НАУЧНЫЙ ОТДЕЛ

МЕХАНИКА

Threshold Values of Morphological Parameters Associated with Cerebral Aneurysm Rupture Risk

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Numerous studies have shown that morphological parameters of aneurysms are associated with their rupture. However, literature data on the values of these parameters vary significantly. The objective of this study is to identify image-based morphological parameter values which correlate with cerebral aneurysm rupture and can be used during preoperative planning to detect aneurysms prone to rupture. Mean values of the morphological factors such as aspect ratio and size ratio were chosen from the literature. These factors were sampled for ruptured and unruptured aneurysms. Statistical analysis of these factors was performed. Statistically significant differences were obtained between mean values in samples of size ratio and aspect ratio for ruptured and unruptured aneurysms. There were no statistically confirmed differences between size ratios for ruptured and unruptured anterior communicating artery aneurysms. In contrast, such differences were revealed for both of examined parameters for posterior communicating artery and middle cerebral artery. ROC analysis revealed critical values of aspect ratio and size ratio which distinguish ruptured aneurysms from unruptured ones. High correlation was obtained between size ratio and aspect ratio. Mean values of aspect ratio and size ratio published in recent articles are smaller than the values published 10–15 years ago. Diagram size ratio — aspect ratio showed threshold value of aspect ratio. It was shown that among considered morphological factors, aspect ratio was meaningful. Moreover, aspect ratio correlates with size ratio, and therefore we assume that size ratio is redundant. The obtained criterion value of AR $= 1.2$ in our opinion is logical. It was also confirmed by ROC analysis.

Keywords: cerebral aneurysm, aspect ratio, size ratio, preoperative planning, statistical analysis, ROC analysis.

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INTRODUCTION

Intracranial aneurysm (IA) is a vascular disorder affecting 2–5% of population [1,2]. Rupture of IA frequently leads to subarachnoid hemorrhage (SAH). The worldwide incidence of SAH is about 9/100000 [3]. Despite the advances in SAH management, the mortality rate still remains very high. According to the authors [4], up to 33% of patients with SAH die before they are hospitalized and approximately 25% die within 24 hours. Moreover, studies report that half of the survivors remain disabled [5].

Today more and more IAs are detected with the help of modern imaging methods such as computed tomography (CT) and magnetic-resonance imaging (MRI). In spite of this fact there is still a dilemma to decide which IA to treat. So the identification of IA prone to rupture is a challenge for a surgeon. Moreover, surgeon must determine which aneurysms need to be treated and which may not be treated because of the high treatment-related risks [6, 7].

Modern researches show that IA morphologies such as aspect ratio (AR) [8, 9] and size ratio (SR) [10, 11] are related to IA rupture status. These parameters can be calculated on the basis of CT and MRI data and are convenient for preoperative diagnosis. However, different authors obtain different threshold values of these parameters, as a result, their applicability is complicated.

This article analyzes published AR and SR values for ruptured and unruptured IAs in order to determine their critical values, by means of which it is possible to identify aneurysms prone to rupture.

1. MATERIALS AND METHODS

A total of 117 articles were found devoted to the study of morphological factors of cerebral artery aneurysm rupture. Articles that did not contain mean values of SR and AR parameters were discarded. Articles in English were considered. Thus, 29 articles devoted to the study of the SR of IAs and 40 articles on the AR of IAs were selected. Search for articles was carried out on Scopus, Pubmed, Elibrary and Google Scholar databases. The review includes articles published from 1999 to 2018. We used the following keywords for article search:

1) cerebral aneurysm aspect ratio;
2) cerebral aneurysm size ratio;
3) cerebral aneurysm morphological rupture factor;
4) factors of cerebral aneurysm rupture.

Articles devoted only to numerical modeling were excluded. Only clinical research articles on the search for aneurysm rupture factors mean values were included. Aneurysm morphologies which were published in reviewed articles were measured using computed tomography angiography images. Since the question of the demographic data of patients is not put in the papers on the factors of aneurysm rupture, it is also not covered in this work. Mean values of SR and AR parameters for ruptured and unruptured aneurysms of the cerebral arteries were chosen from the selected articles.

AR is the maximum perpendicular height of aneurysm divided by the average aneurysm neck diameter. SR is the maximum aneurysm height divided by the mean diameter of branch associated with the aneurysm (Fig. 1). In the third column of Tables 1 and 2 arteries are indicated, for which AR and SR parameters are given: MCA is middle cerebral artery, ICA is internal carotid artery, AcomA is anterior communicating artery, PcomA is posterior communicating artery, All is all cerebral arteries.

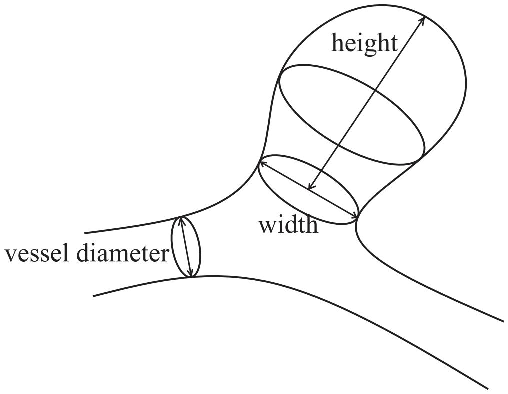


Fig. 1. Schematic image of a brain vessel with an aneurysm

Table 1

Mean values of AR

No.	AR for ruptured	AR for unruptured	Artery	Reference	No.	AR for ruptured	AR for unruptured	Artery	Reference
1	2.70	1.80	All	[12]	21	1.49	0.85	PcomA	[30]
2	2.70	1.50	All	[8]	22	1.80	1.40	All	[31]
3	1.70	1.30	All	[13]	23	1.30	1.10	PcomA	[32]
4	1.24	0.86	MCA	[14]	24	1.56	0.86	All	[33]
5	2.20	1.60	PcomA	[15]	25	1.32	1.02	All	[34]
6	3.40	1.80	All	[16]	26	1.43	0.95	All	[35]
7	1.60	1.10	All	[17]	27	1.31	0.92	All	[36]
8	1.96	1.50	All	[18]	28	1.48	0.86	PcomA	[37]
9	1.39	1.07	AcomA	[19]	29	2.50	1.44	All	[38]
10	1.26	0.97	All	[20]	30	1.40	0.90	All	[39]
11	1.37	1.17	PcomA	[21]	31	1.90	1.30	MCA	[40]
12	2.06	1.03	All	[22]	32	1.70	1.20	All	[41]
13	1.50	1.30	All	[23]	33	1.75	1.01	MCA	[42]
14	1.76	1.29	All	[24]	34	1.90	1.30	All	[43]
15	1.36	1.05	All	[25]	35	2.30	1.70	All	[44]
16	1.18	0.96	All	[26]	36	1.50	1.20	All	[10]
17	1.90	1.50	ICA	[27]	37	2.20	1.50	MCA	[45]
18	1.60	1.03	MCA	[14]	38	1.49	0.96	All	[46]
19	1.84	1.09	All	[28]	39	1.61	1.49	All	[11]
20	1.27	0.84	PcomA	[29]	40	1.51	1.07	MCA	[9]

Table 2

Mean values of SR

No.	SR for ruptured	SR for unruptured	Artery	Reference	No.	SR for ruptured	SR for unruptured	Artery	Reference
1	2.80	1.80	All	[10]	8	1.77	1.44	PcomA	[21]
2	4.07	2.57	All	[47]	9	2.67	0.98	All	[22]
3	2.09	1.55	AcomA	[48]	10	4.300	2.20	All	[51]
4	2.39	1.20	All	[49]	11	1.50	1.10	All	[23]
5	2.60	1.90	AcomA	[50]	12	2.84	2.05	All	[52]
6	3.22	2.34	AcomA	[19]	13	2.81	0.75	All	[24]
7	2.01	1.22	All	[20]	14	2.13	1.46	All	[25]

The end of Table 2

No.	SR for ruptured	SR for unruptured	Artery	Reference	No.	SR for ruptured	SR for unruptured	Artery	Reference
15	1.30	0.90	AcomA	[53]	23	2.26	1.50	PcomA	[37]
16	3.14	1.58	All	[54]	24	3.04	1.86	All	[38]
17	1.04	0.86	All	[55]	25	2.60	1.20	All	[39]
18	1.92	1.00	PcomA	[30]	26	3.28	2.16	MCA	[42]
19	1.84	1.62	PcomA	[32]	27	2.58	1.47	All	[46]
20	1.88	0.84	All	[33]	28	1.86	1.70	All	[11]
21	2.73	2.31	All	[34]	29	1.22	0.79	MCA	[9]
22	2.65	1.85	All	[35]					

Mean values of AR and SR for AcomA, PcomA and MCA were chosen from Tables 1, 2 and are listed in Tables 3, 4.

SR and AR were analyzed according to the following scheme.

Table 3

Mean values of SR for AcomA and PcomA

AcomA		PcomA	
Ruptured	Unruptured	Ruptured	Unruptured
1.30	0.90	1.77	1.44
2.09	1.55	1.84	1.62
2.60	1.90	1.92	1.00
3.22	2.34	2.26	1.50

Table 4

Mean values of AR for PcomA and MCA

PcomA		MCA	
Ruptured	Unruptured	Ruptured	Unruptured
1.27	0.84	1.24	0.86
1.30	1.10	1.60	1.03
1.37	1.17	1.75	1.01
1.48	0.86	1.90	1.30
1.49	0.85	2.20	1.50
2.20	1.60	1.51	1.07

1. Checking the distributions in the samples for normality. Building histograms.

2. Confirming the statistical significance of the differences between groups of ruptured and unruptured aneurysms for AR and SR using Mann – Whitney test.

3. Calculating medians and percentiles for samples of ruptured and unruptured aneurysms for AR and SR for all arteries, as well as for AcomA, PcomA, and MCA, for which separate samples of AR and SR values were formed.

4. ROC analysis for AR and SR. Calculation of ROC areas for AR and SR.

5. Selection of articles in which data on both of ratios (AR and SR) was presented and the formation of a sample for ruptured/unruptured aneurysms to identify critical values of AR and/or SR. Comparison of ROC curves for AR and SR.

6. Spearman correlation analysis.

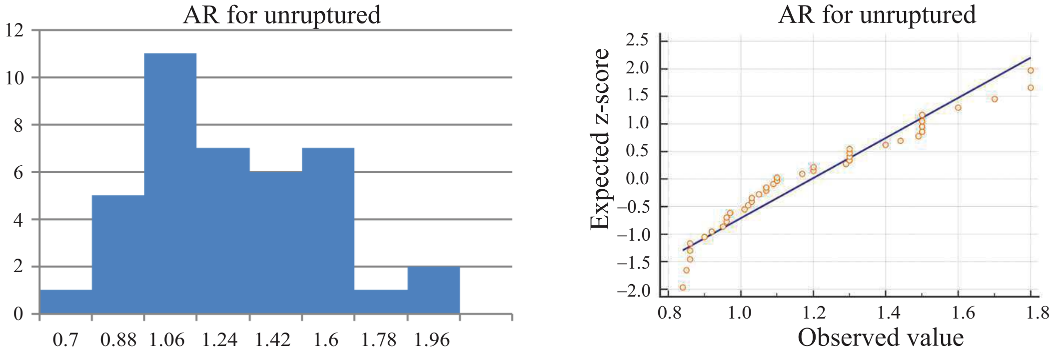
7. Calculation of critical values of AR and/or SR to distinguish groups of ruptured / unruptured aneurysms.

All calculations were carried out in Medcalc 18.11.6 software.

2. RESULTS

1. Normality test for distributions in samples from Tables 1 and 2 was carried out with the help of Shapiro – Wilk test [56].

Histograms for AR and SR samples for ruptured and unruptured aneurysms and normality Shapiro – Wilk test diagrams are shown in Fig. 2–5.



a *b*

Fig. 2. AR histogram for unruptured aneurysms (*a*) and Shapiro – Wilk normality test (*b*)

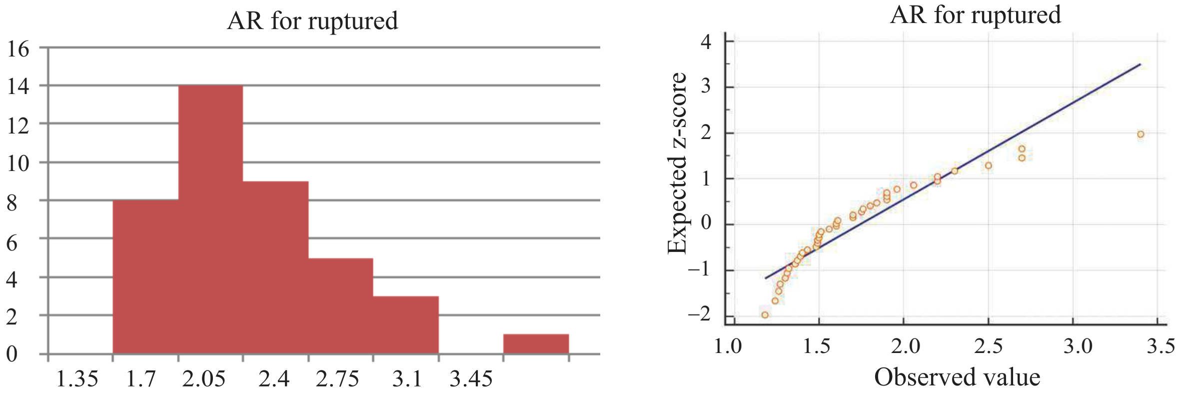


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Fig. 3. AR histogram for ruptured aneurysms (*a*) and Shapiro – Wilk normality test (*b*)

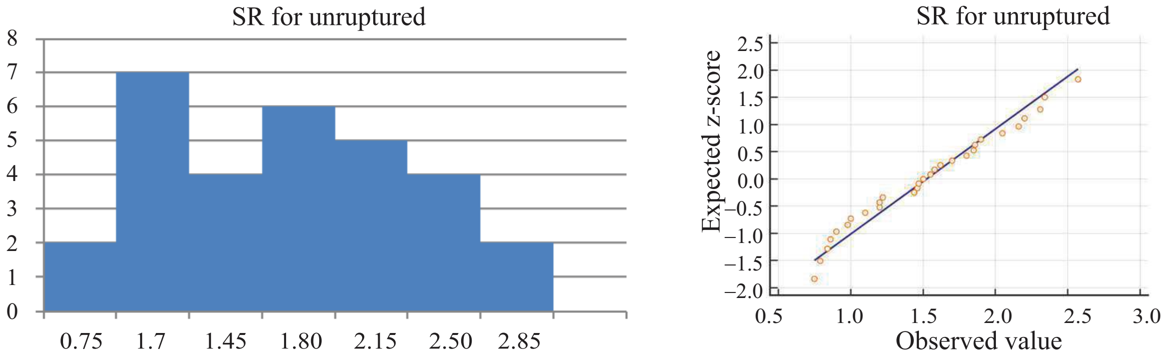

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Fig. 4. SR histogram for unruptured aneurysms (*a*) and Shapiro – Wilk normality test (*b*)

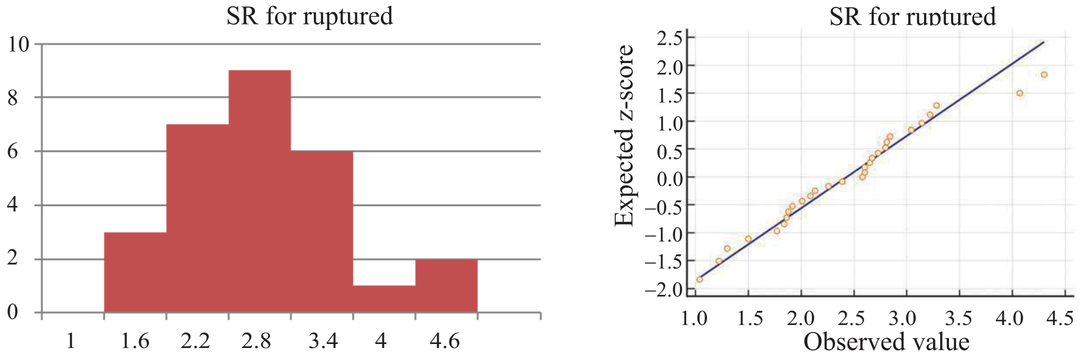

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Fig. 5. SR histogram for ruptured aneurysms (*a*) and Shapiro – Wilk normality test (*b*)

Table 5

Mann – Whitney test for AR and SR ($P = 0.05$)

Parameter	AR	SR
Mann – Whitney criterion	205	114
Critical value	628	314

Shapiro – Wilk test, as well as the type of histograms in Fig. 2–5 showed that in each of the four samples in Tables 1 and 2, the distribution of values was not normal. Therefore, nonparametric methods were chosen for statistical analysis.

2. Mann – Whitney test showed that differences between samples for ruptured and unruptured aneurysms for AR and SR parameters are reliable. Tables 5 and 6 show values of the calculated Mann – Whitney test as well as its critical values [57]. The only case where the differences between samples for ruptured and unruptured aneurysms based on SR were found unreliable is the case of the AcomA (Table 6).

Table 6

Mann – Whitney test for AR and SR for AcomA, PcomA and MCA ($P = 0.05$)

Parameter	SR		AR	
	AcomA	PcomA	PcomA	MCA
Mann – Whitney criterion	4	0	2	0
Critical value	1	1	4	4

3. Medians and percentiles (25%, 75%) for ruptured and unruptured aneurysms for AR and SR parameters for all arteries and for AcomA, PcomA, and MCA were calculated and placed into Tables 7 and 8.

Table 7

Medians (Me) and percentiles (Q25, Q75) for AR and SR (for all arteries)

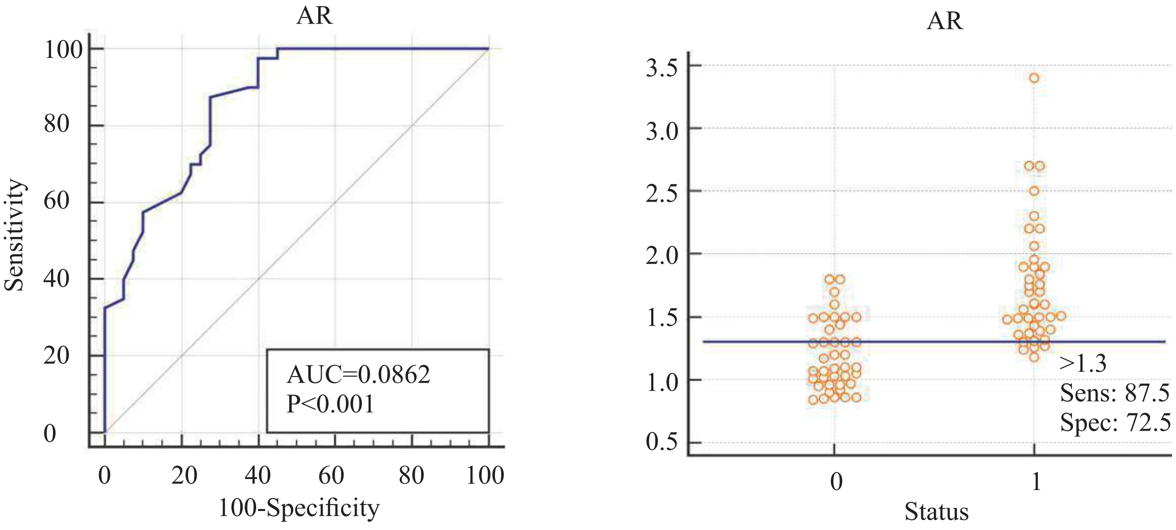
Parameter		Variational-statistical indicators		
		Me	Q25	Q75
AR	Ruptured	1.60	1.39	1.90
	Unruptured	1.09	0.96	1.30
SR	Ruptured	2.60	2.01	2.84
	Unruptured	1.50	1.10	1.90

Table 8

Medians (Me) and percentiles (Q25, Q75) for AR and SR (for AcomA, PcomA, MCA)

Artery	Parameter		Variational-statistical indicators		
			Me	Q25	Q75
PcomA	AR	Ruptured	1.37	1.27	1.47
		Unruptured	0.86	0.70	1.02
	SR	Ruptured	1.88	1.67	2.10
		Unruptured	1.47	1.20	1.74
AcomA	SR	Ruptured	2.35	1.53	3.15
		Unruptured	1.73	1.12	2.33
MCA	AR	Ruptured	1.75	1.39	2.10
		Unruptured	1.03	0.77	1.29

4. The results of ROC analysis for AR and SR are shown in Fig. 6 and 7 respectively.



a *b*

Fig. 6. ROC curve for AR (*a*), criterion value of AR (*b*). ROC area for AR is 0.862 (P<0.001). Status shows ruptured (1) and unruptured (0) aneurysms

Sensitivity for SR> 1.7 was 65.5 and specificity was 86.2.

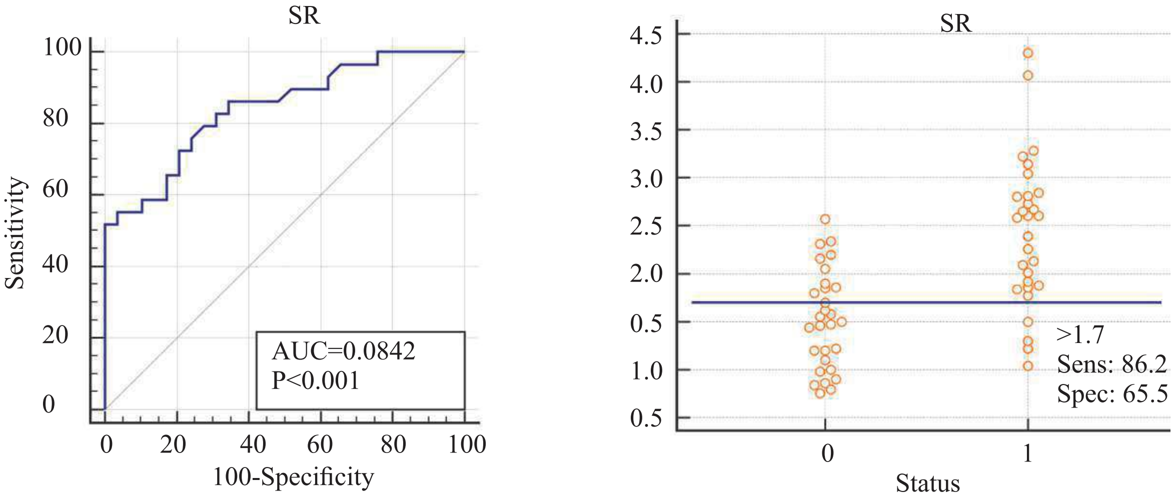


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Fig. 7. ROC curve for SR (*a*), criterion value of SR (*b*). ROC area for SR is 0.842 (P<0.001). Status shows ruptured (1) and unruptured (0) aneurysms

Sensitivity for AR> 1.3 was 87.5 and specificity was 72.5.

5. Then 14 articles were chosen in which both factors were investigated. Two samples of AR and SR were generated with ruptured/unruptured aneurysm status (Table 9). The first author of the corresponding article and reference number were placed into the right column of Table 9. Comparison of ROC curves for AR and SR values from Table 9 was performed (Fig. 8).

6. Spearman correlation analysis showed high correlation (Spearman coefficient was 0.73, P< 0.001) between AR and SR.

7. SR-AR diagram was constructed for the data from Table 9 (Fig. 9). According to the diagram, critical value of AR (vertical green line, AR= 1.2) was calculated,

which distinguishes ruptured aneurysms from unruptured ones. Blue rhombuses on the diagram refer to unruptured aneurysms, red squares refer to ruptured aneurysms.

Table 9

AR and SR values, aneurysm status and first author in reference list

AR	SR	Ruptured/ Unruptured	First author. reference	AR	SR	Ruptured/ Unruptured	First author. reference
1.20	1.80	Unruptured	Dhar S. [10]	1.01	2.34	Unruptured	Lin N. [19]
0.97	1.22	Unruptured	Zheng Y. [20]	1.17	1.44	Unruptured	Jiang H. [21]
1.03	0.98	Unruptured	Qiu T. [22]	1.00	0.80	Unruptured	Qiu T. [22]
1.05	1.46	Unruptured	Li M. [25]	0.85	1.00	Unruptured	Wang G. X. [46]
0.86	1.46	Unruptured	Wang G. X. [14]	1.10	1.62	Unruptured	Zhang Y. [32]
1.02	2.31	Unruptured	Ho A. L. [34]	0.95	1.85	Unruptured	Fan J. [35]
0.90	1.20	Unruptured	Jeon H. J. [39]	1.01	2.16	Unruptured	Lin N. [19]
1.50	2.80	Ruptured	Dhar S. [10]	1.71	3.22	Ruptured	Lin N. [19]
1.26	2.01	Ruptured	Zheng Y. [20]	1.37	1.77	Ruptured	Jiang H. [21]
2.06	2.67	Ruptured	Qiu T. [22]	1.81	2.36	Ruptured	Qiu T. [22]
1.36	2.13	Ruptured	Li M. [25]	1.49	1.92	Ruptured	Wang G. X. [46]
1.30	1.84	Ruptured	Zhang Y. [32]	1.32	2.73	Ruptured	Ho A. L. [34]
1.43	2.65	Ruptured	Fan J. [35]	1.40	2.60	Ruptured	Jeon H. J. [39]
1.75	3.28	Ruptured	Lin N. [19]	1.24	2.51	Ruptured	Wang G. X. [14]

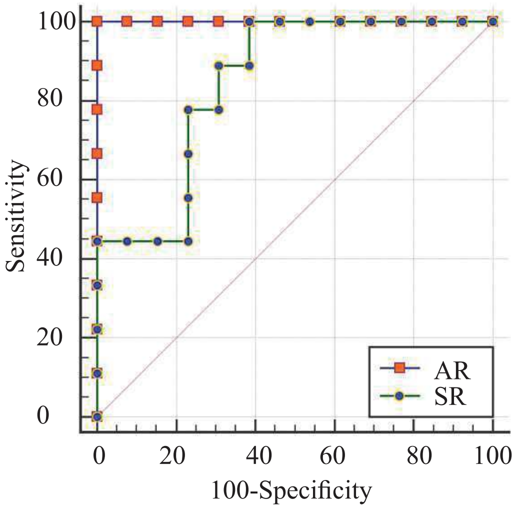


Fig. 8. Comparison of ROC curves for AR and SR (difference between areas is 0.092, P= 0.08)

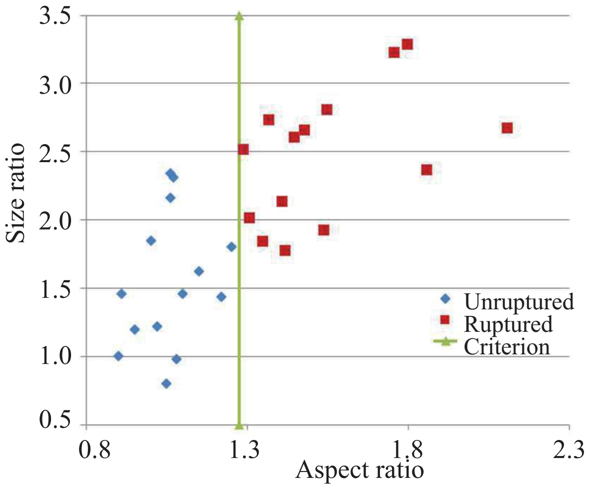


Fig. 9. SR-AR diagram for data from Table 9

3. DISCUSSION

Aneurysms are common pathologies of cerebral arteries. Aneurysm rupture can be catastrophic. Nevertheless, not all aneurysms are prone to rupture, so the surgeon must decide on the need for surgical treatment, assessing the likelihood of an aneurysm rupture. Reliable, easy-to-assess factors can help in assessing the risk of rupture and decision making process.

According to investigations over the past 20–25 years, many risk factors are correlated with rupture of cerebral aneurysms. But none of these factors is used as reliable and independent criterion for analysis of cerebral aneurysm rupture. Many modern studies show that geometric parameters AR and SR are associated with rupture of cerebral aneurysms. The first work on AR was published in 1999 [58]. SR was discovered much later [10]. Moreover, the possibility of differentiation of IAs with the help of these factors is shown by using methods of biomechanics and computational experiment [29, 37, 59]. However, the question still remains open which values of these parameters are considered as thresholds, which could help to identify cerebral aneurysms prone to rupture. The identification of such critical value will provide convenient clinical instrument for differentiating patients with high-risk IAs and elaborating appropriate individual surgery plan.

AR and SR geometrical parameters were selected for the study because they can be easily calculated for almost any aneurysm in CT scan. They have been studied together because both of them are not absolute, but relative values, unlike, for example, the size of aneurysm. Moreover, these parameters are measurable, in contrast to the irregular shape, which is determined subjectively. The subjective factor in the definition of aneurysm irregular shape can introduce a significant error in the diagnosis of an aneurysm and decision making process during preoperative planning.

Although other authors use parametric statistical methods “by default” [9], we deliberately did not use parametric statistical methods, such as, for example, Student’s test, since the distributions in AR and SR samples were not normal. For comparison of medians in AR and SR samples for ruptured and unruptured aneurysms (Tables 7, 8), we used nonparametric Mann – Whitney test.

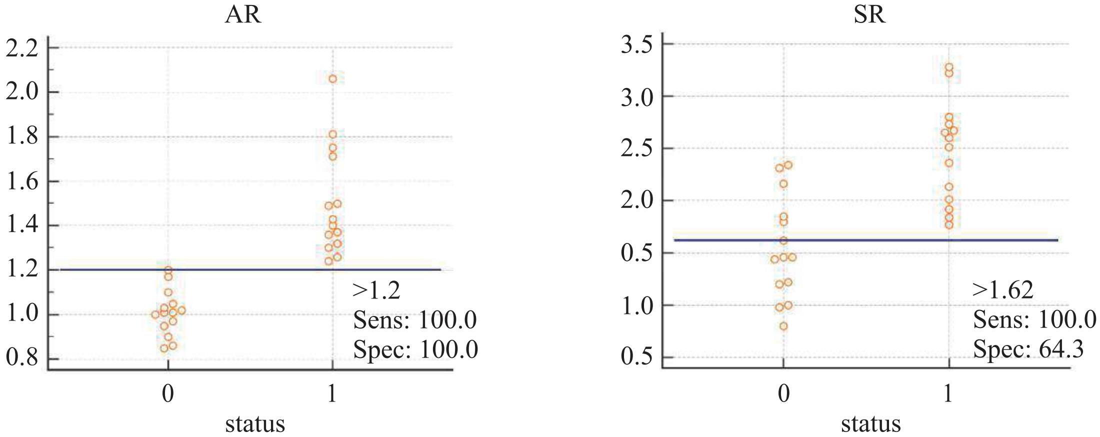
Many authors [19, 48, 50, 53] believe that AcomA among other arteries is most often subjected to the occurrence of aneurysms. However, in this study, there were no statistically confirmed differences between SR samples of ruptured and unruptured AcomA aneurysms. In contrast, such differences were revealed for both of parameters examined (Table 6) for PcomA and MCA. It should be noted that samples of AcomA, PcomA, and MCA were rather small. Nevertheless, Mann – Whitney test can also be applied to such small samples containing 4–5 values.

ROC analysis for AR and SR (Fig. 6 and 7) showed the highest area under ROC curve for AR. But the difference between area under ROC curve for AR and SR was minimal (0.862 and 0.842 respectively for AR and SR). ROC analysis also allowed us to obtain critical values of AR (1.3) and SR (1.7) which distinguish ruptured and unruptured groups of aneurysms. However, sensitivity for SR turned out to be only 65.5 for critical value of 1.7. At the same time, sensitivity and specificity for AR were 87.5 and 72.5 respectively.

Samples were formed for the values of AR and SR (Table 9), which were simultaneously presented in the same articles. This made it possible to compare ROC curves for AR and SR and to reveal the correlation between these parameters and also to reveal threshold of AR. Comparison of ROC curves for both AR and SR factors (Fig. 8) taken from Table 9 showed that AR also has the highest area under ROC curve (1.000 and 0.908 respectively for AR and SR, difference was 0.092, $P = 0.08$).

It was shown that among considered morphological factors, AR is meaningful. Moreover, AR correlates with SR, and therefore we assume that SR parameter is redundant.

The obtained criterion value of AR=1.2 in our opinion is logical. It was confirmed by ROC analysis (Fig. 10) of the data from Table 9 (critical value > 1.20, sensitivity and specificity were equal to 100, area under the ROC curve was equal to 1.000, $P < 0.001$). It can be considered a great success that the diagram shown in Fig. 9 was obtained. It confirms the high correlation between AR and SR, and, at the same time, it makes it easy to determine the criterion value of AR.



a *b*

Fig. 10. Interactive diagrams for AR and SR for data from Table 9 (critical values AR> 1.2, SR> 1.62, $P < 0.001$). Status shows ruptured (1) and unruptured (0) aneurysms

The strength of this study is also that it examines not one group of patients with aneurysms, but this work accumulates many works devoted to the study of morphological factors of cerebral aneurysm rupture.

It should also be noted that values of AR and SR published in recent articles are smaller than the values published 10–15 years ago. We calculated correlation coefficients between mean values of AR and SR and the year of article publication. Spearman correlation coefficients for AR and SR were 0.65 and 0.67 respectively, $P < 0.05$. The highest values of AR and SR were published in the first half of the 2000s [8, 12, 16]. We believe that this can be associated with the development of diagnostic methods. Moreover, the relationship between the values of the parameters and the country where the study was conducted, as well as the population was not identified. However, this question requires more detailed study.

CONCLUSION

High correlation between AR and SR parameters was shown, therefore one of these parameters is redundant. Critical value of AR, which determines ruptured aneurysms, was obtained. We showed that values of AR greater than 1.2 are associated with aneurysm rupture. This morphological parameter specific to cerebral aneurysms is easy to calculate and can be used in the diagnostics of aneurysms and the detection of aneurysms prone to rupture. As a limitation, it is also necessary to note the relatively small sample size, on the basis of which a critical value of AR was obtained. We also did not take into account the age and demographic characteristics of the patients participating in the samples.

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Пороговые значения морфологических параметров, связанных с риском разрыва аневризм сосудов головного мозга

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Многочисленные исследования показывают, что морфологические параметры аневризм связаны с их разрывом. Однако литературные данные о значениях этих параметров значительно различаются. Целью данного исследования является определение значений морфологических параметров, которые коррелируют с разрывом аневризм сосудов головного мозга и могут быть использованы во время предоперационного планирования для выявления аневризм, склонных к разрыву. Средние значения морфологических факторов, таких как соотношение сторон и отношение размеров аневризмы, были собраны из литературных данных для разорвавшихся и неразорвавшихся аневризм. Был выполнен статистический анализ этих факторов. Статистически значимые различия были получены между средними значениями в выборках отношения размеров и соотношения сторон аневризм для разорвавшихся и неразорвавшихся аневризм. Не обнаружено статистически подтвержденных различий между отношением размеров для разорвавшихся и неразорвавшихся аневризм передней соединительной артерии. Напротив, такие различия были выявлены для обследованных параметров для задней соединительной артерии и для средней мозговой артерии. ROC-анализ позволил вычислить критические значения соотношения сторон и отношения размеров, которые отличают разорвавшиеся аневризмы от неразорвавшихся. Была получена высокая корреляция между отношением размеров и соотношением сторон. Средние значения соотношения сторон и отношения размеров, опубликованные в последние годы, существенно ниже значений данных параметров, опубликованных 10–15 лет назад. Было показано, что среди рассмотренных морфологических факторов соотношение сторон аневризм оказалось значимым. Более того, соотношение сторон коррелирует с отношением размеров, и поэтому отношение размеров можно считать избыточным. Полученное значение критерия соотношения сторон, равное 1.2, было также подтверждено ROC-анализом.

Ключевые слова: церебральная аневризма, соотношение сторон, отношение размеров, предоперационное планирование, статистический анализ, ROC-анализ.

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