

# Large-Vessel Occlusion Stroke: Effect of Recanalization on Outcome Depends on the National Institutes of Health Stroke Scale Score

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*Background:* Arterial recanalization is currently considered the main standard of successful early management of acute ischemic stroke. Intravenous (IV) thrombolysis with tissue plasminogen activator (tPA) is the only Food and Drug Administration–approved medical treatment. Large-vessel occlusion, estimated to account for up to 40% of all acute ischemic strokes, is often refractory to IV thrombolysis and is associated with a poor patient outcome. Mechanical recanalization procedures are therefore increasingly used in the treatment of large-vessel occlusion refractory to, or presenting outside the accepted time window for, IV thrombolysis. The aim of this study was to investigate the effect of early vessel recanalization on clinical outcome in patients with large-vessel occlusion stroke. *Methods:* This is a single-center cohort study, analyzing prospectively collected data on 152 patients with large-vessel occlusion and acute ischemic stroke. Seventy-one patients received endovascular treatment (of whom 57.7% also received IV tPA), and 81 (55.6% of whom also received IV tPA) were not treated with endovascular therapy. Clinical outcome was compared for 2 cohorts: patients who recanalized ( $n = 46$ ) and patients with persisting large-vessel occlusion ( $n = 106$ ). *Results:* Early recanalization was an independent predictor of a good clinical outcome in only those patients who presented with a severe ischemic stroke (National Institutes of Health Stroke Scale [NIHSS] score  $>15$ ;  $P = .017$ ). This was not the case for less severe strokes (NIHSS score  $\leq 15$ ) where recanalization did not lead to more patients with functional independence at 90-day follow-up ( $P = .21$ ). *Conclusions:* In this study of acute large-vessel occlusion stroke, we found that clinical outcome following early recanalization was dependent on the patient's pretreatment NIHSS score. A non-negligible proportion of patients with milder strokes did well despite persistent large-vessel occlusion. These results may suggest that in patients who are able to maintain adequate collateral flow despite proximal arterial occlusion, effective adaptive mechanisms are present, which for some patients are long-lasting. This may influence the process of appropriate patient selection for endovascular therapy. **Key Words:** Large-vessel occlusion—ischemic stroke—recanalization—endovascular treatment—thrombectomy.

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Arterial recanalization is currently considered the main standard of successful early management of acute ischemic stroke. Recanalization within 8 hours of symptom onset has been found to be associated with a 4- to 5-fold increase in odds for a good functional outcome and a 4- to 5-fold reduction in the odds of death.<sup>1</sup> Large-vessel occlusions not responsive to intravenous (IV) thrombolysis have been shown to be associated with a poor prognosis. With persistent vessel occlusion (PVO), fewer patients achieve functional independence and mortality rates are higher.<sup>2</sup> The concept that vessel recanalization improves outcome is termed the "recanalization-hypothesis." This is the basis for thrombolytic stroke therapy and the development of new treatment options for acute large-vessel occlusion stroke.

When assessing the approval of retriever devices for use in endovascular treatment, recanalization rates are used as the efficacy end point.<sup>3</sup> However, "futile recanalization," when recanalization is not followed by improved clinical outcome, is well recognized.<sup>4,5</sup> Reperfusion injury is a well-known complication for patients improperly selected for both IV tissue plasminogen activator (tPa) and endovascular therapy. Furthermore, mechanical endovascular intervention is associated with a potential risk of harming the patient. Identifying the factors that translate angiographic recanalization into a favorable clinical outcome is therefore essential.

In addition to vessel recanalization, several other factors including pretreatment stroke severity have been shown to predict clinical outcome after acute ischemic stroke.<sup>6</sup> The National Institutes of Health Stroke Scale (NIHSS) is an accepted clinical tool for assessing stroke severity and clinical outcomes.<sup>7,8</sup> Patients presenting with a pretreatment NIHSS score of more than 15, categorized as a moderate-to-severe stroke, have been found to have a higher probability of a worse outcome and death compared with patients presenting with scores 15 or less (mild-to-moderate stroke).<sup>6</sup> The Prolyse in Acute Cerebral Thromboembolism Trial (PROACT) trial showed a clinical effect of recanalization after intra-arterial thrombolysis only for patients with a pretreatment NIHSS score greater than 11.<sup>9</sup> The Interventional Management of Stroke 3 study also showed a greater potential for endovascular treatment for patients presenting with an NIHSS score of more than 20 compared with patients presenting with a lower NIHSS score (8-19).<sup>10</sup>

Identifying the various factors associated with a good outcome after endovascular treatment with vessel recanalization is essential to enable better selection of patients to treatment. The aim of this study therefore was to investigate the effect of early recanalization on clinical outcome in patients with large-vessel occlusion stroke in a clinical setting.

## Methods

This is a single-center cohort study, analyzing prospectively collected data from 152 consecutive patients with

large-vessel occlusion stroke admitted to Oslo University Hospital (OUH), Rikshospitalet, between 2007 and 2012. OUH is a tertiary referral center providing endovascular service for regional and primary stroke units.

After receiving approval from the Regional Ethics Committee for data collection and analysis, a database of consecutive patients with acute ischemic stroke referred to our hospital for endovascular treatment was established. Study inclusion criteria were acute stroke with clinical ischemic symptoms corresponding to an angiographically proven large intracranial vessel occlusion, absence of intracranial hemorrhage on computed tomography (CT) scan, and a clearly defined time of symptom onset within 6 hours of inclusion. Time of patient inclusion was time of CT angiogram confirming large-vessel occlusion. A limit of 8 hours from symptom onset to vessel recanalization was predefined because early recanalization is believed to have the greatest impact on clinical function.<sup>1</sup> Following admission, all patients were re-examined clinically and if appropriate, new imaging was performed before deciding on further treatment with endovascular recanalization and/or IV thrombolysis, or general medical treatment.

All patients without contraindications to IV thrombolytic therapy were given IV tPa. Contraindications were according to departmental guidelines and in agreement with international guidelines.<sup>11</sup> IV tPa was administered at a dose of .9 mg per kg (maximum 90 mg), with 10% given as an initial bolus and the remaining 90% as a constant infusion over a period of 60 minutes.

Patients who had an ischemic penumbra (mismatch between cerebral blood flow and cerebral blood volume on perfusion imaging) or clinical penumbra (mismatch between established infarct and clinical symptoms) with no contraindications to endovascular therapy were selected for intra-arterial recanalization therapy with intra-arterial thrombolysis alone or with mechanical device, or with mechanical device alone. Contraindications to endovascular therapy were the presence of a too large area of infarction on cerebral imaging defined as more than 50% of the territory supplied by the occluded artery (restricted diffusion on magnetic resonance imaging [MRI] or low attenuation on noncontrast CT), absence of mismatch between cerebral blood flow and cerebral blood volume on perfusion imaging (no ischemic penumbra), absence of clinical mismatch to established infarct on CT or cerebral MRI, technically impossible with lack of groin access (because of previous surgery or severe atherosclerosis), total occluded vessel from the arch of the aorta or extreme vessel tortuosity where catheterization carried increased risk of patient harm, spontaneous clinical improvement, open vessel on reimaging at our institution, and a too high burden of comorbidity with coexisting malignancy, other life-threatening diseases, dementia, major organ-failure, or life expectancy less than 1 year. All patients included in

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