Correlation of Acute M1 Middle Cerebral Artery Thrombus Location with Endovascular Treatment Success and Clinical Outcome

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Abstract

**Purpose**—The location of the arterial occlusion can help with prognostication and treatment triage of acute stroke patients. We aimed to determine the effects of M1 distance-to-thrombus on angiographic recanalization success rate and clinical outcome following endovascular treatment of acute M1 occlusion.

**Methods**—All acute ischemic stroke patients with M1 segment middle cerebral artery (MCA) occlusion on admission CT angiography (CTA) who underwent endovascular treatment were analyzed. The distance between thrombus origin and internal carotid artery (ICA) bifurcation was measured on admission CTA. The modified thrombolysis in cerebral infarction (mTICI) grades 2b (>50% of distal branch filling) and 3 (complete) were considered as successful recanalization. Favorable outcome was defined by 3-month follow-up modified Rankin scale (mRs) score ≤2.

**Results**—Successful recanalization was achieved in 24 (71%) of 34 consecutive patients included in this study. The M1 distance-to-thrombus was shorter among patients with successful recanalization (5.4 ± 5.4 mm) versus those without (11.3 ± 7.6 mm, p = 0.015). The successful recanalization rate was higher among patients with M1 distance-to-thrombus ≤6 mm (odds ratio: 8, 95% confidence interval: 1.37–46.81, p = 0.023) compared with those with distance-to-thrombus >6 mm. There was no significant correlation between M1 distance-to-thrombus and 3-month mRs (rho: −0.350, p=0.043). On the other hand, successful recanalization and admission NIHSS score were the only independent predictors of favorable outcome.

**Conclusion**—Shorter distance of M1 thrombus from ICA bifurcation is associated with higher rate of successful recanalization following endovascular treatment.

Keywords

acute ischemic stroke; CT angiography (CTA); middle cerebral artery (MCA); thrombus; recanalization

Introduction

Appropriate patient selection by advanced neuroimaging in recent clinical trials has been advocated as one of the main reasons for effective endovascular treatment compared with medical treatment alone [1–3]. There is still an ongoing need to identify additional parameters on advanced neuroimaging that can improve identification of stroke patients who will potentially benefit from endovascular treatment, and exclude patients at increased risk of developing complications such as hemorrhagic transformation [4].

Thrombus location is one of the imaging biomarkers that have been evaluated for prognostication of stroke [5,6]. In many centers, CT angiography (CTA) precedes any endovascular treatment of patients with suspected acute ischemic stroke. There is preliminary evidence that the location of thrombus within M1 segment of middle cere-
The MCA thrombus distance from internal carotid artery (ICA) bifurcation may be a quantifiable method for assessment of the location of occlusive thrombus. Recent studies in acute ischemic stroke patients treated with intravenous (IV) thrombolysis have shown that a shorter distance-to-thrombus is associated with higher rates of death and disability and larger diffusion-perfusion mismatch volumes on concurrent MRIs [5,6]. In this study, we aimed to determine the correlation between the distance-to-thrombus measurement on admission CTA scan with angiographic recanalization rate and clinical outcomes in ischemic stroke patients with acute MCA M1 occlusion.

Methods

Patients

This study was a retrospective analysis of prospectively collected data in the stroke registry of two university-affiliated hospitals from December 2006 to June 2010 [8,9]. The local institutional review board approved the data collection methodology. We included all acute ischemic stroke patients who (1) had an admission CTA scan, with (2) unilateral M1 segment MCA occlusion—before the bifurcation/trifurcation, and (3) underwent endovascular treatment. Patients with tandem occlusions of ICA and MCA; double occlusion of MCA and anterior cerebral artery; and those with repeat stroke/reocclusion within 3 months of the presentation were excluded from the analysis. The National Institutes of Health Stroke Scale (NIHSS) score at admission and 3-month follow-up modified Rankin scale (mRs) scores were retrieved from the stroke registry and electronic medical records. Disability or death was defined by a 3-month mRs score ≥2; favorable outcome was defined by a 3-month mRs score ≤2.

Treatment and angiographic recanalization assessment

The protocol for endovascular treatment of ischemic stroke patients during the time span of this study has been described previously [10,11]. All patients who were eligible to receive IV thrombolytic therapy, as per the then-current treatment guideline, received 0.9 mg/kg of IV recombinant tissue plasminogen activators (rt-PAs) [12,13]. Additional endovascular treatment was performed on those patients who had received IV thrombolysis, but had severe clinical symptoms (NIHSS score ≥10), and large artery occlusion on the admission CTA [11]. Moreover, those patients who presented within 8 hours of symptom onset but did not fulfill the criteria for IV rt-PA therapy underwent endovascular treatment based on qualitative and quantitative assessment of admission CT perfusion scan, as described previously [10]. Patients received intra-arterial (IA) rt-PA and/or thrombectomy [8,9]. Recanalization rates were evaluated based on the modified thrombolysis in cerebral infarction (mTICI) scoring system. A successful recanalization was defined by scores of mTICI 2b (perfusion with >50% of distal branch filling) and mTICI 3 (perfusion with filling in all distal branches).

Image acquisition and analysis

All patients underwent CTA using 64-slice multidetector CT scanners (Aquilion ONE Toshiba system, Tokyo, Japan; or Brilliance, CT; Philips Medical Systems, Best, Netherlands). CTA scans were performed following IV administration of approximately 80-cc iodinated contrast (Iohexol 350 [Omnipaque]; GE Healthcare Ireland, Cork, Ireland) at a rate of 4 mL/s, through an 18–20-gauge IV line with “triggering” off at the aortic arch (140-HU threshold). The axial images with 0.75-mm thickness were used for multiplanar and 3-D reconstruction using a dedicated workstation (Vitrea 3-D, Minnetonka, MN). The “M1 distance-to-thrombus length” was determined on curve-linear reformat reconstruction of the MCA, and measured from the center of ICA bifurcation to the beginning of the thrombus (Figures 1 and 2).

Statistical analysis

The data are presented as mean ± standard deviation, number (frequency), or median (interquartile range), wherever appropriate. Categorical variables were compared with Fisher exact tests, continuous variables with student t test, and ordinal variables with the Mann-Whitney U test. The correlations between clinical and imaging variables were calculated using the Spearman rho coefficient. The receiver operating characteristic (ROC) curve analysis was performed, and the “operating point” was determined for dichotomization of M1 distance-to-thrombus length. The multivariate binary logistic regression with stepwise forward likelihood ratio variable selection was performed to determine the independent predictors of favorable outcome. Statistical analyses were performed using SPSS software version 22 (IBM, Armonk, NY).
Results

During a 3.5-year period, 34 patients met the inclusion criteria for our analysis. The average age of patients at the time of presentation was 65.7 ± 14.4 years; 16 (47%) were women. Regarding the type of endovascular treatment, 10 (29%) patients had IA thrombolysis, 6 (18%) underwent mechanical thrombectomy, and 18 (53%) had combination of both IA thrombolysis and thrombectomy. The successful angiographic recanalization was achieved in 24 (71%) of 34 patients. There was no significant difference in successful recanalization rate between different types of endovascular treatment in our cohort ($p = 0.433$).

The M1 distance-to-thrombus was significantly shorter among patients with successful recanalization compared with those with mTICI scores of 0-to-2a (5.4 ± 5.4 mm.

Figure 1. A 77-year-old man presented with acute onset aphasia and right hemiplegia (NIHSS score of 20). on admission CTA (a), he had a proximal left M1 occlusion, with distance-to-thrombus length of 4.7 mm. He received IV thrombolytic therapy, and endovascular treatment was initiated within 4.25 h of symptom onset (B). There was successful complete recanalization of the M1 after thrombectomy (C).

Figure 2. An 83-year-old man presented with left hemiplegia and right gaze deviation (NIHSS score of 10). on admission CTA (a), he had distal right M1 segment occlusion with distance-to-thrombus length of 16 mm. He received IV thrombolytic therapy, and endovascular treatment was initiated within 4 h of symptom onset (B). There was unsuccessful IA thrombolysis without recanalization of the right M1 segment (C). the patient died 1 month after the stroke.
versus 11.3 ± 7.6 mm, \( p = 0.015 \)). The ROC curve analysis showed an area under the curve of 0.752 (95% confidence interval of 0.56–0.945) for the M1 distance-to-thrombus length in prediction of successful recanalization \( (p = 0.022) \), with an operating point of 6 mm for dichotomization of M1 distance-to-thrombus. Table 1 summarizes the clinical characteristics of patients, dichotomized based on M1 distance-to-thrombus of 6 mm. The rate of successful recanalization was higher among patients with M1 distance-to-thrombus of ≤6 mm (Figure 1) compared with those with distance-to-thrombus >6 mm (Figure 2), showing an odds ratio of 8 (95% confidence interval of 1.37–46.81, \( p = 0.023 \)). However, a M1 distance-to-thrombus of ≤6 mm was not associated with higher rate of favorable outcome (Table 1).

Overall, 12 of 34 (35%) patients had favorable outcomes at 3-month follow-up. All patients with favorable outcome had mTICI of 2b or 3 after endovascular treatment. There was no significant correlation between the 3-month mRs scores and the M1 distance-to-thrombus \( (\rho = 0.131, p = 0.461) \). The only independent predictors of favorable outcome were the admission NIHSS score and successful recanalization (mTICI = 2b/3). However, there was a significant negative correlation between the M1 distance-to-thrombus and the admission NIHSS score \( (\rho = -0.350, p = 0.043) \).

**Discussion**

The CTA has gained popularity in assessment of acute stroke patients due to rapid acquisition and wide availability. There have been increasing efforts to identify further prognostic information in addition to the presence of arterial occlusion from admission CTA to assist with stroke patient selection for reperfusion treatment [14,15]. In this study, we found that the odds of achieving successful recanalization were approximately 8 times higher among patients with M1 occlusion of ≤6 mm from ICA bifurcation compared with those with distance-to-thrombus of >6 mm on admission CTA. However, there was no significant correlation between distance-to-thrombus and rate of favorable outcome.

It should be noted that, historically, the M1 segment of MCA was defined as the artery/arteries extending to the insular branches, including the bifurcation [16]. However, the recent consensus statement recommended that M1 should be defined as extending from the ICA terminus to the first bifurcation of the MCA [17]. We have used similar definition for M1 segment in our series.

Different methods have been used to define the location of the MCA occlusive thrombus [5–7]. Some groups have divided M1 segments into proximal and distal portions, either based on the origins of the lenticulostriate perforators or by simply splitting M1 segment into half [7,17]. In our study, the distance-to-thrombus length was measured as a continuous variable using the 3-D curve-reformatted CTA. Then, the operating point from the ROC analysis was applied for dichotomization of study cohort to emphasize on the difference between post endovascular treatment recanalization success rates of patient with proximal versus distal M1 occlusions.

Some studies have suggested that more proximal M1 occlusion is associated with lower rates of favorable outcome following IV thrombolysis or thrombectomy[5–7]. However, these studies have used different methodology and definitions for localization of arterial occlusion. For example, Behme et al. [7] reported that patients with M1 occlusion proximal to the origin of lenticulostriate perforators on digital subtraction angiography had lower rate of disability-free outcome (mRs = 0 or 1) at discharge.

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**Table 1. Demographic and Clinical Characteristics of Patients Dichotomized Based on M1 Occlusive Thrombus Distance from ICA Bifurcation**

<table>
<thead>
<tr>
<th>Distance-to-thrombus ≤6 mm ( n = 18 )</th>
<th>&gt;6 mm ( n = 16 )</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.4 ± 13.6</td>
<td>66.0 ± 15.8</td>
</tr>
<tr>
<td>Gender (men)</td>
<td>8 (44%)</td>
<td>10 (63%)</td>
</tr>
<tr>
<td>M1 MCA occlusion side (left)</td>
<td>13 (72%)</td>
<td>9 (56%)</td>
</tr>
<tr>
<td>Admission NIHSS score</td>
<td>21 (15–23)</td>
<td>18 (14–21)</td>
</tr>
<tr>
<td>Onset-to-CTA interval (hours)</td>
<td>2.16 ± 1.44</td>
<td>3.45 ± 3.38</td>
</tr>
<tr>
<td>Onset-to-microcatheterization interval (hours)</td>
<td>4.29 ± 1.81</td>
<td>5.25 ± 3.19</td>
</tr>
<tr>
<td>IV thrombolytic treatment</td>
<td>12 (67%)</td>
<td>7 (44%)</td>
</tr>
<tr>
<td>IA thrombolytic treatment</td>
<td>3 (17%)</td>
<td>7 (44%)</td>
</tr>
<tr>
<td>Mechanical thrombectomy</td>
<td>3 (17%)</td>
<td>3 (19%)</td>
</tr>
<tr>
<td>IA thrombolysis and thrombectomy</td>
<td>12 (67%)</td>
<td>6 (38%)</td>
</tr>
<tr>
<td>Successful recanalization*</td>
<td>16 (89%)</td>
<td>8 (50%)</td>
</tr>
<tr>
<td>3-month favorable outcome**</td>
<td>8 (44%)</td>
<td>4 (25%)</td>
</tr>
</tbody>
</table>

Intra-arterial, IA; Intravenous, IV; Middle cerebral artery, MCA; National Institutes of Health Stroke Scale, NIHSS.

* Successful recanalization defined by mTICI scores of 2b or 3.

** Favorable outcome defined by 3-month mRs score of ≤2.
and 3-months following thrombectomy. In their series, there was no significant difference in baseline NIHSS scores, ASPECTS, procedural timings, and final mTICI scores between patients with proximal versus distal M1 occlusions [7]. In this study, the distance-to-thrombus was measured as a continuous quantitative variable on CTA rather than dichotomization based on the origin of lenticulostriate perforators on conventional angiography. The variable used in this study is better suited for stratification based on CTA because lenticulostriate arteries are not well visualized, and considerable variation can occur when division is based on half of estimated length of M1 segment due to anatomical variations.

We found no significant relationship between the distance-to-thrombus and the 3-month mRs scores, despite that successful recanalization was more frequent in those with shorter thrombus distance from ICA bifurcation. The difference in definition and measurement of distance-to-thrombus as well as heterogeneity of treatment techniques may partially explain the difference in our findings compared with those of Behme et al. [7].

In addition, greater MCA distance-to-thrombus on admission CTA has shown association with favorable outcome, and smaller perfusion mismatch volume in patients treated with IV rt-PA [5,6]. Prior studies reported that patients with MCA occlusion greater than 16 mm from the ICA terminus were more likely to have favorable outcome. Such dichotomization most likely divides patients into those with M1 versus M2 occlusions [5]. It seems likely that areas of infarction and perfusion mismatch would be smaller with distal branch (M2) occlusions compared with thrombus in M1 segment [6]. In current series, we exclusively focused on patients who received endovascular treatment of M1 occlusion to identify additional prognostic information for patient selection. These are in accordance with recent report that recanalization with endovascular therapy was more frequently achieved in patients with proximal than distal MCA occlusions, but outcome was better with distal than proximal occlusions [18].

The major limitations of our study are retrospective design, small sample size, and heterogeneity of treatment techniques in patients. Lack of a control group with matched clinical severity without endovascular treatment limits our ability to determine the effect of endovascular intervention on clinical outcome. In addition, our results may not be completely applicable to patient cohort treated with newer generation of thrombectomy devices and techniques. Prior studies have shown that stroke patients with higher thrombus burden and longer hyperdense clots on thin-section non-contrast CT scan tend to have higher rates of death and disability and lower probability of revascularization following IV rt-PA treatment [19,20]. Unfortunately, given the lack of thin-section non-contrast CT scan images in our patients, we were unable to determine the thrombus length precisely. Therefore, we cannot comment on whether the relationship between distance-to-thrombus and recanalization was related to thrombus length.

Conclusion

Shorter distance of M1 thrombus from the ICA bifurcation was associated with higher rate of successful recanalization following endovascular treatment. While we were unable to demonstrate any significant relationship between the distance-to-thrombus and the favorable outcome, adjustment of treatment benefits based on thrombus location in larger clinical trials can elucidate the benefits of endovascular interventions in stroke patients with proximal M1 occlusions.

Acknowledgements and Disclosure

None.

References


