

Quantified aneurysm shape and rupture risk

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Object. The authors investigated whether quantified shape or size indices could better discriminate between ruptured and unruptured aneurysms.

Methods. Several custom algorithms were created to quantify the size and shape indices of intracranial aneurysms by using three-dimensional computerized tomography angiography models of the brain vasculature. Data from 27 patients with ruptured or unruptured aneurysms were evaluated in a blinded fashion to determine whether aneurysm size or shape better discriminated between the ruptured and unruptured groups. Five size and eight shape indices were calculated for each aneurysm. Two-tailed independent Student t-tests (significance $p < 0.05$) were used to determine statistically significant differences between ruptured and unruptured aneurysm groups for all 13 indices. Receiver-operating characteristic–area under curve analyses were performed for all indices to quantify the predictability of each index and to identify optimal threshold values. None of the five size indices were significantly different between the ruptured and unruptured aneurysms. Five of the eight shape indices were significantly different between the two lesion groups, and two other shape indices showed a trend toward discriminating between ruptured and unruptured aneurysms, although these differences did not reach statistical significance.

Conclusions. Quantified shape is more effective than size in discriminating between ruptured and unruptured aneurysms. Further investigation will determine whether quantified aneurysm shape will prove to be a reliable predictor of aneurysm rupture.

KEY WORDS • aneurysm • aneurysm rupture • quantified aneurysm shape • subarachnoid hemorrhage

IDENTIFYING indicators of impending cerebral aneurysm rupture has been an area of considerable interest for many years. Among the many variables considered, aneurysm size is the best studied, and a correlation between lesion size and risk of rupture has been documented. Nevertheless, it is well known that many small aneurysms rupture and that many aneurysms reach a large size without causing SAH. Other factors may also have value in predicting which intact aneurysms is likely subsequently to rupture.³⁰ Aneurysm morphology may be such a factor. In a study of 54 patients, Asari and Ohmoto² reported that 35% of multilobular aneurysms ruptured as opposed to 4% of unilobular ones, a finding supported by data from other independent studies.^{5,13,22}

Ujiie and colleagues^{25–27} proposed that the AR of the aneurysm (ratio of depth to neck width) may be a risk factor for rupture. In their retrospective study of angiographic data,

Abbreviations used in this paper: AR = aspect ratio; AUC = area under curve; BF = bottleneck factor; CP = conicity parameter; CT = computerized tomography; D_{max} = maximal aneurysm diameter; D_n = aneurysm neck diameter; EI = ellipticity index; G = gaussian curvature; GLN = norm of gaussian curvature; H = aneurysm height; M = mean curvature; MLN = norm of mean curvature; NSI = nonsphericity index; PCoA = posterior communicating artery; ROC = receiver-operating characteristic; S = surface area of aneurysm wall; SAH = subarachnoid hemorrhage; UI = undulation index; V = aneurysm volume; 2D = two-dimensional; 3D = three-dimensional.

103 (80%) of 129 ruptured aneurysms had an AR greater than 1.6, whereas 70 (90%) of 78 unruptured aneurysms had an AR less than 1.6.²⁷ We performed a similar retrospective study of angiographic data on 57 aneurysms from 42 consecutive patients.²⁰ We found no statistically significant difference in the AR between the 30 ruptured and 27 unruptured aneurysms. Beck, et al.,³ studied retrospective angiographic data on 53 unruptured and 94 ruptured aneurysms. For lesions in the 5- to 9-mm diameter range alone, they found significant differences between the two groups in AR and the presence of lobulation. Interestingly, in contrast to the findings of Ujiie, et al.,²⁷ ruptured aneurysms had a lower AR than unruptured ones (1.8 compared with 2.3, respectively). Beck and colleagues reported that 12 (21%) of 57 ruptured aneurysms had an AR of less than 1.5, whereas 26 (100%) of 26 unruptured aneurysms had an AR greater than 1.5. Ebina, et al.,⁶ also studied the role of a cerebral aneurysm AR but correlated it to postoperative outcome.

In a study of 16 brain aneurysms that grew in size, Sarwar, et al.,²³ noted that all the lesions had an irregular shape. Some authors have proposed physics-based theories for the shape–rupture correlation. Ujiie, et al.,²⁷ found that significant low-flow regions—a possible cause for atherosclerotic inflammation—develop with increasing ARs. Hademenos, et al.,^{11,12} and Chitanvis, et al.,⁴ showed that lesion shape can significantly affect wall tension, a finding confirmed by

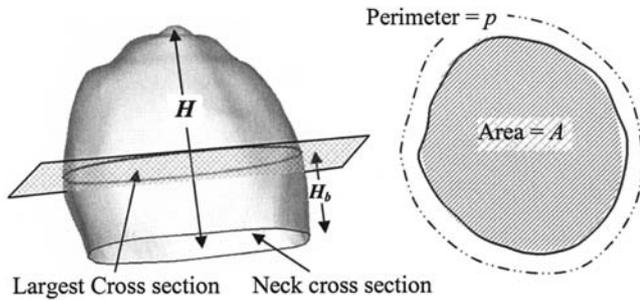


FIG. 1. Illustration of size indices in a representative lesion. Diameter for the noncircular cross-sections are calculated using area and perimeter.

Kyriacou and colleagues¹⁷ who used rigorous mathematical models. The role of aneurysm morphology in the risk of rupture of abdominal aortic aneurysms has also been noted. Elger, et al.,⁷ Vorp, et al.,²⁹ and Raghavan, et al.,²¹ found that abdominal aortic aneurysms of similar sizes have dramatically different tensile wall stress depending on their asymmetry and irregularity. Fillinger and colleagues^{8,9} demonstrated that shape was the one key factor that caused greater tensile wall stress in abdominal aortic aneurysms that ruptured compared with those that did not. There is therefore ample reason for a more sophisticated investigation of cerebral aneurysm shape as a predictor of rupture.

A common limitation in the previous studies on cerebral aneurysm shape is the use of 2D angiographic data for defining and calculating shape features such as the AR. Standard cerebral angiographic projections are 2D images. Cerebral aneurysms are often asymmetrical structures that do not allow for simple extrapolation of 3D morphology from 2D data. Thus the measurements of geometric features can vary with the angiographic projection used, resulting in multiple findings for the same aneurysm. This phenomenon may partially explain the contradictory findings of different reports in regard to the effect of AR and risk of aneurysm rupture.^{3,20,27}

A second limitation in using aneurysm shape as a predictor of aneurysm rupture has been the use of nominal rather than continuous variables to describe shape features (for example, classifying lesions as either unilobular or multilobular). Aneurysms have a spectrum of shapes varying from those that have clearly perceptible daughter lobes to almost imperceptible irregularities of the aneurysm wall. Determining how large an irregularity must be before a lesion is categorized as multilobular is an arbitrary decision. Similar problems arise in other shape categorizations such as regular or irregular, elliptical or spherical, and so forth. A more productive way to study whether aneurysm shape is correlated with risk of rupture is to develop numerical indices that quantify particular shape features within a 3D matrix. Rather than categorizing an aneurysm into a particular group, such indices would quantify the degree of the shape feature in the lesion, which may then be placed within a population spectrum for that shape. This method would allow for a statistically reliable assessment of the use of quantified shape as a predictor of rupture.

Shape, unlike size, is an inherently qualitative feature. Although it is easy to quantify size, it is more difficult to quantify shape. One can study shape by identifying specific morphological features of interest and developing numer-

Shape Index	Low	Medium	High
Undulation index (UI)			
Aspect ratio (AR)			
Ellipticity index (EI)			
Non-sphericity index (NSI)			
Conicity parameter (CP)			
Bottleneck factor (BF)			

FIG. 2. Definitions of selected shape indices and accompanying schematic illustrations.

ical indices that quantify those features. Based on methods in differential and computational geometry, we recently developed and reported¹⁸ a set of global indices for the size and shape of an intracranial aneurysm sac and demonstrated the value of these indices by using anatomically accurate 3D aneurysm geometry reconstructed from CT angiography studies.¹⁵ In the present study, we have used these algorithms to calculate the size and shape indices in a population of ruptured and unruptured aneurysms to determine which index better discriminates between ruptured and unruptured lesions.

Materials and Methods

Study Population

Twenty-seven patients who had presented with a ruptured or unruptured cerebral aneurysm and who had undergone CT angiography were included in this study. Eighteen of these patients harbored unruptured aneurysms and nine harbored ruptured lesions. Computerized tomography angiography scanning was performed at 1.25-mm collimation and 0.6-mm slice thickness. The 3D geometry of the cerebral aneurysm along with the surrounding vasculature was reconstructed using a manually assisted/verified automated edge-detection algorithm (Medical Media Systems, Inc., West Lebanon, NH).

The aneurysms were separated into two groups: those ruptured on presentation (eight lesions) or prior to treatment (one lesion; ruptured group nine lesions); and those intact on presentation, prior to treatment, or during follow up (unruptured group 18 lesions).

In the unruptured group there were seven middle cerebral artery aneurysms, three basilar apex aneurysms, two anterior communicating artery aneurysms, two anterior cerebral artery aneurysms, two ophthalmic artery aneurysms, one internal carotid artery aneurysm, and one PCoA aneurysm. In eight patients with unruptured aneurysms, no treatment was recommended; these patients were followed up for as long as 4 years and no aneurysm rupture occurred. Ten patients underwent successful microsurgical treatment of the unruptured aneurysms.

In the ruptured group there were two basilar apex aneurysms, two

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anterior communicating artery aneurysms, one internal carotid artery aneurysm, and three PCoA aneurysms. Seven patients underwent successful microsurgical treatment for their ruptured aneurysms. One 86-year-old patient did not undergo surgery. Because of the small number of aneurysms in each group, lesions were not stratified according to location in our analyses. Patients were evaluated based on age and sex to determine whether these variables were predictive of aneurysm rupture.

Reconstruction of Lesion Geometry

We developed a suite of custom algorithms (Matlab, version 6.1; Mathworks, Inc., Natick, MA) to automate the determination of size and shape indices of intracranial aneurysms from 3D models of the brain vasculature. The reconstructed computer model is a mesh of triangles in 3D space patched together to form the aneurysm wall. Because its original purpose was visualization, the reconstructed surface contained sharp corners and stair-step effects. The aneurysm model and the surrounding vasculature were first smoothed to eliminate such artifacts while retaining the genuine geometric features. The aneurysm geometry was then isolated from the surrounding vasculature by using a cutting plane that just touched the adjoining branch vessel. All further geometric calculations were performed on the isolated aneurysm model. Detailed description and illustration of the technical aspects of the methodology are provided in an earlier report.¹⁸

Size Indices

Volume of an aneurysm is likely to be the best descriptor of size. For completeness, however, we also calculated the following size indices: S , D_{max} , H , and D_n . Both V and S were calculated using numerical integration.¹⁷ Given that the cross-sections of an aneurysm surface are noncircular, "diameter" was defined as $4A/p$, an approximation commonly used in fluid mechanics,³¹ where A is the area of the cross-section, and p its perimeter (Fig. 1). Maximal diameter was the largest of all cross-sections along the height of the aneurysm, and D_n the diameter of the neck cross-section (that is, at the cutting plane). Aneurysm height was the maximal perpendicular distance from the neck plane to the top of the aneurysm dome.

Shape Indices

Shape features of interest were identified and each feature was quantified by one or more indices. Although a particular index is unlikely to capture all aspects of shape, if calculated with rigor, the index could accurately describe one or more shape features of interest. Figure 2 features illustrations of the meaning of the relevant shape indices.

Undulations in the Aneurysm Wall. Undulations in the aneurysm wall surface are often referred to as irregularities, lobulations, or daughter sacs. Biomechanically, large undulations are likely regions of stress concentrations.^{9,21} Furthermore, earlier findings of the lobulation-rupture correlation^{2,3,23} indicate that undulations are an important shape feature to study. We developed a UI of the lesion surface, $UI = 1 - (V/V_{CH})$, where V_{CH} is the volume of the convex hull of the aneurysm in question. The convex hull of an aneurysm is the smallest surface that completely encompasses the lesion while also being convex at all points,²⁴ similar to a plastic wrap tightened around the aneurysm (Fig. 3). Physically, UI is the volume encapsulated between the aneurysm and its fully convex self (convex hull), expressed as the percentage of the convex hull volume. The UI can vary from 0 to 1. A completely convex aneurysm—that is, one with no undulations—will have an undulation index of 0 (for example, $UI_{sphere} = UI_{hemisphere} = UI_{ellipsoid} = 0$). The greater the undulations of a surface, the greater the volume encapsulated between the aneurysm and its convex hull and hence the greater will be the UI (Fig. 2).

Ellipticity of Aneurysm Sac. One commonly studied shape feature can be described as the ellipticity of the aneurysm, and the AR is one of the indices that attempts to capture this feature. We used two indices to quantify this feature: AR and EI.

The AR (H/D_n) is by definition the same as that used in earlier angiographic studies, except that H and D_n are 3D-averaged variables. Consequently, AR is unique for a given aneurysm sac, although it

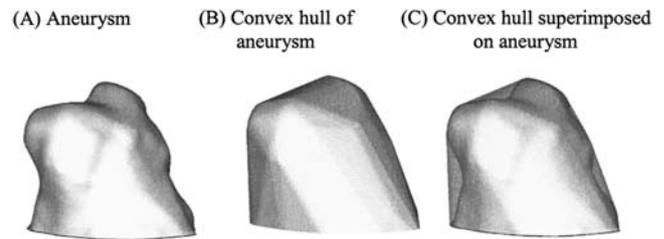


FIG. 3. Illustrations of the convex hull in a highly undulated aneurysm. Note that the convex hull surface touches the convex regions of the sac wall (C) but not the concave regions similar to a tight elastin membrane wrapped around it.

can vary from 0 to ∞ . It is equal to 0.5 for a hemisphere, greater than 0.5 for an egg-shaped (prolate spheroid) lesion, and less than 0.5 for a mushroom-shaped (oblate spheroid) lesion. In practice, the latter types of lesions are far too rare (none in our study population) and hence it is not unreasonable to assume that greater ARs indicate greater ellipticity of a lesion.

To provide a more reliable measure of ellipticity, we defined a new term, "EI." Unlike AR, EI is defined using 3D variables: the volume and surface area of the convex hull of the aneurysm.

$$EI = 1 - (18\pi)^{\frac{1}{3}} \frac{V_{CH}^{\frac{2}{3}}}{S_{CH}}$$

where S_{CH} is the surface area of the convex hull and V_{CH} is the volume of the convex hull. We deliberately use the convex hull of the aneurysm to calculate EI rather than the actual aneurysm to avoid surface undulations from corrupting the index. Consider, for example, a hemispherical aneurysm that has some surface undulations. The surface area of the aneurysm is likely to be greater purely because of the surface undulations. If the actual aneurysm is used for calculating EI, the artificially inflated index will be indicative of an ellipsoidal lesion, which would be erroneous. Instead, by using the formula for the EI, such an aneurysm will have a low index (Table 1). The EI varies from 0 to 1 and is equal to 0 for a hemisphere and increases with increasing ellipticity. Unlike AR, EI will be higher for both egg-shaped and mushroom-shaped lesions.

Deviation From Spherical Shape (Nonsphericity). If a homogeneous distribution of wall tension is likely to result in a stable lesion with a low risk of rupture, then a spherical shape is likely to be the most stable. The level to which an aneurysm surface deviates from a spherical shape therefore could be a good index of instability. This deviation could come from undulations and/or ellipticity, but both will result in a relative increase in surface area of the lesion compared with its volume. We therefore defined an NSI as

$$1 - (18\pi)^{\frac{1}{3}} \frac{V}{S}$$

For all practical purposes, NSI will vary from 0 to 1. It is equal to 0 for a hemisphere and increases with increasing deviation from the spherical shape, be it due to undulation or ellipticity. Indeed, NSI may be thought of as an aggregate of UI and EI.

Conicity of the Aneurysm Wall. Aneurysms that grow rapidly at their dome may be at a different stage of growth and rupture risk compared with those that grow at a region closer to their neck. In the former case, the largest cross-section (where $D = D_{max}$) is likely to be closer to the dome and the lesion will resemble an inverted cone. In the latter case, D_{max} will be closer to the neck plane and the lesion will resemble an upstanding cone. We defined a CP as $0.5 - (H_b/H)$, where H_b is the height of the cross-section from the neck plane at which D_{max} occurs. The CP can vary from -0.5 to 0.5 . It is equal to 0 when D_{max} occurs at the midsection (barrel shaped, quite unlike a cone), 0.5 for D_{max} at the neck plane (an upstanding cone), and -0.5 for D_{max} at the dome (an inverted cone; Table 1). Note, however, that some caution is warranted in interpreting CP. It is not exactly an in-

TABLE 1

Size and shape indices for unruptured and ruptured aneurysms*

Index	Unruptured Aneurysm	Ruptured Aneurysm	p Value	AUC†
age	57 ± 13	56 ± 19	0.857	0.44
sex (% female)	89	67	0.296	—
volume (V)	84 ± 59	146 ± 219	0.264	0.48
max diameter (D _{max})	4.81 ± 1.37	4.87 ± 1.86	0.918	0.45
surface area (S)	83 ± 41	122 ± 128	0.243	0.53
height (H)	5.13 ± 1.54	6.55 ± 3.80	0.175	0.60
neck diameter (D _n)	4.25 ± 1.38	3.79 ± 1.58	0.443	0.42
undulation index (UI)	0.071 ± 0.039	0.137 ± 0.066	0.003	0.80
aspect ratio (AR)	1.27 ± 0.40	1.85 ± 0.79	0.016	0.72
ellipticity index (EI)	0.131 ± 0.047	0.185 ± 0.052	0.011	0.76
nonsphericity index (NSI)	0.156 ± 0.058	0.233 ± 0.061	0.004	0.83
conicity parameter (CP)	0.199 ± 0.194	0.152 ± 0.222	0.579	0.40
bottleneck factor (BF)	1.156 ± 0.171	1.387 ± 0.492	0.082	0.60
mean curvature norm (MLN)	0.333 ± 0.057	0.384 ± 0.057	0.038	0.72
gaussian curvature norm (GLN)	2.051 ± 0.868	2.699 ± 0.899	0.083	0.69

* Values are presented as the means ± standard deviations.

† Represents predictive capability of an index. An AUC of 0.5 indicates an index with zero predictability.

dex of the lesion’s similarity to a cone shape. After all, even a hemisphere will have a CP of 0.5, the maximal possible value. Rather, it is a measure of the location of the largest bulge in the lesion and hence indicative of a useful morphological feature. We chose the word “parameter” rather than “index” to differentiate our term from the more commonly used “conicity index,” an anthropometric indicator of abdominal obesity.^{27,28} Both are similar in principle, but the mathematical definition for CP is more suited to aneurysm topology.

Bottleneck Effect due to the Lesion Neck. An aneurysm with a small neck compared with its size can act as an obstruction to entry of blood flow into the sac, causing abnormal hemodynamics such as low or high shear stress and low velocities. Such changes have been consistently shown to trigger atherosclerotic inflammatory processes.^{10,19} We therefore defined BF as D_{max}/D_n . The value of BF can vary from 1 to ∞. It is equal to 1 for a lesion with no bottleneck ($D_n = D_{max}$) and increases as the bottleneck effect increases (neck diameter becomes relatively smaller).

Curvature of the Aneurysm Wall. Curvature of a point on a surface may be described using two variables: M and G. Using these curvatures, it is possible to determine whether a given point lies in a convex, concave, or saddle region. A saddle region is convex from one plane and concave from another plane (for example, horse saddle, gooseneck, or the Pringles chip). A surface-wide average of M and G provides a global measure of curvature. In a study of differences in cortical shape features between normal and schizophrenic patients, Smith²⁴ reported on two indices of total amount of curvature, namely, the MLN and GLN. Mathematically, they are an average of the M and G for all points on the aneurysm’s surface, but they are normalized against that for a sphere of the same volume. Thus MLN and GLN are nondimensionalized indices. Physically, they provide a measure of the predominating shape characteristic of the aneurysm surface. We used differential geometry techniques reported on by Hamann¹⁴ to develop algorithms for the determination of MLN and GLN. Data in our earlier report¹⁸ details the concept and methodology used to determine the distribution of M and G and calculation of MLN and GLN in an aneurysm model.

Statistical Analysis

The five size and eight shape indices were calculated for all 28 aneurysms in the study population. Two-tailed independent Student t-tests (significance $p < 0.05$) were performed between ruptured and unruptured groups for all 13 indices and for patient age to study sta-

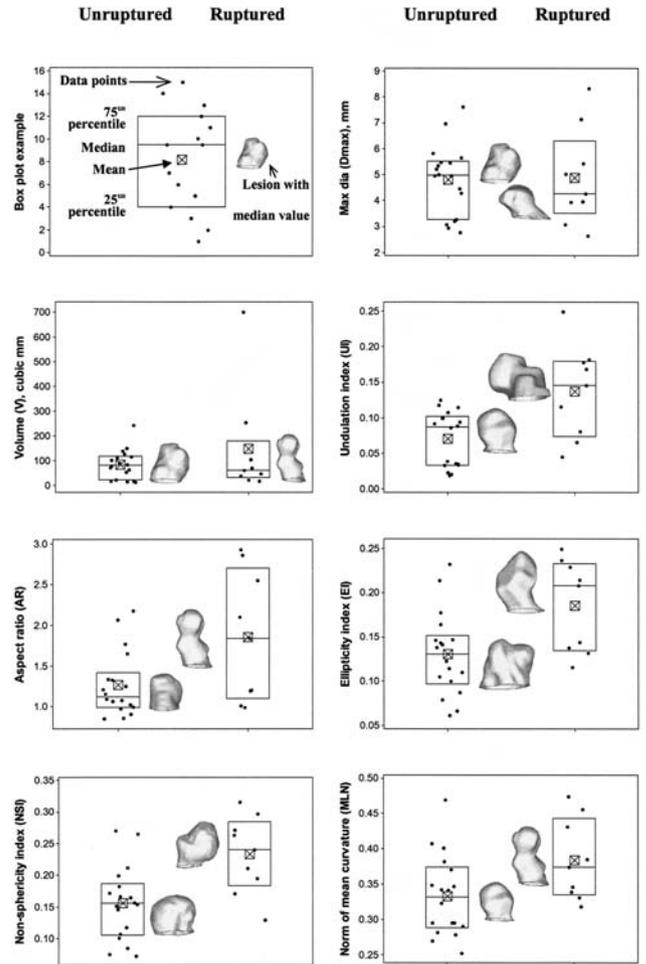


FIG. 4. Box plots of the five shape indices that showed statistical significance for comparison between the ruptured and unruptured lesion groups. Size indices are also shown. The aneurysms shown are shaded surface views of the 3D computer models (not to scale).

tistically significant differences. In the case of nominal variables (sex), we used the Fisher exact test. The ROC curve analyses were performed for all the indices to quantify the predictability of each index and identify the optimal threshold. All statistical analyses were performed using commercially available software (MS Excel; Microsoft Corp., Redmond, WA). To create box plots of the results, we used statistical software (Minitab, State College, PA).

Results

Table 1 shows the comparison of indices between the two lesion groups. Figure 4 shows the box plots for selected size and shape indices. We did not find a statistically significant difference in age ($p > 0.8$) or sex ($p > 0.2$) between the ruptured and unruptured aneurysm groups. There was no statistically significant difference among any of the five size indices between the two groups. Of the shape indices, NSI, UI, EI, AR, and MLN were statistically significantly different between the ruptured and unruptured groups. The GLN and BF also approached statistical significance ($p < 0.085$) in this small group of patients. The CP was not different between the two groups ($p > 0.5$).

The ROC curves, which are representative of the predictive capability of a particular index, were generated for all

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the indices. When sensitivity and specificity are plotted as shown in Fig. 5, an index that has zero predictive capability will be a straight line from bottom left to top right, whereas the 100% accurate predictor will rise vertically from bottom left to top left, then move horizontally from top left to top right. Thus, the shape of the ROC curve may be used to compare the predictive capabilities of different indices of the same condition. Furthermore, the ROC-AUC curve is a quantitative indicator of predictability. We calculated the ROC-AUC for all indices. We found that the nonsphericity index was the best indicator of rupture followed by UI, EI, MLN, and AR, in that order. The AUC for all indices is also listed in Table 1. The ROC curves for selected size and shape indices are shown in Fig. 5.

Discussion

Identifying reliable indicators of risk for rupture of an intact lesion could vastly improve clinical management of intracranial aneurysms. Many possible variables have been studied and reported in the literature, but it is fair to say that there is much room for improvement in our ability to predict which unruptured aneurysm will subsequently produce SAH.³⁰ We believe that aneurysm shape could be an extremely important factor, but our determination of this characteristic remains unsophisticated.

Harbaugh and colleagues¹⁵ were the first to report the use of 3D CT angiography for the diagnosis of cerebrovascular lesions. Since then, CT angiography has come to be used with ever greater frequency for the diagnosis and preoperative evaluation of patients with cerebrovascular disease. The raw information needed to quantify aneurysm shape is now routinely obtained during CT angiography studies (and also in 3D digital subtraction angiography and magnetic resonance angiography). We believe that these data should be used for a more sophisticated analysis of aneurysm shape that might lead to accurate predictors of aneurysm rupture.

Shape is known to show substantial variation among aneurysms and there is a good theoretical basis for its association with rupture risk, although it has not been extensively studied as a predictor of SAH from a previously unruptured aneurysm. The few studies that have been focused on aneurysm shape provided very useful insights but have been confined to one-dimensional (length) or 2D (AR) indices or the use of arbitrary human discretion for nominal categorizations (multilobed). We adopted rigorous geometrical and computational approaches to quantify various shape characteristics. The details of the algorithms were discussed in an earlier study, which was the first to be focused on the 3D shape of cerebral aneurysms.¹⁸ In the present study, we report on some of these earlier indices and new indices that might be related to the risk of aneurysm rupture. Furthermore, we calculated size and shape indices for a population of ruptured and unruptured aneurysms, compared these indices, and identified the best discriminators of aneurysms initially presented with or without rupture.

Size Indices

Our statistical comparisons show that, within this study population, none of the size indices would have been reliable discriminators of aneurysms initially presented with or

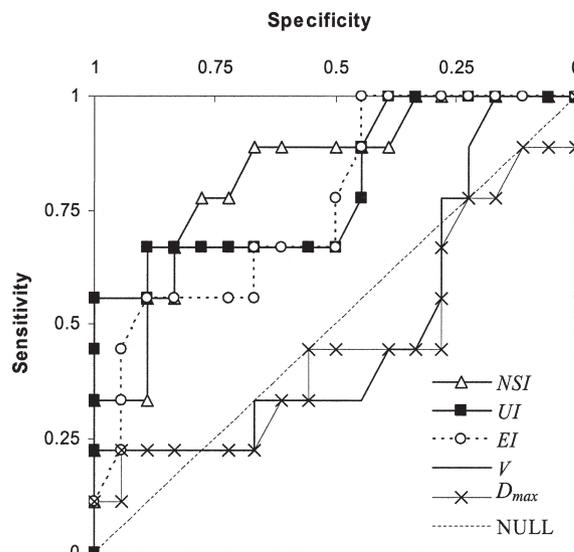


Fig. 5. Graph of ROC curves for rupture predictability demonstrating a comparison of the size indices V and D_{max} with the three most predictive shape indices. NULL denotes a hypothetical index with zero predictive capability. The farther an index's curve is from the NULL curve, the greater its predictive value. Note that V and D_{max} are quite close to NULL, whereas NSI, UI, and EI are much farther away throughout their ranges.

without rupture. The fact that the ROC curves for V and D_{max} were slightly below the null predictor was expected given that the median of the size indices for the ruptured group were slightly smaller than that for the unruptured group, although not statistically significantly so.

Shape Indices

Many of the shape indices were found to be significantly different between the two groups, with their respective ROC curves showing substantially greater ability to discriminate between the ruptured and unruptured groups. The NSI was the best predictor of rupture (AUC 0.83), indicating that the more an aneurysm shape deviates from that of a sphere (that is, greater surface area compared with volume), the greater its risk of rupture. This deviation may be due to undulation and/or ellipticity. At its optimal threshold, based on ROC analysis, 78% of ruptured aneurysms had an NSI greater than 0.183, whereas 78% of unruptured aneurysms had an NSI less than 0.183. We are unaware of any previous report on a variable similar to NSI.

The UI (AUC 0.80) closely followed NSI as a predictor. The UI captures the level of undulations on the lesion surface. Such undulations may come from large perceptible lobulations, localized daughter sacs, or minor concavities. Although UI does not quite differentiate among these undulations, lobulations are likely to more significantly elevate UI. In an expanding membrane, a fully convex surface would be the norm. Nonconvex regions are likely the result of local wall abnormalities that occur during the aneurysm growth process. The level of nonconvexity (that is, undulation) therefore may indicate the level of underlying aneurysm wall abnormality. This concept is the logical basis for the undulation index. Our results indicate that the greater the undulations on a lesion surface, the greater the risk of

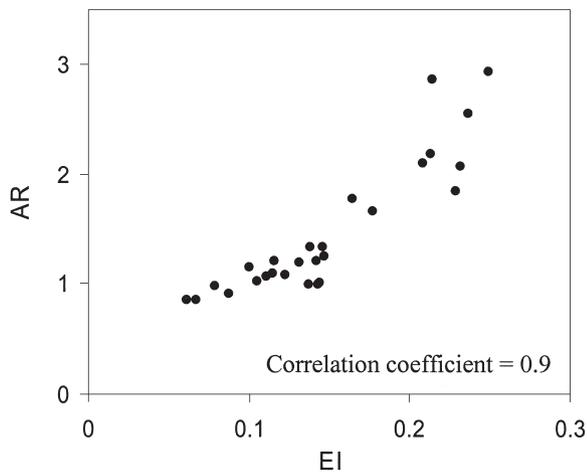


FIG. 6. Graph demonstrating the correlation between the two indices of lesion ellipticity—AR and EI.

rupture. At the optimal threshold, 67% of ruptured aneurysms had a UI greater than 0.116, whereas 89% of unruptured aneurysms had a UI less than 0.116. These results are in agreement with the findings of Asari and Ohmoto,² and Beck, et al.,³ that multilobed lesions are a risk factor for rupture.

The indices representing ellipticity of the lesion—EI (AUC 0.76) and AR (AUC 0.72)—were also found to be statistically significantly different between the two lesion groups and had good predictive value. The EI was defined using inherently 3D variables such as volume and surface area. By defining EI as the relative surface area of the convex hull of an aneurysm normalized to a hemisphere of similar volume, the effects of surface undulations were eliminated. Conceptually, EI is the ellipticity of the convex hull of an aneurysm and truly represents the level to which an aneurysm resembles an ellipsoid. On the other hand, AR is defined using one-dimensional variables like height and diameter, although both are determined from 3D averaging. Although AR has a clear meaning, it can be misleading in the case of lesions whose long axis is oblique or bent and in the case of mushroom-shaped aneurysms. Nevertheless, within our study population, AR appears to be a good a predictor. The correlation between EI and AR is quite high because they both attempt to capture the same feature albeit with different mathematical definitions (Fig. 6). Results from the present study also differ from an earlier study in which we used 2D angiographic measurements to determine AR.²⁰ We have greater confidence in the present analysis because aneurysm shape, as previously discussed, is much more accurately determined using 3D studies than 2D ones. Our results on AR agree with the findings of Ujiie, et al.,²⁷ who found that the greater the AR, the greater the risk of rupture. In contrast, Beck, et al.,³ observed the opposite relationship. We found that five (56%) of nine ruptured lesions had an AR greater than 1.6 (the cut-off value previously reported by Ujiie, et al.,²⁷) and 14 (78%) of 18 unruptured lesions had an AR less than 1.6. Incidentally, the optimal threshold for AR in our study population was 1.77.

The MLN on the lesion surface was statistically different between the two groups and the GLN showed trends toward significance. Globally, the meaning of these curvature in-

dices, MLN and GLN, are rather unclear given that they may be affected by multiple shape features. Mathematically, they are a measure of the deviation from a spherical shape and provide a measure of the predominating shape characteristic.

The BF was not statistically different between the two groups. Its predictability based on ROC curve analysis (AUC 0.60) was lower than most of the aforementioned shape indices. The BF is likely to have a greater role in predicting the success of endovascular coil placement or the ease of microsurgical clip application than the risk of aneurysm rupture.

The CP, a measure of the longitudinal location of the largest bulge, does not differentiate between the two groups. The CP varied from -0.1 to 0.5 , indicating that the maximal bulge was mostly at or below the midsection of the lesions. In other words, none of the aneurysms had an inverted conelike appearance.

Correlation Between Shape and Size Indices

The shape indices were defined as dimensionless quantities with the intention of capturing geometric features independent of size. A study of the correlation between shape indices and aneurysm volume in our study population indicated that abnormal shape characteristics are not confined to larger aneurysms but instead are distributed randomly across all sizes. The correlation coefficients with V for BF (0.14), UI (0.18), EI (0.24), and NSI (0.27) were the lowest, followed by CP (-0.30), AR (0.37), GLN (0.50), and MLN (0.56). Correlation with D_{\max} was consistently lower than with V for all indices.

This is a very important finding and may help to explain the conundrum posed by the data from the International Study of Unruptured Intracranial Aneurysms:¹⁶ If aneurysms smaller than 7 mm rarely bleed, how does one explain the preponderance of ruptured aneurysms smaller than 7 mm in most series? Our data indicate that a small, irregular aneurysm may have a greater risk of rupture than a larger, smoothly contoured aneurysm. In evaluating a patient with an unruptured aneurysm, experienced cerebrovascular surgeons recommend treatment based on many factors including the size, shape, and location of the aneurysm as well as the patient's age, comorbidities, symptoms, family history, habits, and response to the diagnosis. The most parsimonious explanation for the discrepancy between the International Study of Unruptured Intracranial Aneurysms data and case series of ruptured aneurysms may be that, based on a gestalt assessment, cerebrovascular surgeons do a fairly good job of selecting for treatment patients harboring aneurysms that would subsequently rupture if left untreated.

Limitations of the Pilot Study

There are noteworthy limitations in our study. The population size is small. Similar studies on a much larger population are necessary to verify the findings. The comparison of indices between ruptured and unruptured lesion groups stands on the premise that the geometry of cerebral aneurysms does not change following rupture as the CT angiography was performed after SAH in the patients with ruptured lesions. If the aneurysm shape changes dramatically following rupture, then quantified shape analysis may not

Quantified aneurysm shape and rupture risk

be helpful in predicting rupture of a previously intact aneurysm. Previous studies on aneurysm morphology indicate that rupture does not dramatically alter aneurysm shape.^{1,3,27}

Long-term follow up on a large population of patients with unsecured aneurysms will be needed to determine with assurance whether shape analysis can determine the risk of rupture. One of the patients in this pilot study is particularly interesting in regard to this question. This elderly woman had presented with a small, unruptured PCoA aneurysm. All size indices in the patient were below the population mean values in this study. Nonetheless, the shape indices of NSI, UI, EI, and AR were all at or greater than the 90th percentile. She refused treatment and the aneurysm subsequently ruptured within 3 days of her CT angiography evaluation.

Limitations in the methodology of 3D aneurysm reconstruction are minimal and unlikely to affect our findings significantly. Given the limited resolution of CT angiography, the reconstructed models may have surface artifacts such as unrealistic sharp corners. In an earlier study,¹⁸ however, we reported that errors due to the reconstruction process itself have an insignificant effect on the size and shape indices. The shape indices reported here quantify many, but not all, potentially important aneurysm shape characteristics. Evaluation of additional indices that can numerically describe localized aneurysm wall features may be worthwhile.

In the ruptured lesion group (nine lesions), we noted one giant aneurysm whose volume was 700 ml compared with the group mean of 146 ml (Fig. 4). To test the effect this giant aneurysm had on our findings, its data were removed as outliers and the statistical analyses were repeated (eight lesions). The findings did not change much. The NSI, UI, EI, and AR showed statistical significance in their difference between the lesion groups and were the best predictors (AUCs decreased by as little as 0.03 in all four indices). The MLN did not show statistical significance with exclusion of the giant aneurysm. The presence of this giant lesion therefore is unlikely to have biased our findings.

Conclusions

In summary, we have reported on novel 3D sensitive continuous indices for the size and shape of brain aneurysms. We have further assessed their relative predictive value within a study population of ruptured and unruptured aneurysms. We found that the lesion's NSI, UI, and ellipticity (EI and AR) were the best predictors of rupture risk, whereas size indices like V and D_{max} were poor predictors. Future studies of a similar approach on a much larger study population should be performed. Long-term follow up on a large population of patients with unsecured aneurysms will be needed to determine with assurance whether shape analysis can determine the risk of rupture.

Furthermore, to reliably verify the role of shape in rupture risk, such empirical studies need to be accompanied by theoretical modeling that investigates the biomechanical rationale for why a particular aneurysm shape may lead to aneurysm rupture. Biomechanical modeling of blood flow in the aneurysm and pressure-induced wall tension distribution may contribute to a deeper understanding of the role of aneurysm shape and identify particular shape features of interest.

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