Density of Thrombus on Admission CT Predicts Revascularization Efficacy in Large Vessel Occlusion Acute Ischemic Stroke

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Background and Purpose—Can lysability of large vessel thrombi in acute ischemic stroke be predicted by measuring clot density on admission nonenhanced CT (NECT), postcontrast enhanced CT, or CT angiogram (CTA)?

Methods—We retrospectively studied 90 patients with acute large vessel ischemic strokes treated with intravenous (IV) tPA, intra-arterial (IA) tPA, and/or mechanical thrombectomy devices. Clot density [in Hounsfield unit (HU)] was measured on NECT, postcontrast enhanced CT, and CTA. Recanalization was assessed by the Thrombolysis in Cerebral Infarction grading system (TICI) on digital subtraction angiography.

Results—Thrombus density on preintervention NECT correlated with postintervention TICI grade regardless of pharmacological (IV tPA $r=0.69$, IA tPA $r=0.72$, $P<0.0001$) or mechanical treatment ($r=0.73$, $P<0.0001$). Patients with TICI$\geq 2$ demonstrated higher HU on NECT (mean corrected HU IV tPA=1.58, IA tPA=1.66, mechanical treatment=1.7) compared with patients with TICI$<2$ (IV tPA=1.39, IA tPA=1.4, mechanical treatment=1.3) ($P=0.01$, 0.006, <0.0001 respectively). There was no association between recanalization and age, sex, baseline National Institute of Health Stroke Scale, treatment method, time to treatment, or clot volume.

Conclusions—Thrombi with lower HU on NECT appear to be more resistant to pharmacological lysis and mechanical thrombectomy. Measuring thrombus density on admission NECT provides a rapid method to analyze clot composition, a potentially useful discriminator in selecting the most appropriate reperfusion strategy for an individual patient.  

Key Words: Cerebral infarct • CT • revascularization • thrombus

With improved prehospital recognition and faster triage in emergency departments, thrombolysis of acute ischemic stroke has increased across the United States. Nevertheless, thrombolysis fails in many patients, and harmful hemorrhagic complications can occur. Consequently, predicting which patients would likely fail fibrinolytic therapy may be helpful for selecting other recanalization strategies, such as mechanical intervention.

Since the clot itself is the primary target of current stroke treatments, understanding its composition is essential in determining the most effective treatment. Noninvasive imaging can be used as a tool to evaluate clot composition. The purpose of the study was to investigate whether the likelihood of large vessel recanalization in acute large vessel occlusion (LVO) ischemic stroke can be predicted by measuring clot density in Hounsfield units (HU) on admission nonenhanced computed tomography (NECT), postcontrast enhanced CT (CECT), and CT angiogram (CTA).

Materials and Methods

Patients

Under an IRB-approved protocol, a retrospective review of our hospital’s neurointerventional stroke database was performed. We studied 90 patients (47 females, average age 69 years) with acute LVO ischemic strokes treated at our institution with intravenous (IV) tPA, intra-arterial (IA) tPA, and/or mechanical thrombectomy devices (Merci or Penumbra). IV tPA was administered to patients presenting within 4.5 hours of symptom onset. Patients presenting within 6 hours of symptom onset were candidates for IA tPA. Mechanical thrombectomy was implemented on a case by case basis, with patients treated within 6 hours of symptom onset for nondominant anterior circulation LVO, 8 hours for dominant anterior circulation LVO, and up to 12 hours for posterior circulation LVO.

Imaging

All patients underwent 2.5-mm axial NECT and CECT as well as a CTA (acquired at 0.625 mm and reformatted into 1.25 mm). Two authors (P.M. and S.W.H.) retrospectively evaluated NECTs for presence of large vessel thrombus. A region of interest was drawn...
244 Stroke January 2013

Table 1. Baseline Patient Clinical Characteristics

<table>
<thead>
<tr>
<th>IV tPA (n=45)</th>
<th>IA tPA (n=43)</th>
<th>Devices ± tPA (n=77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TICI ≥ 2</td>
<td>TICI &lt; 2</td>
<td>P Value</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.3 ± 8</td>
<td>72.8 ± 15.6</td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td>Baseline NIHSS</td>
<td>13.6 ± 8.2</td>
<td>14.1 ± 7.3</td>
</tr>
<tr>
<td>Time to treatment (min)</td>
<td>200.2 ± 50.4</td>
<td>180.4 ± 40.7</td>
</tr>
</tbody>
</table>

NIHSS indicates National Institute of Health Stroke Scale; TICI, Thrombolysis In Cerebral Infarction scale.

There was a strong correlation between thrombus HU on preintervention NECT and postintervention TICI grade among all patients regardless of pharmacological (IV tPA r=0.69, IA tPA r=0.72, P<0.0001) or mechanical treatment (r=0.73, P<0.0001) (Table 2). Among all treatment modalities (Figure 1), patients with TICI ≥ 2 demonstrated higher HU on NECT (mean corrected HU IV tPA=1.58, IA tPA=1.66, mechanical treatment=1.7) compared with patients with TICI < 2 (IV tPA=1.39, IA tPA=1.4, mechanical treatment=1.3) (P=0.01, 0.006, <0.0001, respectively).

On CECT and CTA, patients with higher TICI scores tended to have a higher HU; however, this did not reach statistical significance (Table 2). There was no correlation between clot volume and likelihood of recanalization.

**Discussion**

In our study, thrombi with lower HU are more resistant to both pharmacological thrombolysis and mechanical thrombectomy. Composition of the thrombus is a factor in determining susceptibility to mechanical and pharmacological clot disruption and thus the degree of successful recanalization. Based on prior studies, 3,4 it is reasonable to posit that thrombi with lower HU have a higher proportion of components (e.g., platelets) that are resistant to fibrinolytic agents and mechanical thrombectomy. This notion is supported by prior experimental studies. 3,5

Table 2. Correlation Between Intracranial Large Vessel Thrombus Density on Preintervention CT Studies and Postintervention TICI Grade on DSA

<table>
<thead>
<tr>
<th>IV tPA Patients (n=45)</th>
<th>P Value</th>
<th>IA tPA Patients (n=43)</th>
<th>P Value</th>
<th>Devices ± tPA Patients (n=77)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation HU and TICI on NECT</td>
<td>0.69</td>
<td>&lt;0.0001</td>
<td>0.72</td>
<td>&lt;0.0001</td>
<td>0.73</td>
</tr>
<tr>
<td>Mean corrected HU on NECT for TICI ≥ 2</td>
<td>1.58</td>
<td>0.01</td>
<td>1.66</td>
<td>0.006</td>
<td>1.7</td>
</tr>
<tr>
<td>Mean corrected HU on NECT for TICI &lt; 2</td>
<td>1.39</td>
<td>1.40</td>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correlation HU and TICI on CECT</td>
<td>0.02</td>
<td>0.44</td>
<td>0.09</td>
<td>0.28</td>
<td>0.09</td>
</tr>
<tr>
<td>Mean HU on CECT for TICI ≥ 2</td>
<td>55 ± 24.8</td>
<td>0.37</td>
<td>55 ± 24.5</td>
<td>0.12</td>
<td>51 ± 22.3</td>
</tr>
<tr>
<td>Mean HU on CECT for TICI &lt; 2</td>
<td>52 ± 14.2</td>
<td>45 ± 19.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correlation HU and TICI on CTA</td>
<td>0.13</td>
<td>0.19</td>
<td>0.18</td>
<td>0.12</td>
<td>0.008</td>
</tr>
<tr>
<td>Mean HU on CTA for TICI ≥ 2</td>
<td>80 ± 29.7</td>
<td>0.54</td>
<td>77 ± 28.0</td>
<td>0.12</td>
<td>76 ± 29.9</td>
</tr>
<tr>
<td>Mean HU on CTA for TICI &lt; 2</td>
<td>75 ± 26.4</td>
<td>65 ± 28.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombus volume (mm³) for TICI ≥ 2</td>
<td>139 ± 124</td>
<td>0.28</td>
<td>129 ± 115</td>
<td>0.44</td>
<td>124 ± 127</td>
</tr>
<tr>
<td>Thrombus volume (mm³) for TICI &lt; 2</td>
<td>106 ± 92</td>
<td>121 ± 90</td>
<td>153 ± 228</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HU indicates Hounsfield units; TICI, Thrombolysis In Cerebral Infarction scale; NECT, nonenhanced CT; CECT, contrast-enhanced CT; CTA, CT angiogram; IV, intravenous; IA, intra-arterial; tPA, tissue-type plasminogen activator.

Within the thrombus on NECT, CECT, and CTA studies in order to obtain the HU, regions that included vessel wall calcification (>100 HU) were excluded from the region of interest. Because hematocrit can affect the measured HU, the HU of the homologous contralateral cerebral artery segment was also measured for calibration. For basilar artery clots, calibration HU was measured in a patent vessel proximal (intracranial vertebral artery or proximal basilar artery) or distal (distal basilar artery or posterior cerebral artery) to the clot. The obtained HU was corrected for hematocrit by the formula HU_{corrected} = HU_{obtained} - 0.0036 × hematocrit. Thrombus volume was calculated using the formula for a cylinder with an elliptical base (πRrH), where R=radius of major axis, r=radius of minor axis, and H=height of cylinder. Intracranial arterial recanalization was determined by DSA after thrombolysis and/or thrombectomy using the TICI grading scale (0 to 3).

**Statistical Analysis**

Means, medians, and standard deviations of ordinal variables were calculated. Correlations were analyzed using the Pearson product-moment correlation function. Means were compared using 2-sided Student t tests. Categorical variables were assessed with a contingency table and the Fisher exact test. The P-value for significance was set at 0.05. Computations were performed with GraphPad Software version 3.1a (La Jolla, CA).

**Results**

Among the 90 patients studied, 45 received IV tPA, 43 received IA tPA, and 77 received a combination of mechanical intervention and IV or IA tPA (Table 1). DSA was performed as early as possible (range 140 to 670 minutes). Successful recanalization (TICI > 2) was achieved in 64 patients.

Based on prior studies, 1,2 it is reasonable to posit that thrombi with lower HU have a higher proportion of components (e.g., platelets) that are resistant to fibrinolytic agents and mechanical thrombectomy. This notion is supported by prior experimental studies. 3,5
Platelet-rich thrombi show lower HU than erythrocyte-rich thrombi because the HU has a linear correlation with amount of hemoglobin. Platelets, atheroma, and cellular debris are all known to decrease the HU of the thrombus on CT.\cite{Kirchhof} Liebeskind et al\cite{Liebeskind} demonstrated on CT that the mean percentage of erythrocytes was higher in thrombi associated with the hyperdense middle cerebral artery sign.

Clot volume may also affect lysability and likelihood of successful mechanical disruption or removal. However, in this study there was no significant difference in thrombus volume among the groups. Consequently, it appears that thrombus composition is more important than thrombus volume in our small cohort of patients.

Determining thrombus composition from radiological signs may help identify patients who are not likely to respond to IV thrombolysis but rather need more aggressive treatment regimens such as endovascular therapy with IA thrombolysis or mechanical thrombectomy. As the stroke center model in the United States evolves to include primary stroke centers that can administer IV tPA and comprehensive stroke centers that can also perform endovascular stroke therapies, predictive noninvasive imaging metrics could facilitate appropriate patient triage.

Our study is limited by its retrospective nature. Prospective studies with pathological specimens of cerebral thrombi in LVO are needed to validate the hypothesis that composition of a thrombus can be determined by noninvasive neuroimaging. Furthermore, several patients in our stroke database were excluded from this study because of the degree of intracranial atherosclerosis (mural calcification) limiting accurate measurement of adjacent thrombus. However, NECT is fast, relatively inexpensive, and widely available, thus arguing in favor of developing further techniques for clot evaluation by this imaging modality.

Conclusions

Our study correlates clot density with the likelihood of large cerebral vessel revascularization by pharmacological lysis and mechanical thrombectomy. Measuring the HU of the intracranial thrombus on the admission NECT provides the stroke team with a rapid method to analyze the clot composition, a potentially useful discriminator in selecting the most appropriate reperfusion strategy for an individual patient.

Disclosures

Dr Hetts is a consultant for Silk Road Medical; is on the scientific advisory board of Medina Inc; and is a grant recipient from the National Institutes of Health—National Institute of Biomedical Imaging and Bioengineering; none of these relationships have any bearing on the work presented. Dr English is a consultant for Silk Road Medical; this relationship does not have a bearing on the work presented.

References

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