ORIGINAL RESEARCH

Influence of observers, threshold values, and measurement methods on volumetric analysis of cerebral aneurysms with three-dimensional rotational angiography

Won-Sang Cho,1 Dong Hoon Shin,2 Joongyub Lee,3 Seung Jin Lee1

ABSTRACT

Introduction Exact measurements of cerebral aneurysms are important in terms of their treatment. However, there is no definitive way to estimate the exact volume of an aneurysm. Our aim was to compare aneurysm volume measured under different conditions: threshold values, observers, and measurement methods.

Methods 40 aneurysms and 7 phantom models were included in the study. Three-dimensional rotational angiography was used, and volumes were compared based on the following factors: two methods (two-dimensional formula calculation and three-dimensional software measurement); three observers; and three threshold values for imaging. In addition, in the phantom models, measured volumes were compared with real volumes. The consistency of the volume measurements under different conditions was assessed using the intraclass correlation coefficient (ICC).

Results The consistency of the measured volumes was excellent in both the patient aneurysms (ICC >0.98) and phantom models (ICC >0.95), irrespective of the influencing factors. Median volume differences were small for observers, threshold values, and methods. When the measured and real volumes of the phantom models were compared, the software measurement achieved the highest reproducibility for real volumes compared with the formula calculation (ICC = 0.86–0.93 vs 0.71–0.80).

Conclusions Measurement of aneurysm volume showed high agreement within each influencing factor, such as methods, observers, and threshold values.

INTRODUCTION

Digital subtraction angiography (DSA) with three-dimensional rotational angiography (3DRA) is considered an inevitable tool for the diagnosis and treatment of cerebrovascular disease. For cerebral aneurysms in particular, one of the major concerns in the field of neurosurgery, DSA with 3DRA can provide the most complete information about the shape of an aneurysm and its spatial relationship to surrounding vessels. Consequently, it is helpful in determining the appropriate treatment plan, reducing procedural complications, and subsequently improving outcome.1

Currently, a considerable number of cerebral aneurysms are being treated by endovascular interventions. An exact measurement of aneurysm volume is very important in selecting the correct device, such as coils and stents, and in evaluating the status of the coiled aneurysms after the procedure. In addition, there have been many reports on aneurysm packing density with coils and its effects on the long-term durability of coiled aneurysms.2–5 However, this is still controversial because there is no exact method of measuring the real volume of cerebral aneurysms, and measurement methods differ between institutions.6–8

The aim of our study was to elucidate the difference in volumes of cerebral aneurysms according to different measurement methods, observers, and threshold values for imaging. In addition, using phantom models of cerebral aneurysms, comparative analysis was performed between real volume and volumes measured with different measurement methods and threshold values.

MATERIALS AND METHODS

Selection of patients and models

A total of 40 cerebral aneurysms in 35 patients were included in the study with approval of the institutional review board. Patients underwent DSA with 3DRA between March 2012 and January 2013. The male to female ratio was 13:22, with a median age of 69 years (range 36–89 years). The locations of the cerebral aneurysms were the internal carotid artery in 16 aneurysms, the middle cerebral artery in 11, the anterior cerebral artery in 10, and the basilar artery in 3 aneurysms. In addition, seven different phantom models of cerebral aneurysms made from glass tubes were selected for the study (figure 1).

Measurement of the aneurysms

All DSA acquisitions were performed using a biplane angiographic system (Axiom Artis Zee; Siemens Medical Solutions, Forchheim, Germany) with a 512×512 matrix. Selective angiography harboring an aneurysm was performed in standard and various oblique projections. 3DRA was also obtained with a bolus of 18 mL of non-ionic iodine contrast medium (Pamiray 300; Dong Kook Pharm Co Ltd, Seoul, Korea) at a rate of 3 mL/s. The 3D datasets were obtained from two rotations: mask run and fill run. The first run (mask run) provided the subtraction mask of bone. The C arm rotated 20° within 5 s at a rate of 26.8 frames/s and a total of 134 two-dimensional (2D) images were acquired. The second run (fill run) was performed during administration of contrast media, and a total of 134 2D images were...
also acquired. All of the images were transferred to the Syngo workstation (Leonardo, Siemens, Forchheim, Germany) and multiplanar images or 3DRA were reconstructed. 3DRA of patients’ aneurysms are presented in the online supplementary figure.

The volume of the cerebral aneurysm was measured using the following two methods: 2D formula calculation and 3D software measurement. All of the measurements were obtained using 3DRA with a predetermined threshold value and the discrimination boundary of the aneurysm neck and parent artery. In the formula calculation, an observer subjectively measured the sizes of the different parts of the cerebral aneurysm: depth, width, and height. Then, aneurysm volume was calculated using the following formula with the assumption that the aneurysm was ellipsoid:

\[ V_{\text{formula}} = \frac{4}{3} \pi \times \left( \frac{\text{depth}}{2} \right) \times \left( \frac{\text{width}}{2} \right) \times \left( \frac{\text{height}}{2} \right) \]

For the software measurement, the aneurysm was manually outlined and segmented from the parent arteries. Then, aneurysm volume was automatically measured using software provided in the Syngo workstation (figure 2). Aneurysm volumes acquired with the formula calculation and with the software measurement are presented in the online supplementary table.

A standard threshold value for the images on 3DRA was subjectively determined by an observer (observer 3); this was considered the best value for imaging to define the cerebral aneurysms and parent arteries. Then, using three predetermined threshold values, including the standard value (a standard value ±500), volume measurements using the formula and software were simultaneously performed to analyze the differences in volume according to the measurement methods and threshold values. In addition, the calculations of cerebral aneurysms were conducted by three different observers (including observer 3) who had worked in the field of neurointervention for more than 7 years to examine interobserver differences.

In the phantom models of cerebral aneurysms, the real volume of the model was obtained as follows: \[ V_{\text{real}} = \left( \text{weight after contrast filling} - \text{weight before contrast filling} \right) / \text{density of the contrast agent} \]. The formula calculation and software measurements of model volumes were also performed by an observer (observer 3) in the same way as described above using the three predetermined threshold values (standard value and standard value ±500). The real volumes of the phantom models were 181.1 mm³ for model 1, 92.3 for model 2, 203.4 for model 3, 49.8 for model 4, 352.2 for model 5, 1000.3 for model 6, and 604.1 for model 7.

**Statistical analysis**

Measured volumes are presented as median (range). To analyze the consistency of the volume measurements based on the threshold values, observers, and measurement methods, visual examination of the data pattern was performed using the Bland–Altman plot, which consisted of the average value of the paired measurements on the x axis and the differences between each pair of measurements on the y axis, with 95% CI of the differences. Agreement was tested statistically using the intraclass correlation coefficient (ICC). An ICC value ≥0.75 indicated excellent reproducibility, 0.4 ≤ICC < 0.75 good reproducibility, and ICC <0.4 poor reproducibility. The analyses were performed using SAS statistical software (V9.2; SAS institute, Cary, North Carolina, USA) and MedCalc (V12; MedCalc software, Mariakerke, Belgium).

**RESULTS**

**Patients’ aneurysms**

Irrespective of the observers, threshold values, or methods for volume measurement of the cerebral aneurysms, reproducibility...
was excellent (ICC>0.98 at least; tables 1–3). Median volume differences for each factor were small, in the order of observers, threshold values, and measurement methods. The lower the threshold value, the larger the aneurysm was measured. Volumes estimated by software measurement were larger than those using the formula calculation.

A Bland–Altman plot comparing volumes measured using the software and using the formula is presented in figure 3. The patterns of the Bland–Altman plots for the other factors (observers and threshold values) were similar to those for the measurement methods (not presented). With increasing aneurysm volume, volume differences also increased. Volumes obtained by software measurement were larger than those obtained by formula calculation, and volumes measured in the lower threshold value were also larger.

### Phantom aneurysms

Comparison of real and estimated volumes are summarized in table 4. Volumes measured by formula and software were larger than real volumes, and volumes measured by software were slightly larger than those measured using the formula calculation. Volume agreement of the phantom models was excellent irrespective of the measurement method, with excellent reproducibility (table 5).

### DISCUSSION

We performed this study to clarify the effects of some factors on volume measurement. In the analysis of patients’ aneurysms, high agreement was achieved, regardless of the factors studied. However, volume differences were small, and in the following order: observers, threshold values for imaging, and measurement methods. To compare measured versus real volumes, we used phantom models. High reproducibility was also identified when comparing measurement methods and different threshold values. However, volumes estimated by software measurements were slightly closer to the real volumes than those obtained by formula calculation.

An exact volume measurement for cerebral aneurysms is important for the selection of appropriately sized coils and for the evaluation of the long-term durability of coiled aneurysms. Oversized coils can cause intraprocedural rupture of cerebral aneurysms or thromboembolism by coil protrusion into the parent artery. Undersized coils can result in incomplete occlusion and recurrence of the cerebral aneurysm. Meanwhile, high packing attenuation is considered to be an important factor for the long-term durability of coiled aneurysms. However, controversy persists, and the major cause is thought to result from the different measurement methods used and the lack of a

### Table 1 Volume differences according to the observers in the patient cases*

<table>
<thead>
<tr>
<th>Threshold value</th>
<th>Volume difference (%) (median (range))</th>
<th>O1 and O2</th>
<th>O1 and O3</th>
<th>O2 and O3</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>10.4 (−40.0 to 80.1)</td>
<td>5.1 (−6.1 to 56.7)</td>
<td>−4.5 (−52.7 to 61.3)</td>
<td>0.989 (0.981 to 0.994)</td>
<td></td>
</tr>
<tr>
<td>Standard +500</td>
<td>11.9 (−37.5 to 106.0)</td>
<td>6.3 (−7.2 to 65.8)</td>
<td>−2.1 (−48.0 to 64.8)</td>
<td>0.987 (0.979 to 0.993)</td>
<td></td>
</tr>
<tr>
<td>Standard −500</td>
<td>9.9 (−40.5 to 67.0)</td>
<td>−1.4 (−19.2 to 33.5)</td>
<td>−9.0 (−50.0 to 47.9)</td>
<td>0.988 (0.980 to 0.993)</td>
<td></td>
</tr>
</tbody>
</table>

*Volumes were obtained using the formula calculation. Volume difference between two observers (ie, O1 and O2) was calculated as follows: (O2−O1)/O1×100 (%). ICC, intraclass correlation coefficient; O1, observer 1; T0, volume at a standard threshold value; T±500, volume at a standard threshold value ± 500.

### Table 2 Volume differences according to the measurement methods (formula calculation versus software measurement) in the patient cases*

<table>
<thead>
<tr>
<th>Threshold value</th>
<th>Volume difference between FC and SM (%) (median (range))</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>45.1 (−12.4 to 92.8)</td>
<td>0.996 (0.993 to 0.998)</td>
</tr>
<tr>
<td>Standard +500</td>
<td>44.0 (−7.3 to 90.1)</td>
<td>0.996 (0.992 to 0.998)</td>
</tr>
<tr>
<td>Standard −500</td>
<td>43.7 (−8.8 to 82.6)</td>
<td>0.997 (0.994 to 0.998)</td>
</tr>
</tbody>
</table>

*Volumes were obtained using both FC and SM only by observer 3. Volume difference between FC and SM was calculated as follows: (VolumeSM−VolumeFC)/VolumeFC×100 (%). ICC, intraclass correlation coefficient; FC, formula calculation; SM, software measurement.

### Table 3 Volume differences according to the threshold values for angiographic imaging in the patient cases*

<table>
<thead>
<tr>
<th>Measurement method</th>
<th>Observers</th>
<th>Volume difference (%) (median (range))</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula calculation</td>
<td>O1</td>
<td>−17.0 (−37.6 to 11.3)</td>
<td>0.994 (0.990 to 0.997)</td>
</tr>
<tr>
<td></td>
<td>O2</td>
<td>−14.3 (−35.7 to −3.6)</td>
<td>0.994 (0.991 to 0.997)</td>
</tr>
<tr>
<td></td>
<td>O3</td>
<td>−12.3 (−35.4 to −2.2)</td>
<td>0.996 (0.993 to 0.998)</td>
</tr>
<tr>
<td>Software measurement</td>
<td>O1</td>
<td>−12.4 (−37.3 to −1.7)</td>
<td>0.994 (0.990 to 0.997)</td>
</tr>
<tr>
<td></td>
<td>O2</td>
<td>−12.4 (−37.3 to 43.5)</td>
<td>0.994 (0.990 to 0.997)</td>
</tr>
</tbody>
</table>

*Volume difference between T0 and T±500 was calculated as follows: (|T0−T±500|)/T±500×100 (%). ICC, intraclass correlation coefficient; O1, observer 1; T0, volume at a standard threshold value; T±500, volume at a standard threshold value ± 500.
definitive method to accurately evaluate aneurysmal volume. Volume measurement is also important when comparing different types of coils for cerebral aneurysms. Recently, the development of new devices as alternatives to coils, made from various types of embolic materials (liquid, metal, polymer, or a combination), has increased, and may replace coils in the near future. Volume measurement would be critical to determine the amount of liquid materials or size of the metal or polymer device for a satisfactory outcome.

There have been some reports on factors affecting measurement of aneurysmal volume, including machine rotation time, injection type for contrast (bolus and continuous infusion), aneurysm shapes (narrow and wide necks), imaging threshold values, measurement methods (a few formulas and software), and boundary between the parent artery and aneurysm sac. According to previous reports, aneurysm volumes measured by software were closer to the real volumes than those calculated using a formula. When the shape of the aneurysm was irregular and very different from the ellipsoid contour, volumes measured by the formulas became inaccurate. In addition, formula calculation showed a tendency to underestimate volumes more than the software measurements. In this study, high agreement for aneurysmal volumes was determined irrespective of the influencing factors. However, the degree of volume differences within each factor was different, and the differences in volume between formula calculation and software measurement were highest in the patients’ aneurysms (>40%).

**Table 4** Volume differences between the real volume and the estimated volume, using formula calculation and software measurement, in the phantom models

<table>
<thead>
<tr>
<th>Threshold value</th>
<th>Volume difference between FC and SM* (%) (median (range))</th>
<th>ICC (95% CI)</th>
<th>Volume difference between FC and RV† (%) (median (range))</th>
<th>ICC (95% CI)</th>
<th>Volume difference between SM and RV‡ (%) (median (range))</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>3.8 (−23.8 to 48.2)</td>
<td>0.951 (0.772 to 0.991)</td>
<td>27.2 (8.3 to 88.6)</td>
<td>0.760 (0.179 to 0.953)</td>
<td>34.9 (14.7 to 86.0)</td>
<td>0.896 (0.562 to 0.981)</td>
</tr>
<tr>
<td>Standard +500</td>
<td>2.9 (−23.6 to 53.2)</td>
<td>0.951 (0.773 to 0.991)</td>
<td>23.4 (2.7 to 77.2)</td>
<td>0.799 (0.272 to 0.961)</td>
<td>28.0 (8.9 to 69.0)</td>
<td>0.927 (0.675 to 0.987)</td>
</tr>
<tr>
<td>Standard −500</td>
<td>2.2 (−23.8 to 41.1)</td>
<td>0.949 (0.764 to 0.991)</td>
<td>44.5 (18.8 to 101.5)</td>
<td>0.710 (0.070 to 0.942)</td>
<td>44.9 (21.7 to 103.8)</td>
<td>0.856 (0.431 to 0.973)</td>
</tr>
</tbody>
</table>

*Volume difference between FC and SM was calculated as follows: \((\text{Volume}_{FC}−\text{Volume}_{SM})/\text{Volume}_{SM}×100\) (%).
†Volume difference between FC and RV was calculated as follows: \((\text{Volume}_{FC}−\text{RV})/\text{RV}×100\) (%).
‡Volume difference between SM and RV was calculated as follows: \((\text{Volume}_{SM}−\text{RV})/\text{RV}×100\) (%).

**Figure 3** Bland–Altman plot of volume differences in patients according to the volume estimation method (software measurement and formula calculation) by observer 3 using a standard threshold value. Two cases with a volume >1000 mm³ were not presented here, all of which were beyond ±1.96 SD.

**Figure 4** Bland–Altman plots of volume differences between real and estimated volumes with formula calculation (FC) and software measurement (SM) in the phantom models. (A) Volume difference between SM and real volumes. (B) Volume difference between FC and real volumes. (C) Volume difference between SM and FC volumes.
In contrast, there was little difference (<4%) between formula calculation and software measurement in the phantom models. The main reason for this is thought to be that the phantom models have more discrete limits between the parent artery and aneurysm sac than real aneurysms. We considered the contrast volume within the phantom model as aneurysm volume without any consideration of the parent artery being filled with contrast media. Part of the parent artery near the aneurysm neck tended to be included more in the software measurement than in measuring the diameter manually with formula calculation. In small aneurysms, such a difference in boundary between the aneurysm and parent artery can cause a significant difference in the measured volume. Nonetheless, these types of differences in measured volumes are thought to occur frequently in the clinical situation.

Volumes measured by both formula and software were larger than real volumes, and volumes determined by software were larger than those determined by formula calculation in real and phantom aneurysms. For the phantom models, volumes by software measurement were closer to real volumes than those calculated using the formula. However, volume differences between formula calculations and software measurements were not significant. Because such a small difference in measurement methods can be confounded by other factors, including observers and threshold values, it is difficult to conclude that formula calculation is inaccurate compared with software measurement. In addition, volumes by both formula calculation and software measurement were higher than real volumes, possibly because observers tend to measure the most outer margin of the aneurysm. Therefore, when selecting a certain size of coil for an aneurysm, a smaller size of coil would be more appropriate to embolize the aneurysm. However, it is more important to know the margin of error between the real volume and measured volume by software for quality control in each institute before considering coil embolization of cerebral aneurysms or evaluating packing attenuation of coils within the aneurysmal sac.

This study has some limitations. First, the number of cases was not sufficient to reach a definitive conclusion with regard to real aneurysms or phantom models. Secondly, although we studied influencing factors for the measurement of aneurysm volume, it is more important how the volumes closest to the real ones were obtained. Hence we would like to suggest that inclusion of the tip of the angiographic catheter, the size of which is already known, within the imaging would be a helpful reference to achieve more accurate volume data while performing cerebral angiography.

CONCLUSION

Agreement for volume measurement was high, irrespective of the influencing factors. Although the volumes of the phantom models estimated by the software were closer to the real volumes than those obtained by formula calculation, the volume difference may have been confounded by other factors because the volume difference was not significantly different between software measurements and formula calculations. Further studies with a large number of phantom models would provide more reliable information about volume measurement and influencing factors, and would help to develop exact methods that result in minimal error when obtaining aneurysm volumes.

Contributors

All authors made a material contribution to this article, revision of the article, and final approval of the article for submission to this journal.

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Competing interests

None.

Ethics approval

Ethics approval was obtained from Kangwon National University Hospital institutional review board.

Provenance and peer review

Not commissioned; externally peer reviewed.

REFERENCES


Table 5 Volume differences according to the threshold values for angiographic imaging in the phantom models*

<table>
<thead>
<tr>
<th>Measurement method</th>
<th>Volume difference (%) (median (range))</th>
<th>ICC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula calculation</td>
<td>$T_{10}$ and $T_{500}$</td>
<td>$-5.4 (-12.1$ to $-3.0)$</td>
</tr>
<tr>
<td>Software measurement</td>
<td>$T_{10}$ and $T_{500}$</td>
<td>$-5.8 (-9.1$ to $-4.7)$</td>
</tr>
</tbody>
</table>

*Volume difference between $T_{10}$ and $T_{500}$ was calculated as follows: $(T_{10}−T_{500})×100%$. ICC, intraclass correlation coefficient; $T_{10}$, volume at a standard threshold value; $T_{500}$, volume at a standard threshold value ±500.
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