Clot length Distribution and Predictors in Anterior Circulation Stroke: Implications for IA Therapy

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Abstract

Background and Purpose—Thin-section non-contrast CT (NCCT) images can be used to measure hyperdense clot length in acute ischemic stroke (AIS). Clots ≥8mm have a very low probability of IV-tPA recanalization, and hence may benefit from a bridging intra-arterial approach. To understand the prevalence of such clots, we sought to determine the distribution and predictors of clot lengths in consecutive anterior circulation proximal artery occlusions.

Methods—Of 623 consecutive AIS patients, fifty-three met inclusion criteria: presentation <8 hours from onset; intracranial ICA-terminus or proximal-MCA occlusion; admission thin-slice NCCT (≤2.5mm); and no IV-tPA pre-treatment. For each patient, hyperdense clot length was measured and recorded along with additional relevant imaging and clinical data.

Results—Mean age was 70 years, and mean time-to-CT was 213 minutes. Median baseline NIHSS was 16.5. Occlusions were located in the ICA-terminus (34% [18/53]), MCA M1 (49% [26/53]) and M2 segments (17% [9 of 53]). Hyperdense thrombus was visible in 96%, with mean and median clot lengths (mm) of 18.5 (±14.2) and 16.1 (7.6-25.2), respectively. Occlusion location was the strongest predictor of clot length (multivariate p=0.02). Clot length was ≥8mm in 94%, 73%, and 22% of ICA-terminus, M1, and M2 occlusions, respectively.

Conclusion—The majority of anterior circulation proximal occlusions are ≥8mm long, helping to explain the low published rates of IV-tPA recanalization. ICA-terminus occlusion is an excellent marker for clot length ≥8mm; vessel-imaging status alone may be sufficient. Thin-section NCCT appears useful for patients with MCA occlusion due to the wide variability of clot lengths.

Keywords

Stroke; Hyperdense MCA; Clot-length; Intra-Arterial Therapy; IV-tPA
INTRODUCTION

The Interventional Management of Stroke (IMS) III randomized controlled trial (RCT) failed to demonstrate the benefit of bridging therapy over IV-tPA alone within 3 hours of acute ischemic stroke (AIS) onset. A major limitation of this trial was that pre-treatment vessel imaging was not mandated for entry. Among the 47% of patients with documented vessel occlusion, there was a significant benefit of intra-arterial therapy (IAT) in the trial.

Nevertheless, vessel imaging may also have significant limitations for identifying patients who will benefit from a bridging approach. In an IMS-III secondary analysis, there was no difference in good outcome rates between the treatment arms for patients with documented middle cerebral artery (MCA) M1 segment occlusions (48% vs. 51% for bridging vs. IV-tPA, respectively). These lesions account for a large fraction of anterior circulation proximal artery strokes. Therefore, there is a clinical need to define imaging biomarkers of IV-tPA resistance for rapid, appropriate patient selection for early-window IAT.

Thin-section non-contrast CT (NCCT) can be used to accurately measure clot lengths based on vessel hyperdensity. Hyperdense clot lengths ≥8mm have a very low probability of IV-tPA recanalization, and may represent an ideal target for bridging IAT. In order to understand the proportion of patients demonstrating this finding, we sought to determine the distribution and predictors of clot lengths in consecutive anterior circulation proximal artery occlusions.

METHODS

The study was approved by our IRB, which waived written informed consent for this HIPAA-compliant retrospective analysis. Between August 2011 and August 2012, we reviewed consecutive AIS patients who presented to the emergency department. Study inclusion criteria were presentation <8 hours from stroke onset, admission stroke-protocol head NCCT with available thin-slice images, CTA-documented occlusion of the internal carotid artery terminus (ICA-terminus) or proximal MCA (M1, M2), and no IV-tPA treatment before imaging.

Imaging

CT was performed using a 64-slice MDCT (LightSpeed, GE-Healthcare, WI), in helical mode: 120kV, Auto-mA with noise-index (NI): 3.5, pitch 0.531:1, rotation speed 0.5s, reconstructed with 90% ASiR™, soft kernel, field-of-view 22-cm. Axial 0.625-mm images were reformatted to 5-mm thick maximum intensity projection (MIP) images. CTA was performed at 120kV, Auto-mA (NI=12), rotation speed 0.5s. 80–100mL nonionic contrast agent (Omnipaque 370; Nycomed, Denmark) was injected, followed by 40mL saline, at a rate of 4mL/s. Images were reconstructed at 0.625-mm thickness, 0.625-mm interval.

Image Analysis

Two neuroradiologists (AJY with >10 years and LTM with >2 years of clinical experience) measured the hyperdense clot length, if present, on axial and coronal MIP-NCCT images with window width and level of 50 HU. To avoid foreshortening, the longer measurement was used for subsequent analysis and reporting.

Statistics

Clot length was analyzed as a continuous variable as well as dichotomized based on the 8mm cutoff as a marker of IV-tPA resistance. Inter-rater agreement, univariate and
multivariate analyses were performed using MedCalc software (v.11.6.1.0, Ostend, Belgium); statistical significance was set at 2-tailed p-value <0.05.

RESULTS

Of 623 consecutive AIS patients, fifty-three patients who met the study inclusion criteria were analyzed. Eighty patients had anterior circulation occlusion based on admission CTA within 8 hours of stroke onset; however, twenty-seven patients were excluded based on transfer from outside hospital where IV-tPA was given before CT imaging at our center. Baseline characteristics are provided in Table 1.

Hyperdense thrombus was visible in 96% of patients (2 M1-MCA clots were not visible on thin-section NCCT). Mean (±SD) clot length (mm) was 18.5(±14.2), and 72%(38/53) of clots were ≥8mm. By occlusion level, mean clot lengths (mm) were 24.6, 17.6, and 8.7 for ICA-terminus, M1, and M2 occlusions, respectively (p<0.001). Bland-Altman plot revealed no significant difference between two observer measurements (Figure 1). In stepwise linear regression, the only independent predictor of clot length was occlusion level (p=0.008).

For dichotomized clot length (<8 vs. ≥8mm), inter-observer agreement was almost perfect (κ =0.91, 95%CI=0.79-1.00). Univariate predictors of ≥8mm-clot were more proximal occlusion level and higher baseline NIHSS score (Table 1). By occlusion level, 94% of ICA-T, 73% of M1-MCA, and 22% of M2-MCA clots were ≥8mm long. In binary logistic regression, clot location was the only independent predictor of clot ≥8mm (p=0.02; adjusted OR 6.43 (95%CI: 1.29 to 31.98) per step from M2 to M1 to ICA-T).

DISCUSSION

This study confirms that at least 90% of anterior circulation proximal occlusions are visible as hyperdense clot using thin-section NCCT. The vast majority (72%) of these occlusions have extensive (≥8mm) clot burden, further suggesting a sizeable population who may potentially benefit from an IV-IAT bridging approach (Figure 2).

The observed recanalization efficiency of IV-tPA based on clot location may correlate with the likelihood of a clot length greater than 8 mm at that location. For example, the proportions of short (<8mm) clots that we found in ICA-T (6%) and M1 (27%) occlusions closely approximate previously reported rates of early IV-tPA recanalization (4.4% for ICA-T and 32.3% for M1).

Furthermore, these findings have important implications for rapid patient triage to intervention. Currently, many centers wait 30 minutes or longer to assess for IV-tPA failure prior to sending a patient to IAT. However, this same delay has been associated with a 10% relative reduction in the probability of good outcome. Because virtually all ICA-terminus occlusions are ≥8mm long, it is reasonable to use CTA-evidence of ICA-terminus occlusion to triage patients directly to IAT during IV-tPA infusion. This approach is supported by IMS-III, which demonstrated a four-times higher rate of good outcome after bridging therapy in patients with CTA-documented ICA-terminus occlusions.

On the other hand, clot length measurement may be critical for triaging proximal MCA occlusions. In IMS-III, there was an equivalent rate of good outcome (~50%) between the treatment arms for M1 occlusions. By removing the 25-30% of M1 clots which are short and likely to respond to IV-tPA alone, patients who may benefit from catheter-based therapy may be rapidly triaged to the interventional suite. This approach is being tested in the THERAPY randomized trial.
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REFERENCES


Figure 1.
Bland-Altman difference plot shows no significant difference between two observer measurements.
Figure 2.
56-year-old female with NIHSS 15 presents 3 hours after onset. Thin-section noncontrast CT data (A) demonstrate a left M1 segment clot measuring 16.6mm. The occlusion is confirmed on CT angiography (B).
# Table 1

Patient characteristics and predictors of clot length

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients n=53</th>
<th>Clot Length &lt;8mm, n=15</th>
<th>Clot Length ≥8mm, n=38</th>
<th>p Univariate</th>
<th>p Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year), mean(±SD)</td>
<td>70.1(±16.6)</td>
<td>66.6(±13.4)</td>
<td>72.4(±17.6)</td>
<td>0.26</td>
<td></td>
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<tr>
<td>Gender (female), % (n)</td>
<td>57%(30/53)</td>
<td>47%(7/15)</td>
<td>60%(23/38)</td>
<td>0.38</td>
<td></td>
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<tr>
<td>Admission NIHSS, median(IQR)</td>
<td>16.5(11-20)</td>
<td>11(5.25-17.75)</td>
<td>18(14.5-20)</td>
<td>0.02</td>
<td>0.26</td>
</tr>
<tr>
<td>ASPECTS, median(IQR)</td>
<td>8(6-9)</td>
<td>8(6.5-10)</td>
<td>7.5(5.9)</td>
<td>0.13</td>
<td></td>
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<tr>
<td>Occlusion side (Right), % (n)</td>
<td>53%(28/53)</td>
<td>73%(11/15)</td>
<td>45%(17/38)</td>
<td>0.07</td>
<td>0.07</td>
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<tr>
<td>Occlusion level, % (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA-T</td>
<td>34%(18/53)</td>
<td>6%(1/18)</td>
<td>94%(17/18)</td>
<td>&lt;0.0001</td>
<td>0.02</td>
</tr>
<tr>
<td>M1-MCA</td>
<td>49%(26/53)</td>
<td>27%(7/26)</td>
<td>73%(19/26)</td>
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</tr>
<tr>
<td>M2-MCA</td>
<td>17%(9/53)</td>
<td>78%(7/9)</td>
<td>22%(2/9)</td>
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<td></td>
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<tr>
<td>Onset-to-CT time, mean(±SD)</td>
<td>3:33(±3:55)</td>
<td>2:31(±1:37)</td>
<td>3:59(±4:29)</td>
<td>0.09</td>
<td>0.39</td>
</tr>
</tbody>
</table>

*Continuous, ordinal and discrete variables compared with unpaired t-test, Mann-Whitney U-test and Fisher's-Exact test, respectively.

(NIHSS=National Institutes of Health stroke scale score; ICA-T=internal carotid artery terminus; MCA=middle cerebral artery)