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Impact of width of susceptibility vessel sign on recanalization following endovascular therapy

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ABSTRACT

Background and purpose: We aimed to investigate the relationship between arterial recanalization following endovascular therapy and the susceptibility vessel sign (SVS) length and width on susceptibility-weighted imaging.

Methods: We retrospectively evaluated consecutive patients with anterior circulation ischemic stroke who underwent magnetic resonance imaging preceded endovascular therapy, and measured the SVS length and width. Successful recanalization was defined as expanded thrombolysis in cerebral infarction grade of 2b to 3. Logistic regression analysis was executed to determine the independent predictors of successful recanalization and first-pass reperfusion (FPR) after endovascular therapy.

Results: Among 100 patients, successful recanalization and FPR were observed in 77 and 34 patients, respectively. The median SVS length and width were 10.3 mm (interquartile range, 6.8–14.1 mm) and 4.2 mm (interquartile range, 3.1–5.2 mm), respectively. In multivariate logistic regression analysis, SVS width was associated with successful recanalization (odds ratio, 1.88; 95% confidence interval, 1.14–3.07; p = 0.005) and FPR (odds ratio, 1.38; 95% confidence interval, 1.01–1.89; p = 0.039). The optimal cutoff value for the SVS width to predict successful recanalization and FPR were 4.2 mm and 4.0 mm, respectively.

Conclusions: Larger SVS width may predict successful recanalization and FPR following endovascular therapy.

1. Introduction

Endovascular therapy for acute ischemic stroke with large vessel occlusion has emerged as a standard therapy [1]. Successful recanalization is significantly associated with good functional outcomes [2,3]. Previous reports have revealed that several factors, such as intravenous thrombolysis [4], a more proximal occlusion site [5,6], and good pre-

treatment collaterals [7], increase the rate of successful recanalization following endovascular therapy.

The susceptibility vessel sign (SVS) is defined as the presence of a hypointense low signal within a vessel on T2*-weighted gradient-echo imaging, which exceeds the diameter of the contralateral or intact portion of the vessel [8]. Histopathological inspection of retrieved thrombi has revealed the SVS to be associated with red blood cell

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Abbreviations: DWI, diffusion-weighted imaging; ICA-T, internal carotid artery terminus; IQR, interquartile range; IV-tPA, intravenous tissue-type plasminogen activator; MCA, middle cerebral artery; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; eTICI, expanded thrombolysis in cerebral infarction; FPR, First-pass reperfusion; NIHSS, National Institute of Health Stroke Scale; SVS, susceptibility vessel sign; SWI, susceptibility-weighted imaging.

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dominant thrombi [9]. Clots containing a higher amount of red blood cells were likely to be observed in patients who had achieved successful recanalization [10–12]. Therefore, the presence or morphology (i.e., length and width) of the SVS could predict successful recanalization after endovascular therapy. However, the association between SVS and successful recanalization is still controversial due to both positive and negative results [13–18]. Excellent recanalization after the first pass of thrombectomy device may be associated with good outcome [19,20]. The relationship between the SVS and first-pass recanalization (FPR) is currently unknown. In this study, we aimed to clarify whether the length and width of the SVS detected by susceptibility-weighted imaging (SWI), which is more sensitive for detecting SVS compared to T2*-weighted imaging [21], were associated with successful recanalization after endovascular therapy in patients with acute ischemic stroke.

2. Methods

2.1. Patient selection

We retrospectively reviewed consecutive patients with acute ischemic stroke admitted to our hospital within 24 h from onset between January 2015 and July 2021. Inclusion criteria for this study were as follows [1]: patients who underwent MRI, including SWI preceded endovascular therapy [2], patients with internal carotid artery terminus (ICA-T), middle cerebral artery (MCA) M1 or proximal M2 segment occlusion. We excluded patients with poor SWI image quality, no SVS, cessation of endovascular therapy, and tandem lesion, which is the occlusion of both ICA and MCA. The institutional review board of Nagasaki University Hospital reviewed and approved the clinical study protocols and waived the requirement for written consent because of the retrospective and record-based study design.

2.2. Clinical information

The baseline characteristics, vascular risk factors (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, and current smoking), histories of coronary artery disease and ischemic stroke, time from symptom onset to groin puncture, time from hospital arrival to groin puncture, initial National Institute of Health Stroke Scale (NIHSS) score, blood tests (brain natriuretic peptide and D-dimer levels), and use of intravenous tissue-type plasminogen activator (IV-tPA) were collected. Ischemic stroke subtype was classified based on Trial of Org 10,172 in Acute Stroke Treatment criteria [22].

2.3. MRI protocol

MRI was performed with a 1.5 Tesla unit (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) using an 8-channel phased-array coil. The acute stroke MRI protocol, which was performed during a single session within 20 min, consisted of diffusion-weighted imaging (DWI), T2-weighted fluid-attenuated inversion recovery, 3D time-of-flight magnetic resonance angiography (MRA), SWI, and 3D arterial spin labeling. The imaging sequence and parameters of SWI were as follows: 43.0 ms repetition time, 35.0 ms effective echo time, 15° flip angle, 3 mm slice thickness, 22 cm field of view, 320 × 195 matrix size, number of echoes = 1, and 188 s total acquisition time.

2.4. Imaging analyses

DWI lesion volume was calculated by summing the infarct area on each slice, taking into accout individual slice thicknesses across the entire outlined area. Hyperintense lesion on DWI was visually determined by comparing to the contralateral, non-affected hemisphere. Arterial occlusion sites were identified using MRA. The SVS was defined as a hypointense signal with blooming artifact on SWI at the occlusion site as revealed by MRA. The maximum length of SVS was measured as the distance between the proximal and distal ends of the SVS, using inplane length measurements of the SVS in the M1 and proximal M2 segments of the middle cerebral artery. Proximal M2 occlusions were defined as occlusions in the horizontal M2 segment within 1 cm from the middle cerebral artery bifurcation [23]. The proximal M2 occlusion may be as readily accessible to endovascular therapy as M1 occlusion [24,25]. In cases of ICA-T occlusion, the length of the SVS perpendicular to the axial acquisition plane (i.e., the thrombus in the supraclinoid internal carotid artery) was not included in the total length of the SVS. The SVS width was defined as the largest diameter of SVS crossing perpendicular to the occlusion site. (Fig. 1) Two investigators (Dr M.M and Dr. R.I) independently assessed the length and width of SVS. Interrater agreement for both length and width of SVS was assessed using the intraclass correlation coefficient.

Collateral grading before endovascular therapy was assessed using the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) scale on angiography by one experienced investigator. (Dr. T.M) [26] This scale rates collateral status on a scale from 0 (no collaterals visible at the ischemic site) to 4 (complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion). Patients were dichotomized into a poor collateral group (score of 0, 1, or 2) and a good collateral group (score of 3 or 4). This grading system was not evaluated in patients with ICA-T occlusion and non-visibility of the A1 segment.

2.5. Endovascular procedures

All endovascular therapy was performed under conscious sedation and using a balloon-guide catheter. The decision to utilize a stentretriever, contact aspiration, or combined techniques [27,28] was left to the discretion of the experienced neurointerventionalists (Dr. N·H and Dr. Y.M). While the operation records indicated the first-line strategy for endovascular therapy, it was unclear in most cases that required multiple passes which specific method ultimately resulted in recanalization. The cerebral reperfusion status was assessed based on expanded thrombolysis in cerebral infarction (eTICI) at the end of the procedure. Successful recanalization after endovascular therapy was defined as an eTICI grade 2b-3. FPR was defined as near to complete recanalization (eTICI 2c/3) after a single pass of the device.

2.6. Statistical analysis

Baseline clinical and imaging parameters were compared between groups with successful and unsuccessful recanalization, as well as between those with and without FPR, using the Mann-Whitney U test for continuous variables and the Fisher exact test for categorical variables. Multivariate logistic regression analyses were conducted to identify independent predictors of successful recanalization in the overall patient population and in those with atrial fibrillation, as well as FPR in the overall patient population. The correlation between SVS width and eTICI grade was assessed using the Pearson correlation coefficient. A pvalue of <0.05 was considered statistically significant. The use of IV-tPA prior to endovascular therapy has been identified as a potential predictor of successful recanalization [4,29,30], and as such was included in the multivariate logistic regression analysis for this purpose. Variables with a p-value of less than <0.1 in univariate analysis were considered potential predictors of favorable recanalization, with the exception of the first-line strategy, which was due to its uncertain impact on the final degree of recanalization in patients requiring more than two passes. The number of passes was also not included as a predictor of successful recanalization, as it is expected that an increase in the number of passes corresponds with an inability to achieve recanalization. Instead, the relationship between SVS width and FPR was analyzed. M1 occlusion and a first-line combined technique have been proposed as predictors of FPR [31,32], and were therefore included as variables in the multivariate logistic regression analysis for this purpose. Cutoff values for SVS



Fig. 1. Susceptibility vessel sign (SVS) on susceptibility-weighted imaging. (A) Magnetic resonance angiography depicted occlusion of the middle cerebral artery M1 segment (white arrow). (B) The method of determining the width (double-headed arrow) and length (double-headed arrow with dotted line) of the SVS is demonstrated.

width capable of distinguishing between the groups were determined using receiver operating characteristic curve analsyis. All the analyses were performed using JMP software version 15 (SAS Institute Inc., Cary, NC, USA).

3. Results

From January 2015 and July 2021, 100 patients were evaluated in this study. Fig. 2 shows the inclusion algorithm. Of these patients, 48 patients were men (48%), median age was 79 years (interquartile range [IQR], 72–86 years). The median NIHSS score was 16 (IQR, 11–21), median initial DWI lesion volume was 15.8 ml (IQR, 5.5–46.0 ml), and median times from symptom onset and door to groin puncture were 179



Fig. 2. Flowchart for the study population. SWI, susceptibility-weighted imaging; ICA-T, internal carotid artery terminus; MCA, middle cerebral artery; SVS, susceptibility vessel sign. min and 73 min, respectively (IQR, 126-433 min and 61-83 min). IVtPA was administered to 44 patients (44%) prior to endovascular therapy. Conventional angiography revealed occlusions in 13 (13%) ICA-T, 73 (73%) M1 segment of the MCA, and 14 (14%) proximal M2 segment of the MCA. Information on collaterals was available for 3 of 13 (23%) ICA-T occlusions, 69 of 72 (96%) M1 segment of MCA occlusions, and 13 of 14 (93%) proximal M2 segment of MCA occlusions. Inter-rater agreement for SVS length and the SVS width were 0.97 and 0.89, respectively. The median SVS length and width were 10.3 mm (IQR, 6.8-14.1 mm) and 4.2 mm (IQR, 3.1-5.2 mm). There was a positive correlation observed between the length and width of SVS. (Pearson correlation coefficient 0.48, p < 0.001) Successful recanalization was achieved in 77 patients (77%), with a median time from groin puncture to recanalization of 32 min (IQR, 26-47 min). FPR was achieved in 34 patients (34%). Patients were treated using stent retriever (n = 49, 49%), contact aspiration (n = 4, 4%), or a combined technique (n = 47, 47%) as the first-line strategy for endovascular therapy. None of the patients received balloon angioplasty as rescue therapy.

3.1. Predictors of successful recanalization

Baseline patient characteristics of patients are shown in Table 1. While there was no significant difference between SVS length in the successful and unsuccessful recanalization groups (10.5 mm [IQR, 6.6–13.7] vs. 10.1 mm [IQR, 7.7–14.8]; p = 0.676), the successful recanalization group had larger SVS widths compared to the unsuccessful recanalization group (4.4 mm [IQR, 3.4-5.3] vs. 3.0 mm [IQR, 2.6–4.1]; p = 0.002). Multivariate logistic regression analysis showed that SVS width (odds ratio [OR], 1.88; 95% confidence interval [CI], 1.14–3.07; p = 0.005) was independently associated with successful recanalization (Table 2). The predictive value of SVS width for successful recanalization had an area under the curve of 0.71 (95% CI, 0.20-1.03), with an optimal cutoff value of 4.2 mm for predicting successful recanalization (sensitivity, 0.58; specificity, 0.78). (Table 3) A scatter plot showed the association between SVS width and end of procedure eTICI grade. (Pearson correlation coefficient, 0.24; p = 0.038) (Fig. 3) Analyses were conducted to validate the association between SVS width and successful recanalization in patients with atrial fibrillation. (Supplementary table 1) SVS width remained consistently associated with successful recanalization (OR, 1.73; 95% CI, 1.02–2.94; p =0.039), with an optimal cutoff value of 3.2 mm for predicting successful recanalization in this patient subgroup. (Table 2 and Table 3).

Table 1

Baseline characteristics of the study population to predict successful recanalization.

| | Successful recanalization | | Unsuccessful recanalization | | p value | |
|---|---------------------------|---------------|-----------------------------|--------------|---------|--|
| | n = 77 | | n = 23 | | | |
| Age, year | 78 | (71–86) | 81 | (76–87) | 0.139 | |
| Sex | 41/36 | | 7/16 | | 0.062 | |
| Vascular risk factors | | | | | | |
| Hypertension | 55 | (71) | 17 | (74) | 1.000 | |
| Diabetes mellitus | 11 | [14] | 1 | [4] | 0.286 | |
| Dyslipidemia | 16 | [21] | 5 | [22] | 1.000 | |
| Atrial fibrillation | 55 | (71) | 12 | (52) | 0.128 | |
| Current smoking | 7 | [9] | 3 | [13] | 0.693 | |
| Past medical history | | | | | | |
| Coronary artery disease | 6 | [8] | 3 | [13] | 0.426 | |
| Ischemic stroke | 14 | [18] | 2 | [9] | 0.349 | |
| Time from symptom onset to groin puncture, min | 173 | (126-425) | 230 | (146–482) | 0.466 | |
| Time from hospital arrival to groin puncture, min | 73 | (62–84) | 73 | (61-82) | 0.838 | |
| Initial NIHSS score | 16 | [12-21] | 17 | [10-19] | 0.465 | |
| Laboratory findings | | | | | | |
| Brain natriuretic peptide, pg/mL | 220.0 | (124.0-304.5) | 195.0 | (45.7-414.0) | 0.667 | |
| D-dimer, µg/mL | 1.4 | (0.9–2.8) | 1.5 | (1.1-2.7) | 0.755 | |
| Use of IV-tPA | 37 | (48) | 7 | [30] | 0.157 | |
| Radiology | | | | | | |
| Initial DWI lesion volume, mL | 15.2 | (5.3–43.7) | 27.6 | (5.7–69.4) | 0.793 | |
| Occlusion site | | | | | | |
| ICA-T | 11 | [14] | 2 | [9] | 0.727 | |
| M1 | 56 | (73) | 17 | (74) | 1.000 | |
| M2 | 10 | [13] | 4 | [17] | 0.732 | |
| SVS length, mm | 10.5 | (6.6–13.7) | 10.1 | (7.7–14.8) | 0.676 | |
| SVS width, mm | 4.4 | (3.4–5.3) | 3.0 | (2.6–4.1) | 0.002 | |
| ASITN/SIR collateral score | | | | | | |
| Grade 3 or 4 (good collateral group) | 38/64 | (59) | 12/21 | (57) | 1.000 | |
| First-line strategy of endovascular therapy | | | | | | |
| Stent-retriever | 35 | (45) | 14 | (61) | 0.238 | |
| Contact aspiration | 2 | [3] | 2 | [9] | 0.226 | |
| Combined technique | 40 | (52) | 7 | [30] | 0.096 | |
| Number of passes | 2 | [1.2] | 3 | [2.3] | < 0.001 | |
| Stroke subtype | | 2, 3 | | 2) 3 | | |
| Cardioembolism | 61 | (79) | 14 | (61) | 0.100 | |
| Large artery atherosclerosis | 2 | [3] | 2 | [9] | 0.226 | |
| Other determined causes | 0 | (0) | 2 | [9] | 0.051 | |
| Undetermined cause | 14 | [18] | 5 | [22] | 0.764 | |
| ondeterminet tatoe | τı | [10] | 5 | رخد | 0.704 | |

Data are presented as median (interquartile range), number (%) and n/N (%). NIHSS, National Institute of Health Stroke Scale; IV-tPA, intravenous tissue-type plasminogen activator; DWI, diffusion-weighted imaging; ICA-T, internal carotid artery terminus; MCA, middle cerebral artery; SVS, susceptibility vessel sign; ASITN/SIR, American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology.

Table 2

Multivariate logistic regression analysis to predict successful recanalization in all patients and patients with atrial fibrillation, and first-pass reperfusion in all patients.

| | OR (95% CI) | p value |
|--|-----------------------|---------|
| Successful recanalization in all patients | | |
| SVS width, per 0.1 mm increase | 1.69 (1.10-2.57) | 0.015 |
| Male | 1.68 (0.57-4.89) | 0.344 |
| Use of IV-tPA | 2.00 (0.70–5.69) | 0.193 |
| Successful recanalization in patients with | h atrial fibrillation | |
| SVS width, per 0.1 mm increase | 1.73 (1.02-2.94) | 0.025 |
| Use of IV-tPA | 1.91 (0.44–8.22) | 0.374 |
| First-pass reperfusion in all patients | | |
| SVS width, per 0.1 mm increase | 1.38 (1.01–1.89) | 0.039 |
| M1 occlusion | 1.14 (0.43-2.99) | 0.790 |
| First-line combined technique | 0.98 (0.41-2.33) | 0.961 |

SVS indicates susceptibility vessel sign; IV-tPA, intravenous tissue-type plasminogen activator; OR, odds ratio; CI, confidence interval.

3.2. Predictors of FPR

The results of univariate analysis to identify predictors of FPR are presented in Supplementary Table 2. The SVS width among patients in the FPR group was larger than that among patients in the No FPR group. (4.8 mm [IQR, 3.9–5.4] vs. 3.8 mm [IQR, 3.0–5.1]; p = 0.041) Multivariate logistic regression analysis indicated that SVS width was independently associated with FPR. (OR, 1.38; 95% CI, 1.01–1.89; p = 0.039) (Table 2) The optimal cutoff value for predicting FPR using SVS width was 4.0 mm, yielding a sensitivity of 0.77 and a specificity of 0.53. (Table 3).

4. Discussion

Our results showed that increased SVS width predicted successful recanalization, while SVS length did not. The cutoff value for SVS width predicting successful recanalization was 4.2 mm.

In this study, successful recanalization achieved through endovascular therapy was more likely in patients with larger SVS widths. A past study revealed that patients with larger SVS widths were more likely to achieve successful recanalization in univariate analysis [15]. However, there is a lack of conclusive evidence on the association between them. Additionally, there is no study examining whether the rate of FPR increases as SVS width increases. The presence of SVS in an occluded vessel has been associated with a high proportion of red blood cells in the thrombus [9]. Previous studies have reported that erythrocyte-rich thrombi retrieved by thrombectomy had higher recanalization rates and required fewer recanalization maneuvers [11,12,33,34]. An enlarged SVS width may reflect a higher proportion of red blood cells in

Table 3

Optimal cutoff values of SVS width for predicting successful recanalization in the overall patient population, in those with atrial fibrillation, and first-pass reperfusion in the overall patient population.

| | AUC (95%CI) | Cutoff value | Sensitivity | Specificity | PPV | NPV |
|---|--------------------------------------|------------------|--------------|--------------|--------------|--------------|
| Successful recanalization in all patients Successful recanalization in patients with atrial fibrillation | 0.71 (0.20–1.03) 0.70 (0.09–1.17) | 4.2 mm 3.2 mm | 0.58 0.87 | 0.78 0.58 | 0.45 0.48 | 0.18 0.07 |
| First pass reperfusion in all patients | 0.63 (0.01–0.62) | 4.0 mm | 0.77 | 0.53 | 0.26 | 0.35 |

AUC indicates area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.



Fig. 3. The linear correlation between the SVS width and the eTICI grade at the end of the procedure is shown by a Pearson correlation coeficient was 0.24, with a *p*-value of <0.038. SVS, susceptibility vessel sign; eTICI, expanded thrombolysis in cerebral infarction.

the thrombus, which could be associated with successful recanalization after endovascular therapy.

SVS length was not associated with recanalization in our study, consistent with a previous report [17]. Longer SVS length could represent a higher clot burden associated with a decreased rate of recanalization, proximal occlusion, more severe neurological symptoms, lower 24-h complete recanalization on MRA, and an unfavorable outcome at 3 months [16,35]. The clot burden score reflecting the length of SVS has been proposed as a predictor of functional outcome [36,37]. Patients with low clot burden scores, corresponding to longer SVS, had poorer outcomes compared with those with high clot burden scores. SVS length and width may reflect the volume and contents of the clot, respectively.

In patients with atrial fibrillation, larger SVS width also predicted successful recanalization. A previous study indicated that SVS was a predictor of atrial fibrillation [38]. The SVS, reflecting a high amount of erythrocytes in the clot, may be associated with successful recanalization [11]. Patients with atrial fibrillation may be more likely to achieve successful recanalization through endovascular therapy, possibly due to the high proportion of erythrocytes in the clot that may result in larger SVS width.

This study has several limitations. First, it is a single-center retrospective study with a small sample size that could result in a type II error. Second, the SVS length in the ICA and M2 segment of MCA may be underestimated because SVS length was measured slice by slice rather than using volumetric imaging. Third, SVS width may be larger when the more proximal vessel is occluded, as it may be affected by the size of the occlusive vessel. A previous study reported that proximal occlusions had higher recanalization rates than distal occlusions [6]. It may be advisable to examine the size at each occluded vessel individually when determining the optimal cutoff value for the SVS width in relation to recanalization following endovascular therapy. Forth, susceptibility is affected by various imaging parameters, which may make reproducibility difficult for other centers. Finally, the collateral flow graded by ASITN/SIR was not associated with recanalization status in our study. This may be due to the fact that the grading system could not be applied to patients with the ICA-T occlusion or hypoplasia of the A1 segment, and patients with internal carotid artery occlusion were not included in this study. Moreover, the reliability of the collateral grading score may be low due to the poor interobserver agreement [39].

5. Conclusion

SVS width may be a predictor of successful recanalization following endovascular therapy. MRI may be a useful initial tool for the evaluation of acute ischemic stroke and obtaining practical information promptly. Future study is warranted to determine the association between SVS width and successful recanalization following endovascular therapy.

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Declaration of Competing Interest

None.

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Appendix A. Supplementary data

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The first author is a graduate student at Nagasaki University while

working at Nagasaki University Hospital. He cannot graduate unless he clearly states in his thesis affiliation that he is a graduate student. This is a very serious problem for us. The authors would like to apologise for any inconvenience caused. Please add Nagasaki University Graduate School to the affiliation of the thesis.

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