Improving the Prediction of Spontaneous and Post-thrombolytic Recanalization in Ischemic Stroke Patients

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Background: Endovascular treatment for acute ischemic stroke patients was recently shown to improve recanalization rates and clinical outcome in a well-defined study population. Intravenous thrombolysis (IVT) alone is insufficiently effective to recanalize in certain patients or of little value in others. Accordingly, we aimed at identifying predictors of recanalization in patients treated with or without IVT. *Methods:* In the observational Acute Stroke Registry and Analysis of Lausanne (ASTRAL) registry, we selected those stroke patients (1) with an arterial occlusion on computed tomography angiography (CTA) imaging, (2) who had an arterial patency assessment at 24 hours (CTA/magnetic resonance angiography/transcranial Doppler), and (3) who were treated with IVT or had no revascularization treatment. Based on 2 separate logistic regression analyses, predictors of spontaneous and post-thrombolytic recanalization were generated. *Results:* Partial or complete recanalization was achieved in 121 of 210 (58%) thrombolyzed patients. Recanalization was associated with atrial fibrillation (odds ratio , 1.6; 95% confidence interval, 1.2-3.0) and absence of early ischemic changes on CT (1.1, 1.1-1.2) and inversely correlated with the presence of a significant extracranial (EC) stenosis or occlusion (.6, .3-.9). In nonthrombolyzed patients, partial or complete recanalization was significantly less frequent (37%, $P < .01$). The recanalization was independently associated with a history of hypercholesterolemia (2.6, 1.2-5.6) and the proximal site of the intracranial occlusion (2.5, 1.2-5.4), and inversely correlated with a decreased level of consciousness (.3, .1-.8), and EC (.3, .1-.6) and basilar artery pathology (.1, .0-.6). *Conclusions:* Various clinical findings, cardiovascular risk factors, and arterial pathology on acute CTA-based imaging are moderately associated with spontaneous and post-thrombolytic arterial recanalization at 24 hours. If confirmed in other studies, this information may influence patient selection toward the most appropriate revascularization strategy. **Key Words:** Ischemic stroke—acute stroke management—IV thrombolysis—recanalization—CT angiography.

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Introduction

Recanalization and reperfusion of threatened ischemic tissue are the most critical predictors for a favorable clinical outcome in acute ischemic stroke.[1] Chances of success also depend on the time to reperfusion,[1,2] the core size, and a favorable penumbra/core ratio.[3–5] The benefit of intravenous thrombolysis (IVT) is also highly time dependent as it is related to the speed and completeness of the clot breakup and the presence of collaterals.[1,6,7] Furthermore, patients with strokes caused by large-vessel occlusions have low recanalization rates with IVT alone and are associated with poor functional outcome despite treatment.[8,9] This may be explained by clot characteristics (composition, size, and location), collateral integrity, and metabolic and genetic factors. More aggressive endovascular treatment strategies are increasingly used to treat large-vessel occlusive strokes as they recanalize these occlusions more effectively and rapidly.[10] Identification of the predictors of recanalization in IVT-treated patients may influence the patient selection for endovascular recanalization therapies. So far, prior studies have detected milder baseline stroke deficits, elevated systolic blood pressures, normal glucose values, smoking history, absence of atrial fibrillation, distal vessel occlusion, and thrombus length to predict post-thrombolytic recanalization.[11–17] However, most of these studies were performed without a logistic regression analysis. The aim of the present study was to identify independent predictors of spontaneous and post-thrombolytic recanalization among multiple demographic, clinical, metabolic, and radiological variables and in a large consecutive cohort of large-vessel occlusive strokes.

Patients and Methods

Study Design and Patient Selection

From January 2003 to July 2012, all consecutive acute ischemic stroke patients admitted to the stroke unit and/or intensive care unit within 24 hours after last known well time were prospectively included in our acute stroke registry.[18] For the current analysis, only patients fulfilling the following inclusion criteria were selected: (1) acute computed tomography angiography (CTA) performed within 12 hours after last known well time, (2) arterial occlusion in cervical and/or cerebral arteries on CTA and in relation to the ischemic territory, (3) availability of a second noninvasive arterial imaging (CTA, magnetic resonance angiography [MRA], or duplex) after 24 hours of the initial treatment (maximal range, 12-48 hours), allowing assessment of recanalization, and (4) treated with IVT within proven time windows or untreated. CTA is performed in all patients without iodized contrast contraindications, such as known allergy or known renal failure. In the original ASTRAL study, 78% of all ischemic strokes had a CTA on arrival.[18] The up to 12 hours time window was selected because significant salvageable brain tissue may still be present, and the recanalization assessment at 24 hours as this time point is a stronger predictor for a favorable outcome at 3 months than earlier assessments (<2 hours).[19,20] IVT with recombinant tissue plasminogen activator was performed whenever indicated by the guidelines of the European Stroke Organization.

Demographics, previous cerebrovascular events, comorbidities, clinical symptoms and signs, and metabolic and physiological parameters were recorded at admission and 24 hours later. Cardiovascular risk factors (pre-existing or newly diagnosed) were systematically collected. National Institutes of Health Stroke Scale (NIHSS) assessment was performed at admission, 6 and 24 hours later, and at 7 days. Prestroke disability and 3-months outcome were assessed using the modified Rankin scale (mRs). Clinical outcome analysis was restricted to patients with prestroke mRs score of 2 or less and was defined as mRs greater than 2 at 3 months. Stroke etiology was categorized following the Trial of Org 10172 in Acute Stroke Treatment classification with dissection and multiple causes added as additional mechanisms.

The study (collection, analysis, and publication of data) was performed according to the ethical guidelines of the commission for research on humans of the Canton of Vaud, subcommission III.

Angiographic Analysis of Arterial Occlusion and Recanalization

On the acute and subacute CTA, extracranial (EC) and large intracranial (LIC) vessels were assessed using continuous axial and reformatted maximum intensity projection pictures of EC and IC arteries for thrombus presence, the most proximal location, and multiple sites of occlusion. The site of the artery occlusion in the ischemic territory (+/− in nonischemic territory) was categorized as follows: IC, EC, LIC, intermediate intracranial (IIC), anterior, and posterior circulation occlusion. LIC occlusion was defined as an occlusion in the trunk of the middle cerebral artery (M1), T-occlusion of the IC internal carotid artery, or basilar artery occlusion. The group of IIC occlusions contained occlusions in the anterior cerebral artery (A1 or A2 segments), distal middle cerebral artery (M2), posterior cerebral artery (P1 or P2 segments), IC part of the vertebral artery (V4), and the siphon of the internal carotid artery without distal T-occlusion; the latter 2 were considered “intermediate” because thrombus load and clinical symptoms are usually minor in the absence of extension into the basilar artery and the carotid T, respectively. Tandem arterial occlusions were defined as a combination of a LIC occlusion and an EC occlusion of the artery leading to the ischemic territory. Occlusion extension was categorized as occlusion