Does Diffusion Lesion Volume Above 70 mL Preclude Favorable Outcome Despite Post-Thrombolysis Recanalization?

Marie Tisserand, PhD; Guillaume Turc, PhD; Sylvain Charron, PhD; Laurence Legrand, MD; Myriam Edjlali, MD; Pierre Seners, MD; Pauline Roca, PhD; Stéphanie Lion; Olivier Naggsara, PhD; Jean-Louis Mas, MD; Jean-François Méder, PhD; Jean-Claude Baron, ScD; Catherine Oppenheim, PhD

Background and Purpose.—Whether to withhold recanalization treatment when the diffusion-weighted imaging (DWI) lesion exceeds a given volume is unsettled. Our aim was to assess the impact of recanalization on outcome in patients with baseline DWI lesion ≥70 mL (DWI≥70 mL) treated ≤4.5 hours from onset. We hypothesized that recanalization is beneficial in a sizeable fraction of these patients and that this is associated with a larger DWI lesion reversal.

Methods.—We analyzed 267 consecutive patients treated with intravenous recombinant tissue-type plasminogen activator for middle cerebral artery territory stroke in whom an occlusion was present on magnetic resonance angiography and 24-hour recanalization and 90-day clinical outcome could be assessed. After stratification relative to the 70-mL DWI lesion cut point, we calculated the odds ratio for recanalization of the primary arterial occlusive lesion (AOL score ≥2) to predict favorable outcome (modified Rankin scale score ≤2). DWI lesion reversal was compared between recanalizers with DWI≥70 mL with favorable and unfavorable outcomes.

Results.—Median (interquartile range) DWI lesion volume was 22 mL (10–60), and median onset time to imaging was 116 minutes (86–151). Twelve (22%) of the 54 patients with DWI≥70 mL experienced favorable outcome, of which 9 had recanalized. In patients with DWI≥70 mL, recanalization was significantly associated with favorable outcome after adjustment for age and National Institutes of Health Stroke Scale (odds ratio = 4.72 [1.09–20.32]; P = 0.0375). Among recanalizers with DWI≥70 mL, absolute and relative DWI reversal volumes were larger in those with favorable compared as with unfavorable outcome (18.8 mL [12.2–47.6] versus 8.5 mL [4.3–31.1]; P = 0.17; and 19.6% [10.9–62.8] versus 8.7% [3.9–16.5], respectively; P = 0.049).

Conclusions.—Patients with DWI lesion volume ≥70 mL can benefit from recanalization after intravenous recombinant tissue-type plasminogen activator. This may partly reflect a larger amount of DWI lesion reversal. (Stroke. 2016;47:1005-1011. DOI: 10.1161/STROKEAHA.115.012518.)

Key Words: acute stroke ■ diffusion-weighted imaging ■ ischemia ■ MRI ■ thrombolysis

The aim of acute stroke treatment is to salvage hypoperfused yet viable tissue by recanalization using intravenous thrombolysis (IVT), endovascular treatment (EVT), or bridging therapy. The size of the infarct core can be approximated by the extent of diffusion-weighted imaging (DWI) signal changes before treatment decision. Most studies but not all have shown that large initial DWI lesion volume was an independent predictor of poor outcome in patients managed conservatively or with IVT or EVT. Because it is associated with symptomatic intracerebral hemorrhage and poor outcome after reperfusion therapy, the term malignant profile was coined for large DWI lesions to identify patients in whom recanalization may be futile. Most studies that identified volumes above which patients had poor outcome included the whole population, irrespective of the occurrence of recanalization. This was clinically relevant because, until recently, IVT was the only approved acute-phase treatment, and recanalization was achieved in less than half of the treated patients. With the advent of thrombectomy, studying the impact of recanalization, which is achievable in most instances, becomes a key question in those patients with large lesions. However, such patients have been excluded from most recent EVT trials. For instance, core volume >70 and 50 mL were exclusion criteria for Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra Arterial (EXTEND-IA) and Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME) trials, respectively.

However, the idea to define a cut point for DWI lesion volume to select patients for reperfusion therapy has been
challenged. In a recently reported large series of patients treated with EVT, favorable outcome was achieved after reperfusion in every third patient with DWI lesions >70 mL, whereas after poor or failed reperfusion, outcome was favorable in only every 12th patient. 

Another point to consider is that DWI lesion cut points above which recanalization may be futile have to date been derived from studies where patients were treated in a late time window, and so may not apply to patients treated earlier. For instance, 2 EVT studies have been discrepant; as in one, the treatment was futile for DWI lesions >70 mL when recanalization occurred at a mean (±SD) 7.4±3.1 hours, whereas in the other, some patients with large DWI lesions benefited from earlier-initiated endovascular recanalization. An important factor to consider regarding these discrepancies is the phenomenon of DWI lesion reversal. The delay from stroke onset to recanalization indeed strongly influences the amount of DWI lesion reversal, and specifically, a DWI lesion ≥70 mL may comprise salvageable tissue in the early time frame, but represent only infarct core when treatment is administered at later times. Thus, recanalization at early time points may be beneficial even despite DWI lesions ≥70 mL, and this would be in part because of substantial DWI lesion reversal.

In a large sample treated in the early time frame by intravenous recombinant tissue-type plasminogen activator, we hypothesized that recanalization would be beneficial in a sizeable fraction of patients with DWI lesion ≥70 mL (DWI≥70 mL). As an explanatory factor, we predicted larger volumes of DWI lesion reversal in good responders.

**Patients and Methods**

**Patients**

Patients were identified from our prospective database of ischemic stroke patients treated by intravenous recombinant tissue-type plasminogen activator between January 2003 and May 2014. Inclusion criteria were middle cerebral artery territory stroke, pretreatment magnetic resonance imaging (MRI), including at least DWI and intracranial magnetic resonance angiography, detectable occlusion on baseline magnetic resonance angiography, assessable 24-hour recanalization, and clinical follow-up with 90-day modified Rankin scale. Exclusion criteria were bridging therapy and marked artifacts on initial DWI. Importantly, a large baseline DWI lesion volume is not an exclusion criterion for IVT in our center. Sites of occlusion were categorized into proximal (internal carotid and proximal segment of the middle cerebral artery) or distal. Recanalization was defined as AOL≥2 (recanalization of the primary arterial occlusive lesion). If not available, angio-computed tomography (CT) or Doppler ultrasound was used. Characteristics of patients, vascular risk factors, admission and 24-hour National Institutes of Health Stroke Scale (NIHSS), on-set-to-treatment and on-set-to-MRI delays, stroke side, initial blood pressure, and blood glucose levels, were collected. The primary study outcome was the percentage of patients who achieved a favorable outcome at 90 days, defined by a modified Rankin scale score ≤2. Symptomatic intracranial hemorrhage was graded according to both the European Cooperative Acute Stroke Study 3 (ECASS3) and Safe Implementation of Thrombolysis in Stroke Monitoring Study (SITS-MOST) definitions. The study was approved by the local ethical committee.

**Magnetic Resonance Protocol**

Pretreatment and follow-up MRI (scheduled =24 hours after recombinant tissue-type plasminogen activator) were performed on a 1.5-T scanner (Signa EchoSpeed; GE Healthcare, Milwaukee, WI) with a 33-mT/m gradient strength and an 8-channel head coil. The standard protocol included at least DWI and intracranial 3D time-of-flight magnetic resonance angiography. A T2-weighted baseline image (b=0 s/mm²) and the DWI (b=1000 s/mm²) were acquired with a single-shot echo planar imaging spin-echo sequence with the following parameters: 6675/81 to 104 (repetition time/echo time range, ms), 24×24 cm² field of view, 128×128 matrix, 2 excitations, 24 sections, 6-mm thick, no gap, 53 s.

**DWI Lesion Measurement**

Blind to clinical data and outcome, DWI lesions were manually segmented using MANGO software version 3.1.2 (Research Imaging Institute, UTHSCSA). Regions of interest were drawn using a combination of interactive thresholding and drawing tools. The segmented DWI voxels were projected onto apparent diffusion coefficient (ADC) maps to exclude any areas of T2 shine-through effect and include areas of decreased ADC with subtle DWI signal changes. Using voxel-based comparison of coregistered initial DWI and 24-hour DWI, reversible acute DWI lesion voxels were automatically determined as those initial DWI voxels that did not overlap with the coregistered 24-hour DWI, as previously described. The relative reversal in each patient was expressed as percentage of DWI lesion volume reversal:

\[
\text{Vol}_{\text{reversal}}/\text{Vol}_{\text{baseline,DWI}} \times 100
\]

**Statistical Analysis**

Continuous variables were described as median (interquartile range) and categorical variables as percentages (percentage). DWI lesions volumes were dichotomized (<70 versus ≥70 mL). For each volume category, we assessed the association between recanalization and favorable outcome using odds ratios (ORs) without and after adjustment for age and for NIHSS using logistic regression. We performed additional sensitivity analyses using an alternative definition for recanalization (AOL=3). Using logistic regression, we also assessed the association between side of the infarct and favorable outcome in patients with DWI≥70 mL. Using a Mann–Whitney U test, we compared absolute and relative DWI reversal (1) between patients with favorable and unfavorable outcome within the subgroup of patients with DWI≥70 mL and (2) between patients with favorable and unfavorable outcome within the subgroup of patients with DWI≥70 mL and who experienced recanalization.

**Results**

During the study period, 473 patients underwent IVT for an acute ischemic stroke. Two hundred and six were excluded because of bridging therapy (n=32), inclusion in a neuroprotection study (n=4), non–middle cerebral artery stroke (n=53), baseline evaluation with CT only (n=36), initial MRI not available in Digital and Communications in Medicine (DICOM) format (n=16), no visible initial occlusion (n=42), no data on recanalization (n=9), or 90-day modified Rankin scale score not available (n=14). Of note, the latter 14 patients had similar NIHSS at 24 hours than the included patients (median 9 [interquartile range 6–14] versus 11 [4–18]; P=0.72). Excluded patients did not differ from the included patients for age or on-set-to-MRI time, but had lower baseline NIHSS (median 10 [6–21] versus 15 [9–20]; P<0.0001).

The characteristics of the 267 included patients are presented in Table 1. Median times from on-set to initial and follow-up MRI were 116 minutes (86–151) and 25.3 hours (21.5–28.9), respectively. Median initial DWI lesion volume was 22 mL (10–60). Fifty-four (20%) patients had DWI≥70 mL. Patients with DWI≥70 mL had higher baseline and 24-hour NIHSS, were imaged and treated later, and had more
proximal occlusion than the others (Table 1). One hundred and thirty-seven patients (51%) experienced recanalization and 130 (49%) had favorable outcome. Of note, the largest DWI lesion volume associated with a favorable outcome was 72 mL in patients who did not recanalize (AOL=0) and 160 mL in patients who recanalized (AOL ≥2).

One hundred and eighteen (55%) of the 213 patients with a DWI volume <70 mL experienced favorable outcome, of which 89 recanalized. Twelve (22%) of the 54 patients with DWI volume ≥70 mL experienced favorable outcome, of which 9 recanalized. Recanalization was significantly associated with favorable outcome in patients with DWI<70 mL (OR=9.61, [5.12–18.02]; P<0.0001) but also in patients with DWI≥70 mL (OR=4.87, [1.15–20.73]; P=0.03; Table 2). Based on a shift analysis over the entire modified Rankin scale range, the association remained significant in patients with either DWI<70 mL (OR=6.99, [4.10–11.90]; P<0.0001) or DWI≥70 mL (OR=3.08, [1.14–8.32]; P=0.03; Figure 1). In patients with DWI≥70 mL, recanalization remained significantly associated with favorable outcome after adjustment for age and admission NIHSS (OR=4.72, [1.09–20.32]; P=0.0375). Recanalizers with DWI≥70 mL experienced an increased

### Table 1. Patients’ Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Whole Sample, n=267</th>
<th>DWI&lt;70 mL, n=213</th>
<th>DWI≥70 mL, n=54</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DWIbaseline volume, mL</td>
<td>21.6 [9.6–60.1]</td>
<td>15.8 [7.5–55.5]</td>
<td>118.3 [94.8–178.4]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, y</td>
<td>71 [59–75]</td>
<td>71 [58–82]</td>
<td>70 [60–79]</td>
<td>0.74</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)*</td>
<td>150 (57)</td>
<td>123 (58)</td>
<td>27 (50)</td>
<td>0.29</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)*</td>
<td>36 (14)</td>
<td>29 (14)</td>
<td>7 (13)</td>
<td>1</td>
</tr>
<tr>
<td>Hyperlipemia, n (%)*</td>
<td>98 (37)</td>
<td>79 (37)</td>
<td>19 (35)</td>
<td>0.88</td>
</tr>
<tr>
<td>Smoking, n (%)†</td>
<td>107 (40)</td>
<td>88 (42)</td>
<td>19 (35)</td>
<td>0.44</td>
</tr>
<tr>
<td>TIA, n (%)†</td>
<td>16 (6)</td>
<td>14 (7)</td>
<td>2 (4)</td>
<td>0.54</td>
</tr>
<tr>
<td>Stroke, n (%)*</td>
<td>19 (7)</td>
<td>15 (7)</td>
<td>4 (7)</td>
<td>1</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)†</td>
<td>71 (27)</td>
<td>57 (27)</td>
<td>14 (26)</td>
<td>1</td>
</tr>
<tr>
<td>Clinical measure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood glucose, mmol/L†</td>
<td>6.4 [5.4–7.5]</td>
<td>6.3 [5.4–7.3]</td>
<td>6.7 [5.8–8.2]</td>
<td>0.08</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg†</td>
<td>80 [70–92]</td>
<td>80 [70–92]</td>
<td>81 [70–92]</td>
<td>0.86</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg†</td>
<td>150 [132–169]</td>
<td>150 [130–166]</td>
<td>149 [133–169]</td>
<td>0.98</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large-artery atherosclerosis, n (%)†</td>
<td>41 (15)</td>
<td>34 (16)</td>
<td>7 (13)</td>
<td>0.68</td>
</tr>
<tr>
<td>Small-vessel occlusion, n (%)†</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cardioembolism, n (%)†</td>
<td>138 (53)</td>
<td>113 (54)</td>
<td>25 (47)</td>
<td>0.36</td>
</tr>
<tr>
<td>Other determined, n (%)†</td>
<td>14 (5)</td>
<td>12 (6)</td>
<td>2 (4)</td>
<td>0.74</td>
</tr>
<tr>
<td>Undetermined, n (%)†</td>
<td>67 (26)</td>
<td>50 (24)</td>
<td>17 (32)</td>
<td>0.29</td>
</tr>
<tr>
<td>Time to MRI, min</td>
<td>116 [86–151]</td>
<td>113 [85–148]</td>
<td>130 [90–173]</td>
<td>0.05</td>
</tr>
<tr>
<td>Time to IVT, min</td>
<td>152 [120–185]</td>
<td>150 [120–180]</td>
<td>168 [134–202]</td>
<td>0.02</td>
</tr>
<tr>
<td>Proximal occlusion, n (%)</td>
<td>181 (68)</td>
<td>138 (65)</td>
<td>43 (80)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Unless specified, all numbers are median [interquartile range]. DWI indicates diffusion-weighted imaging; IVT, intravenous thrombolysis; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; and TIA, transient ischemic attack.

*Assessed in 265 patients.
†Assessed in 264 patients.

### Table 2. Impact of Recanalization on Outcome According to the 70 mL DWI Lesion Cut Point

<table>
<thead>
<tr>
<th></th>
<th>DWI&lt;70 mL (n=213)</th>
<th>DWI≥70 mL (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable outcome</td>
<td>118</td>
<td>12</td>
</tr>
<tr>
<td>No recanalization</td>
<td>29/101 (29%)</td>
<td>3/29 (10%)</td>
</tr>
<tr>
<td>Recanalization</td>
<td>89/112 (79%)</td>
<td>9/25 (30%)</td>
</tr>
</tbody>
</table>

Recanalization was defined as AOL≥2 (recanalization of the primary arterial occlusive lesion). Favorable outcome at 90 days was defined by mRS score ≤2. DWI indicates diffusion-weighted imaging; mRS, modified Rankin scale; and OR, odds ratio.
rate of favorable outcome compared with nonrecanalizers (36% versus 10%). When recanalization was defined as AOL=3, the association between DWI≥70 mL and favorable outcome in recanalizers was no longer significant (OR=2.62, [0.67–10.24]; P=0.17). The right hemisphere was involved in 9 of the 12 patients with DWI≥70 mL who experienced favorable outcome. However, right-sided infarction did not predict good outcome after recanalization in this subgroup (P=0.29). In patients with DWI≥70 mL, 2 (4%) experienced symptomatic intracranial hemorrhage according to either ECASS3 or SITS-MOST definitions.

Among patients with DWI≥70 mL, absolute and relative DWI lesion reversal were larger in patients with favorable outcome than in the others (20.2 mL [13.9–45.2] versus 7.9 [3.5–19.6]; P=0.033 and 19.8% [11.2–55.9] versus 7.4 [2.5–13.5]; P=0.003; Figure 2). Similarly, among patients with DWI≥70 mL who experienced recanalization, absolute and relative DWI lesion reversal were larger in patients with favorable outcome than in the others (18.8 [12.2–47.6] versus 8.5 mL [4.3–31.1]; P=0.17 and 19.6% [10.9–62.8] versus 8.7% [3.9–16.5]; P=0.049), although not statistically significant for the absolute volume.

Discussion

Capitalizing on a large sample of patients treated by IVT, we found that recanalizers with DWI≥70 mL experienced an increased rate of favorable outcome compared with nonrecanalizers (36% versus 10%). This suggests that even patients with large initial DWI lesions benefit from recanalization in the early time window. This good response to recanalization may be partly explained by the novel finding of larger DWI lesion reversal in this subset of patients.

One first inference is that our study, which confirms that advanced MRI in the early time window is feasible, does not support withholding IVT in patients with DWI≥70 mL. Indeed, outcome was favorable in 22% of the cases with DWI≥70 mL, whether recanalized or not. This is consistent with the few studies that reported on the outcome of patients treated despite large initial DWI lesions. Thus, Gilgen et al17 reported that 21% of 66 such patients had favorable outcome, in accordance with the one in 6 with favorable outcome in the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) study.8 A second and even more important finding from our study is that recanalization was associated with favorable outcome in patients with DWI≥70 mL. Available evidence calls into question the existence of a definite DWI volume cut point above which patients do poorly despite recanalization. Combining the impact of DWI lesion extent and of recanalization on outcome, 4 recent studies suggested that large lesions can still benefit from recanalization.16–19 Among 19 patients with DWI>70 mL, complete recanalization tended to be associated with an increased rate of clinical recovery (53% versus 8%).19 In a larger study, favorable outcome was achieved in every third patient with DWI lesions >70 mL (n=66) after successful

Figure 1. 90-day functional outcome as a function of recanalization status and diffusion-weighted imaging (DWI) lesion <70 mL or ≥70 mL. mRS indicates modified Rankin scale.

Figure 2. Diffusion-weighted imaging (DWI) reversal in 2 patients. A, Baseline DWI lesion was 73 mL. After recanalization of the primary arterial occlusive lesion (AOL=3), DWI displayed a large DWI reversal (47 mL). Modified Rankin scale score (mRS) at 3 months was 2. B, In another patient, baseline DWI lesion was 79 mL. After recanalization (AOL=2), DWI displayed a large reversal (49 mL). mRS score at 3 months was 1.
endovascular reperfusion, whereas after poor or failed reperfusion, outcome was favorable in every 12th patient only.17 Two other studies used DWI-Alberta Stroke Program Early CT score (ASPECTS) which can serve as surrogate for large DWI lesion volumes in case of low scores.30 In patients with DWI-ASPECTS <7, favorable outcome was more frequent after early post–recombinant tissue-type plasminogen activator reperfusion than in nonrecanalizers (38% versus 0%, respectively).16 A strikingly similar finding (50% versus 3%, respectively) was found in EVT patients using DWI-ASPECTS <5.18 Our findings are entirely consistent with the above mentioned previous studies.

The above mentioned studies, however, contrast with others that suggested that recanalization/reperfusion would have no benefit or even a detrimental effect in these patients, raising the issue of withholding treatment in this subgroup. Thus, a pooled analysis of the DEFUSE/Echoplanar Imaging Thrombolysis Evaluation Trial (EPITHET) database identified a volume of 80 mL as the best DWI cut point to predict poor outcome despite reperfusion.31 Supporting these findings, Yoo et al found that all 6 patients with DWI lesions >70 mL in their series had poor outcome after EVT.10 Similarly, Ribo et al found that only 12% of patients with infarct core >39 mL achieved favorable outcome after EVT despite recanalization.32 Importantly, however, in the above mentioned 3 studies,10,31,32 most patients were treated well beyond the 4.5-hour time point. This likely explains the discrepant findings between those studies supporting a core cut point to identify a futile group and the remaining cited studies,16–19 including ours. As already mentioned, our study focused on reperfusion therapy administered within 4.5 hours (median 152 minutes for initiation of IVT) and yielded results consistent with studies in which patients were treated in an early time window.16–19

In the hyperacute phase, key factors, including recanalization/reperfusion, can dramatically change the fate of the DWI lesion, owing to DWI lesion reversal seen on MRI obtained at 24 hours. The vast majority of such DWI lesion reversal observed at 24 hours exhibits sustained tissue salvage.22 Among recanalizers with DWI≤70 mL, we found a greater amount (median 19 mL) of lesion reversal in patients with favorable as compared with unfavorable outcome. This finding is consistent with previous work indicating that DWI lesion reversal is mediated by early reperfusion,21,33 is more frequent and sizeable in patients treated in the early time frame,20,22 and is associated with favorable 3-month outcome across all DWI lesion volumes.20 Importantly, the present study is the first to show that the phenomenon of DWI reversal applies to lesion volumes ≥70 mL, which has important implications for patient management.

Our findings were based on manual DWI lesion segmentation, including subtle DWI signal changes with ADC decrease, but without using a specific ADC threshold. To date, the optimal ADC cut point to delineate the true core remains debated, given the overlap in ADC values between core and noncore voxels.34 The use of a definite ADC/DWI threshold, implemented in some automated softwares, may yield different results regarding DWI lesion reversal and prognostic value of the 70 mL cut point. However, recanalization has been shown to be beneficial in patients with large DWI lesions segmented with such an automated software.19 In addition to the issue of volume cut point, lesion topography should also be considered because large volumes may not always induce severe deficits if located in poorly eloquent or even silent areas.2 Because the dogma of lesion cut point as selection criterion for reperfusion therapies is mainly dictated by the consideration of poor functional outcome, the topography issue contributes to the idea that baseline lesion volume may not be a relevant selection criterion. Whether additional imaging information than DWI volume could allow determining a cut point to identify nonresponders to recanalization is another interesting point. For instance, perfusion parameters extracted from CT or MRI might help identify the true core.35 The use of CT to segment the core provided different results from ours in one study, with perfusion CT core >70 mL patients gaining little benefit from IVT.36 Conversely, in another study, perfusion CT core >70 mL was, as expected, useful for predicting functional outcome, but could not reliably identify patients who will not benefit from intra-arterial therapy, in line with our IVT findings.37 So, additional studies based on either CT perfusion or magnetic resonance perfusion combined with DWI-based measurements are needed to reach a consensus on the value of this biomarker to predict the effect of treatments. In our study, the subgroup of patients with available PWI data was too small to permit such additional analysis.

Our study has some limitations. We cannot attribute our results unequivocally to the treatment effect of IVT because of the lack of untreated control group. Because of the retrospective design, we did not obtain perfusion imaging in the follow-up imaging protocol. Because recanalization and reperfusion sometimes depart,5,33 some degree of spontaneous reperfusion probably explains why some nonrecanalizers achieved good outcome. We also cannot exclude that some patients presented futile recanalization because the latter was assessed on the 24-hour follow-up magnetic resonance angiography.38 This possibility refers to the few recanalizers who experienced poor outcome, which would lower the OR of recanalization for favorable outcome. Another limitation is a possible bias from those patients unable to undergo the follow-up MRI or lost to clinical follow-up. However, these patients did not have a worse 24-hour NIHSS. Another potential bias in the present study would have been the exclusion from IVT of patients demonstrating large DWI lesions. Importantly, however, lesion volume is not an exclusion criterion for IVT in our center. Effectively, the fraction of patients with large baseline lesion in our cohort was 20%, in line with that previously reported in unselected acute stroke populations39 and estimate from EXTEND-IA.13 To further ascertain this, we assessed post hoc the reasons for withholding IVT in 338 consecutive patients admitted in our center within 4.5 hours (2008–2013). Of these, 12 had a DWI-ASPECTS <5, and in all except one (volume=218 mL), lesion size was not the main reason for withholding the treatment. Finally, our sample did not allow the assessment of large DWI volumes, such as 100 mL, because the corresponding subgroups were too small after stratification on recanalization for a reliable assessment.
Conclusions
Our results emphasize the frequent clinical benefit from recanalization after IVT even in case of DWI≥70 mL. This good response to recanalization may be partly explained by the novel finding of larger DWI lesion reversal in these patients. By inference, our findings do not support the 70-mL DWI lesion cut point above which recanalization therapies would be futile or dangerous.

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Disclosures
None.

References


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拡散強調画像上の病変体積が 70 mLを超えると血栓溶解療法後に再開通しても良好な転帰は得られないか？

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