by the rupture itself; i.e., the likelihood of shape or size change during aneurysmal rupture could not be completely excluded in this study. Fortunately some studies have indicated that the size and shape of an aneurysm are not affected much by rupture.[3,12,14] Thirdly, our aneurysm data could have been affected by vasospasm. It is well known that vasospasm affects the parent artery on which the hemorrhage occurs from approximately five days after aneurysmal rupture.[15] However, the vast majority of our patients presented for evaluation and had imaging via 3-dimensional DSA within 24 hours of the initial hemorrhage. Therefore, vasospasm was not expected to have a significant effect on our data. Finally, this study has a limited group size, and not all "background" variables can be controlled for even in the setting of mirror location aneurysms, which may have an effect on the results. However, we believe that the 3D study in the current work will lead to parameter measurements with a high degree of accuracy, compensating to an extent, for the small study population.

Conclusion

In conclusion, using a study model in which we compared ruptured and unruptured aneurysms in the same patients harboring mirror location intracranial aneurysms, we identified that only SR is significantly associated with ruptured aneurysms. These findings will need to be confirmed in future larger studies. To provide better means to identify high-risk aneurysms, other disease related factors such as sex, smoking habits, drug abuse, hypertension, and the emerging evidence for a genetic disposition have to be considered as well.

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References

1. Rinkel GJ, Djibuti M, Algra A, van Gijn J. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. Stroke. 1998;29:251-6.
2. Ujiie H, Sato K, Onda H, et al. Clinical analysis of incidentally discovered unruptured aneurysms. Stroke. 1993;24:1850-6.
3. Beck J, Rohde S, Berkefeld J, Seifert V, Raabe A. Size and location of ruptured and unruptured intracranial aneurysms measured by 3-dimensional rotational angiography. Surg Neurol. 2006; 65:18-27.
4. Orz Y, Kobayashi S, Osawa M, Tanaka Y. Aneurysm size: a prognostic factor for rupture. Br J Neurosurg. 1997;11:144-9.
5. Dhar S, Tremmel M, Mocco J, et al. Morphology parameters for intracranial aneurysm rupture risk assessment. Neurosurgery. 2008;63:185-97.
6. Tremmel M, Dhar S, Levy EI, Mocco J, Meng H. Influence of intracranial aneurysm-to-parent vessel size ratio on hemodynamics and implication for rupture: results from a virtual experimental study. Neurosurgery. 2009;64:622-30.
7. Yasuda R, Strother CM, Taki W, et al. Aneurysm volume-to-ostium area ratio (VOR): a parameter useful in discriminating the rupture status of intracranial aneurysms. Neurosurgery. 2011;68: 310-17.
8. You SH, Kong DS, Kim JS, et al. Characteristic features of unruptured intracranial aneurysms: predictive risk factors for aneurysm rupture. J Neurol Neurosurg Psychiatry. 2010;81: 479-84.
9. Hoh BL, Sistrom CL, Firment CS, et al. Bottleneck factor and height-width ratio: association with ruptured aneurysms in patients with multiple cerebral aneurysms. Neurosurgery. 2007; 61:716-22.
10. Kyriacou SK, Humphrey JD. Influence of size, shape and properties on the mechanics of axisymmetric saccular aneurysms. J Biomech. 1996;29:1015-22.
11. Ma B, Harbaugh RE, Raghavan ML. Three-dimensional geometrical characterization of cerebral aneurysms. Ann Biomed Eng. 2004;32:264-73.
12. Raghavan ML, Ma B, Harbaugh RE. Quantified aneurysm shape and rupture risk. J Neurosurg. 2005;102:355-62.
13. Rohde S, Lahmann K, Beck J, et al. Fourier analysis of intracranial aneurysms: towards an objective and quantitative evaluation of the shape of aneurysms. Neuroradiology. 2005;47:121-6.
14. Ujiie H, Tamano Y, Sasaki K, Hori T. Is the aspect ratio a reliable index for predicting the rupture of a saccular aneurysm? Neurosurgery. 2001;48:495-503.
15. Morgan M, Halcrow S, Sorby W, Grinnell V. Outcome of aneurysmal subarachnoid haemorrhage following the introduction of papaverine angioplasty. J Clin Neurosci. 1996;3: 139-42.
16. Bederson JB, Awad IA, Wiebers DO, et al. Recommendations for the management of patients with unruptured intracranial aneurysms: a statement for healthcare professionals from the Stroke Council of the American Heart Association. Stroke. 2000; 31:2742-50.
17. Juvela S.Natural history of unruptured intracranial aneurysms: risks for aneurysm formation, growth, and rupture. Acta Neurochir Suppl. 2002;82:27-30.
18. Morita A, Fujiwara S, Hashi K, Ohtsu H, Kirino T. Risk of rupture associated with intact cerebral aneurysms in the Japanese population: a systematic review of the literature from Japan. J Neurosurg. 2005;102:601-6.
19. Weir B, Disney L, Karrison T. Sizes of ruptured and unruptured aneurysms in relation to their sites and the ages of patients. J Neurosurg. 2002;96:64-70.
20. Wiebers DO. Unruptured intracranial aneurysms: natural history and clinical management. update on the international study of unruptured intracranial aneurysms. Neuroimaging Clin N Am. 2006;16:383-90.
21. Wiebers DO, Piepgras DG, Meyer FB, et al. Pathogenesis, natural history, and treatment of unruptured intracranial aneurysms. Mayo Clin Proc. 2004;79:157-83.
22. Wiebers DO, Whisnant JP, Huston J 3rd, et al. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet. 2003;362: 103-10.
23. Wiebers DO. Patients with small, asymptomatic, unruptured intracranial aneurysms and no history of subarachnoid hemorrhage should generally be treated conservatively: for. Stroke. 2005;36:408-9.
24. Joo SW, Lee S, Noh SJ, Jeong YG, Kim MS, Jeong YT. What is the significance of a large number of ruptured aneurysms smaller than 7 mm in diameter? J Korean Neurosurg Soc. 2009;45:85-9.