Multiple case series have demonstrated the high recanalization rate of endovascular techniques in acute ischemic stroke treatment. In the Multi Mechanical Embolus Removal in Cerebral Ischemia and the Penumbra Pivotal Stroke trials, a recanalization rate of 69.5% and 81.6% was reported, respectively.1,2 Studies with the latest generation of mechanical thrombectomy devices have shown a recanalization rate of ≤90%,3 and similar results were demonstrated by a recent randomized controlled trial with a recanalization rate of 89% (as assessed at the study site; 69% when assessed by the core laboratory). In the majority of published studies, good recanalization outcomes are associated with relatively poor clinical outcomes.4 Thus, patient selection is of critical importance in the endovascular treatment of ischemic strokes for the avoidance of futile recanalizations.5

Previous studies have shown that patients with a favorable baseline computed tomographic (CT) scan (defined by an Alberta Stroke Program Early CT Scale [ASPECTS] of >7) were significantly more likely to achieve favorable outcomes after endovascular treatment than patients with unfavorable scans.6,7 In a recent study on patients with intravenous thrombolytic therapy, a favorable cerebral blood volume (CBV) ASPECTS score was found to be more sensitive in predicting favorable outcome compared with the baseline CT ASPECTS score.8 The goal of this study was to determine the accuracy and reliability of nonenhanced CT images and perfusion CT parameters maps, analyzed with ASPECTS, as final outcome predictors after endovascular stroke treatment.

Alberta Stroke Program Early CT Scale Evaluation of Multimodal Computed Tomography in Predicting Clinical Outcomes of Stroke Patients Treated With Aspiration Thrombectomy

Marios-Nikos Psychogios, MD; Peter Schramm, MD, PhD; Andreas Maximilian Frölich, MD; Kai Kallenberg, MD; Katrin Wasser, MD; Lars Reinhardt, MS; Andreas S. Kreusch, MS; Klaus Jung, PhD; Michael Knauth, MD, PhD

Background and Purpose—Patient selection is crucial in the endovascular treatment of acute ischemic stroke patients. Baseline computed tomographic (CT) images, evaluated with the Alberta Stroke Program Early CT Scale (ASPECTS), are considered significant predictors of outcome. In this study, we evaluated CT images and perfusion parameters, analyzed with ASPECTS, as final outcome predictors after endovascular stroke treatment.

Methods—We analyzed a cohort of patients with acute ischemic stroke and endovascular treatment. Patients with an occlusion of the M1 segment and multimodal CT imaging were included. CT perfusion data were reconstructed using commercial software. Two experienced neuroradiologists separately reviewed and scored CT and CT perfusion images with the ASPECTS score. Parameters were compared between patients with poor and with favorable follow-up outcome. Significantly different variables were further analyzed by forward stepwise logistic regression.

Results—Fifty-one patients were included in our study. Baseline characteristics did not differ between patients with favorable and poor outcomes. No significant difference in recanalization status, the various times, or CT ASPECTS was demonstrated between these 2 groups. Significant differences were demonstrated for age (P=0.0049), cerebral blood volume ASPECTS (P=0.0007), and between cerebral blood volume and cerebral blood flow ASPECTS (P=0.0045). Cerebral blood volume ASPECTS >7 demonstrated the highest sensitivity and specificity for favorable outcome with 84% and 79%, respectively.

Conclusions—CT perfusion parameters, evaluated with ASPECTS, are optimal predictors of outcome and are more sensitive and specific than CT ASPECTS in the prediction of favorable outcome. Use of these parameters in treatment decisions could reduce futile recanalizations. (Stroke. 2013;44:2188-2193.)

Key Words: CBV ASPECTS ■ CT ASPECTS ■ favorable outcome ■ mechanical thrombectomy ■ multimodal CT ■ stroke

Received February 3, 2013; final revision received April 13, 2013; accepted April 23, 2013.
From the Department of Neuroradiology (M.-N.P., P.S., A.M.F., K.K., L.R., A.S.K., M.K.), Department of Neurology (K.W.), and Department of Medical Statistics (K.J.), University Medicine Goettingen, Goettingen, Germany.
Correspondence to Marios-Nikos Psychogios, MD, Department of Neuroradiology, University Medicine Goettingen, Robert Koch 40, Goettingen, Germany. E-mail m.psychogios@med.uni-goettingen.de
© 2013 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org
DOI: 10.1161/STROKEAHA.113.001068
Methods
A cohort of patients with acute ischemic stroke and endovascular treatment with the Penumbra System was analyzed. Only patients with an occlusion of the M1 segment of the middle cerebral artery were included. Inclusion criteria also included the acquisition of a multimodal CT examination consisting of nonenhanced CT and CT perfusion (CTP) of the head before thrombus aspiration. For all patients in this study, nonenhanced CT and CT angiography data were used in making treatment decisions, whereas CTP data were retrospectively analyzed. Exclusion criteria were inability to undergo multimodal CT, history of renal failure, and patient age <21 years. Patients were retrospectively identified for inclusion from a prospectively collected, university Medical Center Göttingen institutional review board–approved database.

Demographic data, vascular risk factors, thrombolysis in cerebral infarction scores, various times, and neurological scores were extracted from the aforementioned database. All neuroradiological scores were assigned in consensus by 2 experienced neuroradiologists, whereas neurological scores were assessed by a stroke neurologist at hospital admission, hospital discharge, and discharge from the rehabilitation unit (follow-up). Successful recanalization was defined as thrombolysis in cerebral infarction 2b or 3.

Images were acquired with a 128-slice multidetector CT scanner (Siemens Definition AS+; Siemens Healthcare Sector, Forchheim, Germany). Scanning order was CT, CTP, and CT angiography. CTP was acquired with a periodic spiral approach consisting of 30 consecutive spiral scans of the brain (96 mm in z axis, 2-second delay, 1.5-second mean temporal resolution resulting in 30×1.5×45-second acquisition time, effective dose of 5.5 mSv) as previously described.8 Contrast medium injections were performed through an 18-gauge cannula placed in a cubital vein. The biphasic injection protocol consisted of 36 mL of highly iodinated contrast medium (Iomeprol 400, Bracco, Konstanz, Germany) followed by 30 mL of saline chaser both injected at a rate of 6 mL/s. CTP data were reconstructed with a slice width of 5 mm every 3 mm (H20f Kernel, 512 matrix) and were further processed using a commercial dynamic analysis package (Volume Perfusion CT Neuro; Siemens) with automatic motion correction and a dedicated noise reduction technique for dynamic data. The total postprocessing time was about 2 minutes. CTP parameter maps were then anonymized and stored on the picture archiving system of our department. This CTP protocol has been broadly used in our routine practice since 2008 without any specific limitations.

Two experienced neuroradiologists (M.K. and M.-N.P.) separately reviewed and scored the CT and CTP scans with the ASPECTS score, a 10-point scoring system to evaluate early ischemic changes in middle cerebral artery strokes. Initially described for baseline CT scans, this system can also be used for the semiquantitative analysis of CBV and cerebral blood flow (CBF) images. Raters were blinded to all clinical information, follow-up scans, and final outcome. CT and CTP examinations were divided into 2 groups, which were rated with a 90-day gap in between. Raters scored all images separately while cases of disagreement were settled by consensus.

Continuous study parameters were compared between patients with follow-up modified Rankin scale (mRS) ≤2 (poor outcome) and those with follow-up mRS ≤2 (favorable outcome) either by Welch t test, in the case of normal distribution, or by the Mann–Whitney U test, in the case of non-normal or ordinal distribution. Categorical variables were compared between the 2 groups by Fisher exact test. In cases with missing follow-up mRS values, discharge mRS was used instead.16 The probability of good outcome at follow-up was assessed by forward stepwise logistic regression using all variables that were significantly different between the 2 groups in the univariate analysis. Selected variables were further examined by receiver operating characteristic analysis and optimal criterion values were calculated. Interobserver agreement was evaluated with weighted κ statistics. Analyses were performed with the MedCalc statistical package (MedCalc, Mariakerke, Belgium). The significance level for all tests was set to α=0.05.

Results
Fifty-one patients were identified for our study (23 women; median age, 69 years; range, 21–86). Four patients were lost to follow-up. National Institutes of Health Stroke Scale at admission was 17.5 (±6) and mean mRS at admission was 4.6 (±0.5). Median CT ASPECTS was 8 (interquartile range, 6.5–9), median CBV ASPECTS was 6 (interquartile range, 5–8); and median CBF ASPECTS was 4 (interquartile range, 3–6). Successful recanalization (thrombolysis in cerebral infarction 2b and 3) was achieved in 61% of the cases with an overall favorable outcome of 27.5% at follow-up. Mean mRS at follow-up was 3.7 (±1.7) with a median follow-up period of 70 days (range, 40–105 days).

Baseline characteristics, such as admission National Institutes of Health Stroke Scale, arterial hypertension, hyperlipidemia, and diabetes mellitus, did not differ between patients with favorable and poor outcomes (Table 1). No significant difference in recanalization status, time from symptom onset to recanalization, time from multimodal CT to recanalization, or CT ASPECTS was demonstrated between the 2 groups. Favorable clinical outcome was greater in patients with CT ASPECTS >7 (36% of the patients) compared with patients with CT ASPECTS ≤7 (18%; Figure 1), without achieving statistical significance (P=0.065).

Significant differences between the 2 groups were demonstrated for age (P=0.0049), CBV ASPECTS (P=0.0007), the difference between CBV and CBF ASPECTS (Δ(CBV−CBF) ASPECTS; P=0.0045), discharge National Institutes of Health Stroke Scale (P=0.0008), and discharge mRS (P=0.0001). Favorable outcome was significantly greater in patients with CBV ASPECTS >7 (65% of the patients) when compared with patients with CBV ASPECTS ≤7 (8%; Figure 1C). Nonrecanalizers with CBV ASPECTS ≤7 did not demonstrate favorable outcome (Figure 2). Fifty-eight percent of recanalizers with CBV ASPECTS >7 had favorable follow-up outcomes, whereas 1 recanalizer with favorable outcome had a CBV ASPECTS of 5 to 7 and another one had a CBV ASPECTS of 0 to 4 (Figure 2B). Favorable outcome was also significantly greater in patients with Δ(CBV–CBF) ASPECTS ≥3 (69% of the patients) when compared with patients with Δ(CBV–CBF) ASPECTS <3 (Figures 1D and 3).

In the stepwise logistic regression model, age (P=0.008, odds ratio, 0.91; 95% confidence interval [CI], 0.85–0.97) and Δ(CBV–CBF) ASPECTS (P=0.01, odds ratio, 1.9; 95% CI, 1.15–3.16) were significant contributors to the prediction of outcome. After using successful recanalization as a selection variable in the model, only Δ(CBV–CBF) ASPECTS remained a significant predictor with a P=0.02 (odds ratio, 1.86; 95% CI, 1.09–3.18).

Receiver operating characteristic analysis is demonstrated in Table 2. For CT ASPECTS >7, the sensitivity was 77% and the specificity 42%. For CBV ASPECTS >7, the sensitivity and specificity were higher with 84% and 79%, respectively. With a favorable outcome prevalence of 30%, the positive predictive value of CBV ASPECTS >7 was 65%, and the negative predictive value was 92%. The positive predictive value of Δ(CBV–CBF) ASPECTS >4 was 71% with a negative predictive value of 78% for favorable outcome.
Overall interrater agreement was very good with \( \kappa_w = 0.86 \) (95% CI, 0.81–0.91), whereas the respective interrater agreement for CT ASPECTS, CBV ASPECTS, and CBF ASPECTS was 0.71 (95% CI, 0.56–0.85), 0.81 (95% CI, 0.69–0.93), and 0.91 (95% CI, 0.82–0.9).

**Discussion**

Our results support previously published data which showed that patients with CT ASPECTS >7 are associated with better clinical outcomes, although in our study the CT ASPECTS score was not significantly different between patients with favorable and poor clinical outcomes.\(^6,\)\(^7,\)\(^11\) Two CTP scores, the CBV ASPECTS, and the difference between CBV and CBF ASPECTS were significantly different between these groups. Overall, the semiquantitative assessment of a CBV map with the ASPECTS score can be a sensitive and a very specific score for the prediction of good outcome. An optimal cutoff value of >7 was calculated for CBV ASPECTS with a positive predictive value of 65% and a negative predictive value of 92%. The respective values for CT ASPECTS >7 were lower. An optimal cutoff value of >8 was calculated for CT ASPECTS, which is greater than the values assessed in previous studies.\(^6,\)\(^5\)

Endovascular treatment of acute ischemic stroke is very expensive, resource-demanding, and exposes patients to significant procedural risks. The in-hospital mortality in a recent study of the US National Inpatient Sample was 24%.\(^12\) This is concordant to our previously published results in a cohort treated with the Penumbra System with an all-cause mortality of 25% and an in-hospital mortality of 22%.\(^4\) Combined with the 50% of patients who are having bad outcomes, it results in 75% of patients with poor outcomes after endovascular therapy. Outcomes are worse in patients >65 years of age with an overall of 85% having poor outcomes.\(^12\) This is consistent to our results as age is a significant predictor of outcome in the logistic regression model. Patients >74 years of age had a 93% probability for bad outcome in our study.

It is obvious that successful recanalization alone is not sufficient for improving clinical outcomes of stroke patients, and proper patient selection is mandatory for better clinical outcomes in patients treated with endovascular techniques. The latest trials,\(^13,\)\(^14\) which compared endovascular procedures with medical treatment for acute ischemic stroke, have raised questions on the usefulness of endovascular procedures, although subgroup analyses indicate a benefit of endovascular treatment for a group of patients.\(^15\) The authors of another recently published study conclude that target mismatch patients with early reperfusion after endovascular stroke treatment had more favorable clinical outcomes.\(^16\) Nonenhanced CT ASPECTS has been previously proposed as a selection criterion, although in our study it is less sensitive and less specific than CBV ASPECTS. CBV ASPECTS and \( \Delta \) (CBV–CBF) ASPECTS allow for a semiquantitative assessment of infarct core, collateral supply, and mismatch volume.\(^17–20\) These parameters can also be assessed with multimodal MRI,\(^21–23\) although this modality is not as widespread and as easy to perform on stroke patients as CT.\(^24\) ASPECTS evaluation can be done without the need for volumetric software and the correlation of ASPECTS mismatch and volumetric mismatch has been shown to be strong.\(^25\)
who evaluate ASPECTS have a steep learning curve and an experienced ASPECTS rater does not need >20 seconds for the evaluation of a scan. Furthermore, our results state that interrater agreement was good for CT ASPECTS and very good for CBV and CBF ASPECTS, which is concordant to earlier studies. Previous reports have supported a shift from elapsed time as a selection criterion and toward imaging assessing the state of ischemic brain. Our results confirm this

Figure 1. Clinical outcomes (modified Rankin scale at follow-up) stratified into 3 groups of (A) National Institutes of Health Stroke Scale, into 3 groups of (B) computed tomography (CT) ASPECTS, and (C) cerebral blood volume (CBV) Alberta Stroke Program Early CT Scale (ASPECTS 0–4, poor scan; ASPECTS 5–7, intermediate scan; and ASPECTS 8–10, good scan) and into 3 groups of (D) Δ(CBV–cerebral blood flow [CBF]) ASPECTS (no difference between CBV and CBF ASPECTS; 1–2 points of difference; >3 points of difference).

Figure 2. Clinical outcomes (modified Rankin scale at follow-up) in the 2 groups of recanalizers and nonrecanalizers, stratified into 3 groups of Alberta Stroke Program Early Computed Tomography scale (ASPECTS) score (ASPECTS 0–4, poor scan; ASPECTS 5–7, intermediate scan; and ASPECTS 8–10, good scan). CBF indicates cerebral blood flow; and CBV, cerebral blood volume.
opinion as time from onset to recanalization or from imaging to recanalization was not significantly different between patients with favorable and poor outcomes.

The main limitation of this study is the retrospective nature of our analysis. Data were extracted from a prospectively collected database, but the CTP images were retrospectively analyzed and not used in treatment decisions. The overall number of the patients analyzed is small, thus reducing the significance of our statistical analysis. Given the importance of our results, a prospective study with CTP maps as

<table>
<thead>
<tr>
<th>Table 2.</th>
<th>Criterion Values and Coordinates of the Receiver Operating Characteristic Curve Regarding Favorable Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criterion</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>≤53</td>
<td>70</td>
</tr>
<tr>
<td>≤61*</td>
<td>71</td>
</tr>
<tr>
<td>≤72</td>
<td>79</td>
</tr>
<tr>
<td>CT ASPECTS</td>
<td></td>
</tr>
<tr>
<td>&gt;7</td>
<td>77</td>
</tr>
<tr>
<td>&gt;8*</td>
<td>62</td>
</tr>
<tr>
<td>CBV ASPECTS</td>
<td></td>
</tr>
<tr>
<td>&gt;6</td>
<td>92</td>
</tr>
<tr>
<td>&gt;7*</td>
<td>84</td>
</tr>
<tr>
<td>&gt;8</td>
<td>31</td>
</tr>
<tr>
<td>∆(CBV–CBF) ASPECTS</td>
<td></td>
</tr>
<tr>
<td>&gt;1*</td>
<td>85</td>
</tr>
<tr>
<td>&gt;2</td>
<td>69</td>
</tr>
<tr>
<td>&gt;4</td>
<td>38</td>
</tr>
</tbody>
</table>

ASPECTS indicates Alberta Stroke Program Early Computed Tomography scale; CBF, cerebral blood flow; CBV, cerebral blood volume; CI, confidence interval; CT, computed tomography; NPV, negative predictive value; and PPV, positive predictive value.

*Optimal cutoff value.
a parameter for imaging decisions is warranted. However, recruiting a large number of patients may be difficult, as there will be an increasing number of interventionalists with ethical considerations regarding endovascular procedures in patients with large CBV lesions/low CBV ASPECTS scores.

**Summary**

Our study validates CTP mismatch as an imaging biomarker and suggests that CTP parameters, analyzed with the ASPECTS score, can be optimal selection parameters for patients with acute ischemic stroke undergoing endovascular procedures. Basing treatment decisions on CBV ASPECTS and $\Delta$ (CBV−CBF) ASPECTS, rather than CT ASPECTS, can lead to further reduction of futile recanalizations.

**Disclosures**

Dr Frölich has received speaker’s honoraria from Siemens Healthcare Sector. The other authors have no conflicts to report.

**References**

Alberta Stroke Program Early CT Scale Evaluation of Multimodal Computed Tomography in Predicting Clinical Outcomes of Stroke Patients Treated With Aspiration Thrombectomy
Marios-Nikos Psychogios, Peter Schramm, Andreas Maximilian Frölich, Kai Kallenberg, Katrin Wasser, Lars Reinhardt, Andreas S. Kreusch, Klaus Jung and Michael Knauth

*Stroke*. 2013;44:2188-2193; originally published online May 28, 2013; doi: 10.1161/STROKEAHA.113.001068

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 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/44/8/2188

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/