Quantification of Subarachnoid Hemorrhage by Three-Dimensional Computed Tomography: Correlation Between Hematoma Volume and Symptomatic Vasospasm

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Abstract

Subarachnoid hemorrhage (SAH) volume was measured by three-dimensional computed tomography (3D-CT) and the correlation examined between the SAH volume and the occurrence of symptomatic vasospasm (SVS). Experimental (in vitro) hematomas were made with blood obtained from 10 volunteers. The hematoma volume was determined by actual measurements and by 3D-CT using a CT number in the range of 40–80 Hounsfield units (HU) on days 1, 4, 7, 11, and 14. The coefficients on days 1 and 4 were relatively high and the correlation between measured and estimated volumes was significant on days 7, 11, and 14. 3D-CT was also performed in 50 patients with SAH at onset (day 0) and on days 1, 4, 7, and 14. The hematoma volume including the volume of normal structures was automatically calculated (V1). The volume of normal structures (V2) with CT numbers of 40–80 HU was calculated in another 50 patients without intracranial lesions as 12 ml. The total hematoma volume was defined as V1 minus mean V2. The mean SAH volume was 44, 36, 21, 11, and 8 ml on days 0, 1, 4, 7, and 14, respectively. The hematoma volumes were significantly larger in patients with SVS than in patients without SVS at all time points. The minimum hematoma volume in patients with SVS was 92, 76, 42, 24, and 12 ml on days 0, 1, 4, 7, and 14, respectively. This method allows the quantitative determination of SAH volume based on 3D-CT, and may be useful in clinical studies of cerebral vasospasm.

Key words: cerebral vasospasm, three-dimensional computed tomography, subarachnoid hemorrhage, hematoma volume, Hounsfield unit

Introduction

Symptomatic vasospasm (SVS) continues to be a major cause of morbidity and mortality after aneurysmal subarachnoid hemorrhage (SAH). Earlier qualitative assessments indicated that patients with large SAH volume on computed tomography (CT) suffered a high incidence of SVS.^{1,3,5} Attempts to quantify SAH volumetrically with a novel software-based technique and two-dimensional (2D)-CT encountered problems posed by the partial volume effect and the absence of SAH in the convex-

ity or posterior fossa.^{4,10} To surmount these problems, we have developed a new method to quantify SAH on three-dimensional (3D)-CT which yield volume data. The present preliminary study was undertaken to develop a method to determine the hematoma volume quantitatively on 3D-CT. Our study was comprised of 3 components: an experimental study (in vitro) to set the CT number in terms of Hounsfield units (HU) and to compare the hematoma volumes acquired in vitro by actual measurements and on 3D-CT; measurement of the SAH volume in patients with aneurysmal SAH; and examination of the correlation between hematoma volume and occurrence of SVS.

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Materials and Methods

I. Experimental measurement of hematoma volume

Experimental (in vitro) hematomas of approximately 60 ml were made in a test tube using venous blood from 10 healthy adult volunteers and kept at 37°C. The actual hematoma volume was measured by elimination of the plasma from the blood. 3D-CT scans of the experimental hematomas were obtained with a 4-channel multidetector row CT (MDCT) instrument (Aquilion, 4 rows; Toshiba Corp., Tokyo) on days 1 (24 hours after sampling the blood), 4, 7, 11, and 14. The scan parameters were: 135 kV, 220 mA, 1 sec/rotation, helical pitch 3, 1-mm slice thickness, reconstruction algorithm (Fc 27). Acquired data were reconstructed on a computer workstation (ZAIOM900; AMIN Corp., Tokyo). The reported CT density of SAH ranges from 40 to 80 HU,¹⁵⁾ so hematoma volume was estimated with HU values between 40 and 80.

II. Clinical measurement of hematoma volume

The study population consisted of 50 patients with SAH, 33 females and 17 males aged 31–84 years (mean 64.5 years), who underwent initial 3D-CT within 24 hours of SAH onset. Informed consent was obtained from all patients or their legal representative before enrollment in this study. The interval between SAH onset and acquisition of the first CT scan was 1–24 hours (mean 11.5 hours). Of the 50 patients, 36 had SAH without intraventricular hemorrhage (IVH) or intracerebral hemorrhage (ICH), 5 had SAH and IVH, 6 had SAH and ICH, and 3 had SAH, IVH, and ICH. All 50 patients underwent direct surgery to the aneurysm within 48 hours of SAH onset. Our institution has adopted a clipping-first policy, and few patients underwent endovascular coil occlusion, so this study excluded these patients. Continuous irrigation therapy with urokinase and ascorbic acid^{8,11)} was used in 10 patients to prevent SVS, 28 underwent cisternal drainage, and 22 were administered fasudil chloride.¹⁴⁾ Patients with SVS received hypertensive, hypervolemic, and hemodilution (triple H) therapy.

All 50 patients underwent 3D-CT using a 4-channel MDCT on days 0 (admission), 1, 4, 7, and 14. The scanning conditions were the same as in the experimental study. Volume data with CT numbers between 40 and 80 HU were shown on a computer screen (Fig. 1A). The CT number of the skull bone was 1000 HU, so was not included in the volume data with CT numbers between 40 and 80 HU. The scalp and subcutaneous tissue were manually excluded from the volume data using the space of the

Fig. 1 A: Volume data in a patient with subarachnoid hemorrhage (computed tomography [CT] number 40–80 HU). B: Estimated volume (volume 1, V1) after manual exclusion of the scalp and subcutaneous tissue. C: Volume data in a normal subject (CT number 40–80 HU). D: Estimated volume (volume 2, V2) of the normal structures such as the venous sinus or falx after manual exclusion of the scalp and subcutaneous tissue.

skull bone (Fig. 1B). Then the volume (volume 1, V1) was estimated. This procedure required 2 minutes. V1 contained the volume of normal structures such as the venous sinus and falx which were difficult to remove manually. Figure 1C shows the volume of normal structures with CT number in the same range (40–80 HU) in another sex- and age-matched 50 patients who provided informed consent and had no intracranial lesions on CT. The scalp and subcutaneous tissue were manually excluded to estimate the volume of the normal structures (volume 2, V2) (Fig. 1D). We defined the total hematoma volume as V1 minus the mean value of V2. In patients with IVH and/or ICH, the IVH and ICH volumes were estimated separately, which were easily separated from the SAH volume on the screen, in contrast to other types such as sylvian hematoma. The SAH volume was defined as total hematoma volume minus IVH and/or ICH volume.

III. Correlation between hematoma volume and SVS

The 50 SAH patients were divided into groups with and without SVS, and intergroup differences

were analyzed statistically. In addition, data on 8 SAH patients with IVH and 9 SAH patients with ICH were examined to assess the possible correlation between IVH and/or ICH volume and SVS. SVS was defined by combined clinical and radiological criteria: Onset between days 4 and 14 after SAH; insidious onset of confusion, disorientation, and/or drowsiness with or without frequently fluctuating focal deficits; negative CT findings excluding other causes of neurological deterioration such as rebleeding, hydrocephalus, intracranial hemorrhage, and/or focal brain swelling; and no other identifiable causes of neurological deterioration such as electrolyte disturbance, hypoxia, or seizures. To be recorded, the change had to persist for a minimum of 8 hours. With respect to reference findings regarding the occurrence of SVS, we evaluated the presence of a new low density area on CT. 3D-CT angiography was performed if SVS was suspected, but not in all cases. The 50 SAH patients were divided into 3 groups: patients without SVS, with SVS and transient symptoms, and with SVS and persistent symptoms. The appearance of a newly developed low density area on CT was also evaluated.

IV. Statistical analysis

Paired Wilcoxon and Spearman coefficient tests were used to assess agreement between the experimental hematoma volume measured and estimated on 3D-CT. The Mann-Whitney U-test was used to evaluate the association between hematoma volume and SVS. Statistical analysis was performed with a commercially available statistical software program (StatMate 3; ATMS Co., Ltd., Tokyo). P values less than 0.05 were considered significant.

Results

I. Experimental measurement of hematoma volume

The volumes of experimental hematoma (in vitro) obtained by measurements and 3D-CT are shown in Fig. 2. Wilcoxon analysis showed significant differences on days 1 ($p < 0.05$) and 4 ($p < 0.01$), but no significant differences on days 7, 11, and 14. The correlation between the hematoma volume obtained by actual measurements and 3D-CT was $r_s = 0.48$ on day 1 (not significant), $r_s = 0.39$ on day 4 (not significant), $r_s = 0.75$ on day 7 ($p < 0.05$), $r_s = 0.98$ on day 11 ($p < 0.001$), and $r_s = 0.88$ on day 14 ($p < 0.01$). The coefficients on days 1 and 4 were relatively high and the correlation between measured and estimated volumes was significant on days 7, 11, and 14.

Fig. 2 Chronological changes in the mean volume of experimental hematoma based on actual measurements (●) and three-dimensional computed tomography (■). Values are means $\pm$ standard deviation.

Fig. 3 Chronological changes in the mean volume of subarachnoid hemorrhage (●), intraventricular hemorrhage (■), and intracerebral hemorrhage (▲). Values are means $\pm$ standard deviation.

II. Clinical measurement of hematoma volume

The V2 value was 12 ± 4 ml (mean $\pm$ standard deviation, $n = 50$). The mean volumes of SAH, IVH, and ICH are shown in Fig. 3. The volume data yielded by 3D-CT can be observed from any direction, so the localization of SAH can be easily understood (Fig. 4). Not only SAH in the convexity and posterior fossa but also ventricular hematoma were visualized and the localization of SAH on 2D-CT and 3D-CT could be compared. In addition, chronological changes in the SAH volume could be easily followed on 3D-CT.

Fig. 4 Upper panel: Axial computed tomography (CT) scans. Lower panel: Volume data acquired by three-dimensional CT in the superior (left), anterior (center), and lateral (right) views. The localization of the subarachnoid hemorrhage (SAH) could be estimated from all directions. SAH could be visualized in the convexity and posterior fossa, as well as the ventricular hematoma.

Fig. 5 Chronological changes in the subarachnoid hemorrhage (SAH) volume in patients with transient (Δ , $n = 2$) and permanent ($\square$, $n = 2$) symptomatic vasospasm (SVS) and without SVS ($\bullet$, $n = 46$). The SAH volume was significantly smaller in patients without SVS than in patients with SVS at all time points examined ($p < 0.01$ on days 0, 1, 4, 7, and 14). The minimum SAH volume in patients with SVS was 92, 76, 42, 24, and 12 ml on days 0, 1, 4, 7, and 14, respectively.

III. Correlation between hematoma volume and SVS

SVS occurred in 4 of the 50 patients. SVS was transient in 2 patients and persistent in 2 patients who manifested a newly-developed low density area. The chronological changes in the SAH volume in the 4 patients with SVS are shown in Fig. 5. At all time points examined, the SAH volume was significantly smaller in patients without SVS than in those with SVS ($p < 0.01$ on days 0, 1, 4, 7, and 14). The minimum SAH volume in patients with SVS was 92, 76, 42, 24, and 12 ml on days 0, 1, 4, 7, and 14, respectively. SVS occurred in 2 of 8 patients with IVH; CT showed that one patient with persistent SVS had developed a new low density area. The mean IVH volume was 18 and 8 ml in the patients with transient and persistent SVS, respectively. None of the 9 patients with ICH developed SVS. Because of the small number of patients, we could not perform statistical analysis.

Illustrative Cases

Case 1 (without SVS): A 72-year-old woman presented with consciousness disturbance of Hunt and Kosnik (H-K) grade IV.⁶⁾ 3D-CT showed massive SAH (99

Fig. 6 Illustrative Case 1 without symptomatic vasospasm. Chronological changes observed on conventional computed tomography (CT) scans (*upper panel*), and volume data acquired by three-dimensional CT with subarachnoid hemorrhage volume (*lower panel*).

Fig. 7 Illustrative Case 2 with transient symptomatic vasospasm. Chronological changes seen on conventional computed tomography (CT) scans (*upper panel*), and volume data acquired by three-dimensional CT with subarachnoid hemorrhage volume (*lower panel*).

ml) (Fig. 6). She underwent neck clipping of 3 aneurysms of the left middle cerebral artery bifurca-

tion, left internal carotid artery-posterior communicating artery, and the basilar bifurcation, and

Fig. 8 Illustrative Case 3 with permanent symptomatic vasospasm. Chronological changes seen on conventional computed tomography (CT) scans (upper panel), and volume data acquired by three-dimensional CT with subarachnoid hemorrhage volume (lower panel).

evacuation of SAH in the left sylvian fissure. 3D-CT obtained on day 1 showed disappearance of the SAH in the left and residual SAH (54 ml) in the right sylvian fissures, and the convexity and posterior fossa. Cisternal irrigation was performed with urokinase and ascorbic acid.^{8,11)} The SAH volume continued to decrease gradually. She did not develop SVS and her Glasgow Outcome Scale (GOS) at discharge was moderately disabled.

Case 2 (with transient SVS): A 52-year-old man presented with consciousness disturbance of H-K grade IV. 3D-CT disclosed massive SAH (115 ml) and IVH (18 ml) (Fig. 7). He underwent trapping of a fusiform aneurysm in the right A₁ portion of the anterior cerebral artery (ACA). Cisternal irrigation was performed with urokinase and ascorbic acid^{8,11)} for 14 days. The SAH volume was 118 and 78 ml on days 1 and 4, respectively. He developed consciousness disturbance on day 5, and manual muscle testing (MMT) demonstrated motor weakness of the left lower extremity (MMT 4/5). 3D-CT angiography revealed marked arterial narrowing at the bilateral A₂ portions of the ACA and triple H therapy was performed. He subsequently recovered and CT showed no newly developed low density area. His GOS at discharge was good recovery.

Case 3 (with permanent SVS): A 66-year-old woman presented with consciousness disturbance of H-K

grade IV. 3D-CT showed massive SAH (130 ml) and IVH (8 ml) (Fig. 8). Her H-K grade was closely monitored and improved to grade III on the next day, so aneurysm neck clipping was performed.¹²⁾ We observed a decrease in the SAH in the sylvian fissure on the axial CT scans acquired on day 1, so rather than performing cisternal irrigation, we administered fasudil chloride.¹⁴⁾ However, 3D-CT revealed residual SAH in the periphery of the sylvian fissure, convexity, and right lateral ventricle. The SAH volume was 126 and 122 ml on days 1 and 4, respectively. She developed consciousness disturbance, hemiparesis (MMT 1/5), and total aphasia on day 11. Subsequent CT detected an extensive low density area, and her symptoms persisted. Her GOS was vegetative survival.

Discussion

Our volumetric analysis using CT showed that the setting of the CT number is highly important. Based on the literature, we chose values ranging from 40 to 80 HU. In previous series of patients, the CT number of SAH at admission ranged from 40 to 80 HU.¹⁵⁾ The CT numbers of the gray and white matter were reported as 25–41 HU (mean 33 HU) and 24–41 HU (mean 30 HU),²⁾ and as 30–40 HU (mean 35 HU) and 25–34 HU (mean 29 HU),¹⁷⁾ respectively. The mean

CT number of the gray matter was measured as 36 HU using the same MDCT instrument as us (Aquilion, 4 rows).¹⁶⁾ Therefore, we decided that setting the CT number at 40–80 HU enabled us to exclude the effect of the volume of the parenchyma. The first step in our volumetric quantification examined found a moderate correlation between the experimental hematoma volume obtained by actual measurements and 3D-CT. Consequently, we adopted CT numbers from 40 to 80 HU in our analyses of 50 SAH patients.

Various attempts to measure the volume of SAH have been reported. A software-based volumetric quantification method using 2D-CT was used to measure the hemorrhagic volume in the sylvian and interhemispheric fissures and in the suprasellar, ambient, quadrigeminal, and prepontine cisterns.⁴⁾ In addition, the hemorrhagic volume was calculated in patients with IVH and ICH. The amount of blood in each discrete region of interest was determined visually based on density and manually outlined on each CT slice, and the hemorrhagic volumes were calculated in cm³ based on the slice thickness and in-plane resolution of the CT scans. The hematoma volume on admission in 40 patients was 2.27–112.3 ml. Using similar methods, the SAH volume on admission in 75 patients was 0.2–38 ml (mean 10.4 ml).¹⁰⁾ However, these methods encountered problems involving the partial volume effect, and the volume in the convexity and posterior fossa was not considered. To surmount these problems, we attempted to quantify the SAH volume using volume data obtained from 3D-CT. We cannot compare the previously reported and present SAH volumes because of differences in the study subjects. Nonetheless, in our study, the mean SAH volume on day 0 (44 ml) was greater than previously reported, which may be attributable to the partial volume effect and the SAH in the convexity and posterior fossa. The method based on 2D-CT⁴⁾ requires 20 minutes to estimate the SAH volume, whereas our method requires only 2 minutes.

All 13 patients in the previous series with cisternal hemorrhage volumes greater than 20 ml developed delayed ischemic neurological deficit.⁴⁾ Univariate logistic model and multivariate analysis have shown that the initial clot volume and the percentage of clot cleared each day are significant predictors of vasospasm.¹⁰⁾ Our study did not attempt to clarify the predictability of SVS due to the large bias introduced by our patients receiving different therapies. Nonetheless, we found that the SAH volume was significantly lower in patients without SVS than in patients with SVS at all time points examined. All 4 patients with SAH volume exceeding 76 ml on day

1 and 42 ml on day 4 developed SVS, whereas no patient with lower values did. The percentage of clot cleared each day may be a significant predictor of vasospasm, but the importance of clearance timing remains unknown.¹⁰⁾ Our results suggest that monitoring the SAH volume until day 4 may help to predict the occurrence of SVS.

We performed continuous cisternal irrigation to prevent SVS.^{8,12)} To dissolve the SAH, we used urokinase and ascorbic acid to degrade oxy-hemoglobin, one of the strongest spasmogenic substances.^{7,9,13)} Even if the SAH volume on day 0 is large, SVS could be prevented by intraoperative clot evacuation and postoperative irrigation. Only one of our patients (Case 1) did not suffer SVS despite the initial SAH volume greater than the minimum SAH volume indicating SVS, but her SAH volume decreased abruptly by day 4. On the other hand, one patient with SAH volume of 42 ml on day 4 developed SVS despite irrigation therapy, indicating that close observation is needed to determine the indication for endovascular treatment in patients developing SVS.

The present method must eliminate possible errors attributable to normal structures with CT numbers in the range of 40–80 HU. The mean volume of normal structures was 12 ml, so we used this value in all patients. If the normal structures had a larger volume, the calculated hematoma volume was larger. On the other hand, if the normal structures had a lower volume, the calculated hematoma volume was smaller, and became negative in some instances. Therefore, errors of approximately 10 ml are unavoidable. However, we were able to observe chronological volume changes in each patient. Artifacts such as aneurysm clips and/or tubes raise another problem. Although titanium clips have little effect on the quantification of the hemorrhage volume, the role of artifacts must not be overlooked.

The present method can rapidly measure SAH volume based on 3D-CT, and allows observation of the hematoma from any direction, so facilitating localization of the SAH. In addition, chronological changes in the SAH volume can be monitored easily. The present study found that SVS occurred in patients with large SAH volume (exceeding 92 ml on day 0, 76 ml on day 1, and 42 ml on day 4). Our method may be a useful tool in clinical studies of cerebral vasospasm, but further experience is necessary.

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