

# Arterial Recanalization Benefits Even Neurologically Improving Stroke Patients After Intravenous tPA

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The “Dense Middle Cerebral Artery (MCA) Sign”, observed in patients with proximal middle cerebral artery occlusion, is seen in the most severe instances of ischemic stroke.

Recanalization, or disappearance of the sign, is seen in about half of patients who receive intravenous (IV) tissue-type plasminogen activator (tPA); this generally heralds a good prognosis, with patients exhibiting lower mortality and better functional outcome.<sup>1</sup> Patients without recanalization, however, may benefit from additional interventions, including intra-arterial thrombolysis or mechanical thrombectomy.

A recent study by Kharotina et al<sup>4</sup> provides indirect evidence for the use of mechanical thrombectomy in patients who fail to recanalize even after neurological improvement. The study analyzed two distinct variables: neurologic improvement with IV tPA alone and presence or absence of arterial recanalization. The primary outcome measure was independence, which was defined as a score of 0-2 on a modified Rankin scale after 3 months.

Patient data was taken from the Safe Implementation of Treatment in Stroke (SITS) register, an international database of patients with acute ischemic stroke who received IV alteplase under typical guidelines. In this study, patients were included that demonstrated occlusion on CT angiogram (CTA) or MR angiogram (MRA), or a dense artery sign on noncontrast CT at admission. After tPA administration, vessel recanalization was identified on repeat imaging 22 and 36 hours later by absence of occlusion on CTA/MRA or resolution of the dense artery sign on CT. Neurological improvement was defined as a 20% improvement from the patient’s admission NIHSS score and was assessed at 2 hours and 24 hours post-treatment.

Of the 28136 registered cases, 5324 met inclusion criteria for the study. Recanalization was seen in about half of patients. Four groups were created from the two variables being studied: neurologic improvement with recanalization (IR), improvement without recanalization (IWR), recanalization without improvement (RWI), and neither recanalization nor improvement (WIWR). In general, recanalization and neurologic improvement were more common in patients that were younger and had reduced risk factors for stroke. Those with recanalization and early neurologic improvement (IR) did best, with 75% having good outcomes at 3 months, versus 49% of patients who did not recanalize despite early neurologic improvement (IWR) (**Figure 1**). The significantly better outcomes in the IR group highlight the importance of recanalization even in the presence of improving neurologic status. In patients who did not show neurological improvement at 2

hours with and without recanalization, improvement at 24 hours was 39% and 17% respectively, with good outcomes at 3 months in 31% and 15%.

This study demonstrates that recanalization is an independent factor from neurological improvement in patient outcome. Although often associated, the assumption that neurologic improvement itself implies recanalization may be incorrect. This is important because in practice, patients who demonstrate neurologic improvement are often not considered for further imaging or endovascular interventions. The superior outcomes in the IR group vs IWR group in this study suggest that even with neurologic improvement after tPA, acute stroke patients warrant additional imaging, and, in the absence of recanalization, endovascular consideration. While the potential benefit of recanalization is demonstrated, the authors note that the optimal method for achieving this, including intraarterial thrombolytics and mechanical thrombectomy, remains unproven as of yet.

It should be noted that the authors in this paper are addressing neurological improvement after IV tPA administration, rather than the issue of symptom improvement prior to IV tPA. Rapidly improving stroke symptoms may indicate spontaneous recanalization, and have long been considered a standard exclusionary criterion for receiving IV tPA. However the Re-Examining Acute Eligibility for Thrombolysis (TREAT) task force recently clarified that any disabling residual symptoms even after improvement (and despite low NIHSS) should still be considered eligible to receive IV tPA<sup>6</sup>. These recommendations reflect the concern for lack of recanalization even in the setting of spontaneous improvement, and parallel the conclusion of this paper which stresses the importance of recanalization in addition to neurological improvement as an independent marker of 3-month good outcome.

Shortcomings identified in this paper include a population drawn from the small proportion of the register (4%) that received angioimaging. If interpretation of a dense artery sign or occlusion on CTA/MRA was unclear, data was excluded, leaving only more obvious occlusions, and thus severe instances of stroke. This limits generalizability of the study to milder strokes. Clot size and location were also not considered. Nonetheless, the findings of this paper are clear: patients who recanalize have better outcomes. These exciting findings support further randomized investigations into an aggressive approach to imaging and further interventions, despite recently published trial data which failed to demonstrate overall benefit of such strategies<sup>2,3,5</sup>. Data from observational studies like this one will help inform design of future studies with the hope of better long-term outcomes in acute stroke patients.

## Figures:

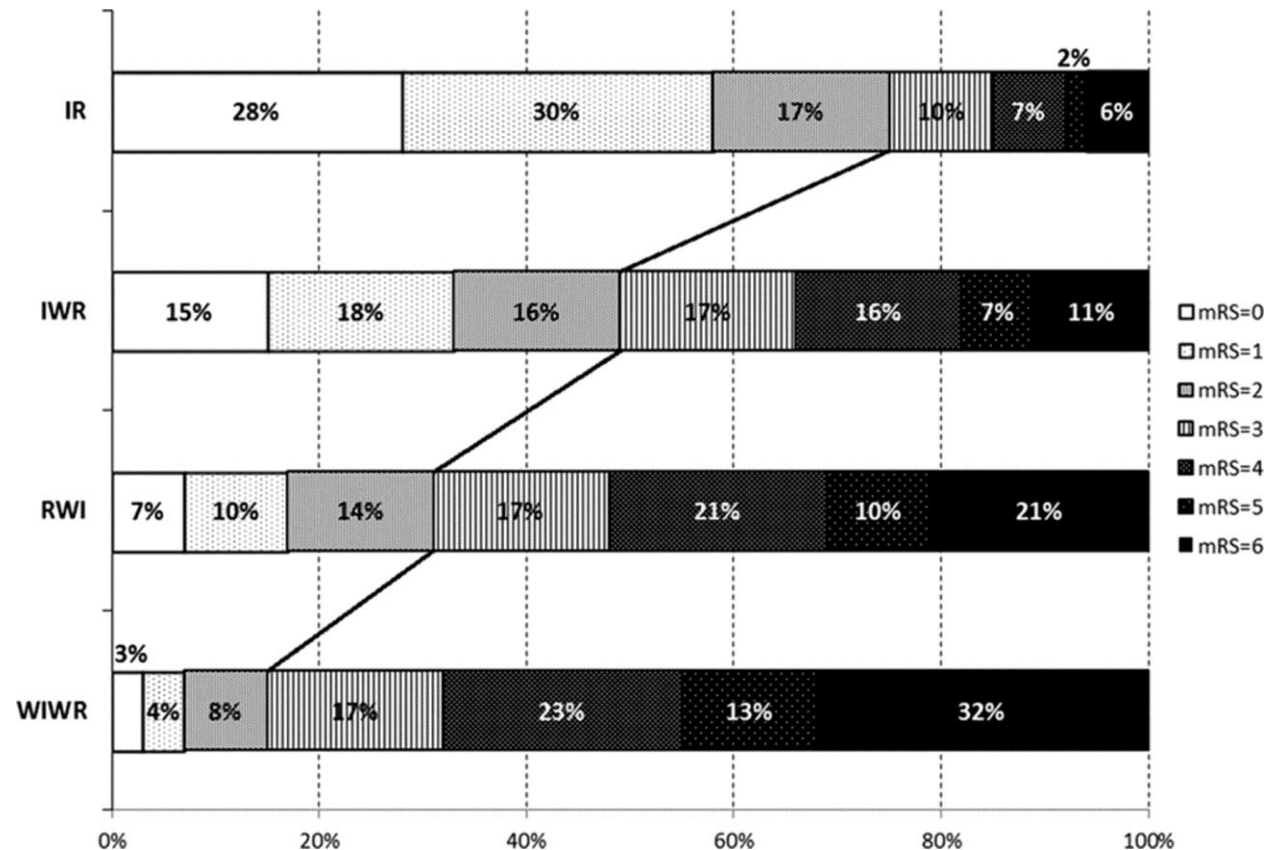


Figure 1 Three-month functional outcome (modified Rankin scale [mRS]) of patients with and without neurological improvement by 20% from baseline at 2 hours post-treatment (n=5324). (Reprinted from Stroke, Vol 44, Kharitonova TV et al, Importance of cerebral artery recanalization in patients with stroke with and without neurological improvement after intravenous thrombolysis, pp. 2513-2518. Copyright 2013, with permission from Lippincott Williams & Wilkins).

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