Size Ratio Performance in Detecting Cerebral Aneurysm Rupture Status is Insensitive to Small Vessel Removal

Alexandra Lauric, PhD
Merih I. Baharoglu, MD
Adel M. Malek, MD, PhD

Cerebrovascular and Endovascular Division, Department of Neurosurgery, Tufts Medical Center, and Tufts University School of Medicine, Boston, Massachusetts

Correspondence:
Adel M. Malek, MD, PhD,
Department of Neurosurgery,
Tufts Medical Center,
800 Washington St #178,
Proger 7, Boston, MA 02111.
E-mail: amalek@tuftsmedicalcenter.org

Received, June 11, 2012.
Accepted, November 27, 2012.
Published Online, December 14, 2012.

Copyright © 2012 by the
Congress of Neurological Surgeons

BACKGROUND: The variable definition of size ratio (SR) for sidewall (SW) vs bifurcation (BIF) aneurysms raises confusion for lesions harboring small branches, such as carotid ophthalmic or posterior communicating locations. These aneurysms are considered SW by many clinicians, but SR methodology classifies them as BIF.

OBJECTIVE: To evaluate the effect of ignoring small vessels and SW vs stringent BIF labeling on SR ruptured aneurysm detection performance in borderline aneurysms with small branches, and to reconcile SR-based labeling with clinical SW/BIF classification.

METHODS: Catheter rotational angiographic datasets of 134 consecutive aneurysms (60 ruptured) were automatically measured in 3-dimensional. Stringent BIF labeling was applied to clinically labeled aneurysms, with 21 aneurysms switching label from SW to BIF. Parent vessel size was evaluated both taking into account, and ignoring, small vessels. SR was defined accordingly as the ratio between aneurysm and parent vessel sizes. Univariate and multivariate statistics identified significant features. The square of the correlation coefficient (R^2) was reported for bivariate analysis of alternative SR calculations.

RESULTS: Regardless of SW/BIF labeling method, SR was equally significant in discriminating aneurysm ruptured status ($P < .001$). Bivariate analysis of alternative SR had a high correlation of $R^2 = 0.94$ on the whole dataset, and $R^2 = 0.98$ on the 21 borderline aneurysms.

CONCLUSION: Ignoring small branches from SR calculation maintains rupture status detection performance, while reducing postprocessing complexity and removing labeling ambiguity. Aneurysms adjacent to these vessels can be considered SW for morphometric analysis. It is reasonable to use the clinical SW/BIF labeling when using SR for rupture risk evaluation.

KEY WORDS: Intracranial aneurysm, Morphology, Rupture risk, Size ratio

Neurosurgery 0:1–7, 2013 DOI: 10.1227/NEU.0b013e318282a513 www.neurosurgery-online.com

Despite improvements in patient management, the incidence of aneurysmal subarachnoid hemorrhage has not declined over time, and aneurysmal rupture continues to be associated with high mortality and morbidity rates.[1] Although aneurysmal subarachnoid hemorrhage is a medical emergency, the management of unruptured incidental lesions, increasingly detected by noninvasive vascular imaging,[2] remains controversial.[1,3] The balance between poorly defined annual rupture risk rates with wide estimated range (0.1%-0.2%[4] to 1%-2%[5]) and the daunting implications of rupture lends great clinical significance to rupture likelihood assessment for any given incidental lesion. At the clinical decision-making level, rupture risk assessment is still predominantly based on the concept of aneurysm size, an index thoroughly analyzed as a potential predictor of aneurysmal rupture.[4-8] However, given that a significant number of rupture events cannot

ABBREVIATIONS: ACHA, anterior choroidal artery; **AUC,** area under the curve; **BIF,** bifurcation-type aneurysms; **D_{max},** largest diameter; **H,** aneurysm maximal height; **OPTHA,** ophthalmic artery; **PCOM,** posterior communicating artery; **PV,** average parent vessel size; **PVsv,** average parent vessel size when considering all small vessels; **ROC,** receiver operating characteristics; **SR,** size ratio; **SR1,** size ratio function of H; **SR2,** size ratio function of D_{max}; **SR1sv SR1,** size ratio function of H when considering all small vessels; **SR2sv SR1,** size ratio function of D_{max} when considering all small vessels; **SW,** sidewall-type aneurysms

be explained by size alone, additional predictors based on relative size,[9,10] location[11] and shape[12-15] have been proposed.

Size ratio[16-19] (SR) was proposed as a morphological feature for discriminating between ruptured and unruptured aneurysms. SR was initially defined by Dhar et al[16] as the ratio of the aneurysm dome height (H) over the average size of the parent and daughter vessels (PV) based on 3-dimensional (3-D) volumetric data, but, in a recent change of definition by Rahman et al,[17] SR was also computed as the ratio of the aneurysm maximal size (D_{max}) divided by the average adjacent vessel size based on 2-dimensional angiographic data. More recent work disputes the utility of SR as a rupture status predictor. Lin et al[20] found SR not to be statistically significant in predicting ruptured status on a group of 79 middle cerebral artery aneurysms. On a dataset of 114 consecutive aneurysms, Patel et al[21] found SR to be a weak indicator of rupture status, whereas Lauric et al,[22] on a dataset of 267 aneurysms, disputed the added predictive value of using SR vs its component features (D_{max}, H, PV).

The PV measurement as used in SR definition is evaluated based on the classification of the aneurysm as sidewall (SW) or bifurcation (BIF).[16] More specifically, in the case of SW aneurysms, PV is calculated as the size of the inflow vessel, whereas in the case of BIF aneurysms, PV is the mean size of inflow and outflow vessels (Figure 1C). Clinical literature[19,23-26] usually labels aneurysms as SW if they originate from only 1 parent vessel with or without a small vascular branch, and as BIF if they are located at major bifurcations in the cerebral vasculature. Carotid ophthalmic artery (OPTHA) and most posterior communicating (PCOM) aneurysms [F1]

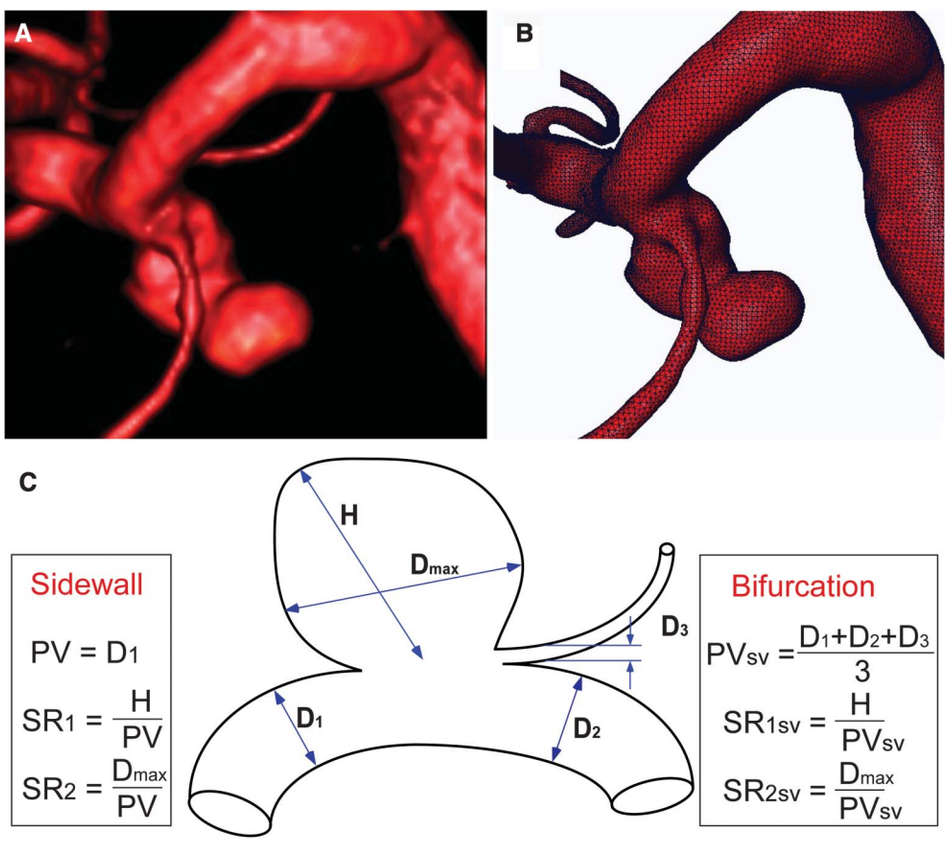


FIGURE 1. *Segmentation and isolation of aneurysms using catheter-based high-resolution 3-D rotational angiography. Shown is a posterior communicating artery aneurysms that was clinically labeled as sidewall (SW), but would have to be considered bifurcation (BIF) for side ratio (SR) calculation purposes.* **A**, *3-D volumetric rendering of the dataset in the right sagittal view* (**B**) *enables segmentation of the vascular structure from surrounding tissue and representation of the vessel surface as a triangular mesh.* **C**, *definition of SR as a function of aneurysm and parent vessel measurements, depending on the SW/BIF labeling rule. D_1, $D2$, and D_3 are measured in planes orthogonal to the vessel, as twice the average distance from the centroid of the plane to the vessel edges. PV, average parent vessel size; SR1, size ratio function of H; SR2, size ratio function of D_{max}; H, aneurysm maximal height; D_{max}, largest diameter; PVsv, average parent vessel size when considering all small vessels; SR1sv, size ratio function of H when considering all small vessels; SR2sv, size ratio function of D_{max} when considering all small vessels.*

are thus accepted as SW aneurysms.[25] This seems to be the labeling rule for SR calculation also, because Dhar et al[16] refer to OPTHA aneurysms as SW, and Xiang et al[19] define SW aneurysms as originating from 1 vessel or from the origin of a small branch whose caliber is one fifth of the parent vessel. The same rule, in which small vessels are ignored from the evaluation of what are clinically considered SW aneurysms, was used by Lauric et al.[22] However, the original proponents of SR have recently argued that the intended definition of SR was for all vessels having direct contact with the aneurysm neck to be considered in PV evaluation, regardless of their size.[22] Because SR calculation requires explicit SW/BIF labeling, it follows that, under this rule, in contrast to common clinical practice, most OPTHA and PCOM aneurysms would be considered as BIF aneurysms. This ambiguity in SW/BIF labeling is problematic when maintaining aneurysm databases, especially if they serve a dual purpose as both clinical and research repositories. As revealed by the comments of Rahman et al,[22] this may lead to potentially ambiguous situations in which, during the same research study, a given aneurysm dataset is first labeled by using 1 rule and resulting in 1 SW/BIF distribution for the purpose of SR calculation, and then relabeled by using a different rule, resulting in a potentially different SW/BIF distribution for the purpose of additional analysis (such as hemodynamic analysis).

The purpose of this study is to evaluate the statistical effect of removing small branches from SR calculation, with the intent of reconciling this SR-proposed SW/BIF labeling with the clinical practice in which small side branches are ignored when evaluating aneurysms that are clinically considered as SW.

TABLE 1. Aneurysm Distribution by Location, and SW vs BIF Classification[a,b]

		Classification With Small Vessels		Classification With One Fifth Rule	
Location	Total	SW	BIF	SW	BIF
ACOM	28		28		28
ICA	17	15		15	
PCOM	31	10	21	22	9
MCA	22		22		22
OPTHA	10	8	4	12	
BA	8		8		8
ICAB	5		5		5
ACHA	6	1	5	6	
VA	3	3		3	
SCA	2		2		2
PCA	1	1		1	
PICA	1		1		1
Total	134	38	96	59	75

[a]ACOM, anterior communicating artery; ICA, internal carotid artery; PCOM, posterior communicating artery; MCA, middle cerebral artery; OPTHA, ophthalmic artery; BA, basilar artery; ICAB, internal carotid artery bifurcation; ACHA, anterior choroidal artery; VA, vertebral artery; SCA, superior cerebellar artery; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery; SW, sidewall; BIF, bifurcation.

[b]Classification as SW/BIF is shown for the same dataset when taking into consideration all small vessels and when removing small vessels by using the one fifth parent vessel ratio rule.

MATERIALS AND METHODS

Patient Selection and Demographics

Consecutive high-resolution 3-D angiographic data of patients with intradural intracranial aneurysms diagnosed over a 4-year period were reviewed for this study. Fusiform, mycotic, and extradural aneurysms were excluded, the latter because of their known different natural history and low risk of subarachnoid hemorrhage. Similar to other studies,[16] only cases in which the rotational angiographic images were of sufficient quality for accurate segmentation and reconstruction were included in this study by a process blinded to ruptured status. A total of 134 aneurysms in 115 patients (mean age, 56 years; 83 women) met the criteria. Aneurysm rupture status was labeled by the treating clinicians at the time of presentation, with a total of 60 (44.7%) aneurysms labeled as ruptured. Details regarding aneurysm location [T1] are provided in Table 1. The temporal aneurysm shape evolution and clinical symptomatology were not followed clinically over a period of time and were not available before rupture. Clinical information, including rupture status, was retrieved from a prospectively maintained database.

Cerebral Angiography and Data Processing

Three-dimensional catheter-based cerebral angiograms were obtained by using a calibrated biplane system, with volume reconstructions performed to yield a 3-D volumetric dataset (Figure 1A-B). Vessel segmentation was performed by using a level-set algorithm based on the open-source Insight Segmentation and Registration Toolkit (ITK, version 3.20) libraries. The segmented volume was then analyzed in the Amira scientific visualization software (version 5.1, Visage Imaging, San Diego, California). For each set, the aneurysm dome was isolated from the surrounding vessels and represented as a 3-D triangular mesh model (Figure 1A-B). A corresponding neck plane was defined for each aneurysm and was represented as a 3-D triangular mesh model. Similar to other studies in the field,[16] the aneurysm neck plane was selected to the best of our ability at the location where the aneurysmal sac protruded outward from the parent vessel. Inflow and outflow planes were defined orthogonal to the vessel for all vessels that had direct contact to the aneurysm neck. The isolated aneurysm dome together with the neck and vessel planes represented the input to an automated measurement tool, previously introduced and validated.[27]

Morphological Feature Extraction

The following measurements were performed in an automated fashion by a validated measurement tool[27]: (1) aneurysm maximal dimension (D_{max}), defined as the largest distance between any 2 points on the aneurysm surface that could be fitted inside the aneurysm dome, (2) aneurysm maximal height (H), defined as the largest distance between the center of the neck and the aneurysm surface that could be fitted inside the aneurysm dome, and (3) vessel size for all vessels that have contact with the aneurysm neck, where an individual vessel size was defined as twice the average distance from the vessel centroid to its edges.[16] Automated measurement of all involved features removed any operator bias that may be associated with manual measurement.

SW and BIF Classification

Classification of aneurysms as SW or BIF was performed by using 2 alternative rules. First, the "one fifth" rule was used—under this rule,

aneurysms were defined as SW if they originate from only 1 parent vessel or from the origin of a branch that was much smaller than the parent vessel (less than one fifth its caliber). Second, aneurysms were defined as BIF if they were located at major bifurcations in the cerebral vasculature. Under this classification system, similar to clinical practice, OPTHA and anterior choroidal artery (ACHA) aneurysms were labeled as SW. PCOM aneurysms, originating at the carotid-posterior communicating artery junction, were classified as either SW or BIF, depending on the size of the PCOM artery relative to the internal carotid artery diameter. Fifty-nine aneurysms were classified as SW and 75 were classified as BIF (Table 1). The parent vessel feature (PV) was calculated according to this classification, namely, small vessels adjacent to SW aneurysms were excluded from analysis. With the use of the SR definition introduced by Dhar et al,[16] SR1 was calculated as the ratio between H and PV. With the use of the definition introduced by Rahman et al,[17] SR2 was calculated as the ratio between D_{max} and PV (Figure 1C). We would like to point out that all aneurysms were initially labeled as SW or BIF by the treating clinicians at the time of presentation. Their labeling was confirmed against this particular one fifth ratio rule, and, in fact, all small branches discussed here were smaller than one fifth of their parent vessels in caliber.

Second, all small vessels visible on the 3-D segmentation of the vasculature, and having direct contact to the neck of the aneurysms, were taken into account, regardless of their size relative to the corresponding parent vessel. With the use of this approach, 38 aneurysms were classified as SW and 96 aneurysms were classified as BIF (Table 1). Compared with the clinical classification, 21 aneurysms (10 ruptured) switched label from SW to BIF (12 PCOM, 5 ACHA, and 4 OPTHA). Figure 2 shows 3 of these aneurysms. The parent vessel feature corresponding to the "all small vessels" rule (PVsv) was calculated according to this classification. SR1sv was calculated as the ratio between H and PVsv, whereas SR2sv was calculated as the ratio between D_{max} and PVsv (Figure 1C) as described by the use of the BIF-specific computation of SR.[16] [F2]

Statistical Analysis

JMP statistical software (Version 8.02, SAS Institute, Cary, North Carolina) was used to evaluate the performance of parameters in rupture status discrimination. Statistical significance was assumed for $P < .05$. All variables were tested independently by using the Student t test. Multivariate logistic regression was performed separately to identify those parameters independently correlated to rupture. Bivariate analysis is used to quantify the correlation between alternative SR calculation and the square of the correlation coefficient is reported (R^2). Receiver operating characteristics (ROC) analysis was used to determine optimal threshold values for rupture status discrimination.

RESULTS

Univariate Analysis

When the analysis was performed on the entire 134 aneurysm dataset, all examined features (D_{max}, H, PV, PVsv, SR1, SR2, SR1sv, and SR2sv) were statistically significant in discriminating between ruptured and unruptured aneurysms. As expected, given the contribution of small vessels, average PV was larger than average PVsv for both ruptured and unruptured aneurysms (Table 2). Consequently, SR1 and SR2 were smaller than SR1sv and SR2sv, respectively. However, our results show no statistical difference between the performances of SR1 ($P < .001$) compared with SR1sv ($P < .001$), or between SR2 ($P < .001$) and SR2sv ($P < .001$). D_{max} ($P < .001$) and H ($P < .001$) performed as well as SR1, SR2, SR1sv, and SR2sv. Bivariate analysis between pairs SR1, SR1sv and SR2, SR2sv resulted in similar correlation with R^2 0.93. [T2]

With the use ROC analysis on the entire aneurysm population, SR1 = 2.29 (70% sensitivity and 73% specificity) was determined as the optimal threshold value to distinguish between ruptured and unruptured aneurysms. In the case of SR2, the optimal threshold value was 3.13 (61% sensitivity and 80% specificity). Similarly, SR1sv = 2.29 (68% sensitivity and 73% specificity) was determined as the optimal threshold value to distinguish between ruptured and unruptured aneurysms. In the case of SR2sv, the optimal threshold value was 3.14 (65% sensitivity and 76% specificity).

When the analysis was performed on the 21 SW aneurysms that become BIF under the "all small vessels" rule, D_{max}, H, SR1, SR2, SR1sv, and SR2sv were statistically significant in discriminating between ruptured and unruptured aneurysms (Table 3). PV ($P = .31$) and PVsv ($P = .55$) were not statistically significant in discriminating rupture status. Again, our results show no [T3]

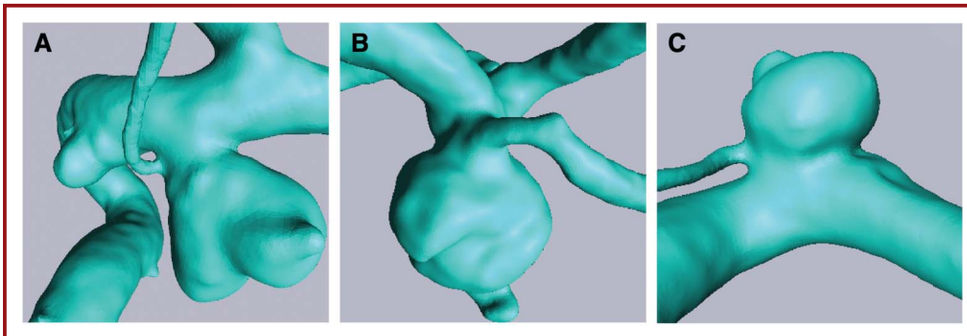


FIGURE 2. *Three instances of aneurysms that were clinically labeled as sidewall, but changed label from "sidewall" to "bifurcation" when the "all small vessels" rule was used.* **A**, *anterior choroidal artery aneurysm viewed from posteromedial view.* **B**, *posterior ~~communication~~ artery aneurysm seen from anteromedial view.* **C**, *ophthalmic artery aneurysm seen from medial view.*

AQ : 5

TABLE 2. Univariate Analysis Results for the Size Parameters Examined (Size, Height, Parent Vessel, Size Ratio)[a,b]

Feature	Ruptured Mean	Unruptured Mean	P
H	7.41 ± 3.55	5.36 ± 2.37	**<.001***
D_{max}	9.05 ± 4.00	6.90 ± 2.78	**<.001***
PV	2.59 ± 0.82	2.98 ± 0.90	**.01***
PVsv	2.39 ± 0.69	2.80 ± 0.87	**.003***
SR1	2.97 ± 1.43	1.89 ± 1.13	**<.001***
SR2	3.65 ± 1.63	2.52 ± 1.27	**<.001***
SR1sv	3.20 ± 1.60	2.11 ± 1.19	**<.001***
SR2sv	3.93 ± 1.82	2.69 ± 1.32	**<.001***

[a]H, maximal height; D_{max}, maximal size; PV, average parent vessel; PVsv, average parent vessel including small vessels; SR1, size ratio function of H; SR2, size ratio function of D_{max}; SR1sv, SR1 when considering all small vessels; SR2sv, SR2 when considering all small vessels.
[b]The values given are means with standard deviation. Analysis was applied on the whole dataset.

statistical difference between the performances of SR1 (P = 03) compared with SR1sv (P = .04), or between SR2 (P = .04) and SR2sv (P = .04). D_{max} (P = .04) and H (P = .03) performed as well as SR1, SR2, SR1sv, and SR2sv. Bivariate analysis between pairs SR1, SR1sv and SR2, SR2sv resulted in similar correlation with R^2 0.98.

With the use of ROC analysis on this 21-aneurysm group, SR1 = 2.53 (60% sensitivity and 82% specificity) was determined as the optimal threshold value to distinguish between ruptured and unruptured aneurysms. In the case of SR2, the optimal threshold value was 2.98 (60% sensitivity and 82% specificity). Similarly, SR1sv = 3.42 (60% sensitivity and 82% specificity) was determined as the optimal threshold value to distinguish between ruptured and unruptured aneurysms. In the case of SR2sv, the optimal threshold value was 4.22 (60% sensitivity and 82% specificity).

TABLE 3. Univariate Analysis Results for the Size Parameters Examined (Size, Height, Parent Vessel, Size Ratio)[a,b]

Feature	Ruptured Mean	Unruptured Mean	P
H	9.15 ± 3.76	6.03 ± 2.85	**.03***
D_{max}	11.12 ± 4.27	7.76 ± 3.01	**.04***
PV	3.23 ± 0.68	3.55 ± 0.77	.31
PVsv	2.36 ± 0.38	2.48 ± 0.57	.55
SR1	3.11 ± 1.90	1.76 ± 0.92	**.03***
SR2	3.79 ± 2.29	2.25 ± 0.95	**.04***
SR1sv	4.11 ± 2.21	2.50 ± 1.23	**.04***
SR2sv	4.99 ± 2.65	3.19 ± 1.23	**.04***

[a]H, maximal height; D_{max}, maximal size; PV, average parent vessel; PVsv, average parent vessel including small vessels; SR1, size ratio function of H; SR2, size ratio function of D_{max}; SR1sv, SR1 when considering all small vessels; SR2sv, SR2 when considering all small vessels; SW, sidewall; BIF, bifurcation.
[b]Values given are means with standard deviation. Analysis applied on the 21 aneurysms with ambiguous SW/BIF labeling.

Multivariate Analysis

Four models related to the 2 definitions of SR and the 2 classification rules were analyzed separately (Table 4). The models corresponding to the one fifth rule included first H, PV, and SR1, and second model $D_{max,}$ PV, and SR2. The models corresponding to the "all small vessels" rule included first H, PVsv, and SR1sv, and second model included $D_{max,}$ PVsv, and SR2sv. In 3 of the 4 models, SR1 and SR2 were not selected as independent parameters correlated to rupture by multivariate statistics. In 1 model (H, PVsv, SR1sv), SR1sv was selected as an independent parameter correlated to rupture together with H and PVsv. However, statistical quantification using the area under the curve (AUC) parameter showed no statistical advantage in adding SRsv to a model made only from H and PVsv (AUC of model H, PVsv, SR1sv was 0.75 vs 0.74 AUC of model H, PVsv). [T4]

DISCUSSION

SR[16-19] was introduced as a morphological parameter for the discrimination of rupture status in intracranial aneurysms and as a potential predictor of aneurysmal rupture. Recently, SR utility has come into question,[20-22] especially on particular groups of aneurysms, such as BIF aneurysms. Published comments by its proponents[22] suggested that the recently described uneven performance of SR may be explained by the removal of small vessels adjacent to SW aneurysms from SR calculation, arguing that the use of the one fifth rule was deleterious to SR performance. It is important to reiterate that SR calculation requires explicit SW/BIF labeling of aneurysms, and, depending on the resulting label, the size of outflow vessels is taken or not into consideration. More specifically, in the case of SW aneurysms, the PV parameter reflects only the size of the inflow vessel, whereas, in the case of BIF aneurysms, the PV parameter is an average of inflow and outflow vessels. As such, taking into account small vessels adjacent to what are clinically recognized as SW aneurysms (such as most ACHA, PCOM, OPTHA) results in a label switch from SW to BIF for the sole purpose of SR calculation.

Of 134 aneurysms available for this study, 21 (15.4%) were clinically classified as SW, but had to be relabeled as BIF when the strict "all small vessels" rule was used. To quantify the effect of small branches to the statistical performance of SR, the 21 aneurysm set was alternatively labeled first as SW and then as BIF. Regardless of SR definition, our statistical analysis showed no influence of the SW/BIF labeling in these aneurysms with small branches, on the statistical performance of SR. That is, removing small branches from SR calculation did not affect SR discriminating performance either on the whole 134-aneurysm set or on the group of 21 aneurysms with alternative SW/BIF labeling.

This result was to be expected, because the 21 aneurysms were all originating from the internal carotid artery, where the vast majority of SW aneurysms are located. It was previously[22] shown that SR performance in this group is mostly determined by its fractional numerator (either D_{max} or H). It follows that alternative PV calculation has little impact on SR performance. The results shown

TABLE 4. Results From Multivariate Statistical Analysis for 2 Models Corresponding to the 2 Definitions of SR[a,b]

	Model With SR1			Model With SR2		
Rule	**Feature**	χ^2	***P***	**Feature**	χ^2	***P***
Using one fifth rule to remove small vessels	H	7.67	**.006**	D_{max}	5.59	**.02**
	PV	7.45	**.006**	PV	5.63	**.02**
	SR1	2.92	.09	SR2	1.45	.23
Using all small vessels	H	9.17	**.003**	D_{max}	7.23	**.007**
	PVsv	9.32	**.002**	PVsv	7.66	**.006**
	SR1sv	4.72	**.03**	SR2sv	3.01	.08

[a]H, maximal height; D_{max}, maximal size; PV, average parent vessel; PVsv, average parent vessel including small vessels; SR1, size ratio function of H; SR2, size ratio function of D_{max}; SR1sv, SR1 when considering all small vessels; SR2sv, SR2 when considering all small vessels.
[b]Analysis applied on the whole dataset.

here confirm that finding. Indeed, regardless of SR definition or SW/BIF labeling scenario, SR performance was statistically similar to that of D_{max} and H. This is confirmed by multivariate analysis, where in 3 of 4 statistical models, SR was not identified as an independent parameter related to aneurysm rupture.

This study evaluated aneurysm and vessel morphology, in the context of SR formulations, to determine those size features that may be relevant to SR ability of identifying aneurysms with higher risk of rupture. By showing that small vessels have no impact to SR discriminating power, the results presented here attempt to clarify for the clinicians the mechanisms through which SR distinguishes between ruptured and unruptured aneurysms.

The results suggest that, clinically, aneurysms adjacent to small vessels (much smaller than the parent vessel) such as ACHA, OPTHA, and most PCOM can be considered SW for morphometric analysis. This should be encouraging for clinicians, because it was previously shown[20,22,28] that rupture status in BIF aneurysms is more challenging to evaluate and predict by the use of size and shape parameters. Based on this aneurysm population, optimal thresholds of 2.29 and 3.13 were established for SR1 and SR2, respectively. Similar values are also reported for SR1sv (2.29) and SR2sv (3.14). These threshold values are only slightly larger than those proposed by Dhar et al[16] (2.05 for SR1sv) and by Rahman et al[17] (3.0 for SR2sv).

However, it should be noted that when optimal threshold values were evaluated on the 21 aneurysms that changed label from SW to BIF, optimal values for SR definitions including small vessels were much higher in comparison with SR excluding small vessels (SR1sv 3.42 vs SR1 2.52, and SR2sv 4.22 vs SR2 2.98). These large SR values reflect the fact that ruptured aneurysms in this group tend to be much larger than ruptured aneurysms in the overall dataset (11.12 ± 4.27 mm vs 9.05 ± 4.00 mm). Because this aneurysmal group represented less than 16% of the whole dataset, these differences had little impact on the overall SR threshold. Still, clinicians who routinely label ACHA, OPTHA, and PCOM aneurysms as SW should be aware that optimal SR values for distinguishing between ruptured and unruptured groups in their population may depend on the particular aneurysm dataset makeup and may be significantly different than values previously proposed. Certainly, larger prospective studies are necessary before clinical certainty can be applied to any potential threshold value.

Regardless of definition, SR seems to have much higher specificity than sensitivity. This is especially true for definitions using the maximal size D_{max}, because SR2 has specificity 80% with sensitivity 61%, and SR2sv has specificity 76% with sensitivity 65%. Thus, when using SR for morphometric aneurysm assessment, the clinicians should be aware that SR has a good performance in identifying unruptured aneurysms, but seems to underestimate ruptured status. These results confirm the performance trend reported by Rahman et al on a 40-aneurysm dataset (reported specificity 75% with sensitivity 69%).

While there is no difference between SR performances when using all small vessels and when employing the $1/5^{th}$ rule as proposed here, we believe there are advantages in using the newly proposed labeling formulations for rupture risk prediction, for both clinicians and researchers.

First, use of the one fifth labeling rule not only simplifies the evaluation of SR (by reducing the processing burden required by small vessel measurements), but likely improves its rupture assessment reliability—with no performance loss. Small vessels are especially difficult to measure accurately, regardless of the method used. If manually measured, these vessels are particularly prone to operator bias, and measurements are highly dependent on windowing settings. If automatically measured, accurate segmentation of small vessels (often less than 1 mm diameter) is a challenging task and still an active research field. Consequently, removing small vessels from calculation increases the reliability and reproducibility of SR for rupture risk assessment.

Second, use of the one fifth labeling rule resolves the ambiguity in SW/BIF labeling and prevents situations in which the same aneurysms are labeled as SW for clinical purposes and as BIF for SR evaluation. A unique labeling methodology results in better maintained aneurysm databases, especially if they are supposed to serve a dual role as both clinical and research repositories. It also makes the transition from SR research to SR use in clinical practice more straightforward.

Study Limitations

Analysis of aneurysm shape to identify rupture status discriminants relies on the hypothesis that aneurysm shape does not change following rupture. Should aneurysm shape change significantly after rupture, the current class of analysis may not be helpful. Even though increasing evidence indicates that such a change does not occur,[29,30] conclusive data on this subject remain scant. The current analysis is retrospective in character and thus can only imply prediction of previously determined rupture status. The conclusions of this study will require validation in prospective randomized studies before their performance can be validated and applied in risk assessment of the incidentally found unruptured aneurysm in clinical practice.

CONCLUSION

The variable definition of size ratio for SW vs BIF aneurysms raises confusion for lesions harboring small-vessel branches, which are clinically considered SW, but are labeled as BIF solely for SR evaluation. This study investigated the effect of removing small branches from SR calculation to comply with the clinical description of SW and BIF aneurysms. The results show that the statistical performance of SR in discriminating between ruptured and unruptured aneurysm is insensitive to the removal of small branches. This suggests that it is reasonable to ignore small-vessel calculation for aneurysms that are clinically considered SW. The proposed methodology (1) reduces postprocessing complexity, (2) simplifies SR formulation, and (3) results in a unique SW vs BIF labeling method shared by both clinical and research practices. Based on this aneurysm population, optimal thresholds of 2.29 and 3.13 were established for SR1 and SR2, respectively.

Disclosure

This work was supported by a grant from the National Institutes of Health (NIH-R21HL102685). The senior author (Dr Malek) has received unrestricted research funding from Codman Neurovascular, Stryker Neurovascular, Microvention Inc., and Siemens Inc. for research that is unrelated to the submitted work. The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. Wardlaw JM, White PM. The detection and management of unruptured intracranial aneurysms. *Brain*. 2000;123(2):205-221.
2. Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. *N Engl J Med.* 2007;357(18):1821-1828.
3. Weir B. Patients with small, asymptomatic, unruptured intracranial aneurysms and no history of subarachnoid hemorrhage should generally be treated conservatively: against. *Stroke*. 2005;36(2):410-411.
4. Wiebers DO, Whisnant JP, Huston J III, et al. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362(9378):103-110. AQ : 3
5. Juvela S, Porras M, Heiskanen O. Natural history of unruptured intracranial aneurysms: a long-term follow-up study. *J Neurosurg.* 1993;79(2):174-182.
6. Juvela S, Porras M, Poussa K. Natural history of unruptured intracranial aneurysms: probability and risk factors for aneurysm rupture. *J Neurosurg.* 2000;93(3):379-387.
7. Wiebers D, Whisnant J, Forbes G, et al. Unruptured intracranial aneurysms—risk of rupture and risk of surgical intervention. International Study of Unruptured Intracranial Aneurysms Investigators. *N Engl J Med.* 1998;339(24):1725-1733.
8. Wiebers DO, Whisnant JP, O'Fallon WM. The natural history of unruptured intracranial aneurysms. *N Engl J Med.* 1981;304(12):696-698.
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(4):716-723.
10. 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(3):495-502.
11. Prestigiacomo CJ, He W, Catrambone J, et al. Predicting aneurysm rupture probabilities through the application of a computed tomography angiography-derived binary logistic regression model. *J Neurosurg.* 2009;110(1):1-6.
12. Lauric A, Miller E, Baharoglu MI, Malek AM. 3D shape analysis of intracranial aneursyms using the writhe number as a discriminant for rupture. *Ann Biomed Eng.* 2011;39(5):1457-1469.
13. Lauric A, Miller EL, Baharoglu MI, Malek AM. Rupture status discrimination in intracranial aneurysms using the centroid-radii model. *IEEE Trans Biomed Eng.* 2011;58(10):2895-2903.
14. Ma B, Harbaugh RE, Raghavan ML. Three-dimensional geometrical characterization of cerebral aneurysms. *Ann Biomed Eng.* 2004;32(2):264-273.
15. Raghavan ML, Ma B, Harbaugh RE. Quantified aneurysm shape and rupture risk. *J Neurosurg.* 2005;102(2):355-362.
16. Dhar S, Tremmel M, Mocco J, et al. Morphology parameters for intracranial aneurysm rupture risk assessment. *Neurosurgery*. 2008;63(2):185-197.
17. Rahman M, Smietana J, Hauck E, et al. Size ratio correlates with intracranial aneurysm rupture status: a prospective study. *Stroke*. 2010;41(5):916-920.
18. 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(4):622-631.
19. Xiang J, Natarajan SK, Tremmel M, et al. Hemodynamic-morphologic discriminants for intracranial aneurysm rupture. *Stroke*. 2011;42(1):144-152.
20. Lin N, Ho A, Gross BA, et al. Simple morphological variables for predicting the rupture risk of middle cerebral artery aneurysms. Presented at: Congress of Neurological Surgeons Annual Meeting; 2010; San Francisco, CA. AQ : 4
21. Patel A, Pravdenkova S, Krisht AF. Does the size ratio indicate a ruptured intracranial aneurysm? Paper presented at: Congress of Neurological Surgeons Annual Meeting; 2011; Washington DC.
22. Lauric A, Baharoglu MI, Gao BL, Malek AM. Incremental contribution of size ratio as a discriminant for rupture status in cerebral aneurysms: comparison with size, height, and vessel diameter. *Neurosurgery*. 2012;70(4):944-952.
23. Lanzer P, Topol EJ, eds. *Pan Vascular Medicine*. 1st ed. Berlin, Germany: Springer; 2002.
24. Xiang J, Tremmel M, Kolega J, Levy EI, Natarajan SK, Meng H. Newtonian viscosity model could overestimate wall shear stress in intracranial aneurysm domes and underestimate rupture risk. *J Neurointerv Surg.* 2012;4(5):351-357.
25. Wilson D, Noble J, Royston D, et al. Automatically finding optimal working projections for the endovascular coiling of intracranical aneurysms. In: Wells W, Colchester A, Delp S, eds. *Medical Image Computing and Computer-Assisted Interventation—MICCAI'98*. Vol. 1496. Berlin/Heidelberg, Germany: Springer; 1998:814-821.
26. Baharoglu MI, Schirmer CM, Hoit DA, Gao BL, Malek AM. Aneurysm inflow-angle as a discriminant for rupture in sidewall cerebral aneurysms: morphometric and computational fluid dynamic analysis. *Stroke*. 2010;41(7):1423-1430.
27. Lauric A, Baharoglu MI, Malek AM. Ruptured status discrimination performance of aspect ratio, height/width, and bottleneck factor is highly dependent on aneurysm sizing methodology. *Neurosurgery*. 2012;71(1):38-46.
28. Baharoglu MI, Lauric A, Gao BL, Malek AM. Identification of a dichotomy in morphological predictors of rupture status between sidewall- and bifurcation-type intracranial aneurysms. *J Neurosurg.* 2012;116(4):871-881.
29. Asari S, Ohmoto T. Natural history and risk factors of unruptured cerebral aneurysms. *Clin Neurol Neurosurg.* 1993;95(3):205-214.
30. Rahman M, Ogilvy CS, Zipfel GJ, et al. Unruptured cerebral aneurysms do not shrink when they rupture: multicenter collaborative aneurysm study group. *Neurosurgery*. 2011;68(1):155-160; discussion 160-161.