Incremental Contribution of Size Ratio as a Discriminant for Rupture Status in Cerebral Aneurysms: Comparison With Size, Height, and Vessel Diameter

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BACKGROUND: Aneurysm size ratio (SR), variably defined as the ratio of dome height (H) or maximal dimension (D_{max}) over average parent vessel diameter (PV) diameter, has been proposed as a promising aneurysm rupture status predictor.
OBJECTIVE: To evaluate the incremental contribution of SR to retrospective rupture status determination in a large high-resolution aneurysm database.
METHODS: Measurements were performed on catheter 3D-rotational angiographic volumetric datasets for 267 aneurysms (98 ruptured). SR was computed both as H/PV (SR1) and as D_{max}/PV (SR2), and its discriminant performance was evaluated on the whole dataset, on aneurysm-type subsets (bifurcation [BIF] vs sidewall [SW]), and at specific aneurysm locations. Univariate and multivariate statistical analyses were performed by the use of area under the curve (AUC) of the receiver-operating characteristics.
RESULTS: Neither SR1 nor SR2 were statistically correlated to rupture status in the BIF group, where only PV (AUC = 0.61) achieved significance. All parameters were statistically significant in the combined group, but with modest performance (AUC range, 0.62-0.74). SR1 (AUC = 0.84) and SR2 (AUC = 0.78) were strong predictors in the SW group, similar to H (AUC = 0.83) and D_{max} (AUC = 0.77). Multivariate statistics failed to support SR as an incremental independent parameter from PV, D_{max}, and H.
CONCLUSION: SR provides an uneven performance that depends strongly on the BIF/SW distribution of the data and is not useful for bifurcation lesions. In the SW subset, the incremental contribution of the SR over its H or D_{max} individual component measurements could not be validated, suggesting prior findings of its utility to be the result of aneurysm-type selection bias.

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

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It is estimated that up to 2% to 5% of the general population harbors asymptomatic intracranial aneurysms,[1] which are being increasingly detected on noninvasive vascular imaging as incidental lesions.[2] While recent studies[3,4] estimate a relatively low annual risk of rupture (0.1-0.2%) for asymptomatic unruptured aneurysms, the mortality and morbidity associated with subarachnoid hemorrhage remains daunting,[5,6] perpetuating the controversy in the management of unruptured incidental lesions.[7,8]

ABBREVIATIONS: ACOM, anterior communicating artery; **AUC,** area under the curve; **BIF,** bifurcation-type; **D_{max},** maximal dimension; **H,** aneurysm height; **ICA,** internal carotid artery; **MCA,** middle cerebral artery; **OPTHA,** ophthalmic artery; **PCOM,** posterior communicating artery; **PV,** average parent vessel diameter; **SR,** size ratio; **SW,** sidewall

At the clinical decision-making level, rupture risk assessment has been predominantly based on the concept of aneurysm size, which has been well described both in prospective and retrospective clinical evaluations.[3,4,9-11] Given that a significant number of very small aneurysms

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present with rupture, additional shape features based on relative size,[12,13] location,[3,4] and shape[12,14-16] have been proposed as superior predictors of rupture status.

Recent work[17-20] has identified size ratio (SR) as one such promising morphological feature for discriminating between ruptured and unruptured aneurysm status. There is growing evidence that aneurysm location[21] and the parent vessel geometry[22] play an important role in rupture discrimination in certain aneurysm groups. SR, by its definition, attempts to incorporate both the geometry of the aneurysm and that of adjacent vessels; SR was initially defined by Dhar et al[17] as the ratio of aneurysm dome height (H) over the average parent vessel diameter (PV) based on 3D volumetric data, but, in a recent change of definition by Rahman et al,[18] it was also computed as the ratio of aneurysm maximal size (D_{max}) divided by the average parent vessel diameter based on 2D angiographic data. Finally, in recent work by Lin et al,[23] on a large sample of 79 middle cerebral artery (MCA) aneurysms, SR was not found to be statistically significant in predicting rupture status.

With the use of a large high-resolution 3D-rotational angiography aneurysm dataset, we were unable to replicate the reported primacy of SR as a rupture status discriminant, and accordingly set out to perform a detailed evaluation of the performance of the size ratio parameter. Specifically, the objective of this study is to evaluate the relative incremental predictive contribution of SR over its component parameters (D_{max}, H, and PV) in the context of the particular aneurysm locational makeup of our patient cohort.

MATERIALS AND METHODS

Patient Selection and Demographics

Consecutive high-resolution 3D angiographic data of patients with intradural intracranial aneurysms that were diagnosed and treated between 2001 and 2008 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.[24] A total of 267 aneurysms in 225 patients were available for analysis. Saccular aneurysms were classified based on shape, and parent and daughter vessels configurations as bifurcation (BIF) (133 aneurysms, 49.8%) or sidewall (SW) (134 aneurysms, 50.2%). Aneurysms were defined as sidewall if they originated from only 1 parent vessel or from the origin of a branch that was much smaller than the parent vessel[25] (less than one-fifth[20]). Aneurysms were defined as bifurcation if they were located at major bifurcations in the cerebral vasculature.[25] Under this classification system, ophthalmic artery (OPTHA) and anterior choroidal artery aneurysms were labeled as sidewall. These are aneurysms that arise from the internal carotid artery near the origin of the ophthalmic and anterior choroidal arteries, respectively. Posterior communicating artery (PCOM) aneurysms, originating at the carotid-posterior communication junction, are classified as either sidewall or bifurcation, depending on the size of the PCOM artery relative to the internal carotid artery (ICA) diameter. Details about the locational distribution of the aneurysm dataset are provided in Table 1. A total of 98 (36.7%) aneurysms were ruptured at the time of presentation; all angiography within this set was obtained emergently and prior to vasospasm onset. Aneurysm status was labeled by the treating clinicians at the time of presentation. The temporal aneurysm shape evolution and clinical symptomatology were not followed clinically over a period of time, and

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

				Classification			
				SW		BIF	
Location	Total Number	Percentage	Parent Vessel Size, mm	Ruptured	Unruptured	Ruptured	Unruptured
ACOM	55	20.59	2.04 ± 0.42			43	12
ICA	52	19.47	3.87 ± 0.59	6	46		
PCOM	49	18.35	3.28 ± 0.74	16	23	5	5
MCA	39	14.60	2.58 ± 0.45			5	34
OPTHA	24	8.99	3.66 ± 0.50	5	19		
BA	12	4.49	2.73 ± 0.44			7	5
ICAB	10	3.74	3.36 ± 0.49			1	9
ACHA	10	3.74	3.34 ± 0.74	3	7		
ACA	4	1.49	2.70 ± 0.80		2	1	1
VA	4	1.49	2.59 ± 0.56	2	2		
SCA	3	1.12	3.03 ± 0.76			1	2
PCA	3	1.12	1.32 ± 0.27	1	2		
PICA	2	0.74	2.55 ± 0.83			2	
Total 267				33	101	65	68
				134		133	

[a]Shown are means with standard deviation. SW, sidewall; BIF, bifurcation; ACOM, anterior communicating artery; MCA, middle cerebral artery; BA, basilar artery; ICA, internal carotid artery; PCOM, posterior communicating artery; OPTHA, ophthalmic artery; ICAB, ICA bifurcation; ACHA, anterior choroidal artery; ACA, anterior cerebral artery; VA, vertebral artery; SCA, superior cerebellar artery; PCA, posterior cerebral artery.

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were not available prior to rupture. Clinical information, including rupture status, was retrieved from a prospectively maintained database.

Cerebral Angiography

Three-dimensional cerebral angiograms were obtained under general anesthesia from either Philips Integris (Bothell, Washington) or Siemens Artis (Malvern, Pennsylvania) biplane systems, and reconstructed by using their respective clinical software packages to yield the 3D volumetric dataset.

Morphological Feature Extraction

Volumetric data sets, including aneurysm and parent vessel (Figure 1A–C), were analyzed in Amira version 5.1 (Visage Imaging, San Diego, California) for segmentation followed by measurement of aneurysm characteristics in 3D space. Size measurements were performed by 2 medical operators in a blinded fashion with respect to the rupture status of the aneurysms. Both operators were provided with the same set of instructions regarding parameter definition and had access to the same 3D model of the vasculature (Figure 1C). The resulting interclass correlation coefficient was 0.92.

Size Ratio

The aneurysm-to-vessel SR was introduced by Dhar et al[17] where it was initially defined as SR = (maximum aneurysm height)/(parent vessel diameter), which we refer to here as SR1. The maximum aneurysm height (H) was measured from the centroid of the aneurysm neck to the farthest point on the aneurysm dome surface. Similar to Dhar et al,[17] the computation of the average parent vessel diameter (PV) depends on the aneurysm type. For SW aneurysms, PV represents the size of the inflow vessel (ie, vessel upstream of the aneurysm). For BIF aneurysms, PV is computed by averaging the size of all vessels that have direct contact to the aneurysm neck (Figure 1D). In both cases, an individual vessel was defined as the mean value of 2 orthogonal measurements of the vessel diameter.

Rahman et al[18] proposed a change in definition in an attempt to improve the SR applicability to 2D angiographic data and to use the parameter in a manner more typical to standard aneurysm measurement practice, that is employing the more commonly used aneurysm size instead of the aneurysm height. Under this new definition SR = (maximum aneurysm size)/(average vessel diameter), which we refer to as SR2 (Figure 1D).The maximum aneurysm size, D_{max}, is defined as the largest distance between any 2 points on the aneurysm dome surface.[22] Note that, although in some cases D_{max} may coincide with either the height of the aneurysm or its width (largest distance parallel to the neck plane), it is usually distinct from both the height and the width of the aneurysm.

Statistical Analysis

JMP Version 8.02 (SAS Institute, Cary, North Carolina) was used to analyze the data. Statistical significance was assumed for $P < .05$. The analysis was performed retrospectively, and the aneurysms were divided into ruptured and unruptured subsets for analysis. All variables were tested independently using the Student *t* test. The analysis was done on the overall group as well as on selected subsets, such as BIF and SW aneurysms, and for specific aneurysm locations. Receiver operating characteristics curve analysis was used to determine sensitivity and specificity. Multivariate logistic regression was performed separately to identify those parameters independently correlated to rupture.

RESULTS

Demographics and Presentation

From a total of 267 aneurysms, 133 were classified as BIF and 134 aneurysms as SW, with location and rupture distribution provided in Table 1. The patients' mean age was 56 years (range, 23-92 years), and 166 (73.7%) patients were women. A total of 33 aneurysms ruptured in the SW group, and 65 ruptured in the BIF group. All catheter angiography was performed within less than 24 to 48 hours from the onset of rupture, prior to onset of vasospasm.

Univariate Analysis

In the combined (SW+BIF) group, all parameters evaluated (D_{max}, H, PV, SR1, and SR2) achieved univariate statistical significance, but with unimpressive performance (Table 2). The rank order of area under the curve (AUC) values was: SR1 (0.74) > SR2 (0.70) > PV (0.69) > H (0.66) > D_{max} (0.62).

Within the BIF group, only PV (AUC = 0.61) was statistically correlated to rupture status (Table 2). Regardless of the definition used (SR1 or SR2), SR showed a poor performance in this group (Figure 2). The analysis was repeated for each of the 3 most common BIF locations from our dataset: anterior communicating artery (ACOM) (55 aneurysms), middle cerebral artery (39 aneurysms), and basilar artery (12 aneurysms) (Table 3). None of the parameters evaluated were statistically significant for these 3 locations.

In the SW group, all parameters, except PV, achieved statistical significance (Table 2). When SR was defined as a function of the aneurysm height, its performance was identical to that of H (SR1 had AUC = 0.84 vs AUC = 0.83 for H). Similarly, when SR was defined as a function of the aneurysm size (D_{max}), its performance was similar to that of D_{max} (SR2 had AUC = 0.78 vs AUC = 0.77 for D_{max}). The analysis was repeated for each of the 3 most common SW locations from our dataset: ICA (52 aneurysms), PCOM (39 aneurysms), and OPTHA (24 aneurysms) (Table 3). All parameters, except PV, showed good performance for these 3 locations.

Multivariate Analysis

Two models related to the 2 definitions of SR were analyzed separately (Table 4). The first model included H, PV, and SR1 and the second model included $D_{max,}$ PV, and SR2. The analysis was again performed on the combined group, as well as on the BIF and SW groups. Regardless of the model and of the group, SR was not selected as an independent parameter correlated to rupture by multivariate statistics, suggesting that the ratiometric definition of the size ratio failed to add any incremental discriminating ability compared with its numerator and denominator separately. In the BIF group, no parameters were statistically significant. In the SW group, H and D_{max} performed

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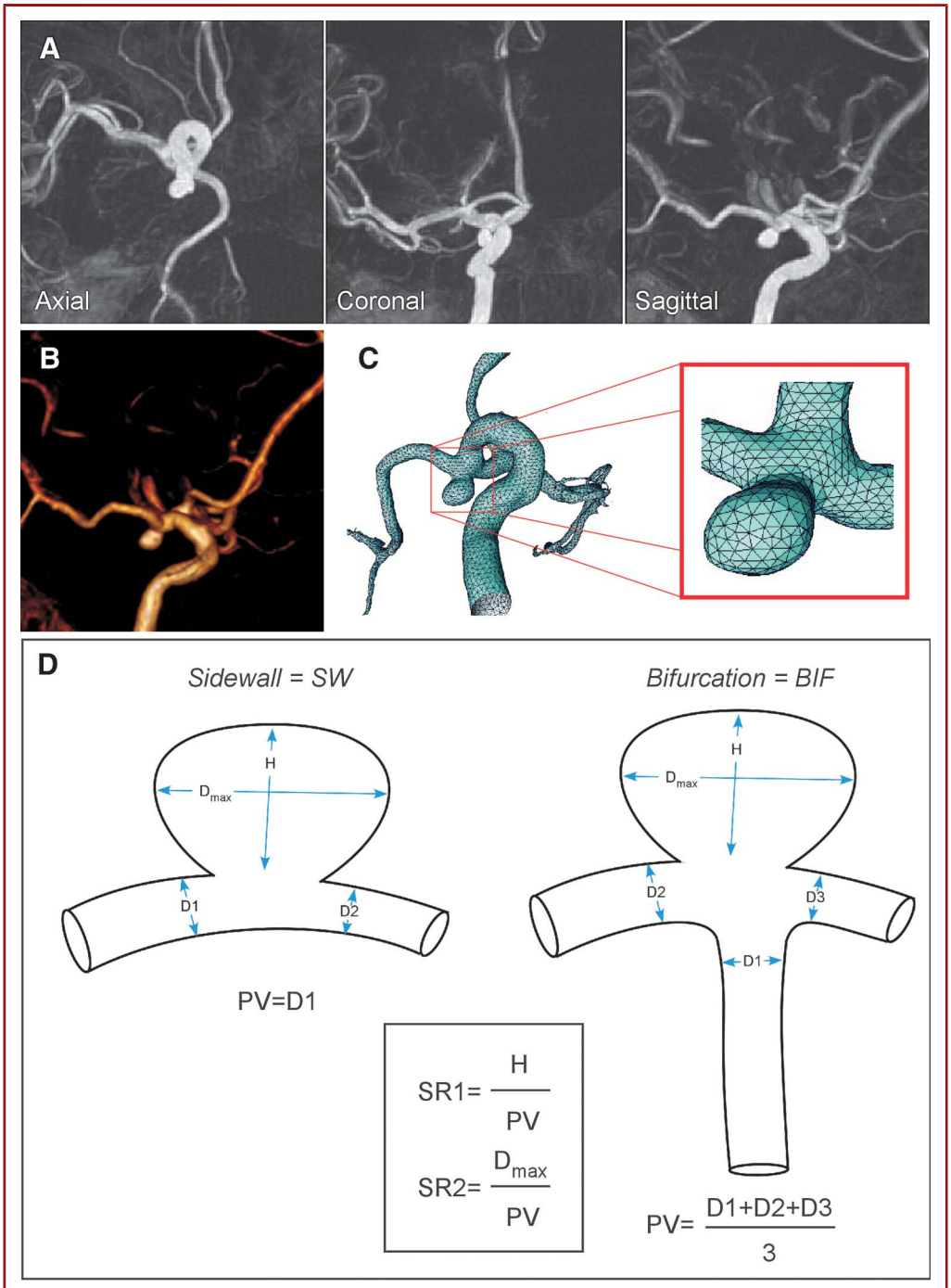


FIGURE 1. *Segmentation and isolation of aneurysms with the use of catheter-based high-resolution 3D rotational angiography.* **A**, *maximal intensity projection of the reconstructed 3D volumetric dataset in axial, coronal, and sagittal projections showing a ruptured posterior communicating artery aneurysm. 3D volumetric rendering (***B***) enables segmentation of the vascular structure from surrounding tissue and representation of the vessel surface as a triangular mesh (***C***), enabling local surface analysis and feature measurement in 3D space.* **D**, *definition of SR as a function of aneurysm and PV measurements for SW and BIF aneurysms. D1, D2, and D3 are defined as the mean value of 2 orthogonal measurements of the vessel diameter. H, height; PV, parent vessel; SW, sidewall; BIF, bifurcation.*

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TABLE 2. Results From Univariate Statistic Analysis for All Parameters Examined[a]

Group	Feature	Ruptured Mean	Unruptured Mean	*P* Value	AUC
BIF	D_{max}	7.96 ± 3.11	6.79 ± 2.96	.75	0.51
	H	6.10 ± 2.99	5.62 ± 2.87	.36	0.55
	PV	2.09 ± 0.53	2.32 ± 0.61	.03*	0.61
	SR1	3.12 ± 1.88	2.60 ± 1.49	.08	0.59
	SR2	3.58 ± 2.04	3.11 ± 1.55	.13	0.56
SW	D_{max}	9.48 ± 3.97	6.10 ± 2.97	<.001*	0.77
	H	8.89 ± 3.89	4.89 ± 2.60	<.001*	0.83
	PV	3.31 ± 0.83	3.57 ± 0.72	.08	0.59
	SR1	2.87 ± 1.59	1.43 ± 0.80	<.001*	0.84
	SR2	3.07 ± 1.66	1.78 ± 0.99	<.001*	0.78
Combined	D_{max}	7.81 ± 3.61	6.38 ± 2.98	<.001*	0.62
	H	7.03 ± 3.55	5.18 ± 2.73	<.001*	0.66
	PV	2.50 ± 0.86	3.07 ± 0.91	<.001*	0.69
	SR1	3.03 ± 1.78	1.92 ± 1.29	<.001*	0.74
	SR2	3.41 ± 1.92	2.31 ± 1.41	<.001*	0.70

[a]Shown are means with standard deviation. AUC, area under the curve; BIF, bifurcation; SW, sidewall; PV, parent vessel; SR, size ratio; H, height; D_{max}, maximal dimension; *, statistically significant parameters.

better than SR. In the combined group, H and PV were independently selected over SR1, whereas D_{max} and PV were independently selected over SR2.

DISCUSSION

Size Ratio Evaluation

SR has been introduced recently[17-20] as a promising parameter for rupture status prediction of intracranial aneurysms. However, when applied in this retrospective study to a dataset of 267 saccular aneurysms, SR performance was found to be somewhat uneven, showing strong dependence on the locational distribution of the dataset.

The univariate statistical analysis shows that, regardless of the definition used, SR is not correlated to rupture status prediction in the subgroup of 133 BIF aneurysms (Table 2). This result is similar to the poor SR performance reported by Lin et al[23]on a dataset of 79 MCA aneurysms. However, a close analysis of (1) the overall contribution of the compounding features (PV, H, D_{max}) to SR performance and (2) the aneurysm distribution by location, suggests that SR may be an unreliable feature in the combined group and a redundant feature in the SW group.

In the combined (SW+BIF) group, the performances of SR1 and SR2 were statistically similar to that of PV. This suggests that the PV contribution to SR prediction performance is very strong. Indeed, 85.2% of the aneurysms correctly identified as ruptured/unruptured by univariate SR1 analysis have also been correctly identified by the univariate PV analysis. In the case of SR2, the overlap is very similar at 84.6%. This is a direct consequence of the SW/BIF distribution in the dataset. The majority of unruptured aneurysms (59.7%) were SW aneurysms, occurring along larger arteries (vessel size 3.49 ± 0.76), whereas the majority of ruptured aneurysms (66.3%) were BIF aneurysms along smaller arteries (vessel size 2.50 ± 0.68). Thus, SR performance in the SW+BIF group, combined with the fact that SR does not discriminate rupture status in BIF aneurysms, suggest that SR discrimination ability is based mostly on the PV values with little contribution from the actual aneurysm morphology.

In the SW group, SR shows strong correlation to rupture. This is true in the overall SW group (Table 1), but also for separate location-based groups (Table 3). However, SR performance is not statistically different from that of the aneurysm measurements used in its definition. When SR is defined as a function of H, its performance is similar to that of H. In this case, 93.3% of the aneurysms correctly identified as ruptured/unruptured by univariate SR1 analysis have also been correctly identified by the univariate H analysis. Similarly, when SR is defined as a function of D_{max}, its performance is similar to that of D_{max}. In this case, 95.2% of the aneurysms correctly identified as ruptured/unruptured by univariate SR2 analysis have also been correctly identified by the univariate D_{max} analysis. The results suggest that even in this group, the use of SR, which requires multiple 3D measurements, is not justified when simpler, established parameters such as aneurysm size and height deliver similar performances (Figure 2).

Regardless of the aneurysm subset analyzed and of the SR definition used, multivariate statistics failed to select SR as a parameter independently correlated to rupture. This suggests that SR usage over its compounding measurements may not be justified.

Size Ratio Is Prone to Aneurysm-Type Distribution Bias

PV is statistically significant in both BIF and the combined group (Table 2), whereas, at the same time, it is not correlated with rupture status for any individual aneurysm location (Table 3). This

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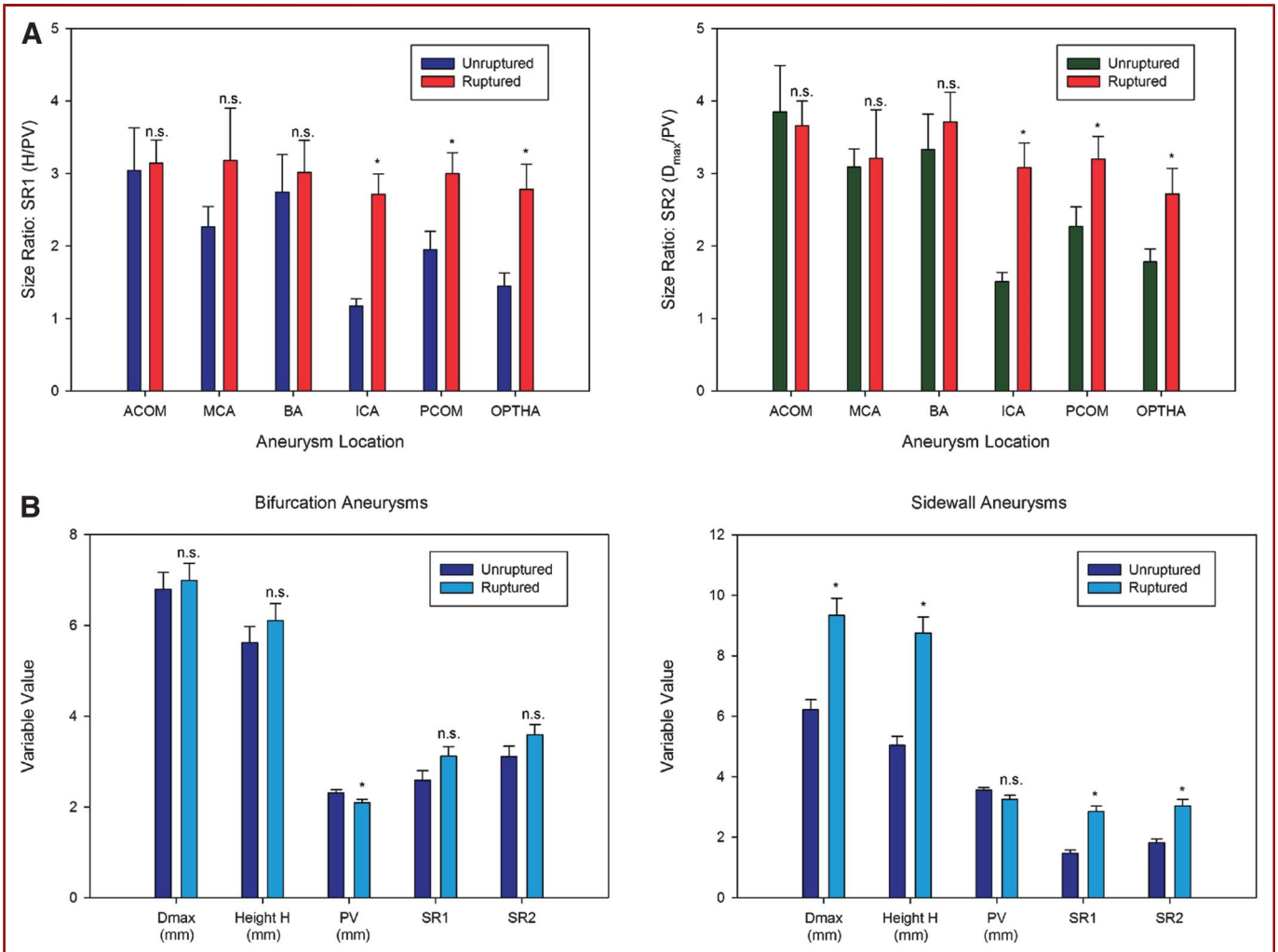


FIGURE 2. **A**, *mean and standard error differences between ruptured and unruptured aneurysms for SR1 and SR2 analysis for specific aneurysm locations (ACOM, MCA, BA, ICA, PCOM, OPTHA).* **B**, *analysis of the 5 parameters evaluated (D_{max}, H, PV, SR1, SR2) for BIF and SW groups. Statistical significant parameter are marked with * in the graph. ACOM, anterior communicating artery; MCA, middle cerebral artery; BA, basilar artery; ICA, internal carotid artery; PCOM, posterior communicating artery; OPTHA, ophthalmic artery; BIF, bifurcation; SW, sidewall; PV, parent vessel; SR, size ratio; H, height; D_{max}, maximal dimension.*

is an indication that PV use in SR definition introduces location bias into what is supposed to be a strictly morphological parameter, based on aneurysm and vessel geometry. Dhar et al[17] argued that the PV contribution over SR performance drops if particular aneurysms are excluded from the dataset; more specifically, aneurysms located on the relatively large ICA, which are suspected to have a low rupture risk. In our dataset, PV remains statistically significant even after ICA aneurysms were removed from the dataset. Most likely, this has to do with our particular location and ruptured/unruptured distribution, in which ICA aneurysms represent only 27.2% of all unruptured aneurysms. This reinforces the idea that SR ability to discriminate rupture status may be more related to the SW to BIF distribution ratio, rather than inherent additional information from its definition.

In recent work, Xiang et al[20] reported good SR discriminating power (AUC = 0.83) using SR1 definition on a 119-aneurysm dataset. The authors did not report performance results for the compounding PV and H, but SR performance can be evaluated from the perspective of the reported aneurysm location distribution (Table 1 in Xiang et al[20]). Indeed, it seems that the unruptured characteristics of the reported statistical model are trained on the SW group, which provides 69.1% of all unruptured aneurysms, whereas the ruptured characteristics are trained on the BIF group, which represents 63.1% of all ruptured aneurysms. Moreover, the majority of unruptured aneurysms (53%) are located on the relatively large ICA (3.87 ± 0.59 mm in our dataset). At the same time, the majority of ruptured aneurysms (52.6%) are located on the relatively small ACOM

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TABLE 3. Univariate Statistical Analysis[a]

Feature	Location *P* Values					
	ACOM n = 55	MCA n = 39	BA n = 12	ICA n = 52	PCOM n = 39	OPTHA n = 24
D_{max}	.60	.42	.70	<.001*	.005*	.06
H	.25	.21	.73	<.001*	.002*	.007*
PV	.27	.59	.58	.33	.41	.51
SR1	.87	.48	.67	<.001*	.01*	.003*
SR2	.80	.75	.57	.001*	.02*	.03*

[a]Shown are *P* values between ruptured and unruptured groups on most common BIF locations (ACOM, MCA, BA) and SW locations (ICA, PCOM, OPTHA), for all parameters examined. SW, sidewall; BIF, bifurcation; ACOM, anterior communicating artery; MCA, middle cerebral artery; BA, basilar artery; ICA, internal carotid artery; PCOM, posterior communicating artery; OPTHA, ophthalmic artery; *, statistically significant parameters.

(2.04 ± 0.42 in our dataset). Because of this strong polarity in ruptured/unruptured locations, it seems very likely that the parent vessel contribution to SR performance was maximized, and this resulted in the SR showing a strong biased behavior against ruptured aneurysms along small vessels. Indeed, the authors acknowledged this possible bias induced by vessel size to the SR performance. This is consistent with our results and suggests that SR is very unlikely to discriminate ruptured vs unruptured aneurysms for same location groups or for the entire BIF group. Other studies[17,18] reporting on SR performance do not provide details about SW/BIF and locational distribution, but we believe the relative importance of SR in rupture status prediction should be judged in the context of each particular dataset makeup.

Evaluation of Size Ratio Alternative Definition

This study also evaluated, in a retrospective manner, the effect on prediction performance of the change in the definition of the size ratio from SR1[17] (function of height and adjacent parent vessels) to SR2[18] (function of maximal size and adjacent parent vessels). Although the authors[18] report that this change will improve the applicability of SR while maintaining the same performance, our results show that SR1 outperforms SR2 in all groups evaluated, but especially in the SW group (Tables 2 and 4), which is the only group where SR shows strong correlation to rupture status.

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

Group	Model With SR1			Model With SR2		
	Feature	χ^2	*P* Value	Feature	χ^2	*P* Value
BIF	H	1.27	0.27	D_{max}	0.25	0.63
	PV	3.68	0.06	PV	2.09	0.15
	SR1	0.49	0.49	SR2	0.06	0.82
SW	H	1.79	0.18	D_{max}	3.89	0.05*
	PV	0.67	0.41	PV	1.98	0.16
	SR1	0.05	0.85	SR2	0.09	0.78
Combined	H	13.09	<0.001*	D_{max}	8.78	0.003*
	PV	18.17	<0.001*	PV	15.1	<0.001*
	SR1	2.74	0.09	SR2	1.74	0.18

[a]SR, size ratio; BIF, bifurcation; SW, sidewall; PV, parent vessel; H, height; D_{max}, maximal dimension; *, statistically significant parameters.

Study Limitations

Analysis of aneurysm shape to identify parameters for prediction of aneurysm rupture status stands on the hypothesis that aneurysm shape does not change after rupture; there is increasing evidence that this is the case.[26,27] Nonetheless, should aneurysm shape change significantly after rupture, shape analysis for a priori risk stratification would be of limited value.

Another potential concern relates to angiographic vasospasm affecting the ruptured aneurysm subset.[28] In the vast majority of our patients, 3D angiography was performed within 24 hours from rupture, making it less likely for vasospasm to have influenced our results. This is reinforced by the fact that for individual aneurysm locations, the size of the parent vessel was not significantly different between ruptured and unruptured aneurysms.

Finally, our analysis is retrospective in character and can only imply prediction of previously determined rupture status. The conclusions of this study will require validation in prospective randomized studies.

CONCLUSION

This study shows that SR has a more limited utility than previously reported in distinguishing between ruptured and unruptured intracranial aneurysms. SR does not introduce a major improvement in rupture prediction accuracy in comparison with its components, and its use over aneurysm size, height, and parent vessel size is not statistically justified. Moreover, SR shows strong bias based on aneurysm location, and, consequently, its performance is highly dependent on the locational distribution of the particular aneurysm dataset.

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Disclosures

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COMMENTS

Size ratio as a measure of aneurysm severity conforms to the plausible theory that aneurysms growing out of a small vessel are likely at a higher risk of rupture than one of the same size, but is growing out of a large vessel. Logic aside, how well would this notion hold up in empirical data? The verdict in the literature is mixed. But the more important question is: is size ratio merely reflecting the fact that rupture status is skewed by aneurysm location? In most reported studies including this one, majority of ACOMs (read small parent vessel) present ruptured, while the majority of ICAs (read large parent vessel) present unruptured. In this study, size ratio did turn out to be a good discriminant, but it was not any better than its component parts. This is a useful contribution to the debate about size ratio.

One important issue to note here is that discriminants of rupture status (ie, ruptured vs unruptured aneurysms) need not necessarily discriminate aneurysms that present unruptured and then evolve toward rupture from those that remain stable as pointed out by the authors. Discriminants of the latter is precisely what will be valuable clinically, so some caution is warranted in drawing conclusions from this study.

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The authors should be commended for their efforts to improve our understanding of factors predicting aneurysm rupture status. As the neurosurgical community endeavors to better understand aneurysm pathophysiology there are bound to be fits and starts regarding our investigative attempts. The authors appropriately seek to identify possible limitations of the newly developed Size Ratio metric. However, this work has several significant limitations that call into question the conclusions that have been generated. A primary limitation is the retrospective nature of this investigation. By its very nature, the evaluation of rupture status can potentially be perceived as being "retrospective" since it does not consist of following unruptured aneurysms forward in perpetuity until they rupture. However, this reality should not be confused with the difference between a retrospective and prospective study design in regard to data collection with a preceding a priori hypothesis. The authors performed a retrospective review of previously acquired data and yet compare their findings to previously reported prospective, blinded data using size ratio (SR) to predict aneurysm rupture status,[1] without identifying this very significant difference between the 2 methodologies. The authors' retrospective

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analysis introduces a number of potential selection biases to their population and weakens the strength of their conclusions.

An additional major concern, and one that is perhaps related to the retrospective study design and potential selection bias, is the unemphasized but significant finding that aneurysm size (H) was not a significant predictor of aneurysm rupture status within their bifurcation aneurysm (BIF) cohort. The authors found only parent vessel diameter (PV) was significant in this cohort. This is in contradiction to landmark studies showing that aneurysm size correlates with rupture risk.[2] This finding, if extrapolated to the population at large, would be much more surprising and potentially impactful than the findings related to SR alone. It is more likely that this contrary finding is an indicator of the limitations of the cohort rather than an important, novel discovery that can be extrapolated to typical patient populations.

For sidewall aneurysms (SW), the authors found that PV was not predictive of rupture, contrary to both the BIF cohort within this study and to the current literature. This is likely secondary to the fact that many of the aneurysms analyzed were internal cerebral artery (ICA) aneurysms, thereby, according to the authors' methodology, holding the PV size essentially constant across the analysis. By keeping PV constant, SR and size would be expected to have a similar predictive ability for detecting those aneurysms that ruptured, which is exactly what the authors found. This is directly secondary to the authors discounting small contributory arteries in their calculations. The authors justify their methodology by referring to one of the initial Size Ratio publications by Xiang et al wherein a 1/5ths rule was used to clarify "SW" vs "BIF" classification.[3] Xiang et al created the 1/5ths rule to broadly classify hemodynamic profiles for aneurysms for the purposes of their hemodynamic analysis. This was separate from their methodology of measuring SR. In fact, Xiang et al still used the methodology of Dhar et al for the determination of Size Ratio. The authors applied this 1/5ths rule to their measurement of SR, which is contrary to the prior publications ("the average diameter of the feeding and all branching vessels was used for the "average vessel diameter"[4]; "Parent vessel diameter was measured at the nearest region of definable vessel for all vessels that had direct contact with the aneurysm neck"[1]) and, as a result, removed the important contribution of such associated vessels from the analysis. This error in the authors' interpretation of the preceding publications methodology likely contributes to their contrasting findings.

In the combined group multivariate analysis SR is removed from the cohort. This is an interesting finding, but given the already acknowledged, inconsistent application of SR methodology, as well as the already acknowledged unique attributes of this data set (such as size (H) being nonpredictive in the BIF cohort) this is not particularly surprising. More surprising is that in the multivariate analysis of the BIF cohort none of the parameters achieved significance, including size and parent vessel size. This contrasts with the findings of a great number of publications.

It is well commented upon, in multiple prior publications, that part of the theorized benefit of SR is that it incorporates aneurysm location in its analysis.[4-6] The authors imply that this is a weakness of the metric; however, in reality, this is an acknowledged and emphasized strength, allowing 1 simple evaluation to account for the relative contribution of both aneurysm size and aneurysm location.

We are appreciative of all efforts to refine our mutual understanding of aneurysm pathophysiology, for such inquiries further our knowledge of this devastating disease. Additionally, as the authors rightly point out, the findings of investigations into aneurysm rupture status require confirmation in prospective observational cohorts, such as the ISUIA database, prior to gaining acceptance as practice-influencing, evidence-based indications for management decisions. In fact, such efforts are currently underway and will hopefully lead to clear-cut conclusions regarding the wealth of varied morphometrics currently described in the literature. Until that time we must rely on the best data in hand to generate hypotheses and guide future investigations. Unfortunately, the data presented by Malek et al contain significant limitations and do not, as of yet, counterbalance the growing body of literature suggesting a potential value to the SR metric.

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The authors analyzed size ratio either as height/parent vessel or as maximum diameter/parent vessel in 98 ruptured and 169 unruptured cerebral aneurysms, and found that neither version of size ratio was associated with rupture status. Studies such as this one that compare geometric findings of ruptured aneurysms vs unruptured aneurysms may help the clinician to identify a ruptured aneurysm in a patient with multiple aneurysms and no helpful clues (such as pattern of subarachnoid hemorrhage) to discriminate which aneurysm ruptured. It is unclear, however, that studies such as this one can be used to predict which unruptured aneurysms are at higher risk of rupture. For this aim, prospective studies with imaging prior to and after rupture are necessary. This type of study is, for obvious reasons, much more difficult to perform, and would require a multicenter collaborative effort (such as Rahman et al[1]) or a multicenter natural history study (such as ISUIA[2]) to accumulate enough patients with sufficient imaging. Further studies with prospective "before and after" imaging are needed so we can gain better understanding and better counsel our patients with unruptured aneurysms.

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