Interobserver variability in angiographic measurement and morphologic characterization of intracranial aneurysms: a report from the International Study of Unruptured Intracranial Aneurysms.

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Interobserver Variability in Angiographic Measurement and Morphologic Characterization of Intracranial Aneurysms: A Report from the International Study of Unruptured Intracranial Aneurysms

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PURPOSE: To determine the variability in assessment of the principal inherent characteristics of intracranial aneurysms through the evaluation of interobserver variability for material with uniform quality. **METHODS:** Blinded interpretations of a single set of cerebral arteriograms of 55 aneurysms were evaluated by several statistical approaches. **RESULTS:** Excellent correlations were found for the detection and measurement of aneurysms after adjusting for geometric distortion caused by magnification. Progressively decreasing correspondence was found for factors that characterized morphology, including, in order, determination of margins, assessment of accessory appendages, and identification of a neck. **DISCUSSION:** Correction for geometric distortion was the most critical factor that influenced uniform measurement of size. Standards for measurement and morphologic characteristics were subsequently established for use in the International Study of Unruptured Intracranial Aneurysms.

Index terms: Aneurysm, intracranial; Cerebral angiography

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The International Study of Unruptured Intracranial Aneurysms (ISUIA) is a multicenter investigation designed to evaluate the risk of rupture of previously unruptured intracranial aneurysms and the risk of hemorrhage associated with repair of these lesions (see the Appendix). Previous smaller studies suggested that among patients with unruptured aneurysms and no history of subarachnoid hemorrhage from a different source, aneurysmal size at the time of discovery is the most important variable determining the risk of future rupture (1, 2). Another study suggested that the risk of hemorrhage associated with repair of unruptured intracranial aneurysms may depend on both the size and the location of the aneurysm, but the number of patients in that study was too small to establish a definitive risk for subgroups (3). Earlier series have implicated size as an important factor in defining groups related to ruptured or unruptured aneurysms (4–8). Most angiographic studies have not used rigorous criteria for making measurements, and it is unclear how specific variables, variations in measurement techniques, and geometric radiographic distortion were evaluated.

A study was conducted to determine interobserver variability for the purposes of the ISUIA to establish methods to evaluate angiograms with regard to the size, location, and other angiographic characteristics of aneurysms. The results of this study were used to refine the standard procedure for measuring aneurysms in the multicenter analysis in order to achieve optimal uniformity. This report describes the evaluation of the measurement criteria. Assessment of interobserver variability in interpretations of the nonuniform clinical imaging material of the ISUIA was not a goal of this study. Both intraob-

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server and interobserver variability as well as quality assessment of different techniques will be addressed in future reports.

Materials and Methods

Selected angiograms of 55 intracranial aneurysms were coded by initials, date of examination, and study number. All angiograms were cut-film studies of similarly high quality, with magnification ranging from ×1.0 to ×1.6, and were obtained at one institution. The cases were purposively selected to include both ruptured and unruptured aneurysms. The size and morphologic characteristics were intended to span a full range of presentation anticipated in the clinical environment. The quality was uniform and the cases were not expected to represent the more varied technique of the material in the ISUIA. The range of size and characteristics of the aneurysms was intended to guide the process of measurement technique.

The angiograms were interpreted independently by two experienced neuroradiologists without knowledge of previous findings or of each other's results. Each of the 55 angiograms showed aneurysms, and each was reviewed by the two neuroradiologists in separate locations. The examinations in this study included injection of 22 right carotid arteries, 25 left carotid arteries, two right vertebral arteries, and nine left vertebral arteries as parent vessels of the intracranial aneurysms. Aneurysms ranged in size from 3 to 30 mm, with a mean maximum diameter of 5 to 10 mm in any one of the three axes. Diameters were measured to the nearest millimeter and represented the internal lumen. Comparisons were made for angiographic content (magnification, aneurysmal location, aneurysmal morphology, and measured size) in the anteroposterior, mediolateral, and cephalocaudal dimensions. Statistical analysis of categorical variables was performed with contingency table analysis and significance was determined by a χ^2 statistic. Aneurysmal size was compared by correlation analysis and by unpaired and paired t tests. Percentage of agreement was calculated for multiple size strata.

All angiograms had less than 50% atherosclerotic stenosis in the arteries supplying the aneurysm. Two patients had an arteriovenous malformation in addition to the aneurysm. These parameters were not a focus of the study.

Although estimation of the degree of geometric distortion of the image was not a factor under investigation in this study, it is important to correct for image magnification and/or minification. To simplify the correction for geometric distortion of the image, a special ruler called the *cerebral angiogram magnification/minification ruler* was devised by one of the authors. The ruler incorporated film magnification and digital subtraction angiographic magnification/minification corrections when used retrospectively with cerebral arteriograms (Fig 1). These corrections were based on measurements from a standardized cohort of 200 adult patients undergoing cerebral angiography and from literature reviews of skull anthropometric studies (9).

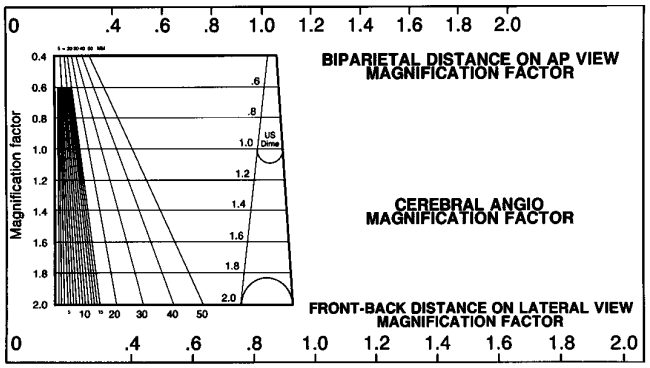

Fig 1. Cerebral angiogram magnification/minification ruler (not reproduced to scale). To make a measurement, the magnification or minification factor is first determined. The top of the ruler is placed over the anteroposterior (*AP*) view along the biparietal diameter, and the distance between the two external tables provides the anteroposterior view magnification factor. The corresponding measurement scale on the left-hand grid is then used to measure structures on the anteroposterior view directly. Similarly, the bottom of the ruler is placed along a line from the brow to the occiput on the lateral view; this distance provides the magnification factor for the lateral view. For example, if the biparietal distance is marked at 1.6 on the top of the ruler, the horizontal scale at 1.6 on the grid is used to directly measure a structure on the anteroposterior view. A similar but usually different magnification factor and its corresponding scale would be used for measurements on the lateral view.

If a US dime is placed on the head during imaging, the maximum diameter of the disk (actual diameter, 17.5 mm) on the film is adjusted within the two diverging lines on the right side of the grid to determine precisely the magnification factor.

Such retrospective calibration provides correction within ±10% for either sex in a normal adult population. Without such correlation for geometric distortion, direct measurement on images may vary within a 150% range of error.

The interpreters were asked to characterize the aneurysms with regard to the smoothness or irregularity of the margin of the lumen, the presence of a neck, and the presence of accessory appendages. Similar definitions of these variables were presented to both observers but collaboration on the interpretation of these definitions did not occur before the study.

Results

Four separate analyses were performed on the reliability of determining the size of the aneurysms, which was the main focus of the study. First, a comparison was made of the means of the anteroposterior, mediolateral, and cephalocaudal diameters (Table 1). The mean diameters were not significantly different. Reader 1 had a higher mean of 8.5 mm on the anteroposterior view as compared with reader 2, who had a mean of 8.3 mm. A similar relationship of the means was observed for both the

TABLE 1: Group comparison of aneurysmal size

View	Size, mm					*P*
	Mean	Median	Minimum	Maximum	SD	
Anteroposterior						
Reader 1	8.509	8	3	25	4.264	0.792
Reader 2	8.287	7	2	27	4.618	
Mediolateral						
Reader 1	8.509	7	3	22	4.417	0.572
Reader 2	8.040	7	1.6	19	4.102	
Cephalocaudal						
Reader 1	8.400	7	2	22	4.609	0.816
Reader 2	8.200	8	0.5	23	4.623	

TABLE 2: Pair analysis of aneurysmal size

View	Size, mm				*P*
	Mean	Minimum	Maximum	SD	
Anteroposterior					
Difference	0.123	−2	4	1.168	0.448
Mediolateral					
Reader 1	0.469	−2	6	1.343	0.0123
Cephalocaudal					
Difference	0.2	−7.5	6.5	1.739	0.3975
Maximum					
diameter	0.225	−3.5	3	1.122	0.1422

TABLE 3: Correlation of values

	Pearson	Spearman
Anteroposterior	0.968	0.916
Mediolateral	0.953	0.951
Cephalocaudal	0.929	0.922
Maximum	0.972	0.954

mediolateral and cephalocaudal views. Comparison of first (largest) aneurysm pairs showed no difference in the anteroposterior and cephalocaudal views (Table 2). The mediolateral difference was marginally significant. No significant difference was found for the maximum diameter. The correlation of values was high whether a Pearson or rank (Spearman's) correlation coefficient was used (Table 3). Analysis was also performed on the distribution based on size strata (Table 4), which would include the range of sizes used for clinical decision making. The results showed that reader 2 classified small aneurysms more often in lower categories. The overall actual agreement was 84%.

Measurements of the maximum diameter were most consistent between the two readers for aneurysms in the middle and large size categories (Fig 2). A slight discrepancy occurred in the smallest category near the threshold of resolution for measurement (Fig 3).

Magnification correction factors and aneurysmal location were reported consistently between the two readers. Slight inconsistencies in description of the parent vessel anatomy occurred, but they were not considered significant for the purposes of this study.

Differences in morphologic classification were found between the two readers (Table 5). Reader 2 classified more aneurysms as having smooth and even margins, whereas reader 1 graded more of them as irregular and uneven. There was a slight difference in the determination of accessory appendages and a larger difference in the categorization of these appendages as either daughter sacs or extra lobes. A difference in reporting the presence of an aneurysm neck was found between the two (Table 6). No difference was found for presence or severity of atherosclerosis. All films had less than 50% atherosclerotic stenosis in the arteries supplying the aneurysm (North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria). An arteriovenous malformation was present in two patients and was detected by both readers. Vasospasm was present in 5% of the films, and the assessment was significantly different between the two readers. The numbers were too small to determine differences and severity of location of vasospasm, and this was not a primary objective for this study.

Discussion

This study was part of the effort to standardize the measurement and characterization of intracranial aneurysms for the multicenter ISUIA. The principal objective was to determine interobserver variability for specific measurement

TABLE 4: Comparison of maximum diameter based on size strata*

			Reader 1					
			3.0 to 5.9 mm	6.0 to 9.9 mm	10.0 to 14.9 mm	15.0 to 24.9 mm	25+ mm	Total of reader 1
			7	24	19	4	1	55
Reader 2	3.0 to 5.9 mm	10	6	4				
	6.0 to 9.9 mm	22	1	19	2			
	10.0 to 14.9 mm	19		1	17	1		
	25.0 to 24.9 mm	3				3		
	25+ mm	1					1	
	Total of reader 2	55						

* The measurement of each reader can be classified into five groups. The composite of each group can be compared between the two readers by moving horizontally (reader 2's group as classified by reader 1) or vertically (reader 1's group as classified by reader 2). Percentage of agreement = 0.836.

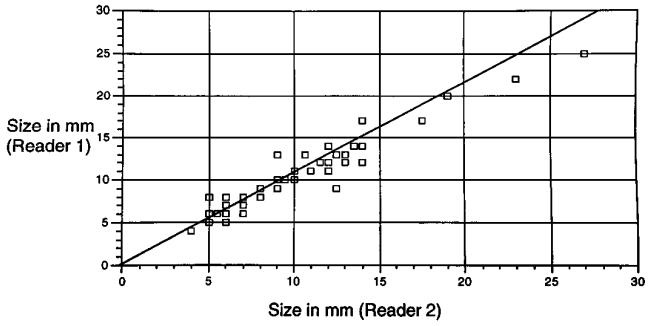

Fig 2. Correlation of size. A high correlation was found between the two readers for measurements throughout the range of maximum diameters of aneurysms.

TABLE 5: Comparison of morphologic classification of aneurysms

Reader	Single Smooth	Single Irregular	Daughter Sacs	Extra Lobes	Not Coded
1	23	14	9	7	2
2	36	4	11	2	2

Note.—$\chi^2 = 11.4$, $P = .022$.

TABLE 6: Comparison of reporting aneurysm neck

Reader	No	Yes	Unknown	Not Coded
1	30	9	16	0
2	2	45	7	1

Note.—$\chi^2 = 53.02$, $P < .001$.

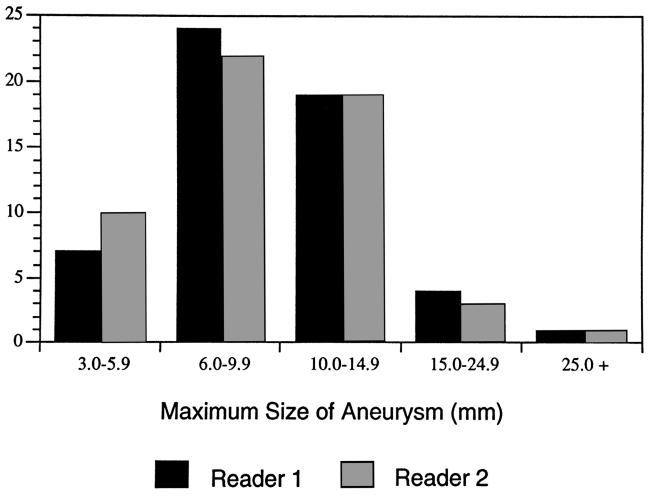

Fig 3. Distribution of size. The majority of aneurysms were between 6 and 15 mm in size, although both small and large lesions were represented.

variables to be used in the ISUIA. Another objective was to identify those variables that would be most appropriate for data collection in the ISUIA.

This study should be considered a preliminary effort to understand interobserver variability in the assessment of cerebral aneurysms, which is notably lacking a structured approach. Existing reports regarding intracranial aneurysms lack analyses of intraobserver or interobserver variability and generally lack standardized approaches toward the categorization of aneurysms in terms of size and morphology. Neither assessment of the quality of examination technique nor variability of an individual observer was a goal of this study. Both these issues will be addressed in subsequent reports. The focus of this study was to determine the principal inherent characteristics of intracranial aneurysms that affect interobserver variability. This was best addressed through the evaluation

of interobserver variability for material with uniform quality. The interobserver variability was not directed toward parameters that would be affected by examination technique, such as the threshold of size for detection. At present, we still do not know the final profile and critical thresholds for unruptured aneurysms in the ISUIA. Variability in technical quality clearly poses an additional challenge that should be the subject of further investigation.

Excellent interobserver correlation was found in reporting imaging technique, injected and opacified vessels, number of aneurysms, location of aneurysms, number of accessory appendages, presence or absence of arteriovenous malformations, atherosclerosis, and vasospasm.

The correlation between the two readers in regard to aneurysmal size and correction for magnification was good. This was facilitated by the use of a specially designed cerebral angiogram magnification ruler. Further analysis revealed that discrepancies occurred primarily because of arbitrary differences in measuring aneurysmal diameters according to axis and film plane (ie, measuring the maximum diameter along any axis in the film plane versus measuring the diameter only along a given axis at 90° or 180° to the film plane). There was significant discrepancy between the readers in regard to reporting the presence or absence of an aneurysm neck, the specific morphologic classification of aneurysms, the wall characteristics and nature of accessory appendages, and the number of abnormalities of the circle of Willis. The primary reason for discrepancies in reporting the presence of aneurysm necks was related to the practice of one reader to infer the presence of a neck even if it was not adequately visible. In the established definitions, it was decided to report only what appears directly on the images. In regard to morphologic classification, discrepancies were related to the initial lack of a specific definition for *daughter sac* as opposed to *aneurysmal lobe*. The discrepancies in regard to abnormalities within the circle of Willis related to lack of a specific definition of *abnormalities*.

To achieve uniformity in these measurements for the ISUIA, specific definitions and procedures were developed for size and magnification, as listed below.

1. Image Interpretation. A standard procedure for measuring aneurysms was developed to ensure uniform characterization and measurement of unruptured intracranial aneurysms. The measurement variables consider diameters in three planes, inclusion of aberrant morphology (such as lobes and accessory sacs), and geometric radiographic magnification.

2. Geometric Distortion. Geometric film magnification or digital image magnification/minification must be considered when determining the size of an aneurysm. Techniques used by participating ISUIA centers for producing digital images and magnified films for cerebral angiography create distortions ranging from 0.5 to 2.5 relative to the actual size. Failure to consider this distortion when reporting aneurysmal measurements introduces a 50% to 150% uncertainty factor that precludes useful comparison of data.

Any credible attempt to consider image magnification/minification is acceptable because the measurement error for this variable will be reduced to a negligible level compared with the range of uncertainty if geometric distortion is not considered (10). Various techniques that use calibration rulers, markers placed on the head, external stereo frames, or intrinsic baseline anatomic markers on the image decrease this potential error to 10% or less (11, 12). For the ISUIA, markers such as a ruler or a US dime placed in the image plane are encouraged for prospective examination; skull size calibration methods with special rulers are used for retrospective measurements. Small differences in geometric distortion within the head have not been considered (eg, a middle cerebral artery trifurcation aneurysm is off center on the lateral view from a marker placed on the midline of the head).

The magnification factor refers to the number that 1.0 is multiplied by to obtain the apparent size on the given film. This number may be predetermined from a retrospective examination of film with a cerebral angiography magnification/minification calibration device or a corresponding analysis of a prospective case with a standardized marker placed within the film plane.

3. Aneurysmal size. For the ISUIA, the maximum diameter reported for an intracranial aneurysm is the largest measurement that is corrected for geometric distortion and includes any appendage in any one of the three film planes (ie, anteroposterior, mediolateral, or cephalocaudal). The anteroposterior and cephalocau-

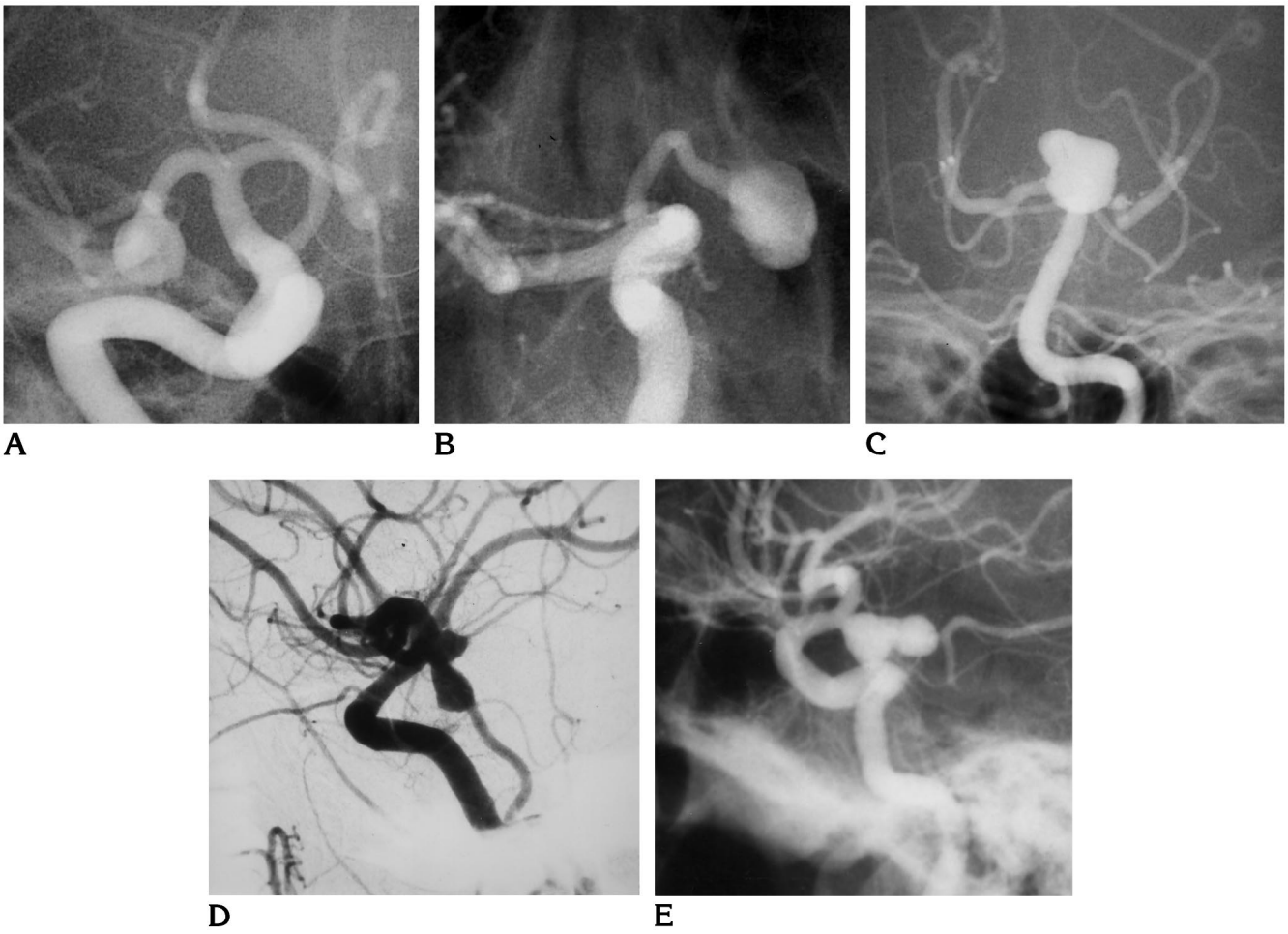

Fig 4. Aneurysmal morphology for ISUIA classification.

Type 1 aneurysm (*A*) has a single sac with even margins. Type 2 aneurysm (*B*) has an irregular surface. Type 3 aneurysm (*C*) consists of a parent sac and one or more secondary sacs. Each secondary sac represents less than 25% of the estimated total volume. Type 4 aneurysm (*D*) represents a structure with more than one lobe. A lobe arises directly from the neck of the aneurysm or represents a protuberance of more than 25% of the estimated total volume (*E*).

dal diameters are measured in the lateral view. With views of the lateral image, the maximum diameter is identified and measured by using the previously determined magnification or minification correction factor. It is then determined whether this maximum diameter is most appropriately defined as an anteroposterior or cephalocaudal axis. The companion measurement is determined as the diameter at a 90° angle to the previous measurement. The mediolateral diameter is defined as the maximum mediolateral measurement determined on the anteroposterior view. As with the other measurements, the mediolateral diameter may be off-axis with the orthogonal mediolateral plane of the image.

Diameters are measured to the nearest millimeter. The range of error induced by geometric

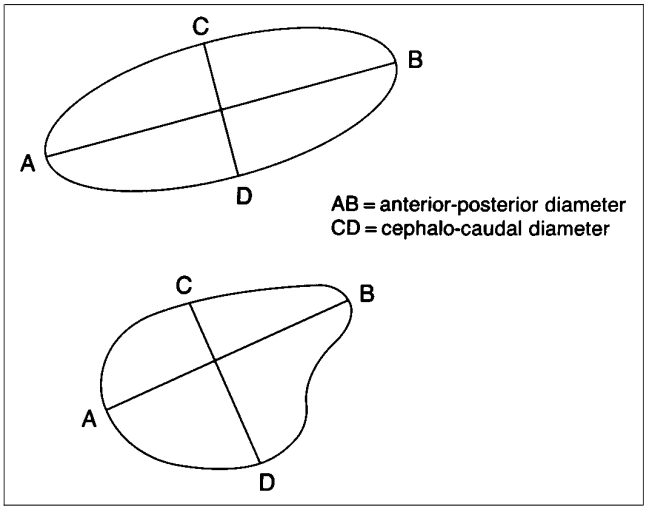

Fig 5. Diameters of irregular or asymmetric aneurysms include maximum measurements in each plane.

distortion far exceeds specific submillimeter direct measurements from hard copy. This is particularly true for a data set that by necessity includes a wide range of techniques neither controlled nor monitored by ISUIA investigators. Levels of precision in a study of uncontrolled data are presumably lower than those that might be achieved in a controlled study with uniform technique and on-line measurement. The inherent error of assessment of geometric distortion of nonuniform technique is less well understood. This error was intentionally removed from this study in order to focus specifically on interobserver variability for purposes of adjudication.

4. Aneurysmal Morphology. Four morphologic classifications were developed for use in the ISUIA: a single sac with a smooth margin; a single sac with an irregular corrugated margin; a primary sac with a secondary daughter sac, defined as a separate protuberance arising from the main sac that is less than 25% of the total volume of the sac; and a multilobed structure, defined as a protuberance arising directly from the primary neck of the aneurysm or arising from the main body and representing 25% or more of the apparent volume of the main sac.

The location of the aneurysm is defined in terms of the junction of a secondary vessel arising from a parent vessel. When an aneurysm arises from such a junction, the name of the secondary vessel is used to label the aneurysm. Thus, an aneurysm arising at the junction of the anterior cerebral artery and the anterior communicating artery is described as an anterior communicating artery aneurysm.

The presence of an aneurysm neck is determined from what is seen directly on the images. This presence is not inferred but is only recorded if the neck is definitely seen. The presence of the neck was subject to the widest range of interpretation between the two readers and was subsequently considered a subjective marker that is highly dependent on the number of views and the technique used in a retrospective imaging examination (Figs 4 and 5). The significance of detailed assessment of neck size and morphology is well recognized in the endovascular management of aneurysms (13).

Other Angiographic Features

For the purposes of the ISUIA, other vascular features are recorded according to standard criteria used for angiographic definitions. These include the description of anatomic anomalies within the circle of Willis and the presence or absence of associated atherosclerosis, arteriovenous malformations, and other intracranial lesions. Atherosclerosis within the feeding carotid or vertebrobasilar vessels is recorded in terms of percentage of stenosis. The presence of an arteriovenous malformation is recorded according to standard convention (14). This includes the description of the malformation relative to the supply of the vessel containing the aneurysm, the distance of one or two branching points from the aneurysm on the supplying vessel and the malformation, or the presence of the arteriovenous malformation on a parent vessel unrelated to the intracranial aneurysm. The presence of associated vasospasm is also recorded as part of the general intracranial description.

Summary

It is important to establish standardized criteria for measuring and characterizing intracranial aneurysms. To advance our understanding of the natural course and surgical morbidity and mortality of unruptured intracranial aneurysms, it is necessary to develop collaborative efforts among many medical centers to study an adequate number of patients in a reasonable period of time. This requires maximal uniformity among participating medical centers in regard to characterizing and measuring aneurysms. This is particularly true in our assessment of cerebral aneurysms, because aneurysmal size and morphologic characteristics may be critical factors in determining their natural course and their surgical morbidity and mortality. Uniformity of measurement and morphologic characterization are also important criteria for making comparisons of data from different medical centers.

Appendix

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