Additional Diagnostic Value of Computed Tomography Perfusion for Detection of Acute Ischemic Stroke in the Posterior Circulation

Erik J.R.J. van der Hoeven, MD; Jan Willem Dankbaar, MD; Ale Algra, MD; Jan Albert Vos, MD; Joris M. Niesten, MD; Tom van Seeters, MD; Irene C. van der Schaar, MD; Wouter J. Schonevile, MD; L. Jaap Kappelle, MD; Birgitta K. Velthuis, MD; on behalf of the DUST Investigators

Background and Purpose—Detection of acute infarction in the posterior circulation is challenging. We aimed to determine the additional value of tomography (CT) perfusion to noncontrast CT and CT angiography source images for infarct detection and localization in patients suspected of acute ischemic posterior circulation stroke.

Methods—Patients with suspected acute ischemic posterior circulation stroke were selected from the Dutch acute Stroke Trial (DUST) study. Patients underwent noncontrast CT, CT angiography, and CT perfusion within 9 hours after stroke onset and CT or MRI on follow-up. Images were evaluated for signs and location of ischemia. Discrimination of 3 hierarchical logistic regression models (noncontrast CT [A], added CT angiography source images [B], and CT perfusion [C]) was compared with C-statistics.

Results—Of 88 patients, 76 (86%) had a clinical diagnosis of ischemic stroke on discharge and 42 patients (48%) showed a posterior circulation infarct on follow-up imaging. Model C (area under the curve from the receiver operating characteristic curve=0.86; 95% confidence interval, 0.77–0.94) predicted an infarct in the posterior circulation territory better than models A (area under the curve from the receiver operating characteristic curve=0.64; 95% confidence interval, 0.53–0.76; P<0.001) and B (area under the curve from the receiver operating characteristic curve=0.68; 95% confidence interval, 0.56–0.79; P<0.001).

Conclusions—CT perfusion has significant additional diagnostic values to noncontrast CT and CT angiography source images for detecting ischemic changes in patients suspected of acute posterior circulation stroke. (Stroke. 2015;46:00-00. DOI: 10.1161/STROKEAHA.115.008718.)

Key Words: brain infarction ■ multidetector computed tomography

Posterior circulation stroke accounts for 20% of ischemic strokes. Clinical signs and symptoms of anterior and posterior ischemic stroke may overlap, causing a delay in making the correct diagnosis.1 In the acute stage, noncontrast computed tomography (NCCT) is used to exclude cerebral hemorrhage and pathologies other than ischemic stroke and to detect early signs of ischemia. CT angiography (CTA) can provide information on the presence and site of an arterial occlusion. CTA source images (CTA-SI) can also help to detect ischemic changes.2 CT perfusion (CTP) can detect ischemic perfusion defects, with a pooled analysis sensitivity of 80% (95% confidence interval [CI], 72%–86%) and a specificity of 95% (95% CI, 86%–98%) for early diagnosis of stroke.3 The additional diagnostic value of CTP compared with NCCT and CTA for posterior circulation stroke has not been analyzed.

We investigated the additional diagnostic value of CTP to CTA-SI and NCCT for infarct detection and localization in patients suspected of acute ischemic posterior circulation stroke.

Methods

Patients

All patients participated in the prospective, multicenter, observational Dutch acute stroke study (DUST; ClinicalTrials.gov NCT00880113) in which the diagnostic values of CTA and CTP within 9 hours after onset of the neurological deficit were investigated in patients with acute ischemic stroke.4 We selected consecutive patients between May 2009 and December 2012 with suspected acute posterior circulation ischemic stroke as defined in the Oxfordshire classification.5 Reasons for exclusion were poor image quality, not all 3 posterior circulation Alberta Stroke Program Early CT Score (PC-ASPECTS)6 levels included in the CTP slab or missing follow-up imaging.
Imaging

Protocols of NCCT, CTA, and CTP imaging have been reported previously. Location of ischemic changes in the posterior circulation territory was allocated according to the 8 PC-ASPECTS regions: pons, midbrain, right or left thalamus, right or left cerebellum and right or left posterior cerebral artery territory (Figure). Follow-up imaging consisted of NCCT, or if clinically indicated MRI (including diffusion-weighted imaging and fluid attenuated inversion recovery), and was performed around day 3 after admission or earlier if patients deteriorated or were discharged from hospital.

Statistical Analysis

Three logistic regression models were developed, including NCCT (model A), with addition of CTA-SI (model B) and addition of CTA-SI and CTP (model C). The diagnostic value of each model was assessed with the area under the curve from the receiver operating characteristic curve. The additional diagnostic value of the models was assessed by comparing the area under the curve receiver operating characteristic curves.

Results

Eighty-eight patients with suspected posterior circulation stroke fulfilled the inclusion criteria (Table 1). Mean time from symptom onset to imaging was 227±154 minutes. Admission NCCT detected 13 (31%), CTA-SI 14 (33%), and CTP 31 (74%) of the 42 patients with an infarct in the posterior circulation on follow-up imaging (Table 2). Positive predictive values were high for all diagnostic modalities. The negative predictive value of CTP (80%) was higher compared with that of NCCT (61%) and CTA-SI (62%). Small infarct size or artifacts caused false-negative CTP in 11 patients, including 6 in the brain stem.

Follow-up imaging showed 62 infarcts in 704 assessed regions (Table 2). NCCT detected 15 (24%), CTA-SI 17 (27%), and CTP 41 (66%) infarcts. CTP detected significantly more ischemic lesions in the cerebellum, posterior cerebral artery territory, and thalami than NCCT and CTA-SI. For all techniques, lesion detection was the poorest in pons and midbrain.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>88</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean (SD)</td>
<td>63 (13)</td>
</tr>
<tr>
<td>Sex, male</td>
<td>59 (67)</td>
</tr>
<tr>
<td>NIHSS, median (IQR)</td>
<td>2.5 (2–5)</td>
</tr>
<tr>
<td>Time of symptom onset to start CT protocol</td>
<td></td>
</tr>
<tr>
<td>0–4.5 h</td>
<td>61 (69)</td>
</tr>
<tr>
<td>4.5–9 h</td>
<td>27 (31)</td>
</tr>
<tr>
<td>Intravenous thrombolysis</td>
<td>43 (49)</td>
</tr>
<tr>
<td>Mechanical thrombectomy</td>
<td>3 (3.4)</td>
</tr>
<tr>
<td>Follow-up imaging</td>
<td></td>
</tr>
<tr>
<td>NCCT</td>
<td>75 (85)</td>
</tr>
<tr>
<td>MRI</td>
<td>13 (15)</td>
</tr>
<tr>
<td>Final clinical diagnosis</td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke*</td>
<td>76 (86)</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>71 (93)</td>
</tr>
<tr>
<td>Detected on FU imaging</td>
<td>42 (59)</td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Detected on FU imaging</td>
<td>3 (50)</td>
</tr>
<tr>
<td>TIA</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Nonischemic</td>
<td>9 (10)</td>
</tr>
</tbody>
</table>

All values are given as number (%), unless otherwise indicated. CT indicates computed tomography; FU, follow-up; IQR, interquartile range; NCCT, noncontrast computed tomography; NIHSS, National Institutes of Health Stroke Scale; and TIA, transient ischemic attack.

*One patient had both anterior and posterior circulation stroke.
The area under the curve was 0.64 (95% CI, 0.53–0.76) for model A (NCCT), 0.68 (95% CI, 0.56–0.79) for model B (NCCT+CTA-SI), and 0.86 (95% CI, 0.77–0.94) for model C (NCCT+CTA-SI+CTP). There was no significant difference between model A and model B ($P=0.08$). Model C predicted an infarct in the posterior circulation territory significantly better than both model A ($P<0.001$) and model B ($P<0.001$).

**Discussion**

Our findings show that adding CTP to NCCT and CTA-SI in the diagnostic work-up in patients suspected of an ischemic posterior circulation stroke significantly increases diagnostic accuracy. Detection of acute ischemia in the brain stem remains challenging.

We are aware of only one other study investigating stroke detection with CTP in posterior circulation stroke. In this study, no significant differences between detection of infratentorial and supratentorial stroke lesions were found. Sensitivity and specificity for detection of infratentorial ischemic lesions were, respectively, 91% and 93%. The longer duration from stroke onset to imaging in this study (mean 540 versus 227 minutes) probably accentuated ischemic changes and therefore increased sensitivity. Lacunar strokes were excluded, whereas small infarcts caused false-negative findings in our study.

Intravenous thrombolytic therapy may also have influenced sensitivity and specificity because it can achieve timely reperfusion. Consequently, ischemic but still viable regions may not progress to infarction in treated patients, leading to false-positive findings. False-positive findings may also be caused by follow-up NCCT as small (lacunar) infarcts, and brain stem infarcts can be difficult to visualize on NCCT.

**Acknowledgments**

We thank the Dutch acute Stroke Trial (DUST) investigators.

**Sources of Funding**

This work was supported by the Dutch Heart Foundation to DUST (grant 2008T034), Dr van der Hoeven (grant 2010B151), and Dr Dankbaar (grant 2012T061) and the Nuts Ohra Foundation to DUST (grant 0903-012).

**Disclosures**

None.

**References**

Additional Diagnostic Value of Computed Tomography Perfusion for Detection of Acute Ischemic Stroke in the Posterior Circulation

Erik J.R.J. van der Hoeven, Jan Willem Dankbaar, Ale Algra, Jan Albert Vos, Joris M. Niesten, Tom van Seeters, Irene C. van der Schaaf, Wouter J. Schoenewille, L. Jaap Kappelle and Birgitta K. Velthuis

on behalf of the DUST Investigators

*Stroke.* published online March 5, 2015;

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 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/early/2015/03/05/STROKEAHA.115.008718

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/