Can DWI-ASPECTS Substitute for Lesion Volume in Acute Stroke?

Constance de Margerie-Mellon, MD*; Guillaume Turc, MD*; Marie Tisserand, MD; Olivier Naggara, PhD; David Calvet, PhD; Laurence Legrand, MD; Jean-François Meder, PhD; Jean-Louis Mas, MD; Jean-Claude Baron, ScD; Catherine Oppenheim, PhD

Background and Purpose—The extent of diffusion lesion on pretreatment imaging is a risk factor for poor outcome and hemorrhagic transformation after thrombolysis, and volumes of 70 to 100 mL have been advocated as cut-offs. However, estimating diffusion-weighted imaging (DWI) lesion volume (Vol\textsubscript{DWI}) in the acute setting may be cumbersome. We aimed to determine whether the DWI-Alberta Stroke Program Early CT Score (DWI-ASPECTS) can substitute for Vol\textsubscript{DWI}.

Methods—DWI-ASPECTS and Vol\textsubscript{DWI} were measured retrospectively on pretreatment MRI (median onset-to-MRI delay=122 minutes) in 330 consecutively treated patients with middle cerebral artery stroke.

Results—DWI-ASPECTS and Vol\textsubscript{DWI} were strongly correlated (p=−0.82), but each DWI-ASPECTS point corresponded to a wide range of Vol\textsubscript{DWI}. All patients with DWI-ASPECTS ≥7 (n=207) had Vol\textsubscript{DWI} <70 mL, whereas 32 of the 34 patients with DWI-ASPECTS ≤4 had Vol\textsubscript{DWI} >100 mL. However, intermediate DWI-ASPECTS (4–6; n=89) corresponded to highly variable Vol\textsubscript{DWI} (median, 66 mL; interquartile range, 40–98).

Conclusions—Although each DWI-ASPECTS point corresponds to a wide range of volumes, DWI-ASPECTS ≤4 or ≥7 may be used as reliable surrogates of Vol\textsubscript{DWI} >100 or ≤70 mL, respectively. (Stroke. 2013;44:00-00.)

Key Words: ASPECTS • diffusion-weighted imaging • stroke • thrombolytic therapy

In acute anterior circulation stroke, the extent of the diffusion-weighted imaging (DWI) lesion is a predictor of poor outcome and symptomatic hemorrhage after reperfusion therapy.1,2 Specifically, volumes of 70 and 100 mL have been advocated as reliable cut-offs.3,4 Accordingly, the DWI lesion volume (Vol\textsubscript{DWI}) is used as exclusion criterion in ongoing recanalization trials. However, manual outlining for Vol\textsubscript{DWI} measurements is time consuming, whereas automated tools are not widely available and may imply manual correction.5 Conversely, the semiquantitative DWI-Alberta Stroke Program Early Computerized Tomography Score (DWI-ASPECTS) is increasingly used because it is straightforward, reproducible,6 and assessable at bedside. One study showed that DWI-ASPECTS ≤4 predicted Vol\textsubscript{DWI} ≥100 mL within 48 hours after stroke onset.7 Our aim was to determine whether DWI-ASPECTS can reliably substitute for Vol\textsubscript{DWI}. In the first 6 hours, we assessed the relationships between DWI-ASPECTS and Vol\textsubscript{DWI} in patients with middle cerebral artery stroke. We particularly focused on one hand, on DWI-ASPECTS cut points previously reported to be associated with Vol\textsubscript{DWI} >100 mL (≤4), hemorrhagic transformation (≤6 and <8), or outcome (≤5, ≤6, <7, and ≤8) and, on the other hand, on the 70 and 100 mL Vol\textsubscript{DWI} cut-offs.3,4,11

Patients and Methods

Data were extracted from a monocentric prospective register of consecutive patients treated by intravenous and intra-arterial thrombolysis for ischemic stroke (2001–2013), where MRI was implemented as first-line pretherapeutic imaging. Patients were included if they had a middle cerebral artery stroke confirmed by pretreatment MRI (1.5 Tesla; DWI: 3 directions; b=0–1000 s/mm\textsuperscript{2}; 6-mm contiguous slices). DWI-ASPECTS was scored by a stroke neurologist and Vol\textsubscript{DWI} measured by a neuroradiologist using a semiautomated method.12 In 20% of the population, DWI-ASPECTS and Vol\textsubscript{DWI} were reassessed independently by another neuroradiologist. Interobserver agreement for DWI-ASPECTS and Vol\textsubscript{DWI} was assessed using weighted-kappa and intraclass correlation coefficients, respectively. Correlation between DWI-ASPECTS and Vol\textsubscript{DWI} was determined using Spearman rank correlation coefficient. Based on the current literature, specific ASPECTS bins1,2,7–10 were assessed against Vol\textsubscript{DWI} values, with particular focus on the 70 and 100 mL cut-offs.3,4,11

Results

During the study period, 473 patients underwent intravenous and intra-arterial thrombolysis for acute stroke. Excluded patients (n=143; posterior circulation or pure anterior cerebral artery stroke, n=83 and no pretreatment MRI, n=60) did not differ from included patients on baseline characteristics (data not shown). The remaining 330 patients (178 [54%]...
men; median [interquartile range] age, 68 [56–79] years; admission National Institutes of Health Stroke Scale score, 15 [10–20]) had onset-to-MRI delay of 122 (90–164) minutes. Medians (interquartile range) for DWI-ASPECTS and Vol\textsubscript{DWI} were 7 (6–8) and 23.3 mL (9.6–63.4), respectively. Weighted-$\kappa$ and interobserver intraclass correlation coefficient were 0.94 (95% confidence interval, 0.91–0.96) and 0.98 (95% confidence interval, 0.98–0.99), respectively. There was a strong negative correlation between Vol\textsubscript{DWI} and DWI-ASPECTS ($\rho$=-0.82; 95% confidence interval, −0.86 to −0.77; $P<0.001$). The Table shows that the highest Vol\textsubscript{DWI} in the 207 patients with DWI-ASPECTS $\geq$7 was 67 mL, whereas the lowest Vol\textsubscript{DWI} in the 34 patients with DWI-ASPECTS <4 was 93 mL (Figure). However, Vol\textsubscript{DWI} values were extremely variable in the 88 patients with ASPECTS 4 to 6 (median [interquartile range], 66 [41–97]; range, 10–197 mL). Post hoc analysis showed similar results for Vol\textsubscript{DWI} versus modified DWI-W-ASPECTS\textsuperscript{13} (142/330 [43%] patients had lesion in the corona radiata).

## Discussion

Although each DWI-ASPECTS point corresponded to a wide range of Vol\textsubscript{DWI}, all patients with extensive changes on DWI-ASPECTS (0–3) had large Vol\textsubscript{DWI}, whereas all patients with limited DWI-ASPECTS changes (≥7) had Vol\textsubscript{DWI} <70 mL. DWI-ASPECTS is increasingly used for description or prognostic purposes in stroke populations. Although not designed to substitute for Vol\textsubscript{DWI}, DWI-ASPECTS does provide some semiquantitative estimate of it. However, DWI-ASPECTS overlooks lesions within the striatocapsular region and only partially covers the middle cerebral artery territory. This explains the wide range of true lesion volumes for a given DWI-ASPECTS point found here, in line with other studies.\textsuperscript{2,7}

Our finding that DWI-ASPECTS <4 invariably predicted Vol\textsubscript{DWI} ≥93 mL is entirely consistent with 1 previous report\textsuperscript{3} and highly relevant to the Diffusion and perfusion imaging Evaluation For Understanding Stroke Evolution (DEFUSE)-2 malignant profile 100 mL cut point.\textsuperscript{4} However, patients with DWI-ASPECTS ≥7 all had Vol\textsubscript{DWI} <70 mL, which corresponds to the cut point incorporated in the target mismatch definition.\textsuperscript{4} Although debated,\textsuperscript{11} these volume cut-offs are proposed to identify poor or good responders to reperfusion therapy,\textsuperscript{3} and particularly the 100-mL cut point serves as an exclusion criterion in several ongoing trials. However, fully automated softwares to calculate Vol\textsubscript{DWI} are not yet commonly used and can fail in real time. This may lead to imbalanced groups on baseline characteristics in trials where randomization is based on automated MR-image segmentation.\textsuperscript{14} Failure of automated volumetry may also restrain patient’s inclusion in trials. To overcome these difficulties, DWI-ASPECTS <4 could replace the poorly reproducible greater than one third of the middle cerebral artery territory CT rule as an alternative exclusion criterion in MR-based trials.

The tight relationships between extreme DWI-ASPECTS values (ie, <4 or ≥7) and the >100- or <70-mL, respectively, cut points found here suggest that DWI-ASPECTS could serve as a surrogate for these volumes. This concerned almost 3 quarters (241/330) of the studied population and may have clinical relevance. However, in those patients with intermediate DWI-ASPECTS (4–6), Vol\textsubscript{DWI} straddled widely across the above cut point volumes, indicating that intermediate DWI-ASPECTS cannot substitute for Vol\textsubscript{DWI} to identify patients with target mismatch or malignant profile. Of note, no DWI-ASPECTS cut point identified lesion volume >145 mL,\textsuperscript{15} above which decompressive hemicraniectomy is indicated.

Limitations of our study include its retrospective and single-center nature, and the focus on patients who underwent thrombolysis, which limits generalizability to nonthrombolized patients and may, in part, explain the low proportion of patients with large Vol\textsubscript{DWI} and consequently the relative large 95% confidence interval for patients with low ASPECTS.

In conclusion, in the first 6 hours, each DWI-ASPECTS point corresponds to a wide range of Vol\textsubscript{DWI}. However, extreme DWI-ASPECTS scores could serve as surrogates for important volume cut points. Further studies are needed prospectively to confirm this observation and to strengthen the value of existing Vol\textsubscript{DWI} cut points in predicting outcomes after recanalization.\textsuperscript{11}

## Table. DWI-ASPECTS Cut Points and Corresponding Volumes

<table>
<thead>
<tr>
<th>DWI-ASPECTS</th>
<th>n</th>
<th>Median</th>
<th>IQR</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>34</td>
<td>164</td>
<td>125–214</td>
<td>93–287</td>
</tr>
<tr>
<td>≥4</td>
<td>296</td>
<td>19</td>
<td>9–47</td>
<td>0–197</td>
</tr>
<tr>
<td>&lt;5</td>
<td>52</td>
<td>145</td>
<td>104–186</td>
<td>60–287</td>
</tr>
<tr>
<td>≥5</td>
<td>278</td>
<td>18</td>
<td>8–37</td>
<td>0–197</td>
</tr>
<tr>
<td>&lt;6</td>
<td>81</td>
<td>114</td>
<td>84–171</td>
<td>29–287</td>
</tr>
<tr>
<td>≥6</td>
<td>249</td>
<td>16</td>
<td>7–30</td>
<td>0–166</td>
</tr>
<tr>
<td>&lt;7</td>
<td>123</td>
<td>92</td>
<td>49–148</td>
<td>10–287</td>
</tr>
<tr>
<td>≥7</td>
<td>207</td>
<td>13</td>
<td>6–23</td>
<td>0–67</td>
</tr>
<tr>
<td>&lt;8</td>
<td>187</td>
<td>50</td>
<td>24–109</td>
<td>3–287</td>
</tr>
<tr>
<td>≥8</td>
<td>143</td>
<td>9</td>
<td>5–18</td>
<td>0–67</td>
</tr>
</tbody>
</table>

DWI-ASPECTS indicates diffusion-weighted imaging-Alberta Stroke Program Early CT Score; and IQR, interquartile range.
Disclosures
None.

References
Can DWI-ASPECTS Substitute for Lesion Volume in Acute Stroke?
Constance de Margerie-Mellon, Guillaume Turc, Marie Tisserand, Olivier Naggara, David Calvet, Laurence Legrand, Jean-François Meder, Jean-Louis Mas, Jean-Claude Baron and Catherine Oppenheim

Stroke. published online October 3, 2013;
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/early/2013/10/03/STROKEAHA.113.003047

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/