Evaluation of Anatomical and Morphological Factors Correlation with Rupture Risk for Intracranial Aneurysms

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SUMMARY
Introduction. The ruptured intracranial aneurysm (IA) is the most common cause of subarachnoid hemorrhage (SAH) (up to 85%), and it can cause a significant morbidity and mortality. However, with the wider availability of non-invasive intracranial imaging techniques, the increasing number of unruptured IAs is incidentally being detected. That is why the life threatening SAH can be prevented if the aneurysm can be treated before rupture. When the unruptured IA is detected, the risk of rupture has to be balanced with the risks of preventive treatment. Therefore prognostic criteria for the risk of rupture are necessary for the effective management of patients with unruptured IA.

Aim of the study. To analyse the localization and geometry of ruptured intracranial aneurysms including the aneurysm height, the neck width, the dome width, the aneurysm shape, the aspect ratio (height/neck), the bottleneck factor (dome width/neck width) and the multiplicity of aneurysms and its association with rupture risk.

Material and methods. Patients with the intracranial aneurysm rupture and SAH, who underwent endovascular treatment in the interventional radiology department of Riga East Clinical University Hospital “Gaļiezers” from January 2012 until December 2014, were selected for research. The characteristics of aneurysms were retrospectively reviewed using clinical charts and radiologic findings – 3D digital subtraction angiography, CT angiography.

Results. 128 patients with 132 ruptured IA were assessed, 46 of them were males (36.9%) with mean age 47.0 ± 12.93 years and 82 females (64.0%) with mean age 60.0 ± 13.30 years. 2 aneurysms were considered to be probably ruptured in 4 patients with multiple IA. The most common localization of ruptured aneurysms was the anterior communicating artery (ACoA) - 46 patients (34.8%). The number of regular shape aneurysms was 91 (68.9%), with a daughter sac - 17 (12.9%) cases, polycyclic - 21 (15.9%). The mean height of an aneurysmal sac was 6.1 ± 3.64 and the mean aspect ratio (height/neck width) was 1.8 ± 0.81. The bottleneck factor (dome width/neck width) was 1.6 ± 0.64. In 31 (24.2%) cases the multiple aneurysms were verified in a single patient.

Conclusion. The study showed the female predominance in the group of patients with ruptured intracranial aneurysms. The registered ruptured aneurysms had the small mean aspect ratio that might reasonably influence the decision to treat the unruptured aneurysm actively despite its size.

Key words: angiography, aneurysm, ruptured, intracranial aneurysm, subarachnoid hemorrhage.

INTRODUCTION
Intracranial aneurysms are relatively common, occurring in an estimated 0.2% to 9% of the general population. The ruptured IA is the most common cause of SAH (up to 85%) (10), and it can cause a significant morbidity and mortality (21, 5, 16). However, with the wider availability of noninvasive intracranial imaging techniques, the increasing number of unruptured intracranial aneurysms is being incidentally detected (3, 12, 14, 15). That is why the life threatening and debilitating sequelae of SAH may be prevented if the aneurysm can be treated before rupture.

The optimal management of the incidentally discovered IA remains a controversial topic in neurosurgery. When the unruptured aneurysm is detected, the risk of rupture has to be balanced with the risks of preventive treatment. However, the assessment of rupture risk is inaccurate (3, 5, 12). Therefore the prognostic criteria for the risk of rupture are necessary for the effective management of patients with unruptured IA.

Various parameters have been proposed to identify the risk of rupture. In several studies there have been shown that the aneurysm location, the neck width, the dome width, the dome height, the aneurysm shape, the aspect ratio and the multiplicity are important prognostic factors in rupture risk that have been widely studied between ruptured and unruptured aneurysms. Many studies even try to determine a specific location and a critical size at which an aneurysm was likely to rupture (5, 8, 9, 15, 21, 22).

Knowing the critical size of the aneurysm and a specific location and other morphological parameters at which the incidence of rupture increases may help in patients’ selection for treatment of unruptured aneurysms (3, 22). The major ethical issue in evaluating the natural history of unruptured aneurysms is that patients with
a high risk of aneurysms cannot be left untreated (15). The aim of the study was to review patients with ruptured IA of Interventional radiology department in Riga East University Hospital “Gaiļezers”, to analyse the most common localization and morphological parameters – the neck width, the dome height, the dome width, the aneurysm shape, the aspect ratio (height/neck width), the bottleneck factor (dome width/neck width) and the multiplicity of aneurysms according to its association with rupture risk.

AIM OF THE STUDY
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MATERIAL AND METHODS
166 patients with the diagnosis of intracranial aneurysms were treated in the Interventional radiology department of Riga East University Hospital “Gaiļezers” during the period from January 2012 until December 2014. Patients were categorized into two groups: ruptured aneurysm group (with SAH) and unruptured aneurysm group. SAH was diagnosed by the head computed tomography. All patients with unruptured aneurysms were excluded from the study. The medical charts and radiological imaging findings of 128 patients with the diagnosis of 132 ruptured intracranial aneurysms were retrospectively reviewed. In 4 patients 2 aneurysms were considered as ruptured. The characteristics of ruptured aneurysms were retrospectively reviewed using the digital subtraction of 3D angiography (Fig. 1. a and b.). The 3D angiography images were obtained with the Philips Allura 3D-RA working station. Computer tomography angiographies were used in 4 cases in absence of 3D angiograms. The localization of ruptured IA was categorized into anterior circulation (including anterior cerebral artery, anterior communicating artery, internal carotid artery, middle cerebral artery) and posterior circulation (including basilar artery, posterior communicating artery, vertebral artery and cerebellar arteries).

Most aneurysms included in the study were saccular or berry like, the aneurysm shape was categorized into regular (defined as aneurysm width is 80% to 100% of its length) and irregular: with a daughter sac (an irregular protrusion of the aneurysm wall) and polycyclic (multiple lobes with equal diameter were present). The measurements of the maximal neck-width, the aneurysm dome height (length from the neck center to the dome of the aneurysm), and the aneurysm dome width (measured perpendicular to the length) were performed using the angiographic program. The aspect ratio describes the relation between the aneurysm length (dome height) and the aneurysm neck. It was calculated by dividing aneurysm dome height by aneurysm neck-width. The bottleneck factor describes the relation between the aneurysm width and the aneurysm neck, and it was calculated by dividing aneurysm width by aneurysm neck-width.

In patients with multiple aneurysms, the aneurysm responsible for rupture was determined by SAH distribution or cerebral hematoma localization on CT, aneurysm morphology and localization.

Statistical Analysis
All statistical analysis for the obtained data was processed by the statistical software SPSS 22. A statistical difference of p < 0.05 was considered significant.

RESULTS
From 128 reviewed patients with intracranial ruptured aneurysms, the definite measurements were obtained for 132 ruptured aneurysms. In 4 patients 2 aneurysms were considered as ruptured.

Age and sex
The mean age of patients in this study was 55.3±14.56 years (range 17-85 years). The most common age group was 51 - 60 years. There were 46 (36.9%) males with mean age 47.0±12.94 and 82 females (64.0%) with mean age 60.0±13.38 years (SD). The study demonstrated the female predominance with ruptured intracranial aneurysms, with the male to female ratio of 1:1.8 (46/82) Males were presented with ruptured intracranial aneurysms at a younger mean age than females (mean age difference, 12.9 years; 95% confidence interval, p < 0.005). The age and sex distribution is shown in the figure 3.

Aneurysm location
The aneurysm location was: the anterior communicating artery (AComA) in 46 patients (34.8%), the internal carotid artery (ICA) was in 34 patients (25.8%), the middle cerebral artery (MCA) was in 25 patients (18.9%), the top of the basilar artery (BA) was in 8 patients (6.0%), the anterior cerebral artery (ACA) was in 8 patients (6.1%), the posterior communicating artery (PCoA) was in 6 patients (4.5%), the vertebral artery (VA) was in 2 patients (1.5%), the posterior inferior cerebellar artery (PICA) was in 3 (2.3%). The distribution of ruptured intracranial aneurysms is shown in Table 1.

Most aneurysms (119/132, 90.2%) were located in the anterior circulation. The most common site of the rupture was the anterior communicating artery (46/132, 34.8%). The number of regular shape aneurysms was 91 (68.9%), with a daughter sac - 17 (12.9%) cases, polycyclic - 15.9 (15.9%).

Size of aneurysms
All measured parameters of the ruptured IA are shown in Fig.2. The mean dome width was 5.8±3.50 mm. The mean height was 6.1±3.64 mm. There was no significant difference in the size parameters of the ruptured aneurysms (t test, p < 0.05) in men and women. But the statistically significant difference between the mean height of AComA artery aneurysms and the aneurysms of other localizations was found there. The aneurysms on AComA had a significantly smaller mean height.
It is observed that 51.5% (68/132) of the reviewed ruptured aneurysms in our research had a small height (size ≤5 mm) and 54.5% (72/132) of aneurysms had a small width (size ≤5 mm). Notably, the percentage of small aneurysms (height and width ≤5 mm) rupturing on the anterior communicating artery was higher (26/46, 56.5% for height) compared with the ACI localization with small aneurysms in 15/34 cases (44.1%) and MCA - 13/25 of cases (52.0%), 95% confidence interval, p<0.05.

The mean neck width for the ruptured aneurysms was 3.5±1.69 mm. 99/132, 75.0% of the analyzed aneurysms neck size was less than 4 mm. The mean neck width of the AComA aneurysms was 3.1±1.03 mm, for MCA = 3.4±1.2, for ICA = 4.2±1.78. These parameters are statistically different (95% confidence interval, p>0.05).

The mean aspect ratio (height/neck width) in our study was 1.8±0.81. The mean bottleneck factor (dome width/neck width) was 1.7±0.65. The mean aspect ratio of AComA aneurysms was 1.7±0.67, the mean bottleneck factor was 1.6±0.57. The mean aspect ratio of AComA aneurysms was significantly different from other localizations of aneurysms. The mean aspect ratio of ICA aneurysms was 2.0±0.83 and the bottleneck factor was -1.6±0.66. The mean aspect ratio of the MCA aneurysms was 1.9±0.96 and the bottleneck factor was -1.6±0.62. The statistical analysis didn’t show the significant difference between these parameters (p=0.112). 59/132, 45% of the ruptured aneurysms of our study had the aspect ratio of less than 1.6.

When the size of aneurysms was assessed in accordance with the age using the Mann-Whitney test, the mean aspect ratio of aneurysms in patients below age 65 years was 1.9±0.86 and the mean aspect ratio of aneurysms in patients above age 65 years was 1.6±0.61 mm. In the older age group (above 65 years), the aspect ratio was smaller than in the younger age group (below 65 years), which was statistically significant (p<0.05). The aneurysm size in accordance with the age is shown in Fig. 4. All measured parameters are shown in Fig. 5.

**Multiplicity**

Multiple aneurysms occurred in 31/128 (24.2%) patients. In our series, there was no significant difference in the proportion of the multiple aneurysms between men (11/46, 23.9%) and women (20/82, 24.4%).

**DISCUSSION**

The cerebral aneurysm rupture is a highly dangerous condition which results in subarachnoid hemorrhage (SAH), interventricular hemorrhage and intracerebral hematoma, thus it can cause life threatening conditions, including fatal in about 40% of cases (17). It is crucial to recognize the main rupture risk factors of incidentally discovered unruptured aneurysms.

Various parameters have been proposed to identify the risk of rupture. Several studies have shown that the aneurysm location, the neck width, the dome width, dome height, the aneurysm shape, the aspect ratio and the multiplicity are important prognostic factors of rupture, that have been widely studied between ruptured and unruptured aneurysms (5, 8, 9, 15, 21, 22). Two large prospective studies have reported the natural history of unruptured intracranial aneurysms - the International Study of Unruptured Intracranial Aneurysms (ISUIA), which prospectively assessed 4060 patients with unruptured aneurysms in the United States, Canada, and Europe, and the Unruptured Cerebral Aneurysms Study (UCAS), a Japanese cohort which followed 5720 patients with 6697 aneurysms. Both these studies noted that the aneurysm size and location were associated with a higher risk (8). In the UCAS study it was shown that the presence of the daughter sac was associated with a higher rupture rate contrary a regular shaped, smooth wall aneurysm (8). Additional risk factors have been investigated, such as familial predisposition, smoking, hypertension, female sex, connective tissue disorder, aneurysm growth rate (15, 16).

In our study we described the anatomical and morphological risk factors to determine the aneurysms with a higher rupture risk.

The study demonstrated the female predominance with ruptured intracranial aneurysms, with the male to female ratio of 1:1.8 (46/82). The same pattern of the female predominance in the group of patients with intracranial aneurysms has been shown in several previous studies (1, 4, 5). Nevertheless, there was no significant difference in the size of the ruptured aneurysms in men and women.

Male patients tended to have ruptured aneurysms at a younger age (mean age 47) than females. The incidence increased slightly with age among women. That is similar with Chinese population studies (5, 6). However, the main age difference in our study was bigger. Female predominance and age related changes could be explained by the lifestyles and other environmental differences between men and women (5). Some studies state that as the gender discrepancy is present in older (>50 years) but not younger individuals, so hormonal influences have been suggested to play a role in the risk of SAH. In one case-control study, premenopausal women without a history of smoking or hypertension were at a reduced risk of SAH compared with age-matched postmenopausal women. Furthermore, the use of estrogen replacement therapy was associated with a reduced risk of SAH in postmenopausal women. This study example shows us that estrogen deficiency of menopause can increase aneurysm rupture risk (7).

Concerning the location, several studies have described the most common aneurysms placement and have related the rupture risk to the aneurysm location. It is reported that a particularly high rupture risk there exists in the anterior regions of the circle of Willis and a large percentage of aneurysms that rupture are located on the anterior communicating artery (AComA) (5, 8, 16, 22). Our results are similar to the pattern reported in literature - the majority of the measured ruptured aneurysms were located in the anterior circulation.

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4.9±1.78 (95% confidence interval, p<0.05).

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The most common site of rupture was the anterior communicating artery.
Most studies show the size correlation to rupture rates. For example, UCAS research finds out that the aneurysms of 7 mm or larger were associated with a significantly increased risk of rupture according to their analysis (8). However, this pattern is different from smaller studies that report about the small ruptured aneurysms. For instance, HP Lai et al. conducted research where 64% of the Chinese patients with SAH had small ruptured aneurysms (sized ≤5 mm) (5). Our series also demonstrated a significantly large proportion of small aneurysms less than 5 mm. Other factors, such as lifestyle and other environmental factors probably may contribute to these differences.

Notably, the highest percentage of small ruptured aneurysms are located on the anterior communicating artery (95% confidence interval, p<0.05). In literature it is reported a particularly higher rupture risk for aneurysms of the anterior communicating artery (5, 16, 22). One such study was conducted by Young-Gyun Jeong, M.D et al. (22), who analyzed 239 ruptured aneurysms, and proved that 44% of aneurysms on AComA were smaller than 5 mm, that is similar to our results. This can be explained by the relatively smaller thickness and diameter of the anterior communicating artery, which limits the size of the aneurysm at the time of rupture (5).

The neck width has been examined in multiple studies, mostly placing the mean width for unruptured and ruptured lesions between 2 and 3 mm. (14, 15). 75.0% analyzed aneurysms had the neck size of less than 4 mm. This parameter may influence the choice of treatment technique (20). However, the neck size doesn’t have a separate influence on the rupture rate, therefore the aspect ratio and bottleneck ratio are used.

The mean aspect ratio in our study for the ruptured aneurysms (height/neck width) was 1.8±0.81. Several studies show that the unruptured aneurysms mean aspect ratio is 1.6-1.8, but for the ruptured ones the aspect ratio is more often higher than 2.0 (2, 14). It shows the aspect ratio limitations as a predictor of the aneurysm rupture risk. The aspect ratio between 1.6 and 2.2 is consistently considered to be the borderline and it couldn’t show the real rupture risk potential (14).

The aneurysms with aspect ratios < 1.6 are less likely to be at a high rupture risk potential, but our results showed that approximately half (44.7%) of patients had the aspect ratio of less than 1.6. This could be influenced by the additional risk factors, such as hypertension, smoking, lifestyle and environmental factors, that weren’t included in this study.

The literature data shows that the patient’s age could be an additional factor in rupture risk. The prevalence of both unruptured and ruptured aneurysms increases with age and it is reported that older patients have larger intracranial aneurysms (19, 22). Our study shows that the aspect ratio of aneurysms in older age group (above 65 years) was significantly smaller than that of aneurysms in younger age group (below 65 years). That could be explained by the age related changes in blood vessel walls, that is no longer associated with aneurysm parameters but with the fragility and morphological changes of the arterial walls. When elastic arteries age over the years, their diameters increase and become stiffer, and their walls thicken. The major structural changes caused by aging occur in the median layer, which thins out and loses its orderly arrangement of elastin laminas and fibers and become fragmented and unorganized (23). The degeneration of elastic fibers is accompanied by an increase in the collagenous substance and the vessel progressively loses its elasticity. The stiffening of the wall causes an increase in the speed of the pulse wave. The increase in the cyclic stresses on the arterial wall can lead to a fatigue-like remodeling process in the elastin sheets and fibers leading to a higher fragility of existing arterial aneurysm wall.

Many studies have listed the risk factors of multiple aneurysms such as smoking, hypertension and family history of cerebrovascular diseases (5, 13). Thus, the difference in the prevalence of multiple aneurysms may be related to the prevalence of risk factors in various layers of populations. The prevalence of multiple aneurysms in our series was comparable to the population data in literature, where the number of patients with intracranial aneurysms is around 15%-33.5% (15). There was no significant difference in the proportion of multiple aneurysms between men and women, which is contrary to the general finding where female gender is a risk factor for multiple aneurysms (13, 11). However, as our series do not consider other risk factors for the multiple aneurysms, a confounding effect cannot be excluded.

CONCLUSIONS

Our research has studied the pattern of the ruptured intracranial aneurysms in Interventional Radiology department of Riga East University Hospital “Gaiļezers” during the three-year period in terms of the size, location, and the point prevalence of multiple aneurysms.

Table 1. Location of ruptured intracranial aneurysms

<table>
<thead>
<tr>
<th>Location</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior circulation</td>
<td></td>
</tr>
<tr>
<td>AComA</td>
<td>46</td>
</tr>
<tr>
<td>ICA</td>
<td>34</td>
</tr>
<tr>
<td>MCA</td>
<td>25</td>
</tr>
<tr>
<td>ACA</td>
<td>8</td>
</tr>
<tr>
<td>AComP</td>
<td>6</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>8</td>
</tr>
<tr>
<td>PICA</td>
<td>3</td>
</tr>
<tr>
<td>VA</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>132</td>
</tr>
</tbody>
</table>

Abreviations: anterior communicating artery (AComA), the internal carotid artery (ICA), the middle cerebral artery (MCA), the basilar artery (BA) the anterior cerebral artery (ACA), the posterior communicating artery (PCoA), the vertebral artery (VA), the posterior inferior cerebellar artery (PICA).
There was a female predominance of patients with ruptured intracranial aneurysms. The statistically significant difference in the peak age of incidence between men and women was observed. The incidence significantly increased slightly after 50 years among women. Most intracranial aneurysms were located in the anterior circulation part of the circle of Willis. The most common localization of the ruptured aneurysms was the anterior communicating artery, which more commonly had a small height (≤ 5 mm). According to the results of our research the majority of the aneurysms ruptured, while they were small in size, had the small aspect ratio and the bottleneck factor. These results contradicted with the previously published studies which stated that small aneurysms are safe and tend not to rupture easily. Therefore we cannot consider small aneurysms as safe lesions and that might reasonably influence the decision to treat actively the unruptured aneurysm despite its size, especially those which are located in the areas of the hemodynamic stress. In our series there was no significant difference in the proportion of the multiple aneurysms between men and women which disagreed with the published considerations of other authors that female gender could be a risk factor for multiple aneurysms.

Table 2. Point prevalence of multiple aneurysms

<table>
<thead>
<tr>
<th>Sex</th>
<th>single aneurysm</th>
<th>single aneurysm. %</th>
<th>Multiple aneurysms</th>
<th>Multiple aneurysms, %</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>35</td>
<td>76,1%</td>
<td>11</td>
<td>23.9%</td>
<td>46</td>
</tr>
<tr>
<td>Female</td>
<td>62</td>
<td>75,6%</td>
<td>20</td>
<td>24.4%</td>
<td>82</td>
</tr>
<tr>
<td>total</td>
<td>97</td>
<td>75,8%</td>
<td>31</td>
<td>24.2%</td>
<td>128</td>
</tr>
</tbody>
</table>

![Fig. 1. a. Digital subtraction angiography (DSA) in AP and LL view showing AcomA aneurysm](image)

![Fig. 2. Diagram detailing common morphological parameters used in the assessment of the aneurysm rupture risk](image)

![Fig. 1. b. 3D DSA angiography](image)
Conflict of interest: None

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