The Importance of Size: Successful Recanalization by Intravenous Thrombolysis in Acute Anterior Stroke Depends on Thrombus Length

Christian H. Riedel, MD; Philip Zimmermann, MD; Ulf Jensen-Kondering, MD; Robert Stingele, MD; Günther Deuschl, MD; Olav Jansen, MD

Background and Purpose—We hypothesize that in acute middle cerebral artery stroke, thrombus lengths measured in thin-slice nonenhanced CT images define a limit beyond which systemic thrombolysis will fail to recanalize occluded arteries.

Methods—In 138 patients who presented with acute middle cerebral artery stroke and who were treated with intravenous thrombolysis (IVT), we measured lengths of thrombotic clots depicted as arterial hyperdensities in admission nonenhanced CT images with 2.5-mm slice width. Vascular recanalization was investigated after thrombolysis and recanalization results were related to thrombus lengths by logistic regression.

Results—In 62 patients, IVT resulted in recanalization; among these patients, no thrombus length exceeded 8 mm. The median modified Rankin scale score at hospital discharge was 2. In the remaining 76 patients, thrombus lengths mostly exceeded 8 mm and IVT failed in recanalization. These patients were discharged with a median modified Rankin scale score of 5.

Conclusions—This study shows that in acute middle cerebral artery stroke, IVT has nearly no potential to recanalize occluded vessels if thrombus length exceeds 8 mm. (Stroke. 2011;42:1775-1777.)

Key Words: cerebral ischemia | computed tomography | ischemic stroke

In acute middle cerebral artery strokes, successful intravenous thrombolysis (IVT) depends on the quantity of intravascular thrombus.1 Thrombotic clots can be detected in nonenhanced cranial CT images as intra-arterial hyperdensities (hyperdense middle cerebral artery sign).2,3 Despite its high specificity,4 the hyperdense middle cerebral artery sign has been of limited use in acute stroke management because of its low sensitivity.5 To achieve high sensitivity, CT image slices have to be reconstructed with significantly thinner slice width compared to standard protocols.6 We recently demonstrated that this technique allows for quantifying thrombus length with high accuracy.7 In this study, we investigated if thrombus lengths, measured in thin-slice nonenhanced CT images, can be used to predict the likelihood of a successful recanalization by IVT.

Materials and Methods

Patients
Patients with acute middle cerebral artery strokes treated at our center between April 2007 and March 2009 were studied in a retrospective case series. Included patients had to present within 3 hours from symptoms onset and been treated by IVT. Furthermore, they were only followed-up if they had received a nonenhanced CT scan reconstructed with 2.5-mm slice width before IVT was started. After IVT, transcranial Doppler sonography, MRA, or CTA had to prove either successful recanalization or persistent occlusion of the initially obstructed vessel. A total of 138 patients (75 male, 63 female; median age, 69 years) matched these inclusion criteria.

Data Acquisition
For all cases, baseline demographical data, NIHSS score at the time of admission, time of recanalization control, duration of hospital stay, and modified Rankin scale score at discharge were collected. In all nonenhanced CT datasets, thrombus in the middle cerebral artery was automatically detected and clot lengths were quantified as described previously.7

Statistical Tests
Demographical data were analyzed with Fisher exact test for categorical data and Student t test for continuous variables. The relations between thrombus lengths and recanalization success were evaluated using logistic regression. The quality of the underlying model was tested with χ² statistic. We evaluated the probability of the recanalization of the occluded vessels by taking samples from the regression model at selected lengths.

Results
Demographic and clinical features of the 138 patients enrolled in this study are shown in the Table.
In 15 patients (10.9%), no hyperdense middle cerebral artery sign was detected. Subsequently, a vascular obliteration was found on the follow-up assessments after intravenous thrombolysis in none of these patients. In 62 patients, the occluded artery could be recanalized by IVT, whereas 76 patients showed vessel occlusion after IVT in the follow-up studies.

According to the logistic regression (Figure 1), short clots (length $<5$ mm) are highly likely to be dissolved completely, but recanalization can be expected in $<1\%$ of cases if the thrombotic clot extends further than 8 mm. The predictive power of thrombus length measurement for successful recanalization after IVT proved to be highly significant ($P<0.001$).

The median value of the modified Rankin scale score at hospital discharge was 2 in patients with recanalization and 5 for those without recanalization (Figure 2). Modified Rankin scale score differed significantly between patients with and without recanalization ($P<0.001$).

**Discussion**

Our study shows that IVT has nearly no potential to recanalize occluded vessels with a thrombus length exceeding 8 mm. This is in line with other studies demonstrating the strong dependency of clinical outcome on recanalization rate.\(^8,9\) Loss of the hyperdense middle cerebral artery sign during follow-up was found to be an indicator of favorable outcome after IVT.\(^10\) Two recent studies related the success of recanalization by IVT and patient outcome to scores that were derived from CTA studies.\(^1,8\) These results compare to ours with respect to outcome. However, our measurement of thrombus length is easier to apply and unambiguous.

Our results can help to identify patients in whom IVT will most likely fail in open occluded arteries. In these patients, immediate intra-arterial therapy might be the treatment of choice.

The results of our study must be interpreted with caution because the data were analyzed retrospectively, although blind for the clinical and thrombus length outcome. Second, the sample size is limited for a stroke study. However, the threshold for the thrombus length indicating a favorable outcome was found to be so well-defined that a major quantitative deviation of future studies with larger sample sizes is unlikely.

We conclude that the present results justify a prospective study that should address the question of whether IVT should be replaced by intra-arterial thrombolysis when the thrombus length measured with our protocol exceeds 8 mm.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients (N=138)</th>
<th>Recanalized (N=62; 44.9%)</th>
<th>Not Recanalized (N=76; 55.1%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n/total n (%)</td>
<td>63/138 (45.7)</td>
<td>28/62 (45.2)</td>
<td>35/76 (46.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>Age, years</td>
<td>67.9±12.8</td>
<td>66.8±14.2</td>
<td>68.5±11.1</td>
<td>0.03</td>
</tr>
<tr>
<td>NIHSS score (admission)</td>
<td>11.2±4.2</td>
<td>9.3±3.3</td>
<td>12.6±4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>11.0±5.3</td>
<td>10.8±5.5</td>
<td>4.2±0.8</td>
<td>0.39</td>
</tr>
<tr>
<td>Modified Rankin scale score (discharge)</td>
<td>3.4±1.9</td>
<td>1.9±1.0</td>
<td>4.4±1.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recanalization control (N), TCD/MRA/CTA</td>
<td>127/9/2</td>
<td>58/3/1</td>
<td>69/6/1</td>
<td></td>
</tr>
<tr>
<td>Time to recanalization control (hours)</td>
<td>20.7±6.0</td>
<td>20.9±5.8</td>
<td>20.5±6.3</td>
<td>0.42</td>
</tr>
</tbody>
</table>

CTA indicates computed tomography angiography; MRA, magnetic resonance angiography; NIHSS, National Institutes of Health Stroke Scale; TCD, transcranial Doppler.

In 15 patients (10.9%), no hyperdense middle cerebral artery sign was detected. Subsequently, a vascular obliteration was found on the follow-up assessments after intravenous thrombolysis in none of these patients. In 62 patients, the occluded artery could be recanalized by IVT, whereas 76 patients showed vessel occlusion after IVT in the follow-up studies.

According to the logistic regression (Figure 1), short clots (length $<5$ mm) are highly likely to be dissolved completely, but recanalization can be expected in $<1\%$ of cases if the thrombotic clot extends further than 8 mm. The predictive power of thrombus length measurement for successful recanalization after IVT proved to be highly significant ($P<0.001$).

The median value of the modified Rankin scale score at hospital discharge was 2 in patients with recanalization and 5 for those without recanalization (Figure 2). Modified Rankin scale score differed significantly between patients with and without recanalization ($P<0.001$).
Sources of Funding
This study was supported by a grant from the Medical Faculty of the Christian Albrechts University Kiel.

Disclosures
None.

References
The Importance of Size: Successful Recanalization by Intravenous Thrombolysis in Acute Anterior Stroke Depends on Thrombus Length
Christian H. Riedel, Philip Zimmermann, Ulf Jensen-Kondering, Robert Stingele, Günther Deuschl and Olav Jansen

Stroke. 2011;42:1775-1777; originally published online April 7, 2011; doi: 10.1161/STROKEAHA.110.609693

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/42/6/1775

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/